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ABSTRACTS E-BOOK



Adrenal

ICE2020-1108

CLINICAL AND MORPHOLOGICAL CHARACTERISTICS OF NON-FUNCTIONAL ADRENAL ADENOMA

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Introduction: An adrenal incidentaloma is now established as a common endocrine diagnosis that requires a multidisciplinary approach for effective management. The patients need an personalized approach based upon image analysis, endocrine workup and clinical symptoms and signs are required in every case.

Objectives: To reveal clinical and morphological characteristics of nonfunctional adrenal adenoma (NFAA) and to establish appropriate management and therapeutic regimens in Yekaterinburg.

Methods: A total of 202 patients with AIs were retrospectively evaluated. $p < 0.001$.

Results: Endocrinological evaluations demonstrated of total AIs were 8 (4.8%) with Cushing's syndrome, 36 (21.7%) as pheochromocytomas, 11 (6.6%) as aldosterone-producing adenomas, Adrenocortical carcinoma (ACC) were accounted for 1 (0.6%). 110 patients with NFAA followed-up for a mean time of $2,12 \pm 3,3$ (M \pm SD) months before adrenalectomy at departments of endocrinology and surgical department of hospital № 40 and 36 patients with one followed-up at for present time $4,97 \pm 3,1$ in clinic №40 in Yekaterinburg. The mean age in operated group $47,0 \pm 12,7$ years, 24 (21.8%) males and 86 (78.2%) females. The mean nodule size of tumor based on computed tomography was $6 \pm 2,9$ cm, the right NFAA – 53 (48.2%), the left – 48 (43.6%), bilateral – 9 (8.2%). The prevalence of diabetes were 11 (10%), high blood pressure – 59 (53.6%), the obesity was 37 (34.3%). The cortisol in morning blood serum were $381,64 \pm 173,2$ nmol / l; the total methanephrine in daily urine – $106,78 \pm 85,75$ mcg / day; the DHEA-s - $3,63 \pm 1,96$ μ mol / l. The most frequently histological diagnosed is clear cell adenoma - 42 (38.2%).

Conclusion: the most of AIs are NFAAs and histological diagnosed was clear cell adenoma.

Disclosure of Interest: None Declared

Adrenal

ICE2020-1134

RELIABILITY OF ADRENAL COMPUTED TOMOGRAPHY IN PREDICTING THE MALIGNANCY OF NON-FUNCTIONAL ADRENAL ADENOMA

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Introduction: Adrenal incidentaloma (AI) is an adrenal mass discovered accidentally during abdominal or chest imaging techniques not aimed to adrenal gland assessment. The management of non-functional adrenal adenomas (NFAI) at least 4 cm is still a matter of debate as it is unclear whether imaging can be used to characterize their potential malignancy. Moreover, the risk of new hypersecretion in nonoperated tumors is uncertain. Our aim was to better characterize these large NFAIs.

Objectives: This study evaluated the reliability of computed tomography (CT) scan radiological parameters in predicting the malignancy of NFAI.

Methods: We performed a retrospective study in City Hospital № 40 in Yekaterinburg from January 2015 to December 2019, involving 49 operated patients NFAI and 56 non-operated ones for evaluation. For all patients, we assessed history, physical examination, radiological parameters of NFAI by CT scan (native Hounsfield unit [HU]), maximum diameter and blood investigations (glycated haemoglobin, adrenocorticotrophic hormone, aldosterone, renin, aldosterone/renin ratio, normetanephrine, metanephrine, dehydroepiandrosterone sulphate, cortisol and 1 mg overnight dexamethasone suppression test).

Results: Criteria for the diagnosis of malignant NFAI were: a combination of size and HU. In group with native CT HU ≤ 10 (n-19) adrenal mass 5.1 ± 2.0 cm, aged 48.5 ± 11.2 years. All adenomas have accumulated contrast medium. In group with native CT (n-6) adrenal mass 6.0 ± 2.1 cm, aged 62.5 ± 9.9 years. In group with native CT HU ≥ 10 (n-24) adrenal mass 6.3 ± 3.4 cm, aged 43.0 ± 13.7 years. Observation time before surgery $2,12 \pm 3,3$ years.

The non-operated patients (n-56) adrenal mass 2.44 ± 1.45 cm, aged 64.41 ± 10.72 . Native CT varied from -69 HU to $+50$ HU, Me 6 ± 26 HU, Arterial phase Me 72 ± 24 HU, Venous phase Me 55 ± 23 HU, washout (6 min) Me 27 ± 11 HU. Observation time 5.27 ± 3.05 years. Patients treated by adrenalectomy had larger tumors, higher CT unenhanced density than non-operated ones.

Conclusion: Native HU was the most significant radiological parameter in predicting the malignancy of NFAI. The risk of malignancy significantly increases with the CT ≥ 10 HU, accumulated contrast medium and decreases with the CT ≤ 10 HU, size less than 2.44 cm.

Disclosure of Interest: None Declared

Adrenal

ICE2020-1148

THE CASE OF A 17-YEAR-OLD FEMALE WITH PARAGANGLIOMA AND AN SDHB MUTATION CLINICALLY COMPARED WITH CASES OF ADULT PHEOCHROMOCYTOMA

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Introduction: Takotsubo cardiomyopathy (TTC) is a reversible cardiomyopathy with a unique morphological feature of the left ventricle characterized by an apical ballooning appearance. The condition develops as a complication of PPGL (pheochromocytomas (PHEO) and paragangliomas (PGL)). TTC is a rare condition, but the number of reported cases has increased in recent years. Epidemiologically, psychological stress and physical stress are often observed before the onset of TTC.

Case Description: A 17-year-old female high school student was hospitalized emergently after suffering sudden palpitations and losing consciousness on the morning of a test day. On admittance she was in a state of shock. Echocardiography revealed a diffuse wall hypokinesis, and acute heart failure was diagnosed. Myocardial biopsy suggested fulminant TTC on the basis of catecholamine hypersecretion with urinary normetanephrine 1350 ng/mg/Cr and urine noradrenaline 728 µg/day. Other endocrine hormones were in the normal ranges. An abdominal CT and MRI depicted a well-defined 33 × 22 mm tumor in the right retroperitoneum. A 123I-MIBG scintigram and PET-CT accumulated confirmed solitary PGL. After the diagnosis, the tumor was surgically removed and the patient's hemodynamics and hormonal value were normalized. An SDHB mutation was found in an ensuing analysis of tumor samples.

Comparison with 13 adult cases with PHEO (average age 49.7 years, 6 males) treated at our institution: This teenage case was the youngest of the patients treated for TTC at our institution. Her urinary adrenaline was normal, and significantly lower than the mean (65 µg/day), falling below all of the other recorded values (7.6 µg/day). Her urinary noradrenaline was 1.9 times higher than the average value (377 µg/day), reaching an extremely high level exceeding all of the other recorded values (728 µg/day).

Clinical discussion: This teenage case is rare. Acute TTC is seen in up to only 3% of patients with PPGL, and typically in postmenopausal women. Among the various genetic mutations that influence PPGL, those in genes encoding subunits of succinate dehydrogenase are the most relevant. Our case has an SDHB mutation. While the variation in the forms manifested, such as TTC or inverted TTC, can be attributed to anatomical differences in the sympathetic innervation of the heart and individual differences in adrenergic receptor distribution, further details are unknown. The incidence and severity of TTC in PHEO or PGL with/without SDHB mutation are issues for future study.

Disclosure of Interest: None Declared

Adrenal

ICE2020-1212

ADRENAL LARGE B CELL LYMPHOMA PRESENTING AS INCIDENTAL ADRENAL MASS AND HYPERCALCEMIA

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Introduction: Malignant lymphoma arising primarily in the endocrine organs is rare, accounting for less than 8% of extranodal presentations, and among the endocrine organs, the thyroid gland is most commonly involved.

Primary adrenal lymphoma is a rare condition and may present as bilateral adrenal masses which may be rapidly growing.

Case Description: A case of a 72 year old gentleman is presented who was admitted with a protracted history of weight loss, fatigue and intermittent abdominal pain with an unremarkable physical examination. He underwent transfusion and gastrointestinal endoscopies for anemia which were unremarkable. He had CT of chest, abdomen and pelvis which showed bilateral adrenal masses. Endocrine investigations were carried out as an outpatient, all of which were negative. He was readmitted 4 weeks after initial discharge with hypercalcaemia with a PTH of 4 and a normal bone scan, it was refractory to cinacalcet needing zoledronic acid. He then underwent adrenal biopsy which showed diffuse large B cell lymphoma and was started on prednisolone pending tissue diagnosis and results of bone marrow biopsy. He received 6 courses of R CHOP with good effect.

Clinical discussion: Primary adrenal lymphomas are rare tumours and should be considered in the differential diagnosis of unilateral and bilateral adrenal masses. Patients usually do not have disease elsewhere and this makes the diagnosis more difficult. Symptoms of the disease are variable and is usually diagnosed incidentally on abdominal imaging.

Disclosure of Interest: None Declared

Adrenal

ICE2020-1221

PURE ANDROGEN SECRETING UNILATERAL ADRENAL HYPERPLASIA WITH CONTRALATERAL ADENOMA. CASE REPORT AND LITERATURE REVIEW

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Introduction: Pure androgen-secreting adrenal tumors (PASAT) are extremely rare. 80% occur in females. Clinically, it presents with hirsutism, menstrual disturbances and virilization.

Case Description: A 47-year-old female patient with no relevant background presents with history of 5 years of hirsutism and amenorrhea, intensified in the previous year adding alopecia, increased muscle mass and voice deepening. The physical examination reports a normal weight, normal blood pressure, moderate hirsutism (18 on the Ferriman-Gallway scale) and clitoromegaly without elements of Cushing's syndrome.

Laboratory tests highlight a value of total testosterone of 937 ng/dl (8.4 - 48.1), DHEAS 331 ug/dl (56.2-282.9), normal FSH, LH, PRL and a cortisol level of 1.6 ug/dl after a dexamethasone suppression test.

Abdominal computed tomography (CT) shows a solid nodular right adrenal mass with hypodense areas inside, 40x34x32 mm, washout of 16.3%, deemed uncharacterizable, and on the left adrenal, an adenoma 12x10x10 mm is reported. Positron Emission Tomography (PET-CT), shows poor and diffuse metabolism in the right lesion and confirms the left adenoma.

Right adrenalectomy was decided by laparoscopic approach, without complications. 2 months after surgery, the signs and symptoms of hyperandrogenism and virilization subside almost completely, total testosterone and DHEA-S levels decrease, being normal for age and sex.

Clinical discussion: PASAT are rare tumors that predominate in females. The androgen excess in women clinically shows with hirsutism and progress to virilization with clitoromegaly, voice deepening, alopecia, increase of muscle mass, changes in the distribution of body fat, decrease in breast volume, among others. The diagnosis is of clinical suspicion with signs of hyperandrogenism and virilization, elevated serum androgen levels, and imaging evidence of adrenal tissue injury. However, these are not enough to make an accurate diagnosis, being of main importance the pathology report for the definitive diagnosis. Treatment is surgical and the approach will depend on the size and behavior of the tumor. Pathology findings will determine the medium and long-term prognosis.

Disclosure of Interest: None Declared

Adrenal

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HISTOPATHOLOGICAL ANALYSIS OF TUMOR MICROENVIRONMENT IN PHEOCHROMOCYTOMA

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Introduction: Recently, tumor microenvironment (TME) has been reported to play pivotal roles in many human malignancies in tumorigenesis, progression and metastasis. However, rare studies have explored TME in pheochromocytomas (PHEOs), although malignant PHEOs were reported to harbor lower sustentacular cells and activated angiogenesis.

Objectives: Therefore, in order to explore the details of TME in PHEOs, we examined tumor infiltrating lymphocytes (TILs), tumor associated macrophages (TAMs) and angiogenic markers in PHEOs. We then compared the results with PASS (pheochromocytoma of the adrenal gland scaled score), GAPP (grading system for pheochromocytoma and paraganglioma) and the status of catecholamine-synthesizing enzymes as well as the clinicopathological factors of the patients.

Methods: We immunohistochemically evaluated TILs (CD4 and CD8), TAMs (CD68 and CD163), sustentacular cells (S100p), angiogenic markers (CD31 and areas of intratumoral hemorrhage) and catecholamine-synthesizing enzymes (TH, DDC and PNMT) in 39 PHEOs.

Results: CD8 ($p=0.0400$), CD31 ($p=0.0256$) and PNMT ($p=0.0498$) were all significantly more abundant in PHEOs with PASS < 4 than PASS ≥ 4 . In addition, CD8⁺T cells were also significantly more abundant in well- than moderately differentiated PHEOs according to GAPP score ($p=0.0108$). CD68⁺macrophages were significantly higher in PHEOs with regular histological patterns than those not ($p=0.0379$) and positively correlated with DDC status ($p=0.0168$). CD163⁺ macrophages were significantly positively correlated with CD8⁺T cells ($p=0.0032$). The proportion of intratumoral hemorrhagic areas was significantly higher in PHEOs with PASS ≥ 4 ($p=0.0172$) and capsular/vascular invasion ($p=0.0031$) than those not. DDC was significantly positively correlated with PASS score ($p=0.0356$) and TH was significantly higher in PHEOs harboring regular histological patterns ($p=0.0236$) and cellular monotony ($p=0.0219$) than those not.

Conclusion: We demonstrated that CD8⁺T cell may be suppressed by excessive catecholamine and its abundance in PHEOs can represent a histologically low-scored tumor. Excessive catecholamine can also activate angiogenesis resulting in an increased intratumoral hemorrhage in malignant PHEOs. Therefore, in situ excessive status of catecholamine could modulate tumor immune system and neoplastic angiogenesis in PHEOs.

Disclosure of Interest: None Declared

Adrenal

ICE2020-1261

BILATERAL PHEOCHROMOCYTOMA

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Introduction: Bilateral pheochromocytoma is a rare entity. It's usually seen in the context of a family illness. However, sporadic bilateral forms can be observed as in our case. It still poses several problems relating to its diagnosis, criteria of malignancy, genetic aspects, and treatment, especially in the absence of a family history.

Case Description: This is a 29-year-old patient, who had an intense headache resistant to analgesics, palpitation and profuse sweating; Clinical examination revealed a very high blood pressure (200/110 mmHg) and tachycardia. The urinary methoxylated derivatives returned very high; the abdominal MRI revealed 2 adrenal masses, malignant in appearance. The diagnosis of bilateral pheochromocytoma was retained. The investigation for multiple endocrine neoplasia and family form was negative.

Clinical discussion: Our initial behavior was a unilateral adrenalectomy by laparoscopy, subsequently totaled in view of the persistence of catecholamine secretion on the other side. The evolution under hydrocortisone replacement therapy was favorable with normalization of blood pressure levels.

Disclosure of Interest: None Declared

Adrenal

ICE2021-1292

HYPOPITUITARISM AFTER INFLUENZA VIRUS INFECTION - CASE REPORT

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Introduction: Hypopituitarism is defined as the total or partial loss of anterior and posterior pituitary gland function that is caused by pituitary or hypothalamic disorders. It is a disease of varied etiologies, a serious endocrine illness that requires early recognition and prompt treatment to avoid its severe deleterious effects. It is often missed in adults, due to non-specific symptoms of growth hormone deficiency and hypogonadism or mild deficiencies of other pituitary hormones. Here, we represent a 59-years old female patient with hypopituitarism after a influenza virus infection

Case Description: At the endocrinology outpatient clinic, a 59-year-old female patient arrives due to severe fatigue and a large weight loss in the last two years, despite her preserved appetite. In these two years, she has lost about 20 kg. Earlier registered as an endocrinology patient and being treated for hypothyroidism, caused by Hashimoto's thyroiditis. On substitution therapy, she takes 25 mcg of Euthyrox. Due to vitamin D deficiency, she also takes vitamin D. In the History of the Disease we have noticed that, two years ago, she was treated in our hospital for bilateral pneumonia developed as a complication of influenza virus infection. The influenza virus H1N1 was confirmed. Due to the severe clinical condition and the newly developed encephalopathy, the treatment was continued in tertiary level care. At that time, the greatest weight loss was detected

Clinical discussion: Based on diagnostics and laboratory tests, we conclude that this is a patient with hypopituitarism with reduced secretion of corticotropic as well as gonadotropic hormones. Thyrotropic hormone values were not significantly changed, which immediately suggested the prescription of a hormone replacement therapy, hydrocortisone. We have not examined the values of other pituitary hormones, but we can certainly say that this is a patient with hypopituitarism of post-infectious aetiology. For further treatment, we recommended hydrocortisone in a total daily dose of 20 mg, divided into two doses. A morning dose 15 mg and an evening dose 5 mg. We performed control analyzes 15 days after the hospital discharge. Morning levels of cortisol, prolactin and thyroid hormones were checked. The results were: cortisol at 8 am 213.5 nmol / l; prolactin less than 12.60 IU / ml; TSH 3.21 mIU / L and fT4 7.64 pmol / l. The patient felt better, she had more strength for daily activities and could have already boasted about weight gain.

Disclosure of Interest: None Declared

Adrenal

ICE2021-1306

PHEOCHROMOCYTOMA SECRETING IL-6; AN ATYPICAL PRESENTATION

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Introduction: Pheochromocytoma (PCC) is a rare tumor that arises from the adrenal medulla, usually presents with headache, sweating and palpitations due to excessive catecholamine release. However, PCC may secrete neuropeptides, hormones and cytokines, such as interleukin-6 (IL-6)) resulting in unusual clinical manifestations

Case Description: A 48-year-old woman with a previous history of type 1 neurofibromatosis (NF1) and hypertension was referred to discarded PCC. Laboratory tests revealed leukocytosis and thrombocytosis with increased erythrocytation rate (ESR) and elevated urinary metanephrine [White blood cells account: 20530 RR 4000-10000; ESR: 50 mm/h RR <22; Platelets: 635000 uL RR 150000-400000, Urinary metanephrine: 673 ug/24hs, RR 30-180; Urinary Adrenaline: 53 ug/24 hs RR <20; Urinary Noradrenaline: 265 ug/24hs RR <80] Abdominal CT revealed a left bilobed adrenal tumor 33 x 32 mm in the largest dimension (40 HU). Oncohematological and myelodysplastic disease were discarded (mutation JAK2- V617F, trasloc 9-22 and bcr-abl were negative). She had no fever but cytokines secretion was suspected and IL-6 was elevated (11,4 pg/ml RR <5,9). Uneventful laparoscopic adrenal surgery was performed. After surgery all biochemical parameters were within the reference range and blood pressure normalization was achieved.

Clinical discussion: It has been previously described that PCC may secrete cytokines with systemic inflammatory response syndrome (SIRS). IL-6 is a multifunctional molecule that plays an important role in hematopoiesis and immune and inflammatory responses. IL-6 over-production can be either ascribed directly to the tumor or indirectly accounted for tumoral production as a consequence of the high levels of circulating catecholamines. Symptoms relief, inflammatory marker and hematologic parameters normalization following the decrease in IL-6 level after tumor resection strongly supports the role of IL-6 in the unusual presentation of our case. Our patient had mild hypertension despite high catecholamine levels and could be explained by the increased nitric oxide synthesis due to IL-6 activity, which might have led to vasodilation. PCC may be a cause of paraneoplastic syndrome with marked increase in the levels of inflammatory markers. IL-6 appears to be the primary mediator. PCC has to be considered in the vast differential diagnosis of oncohematological and myelodysplastic syndromes when common causes are ruled out.

Disclosure of Interest: None Declared

Adrenal

ICE2021-1336

HYPOKALEMIA – COMMON YET WITH MULTIPLE POSSIBILITIES

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Introduction: Hypokalemia is a common entity in hospitalized patients. Severe hypokalemia, defined as potassium less than 2.5 mEq/L, can be life threatening. Though diuretic use and loss of potassium through GI tract are the most common causes of hypokalemia, diagnosis of other causes of hypokalemia can be challenging. We present a case of severe hypokalemia secondary to a functional adrenal myelolipoma.

Case Description: A 58-year-old, female was brought to the hospital for confusion, poor oral intake. She had a past medical history significant for schizophrenia, not on any medications. On exam, she was febrile, tachycardic, hypotensive, confused, and had an abscess over right axilla with easily expressible thick exudate. Laboratory exam revealed leukocytosis, profound hypokalemia, and an ABG showed metabolic alkalosis. CT brain was normal. She was treated with fluids, broad spectrum antibiotics, and potassium replacement. Improved hemodynamically but continued to have profound hypokalemia. Patient was also noted to have elevated blood pressure, mild hirsutism, acne, and truncal obesity. Further work up for evaluation of hypokalemia was done.

A spot urine K+, urine K+/Creatinine levels obtained indicated renal loss of potassium. Serum renin, aldosterone, and a.m. cortisol were normal. CT abdomen revealed a 10 cm, mass in left adrenal gland, suggestive of adrenal myelolipoma. Due to a high clinical suspicion of Cushings, low dose dexamethasone suppression test, 24-hour urine cortisol, serum ACTH levels, DHEAS were obtained. Plasma metanephrine was obtained to rule out pheochromocytoma.

The patient had a serum cortisol above 5 after a low dose dexamethasone suppression highly suggestive of Cushings. 24-hour urinary cortisol levels were in the upper limit of normal range. ACTH was at the 30th percentile. Surgery was recommended as the treatment of choice and performed; histology confirmed a benign adrenal myelolipoma.

Clinical discussion: Hypokalemia is a common entity encountered by internists. Though the common causes are easy to ascertain, other etiologies like an underlying endocrine disorder may be missed due to subtle clinical features. Adrenal myelolipomas are common, yet largely non-functional. A high clinical suspicion, broad differential, requiring a multidisciplinary, stepwise approach to diagnose these rarer causes of hypokalemia like a functional adrenal myelolipoma.

Disclosure of Interest: None Declared

Adrenal

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THE LONG SOUGHT EXTRAPANCREATIC SOURCE OF INSULIN PRODUCTION IN CHICKENS: THE ADRENAL GLAND

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Introduction: The increasing prevalence of diabetes mellitus in the western world urges the search for discovering extra pancreatic sources of insulin. This reminded us about the century long puzzle raised by experiments in birds showing that pancreatectomy does not lead to profound diabetes. However, the putative extrapancreatic tissue that produces insulin in birds has never been identified.

Objectives: We sought to find the source of insulin production in a non-pancreatic tissue of chickens for several purposes: deciphering the evolution of endocrine specifications of tissues; expanding our understanding of chicken physiology; and finding new directions for insulin induction outside of the pancreas that may be used in diabetes.

Methods: The methods used included bioinformatic searches in GenBank available datasets of human and chicken mRNA sequencing datasets, qPCR, blood glucose measurements and immunohistochemistry (IHC). The specificity of the antibodies used was verified based on their well characterized expression pattern in pancreatic (insulin and somatostatin, SST) and adrenal (tyrosine hydroxylase, TH) tissues. We produced pancreatectomized chickens and compared adrenal gene expression between operated and sham operated chickens.

Results: Our study revealed that chicken adrenal normally expresses insulin mRNA at a level 18 fold lower than the pancreas (471 and 26 RPKM, respectively), whereas in human insulin mRNA is very lowly expressed in the adrenal (514 and 0.1 RPKM, in pancreas and adrenal, respectively). In pancreatectomized compared to sham operated chickens we found tenfold induction of insulin mRNA, 24 hr after surgery, indicated also by IHC analysis. The pancreatic-d cell peptide, SST, that regulates insulin secretion has also been found in the adrenal of chickens and not in rat, at both the mRNA and protein levels. IHC analysis with TH antibodies, confirmed the morphology of the adrenal medulla in chickens, which resemble pancreatic islets, and its identification as the source of the adrenal insulin and SST production.

Conclusion: Our study suggests some pancreatic islet activity in the adrenal medulla cells of chickens, thus resolving a century long puzzle about extrapancreatic source of insulin. It will be of high interest to find out if some insulin induction potential may still be present in human adrenal and if this explains the recent suggestion that human adrenal is the preferred target for pancreatic-cells implantation.

Disclosure of Interest: None Declared

Adrenal

ICE2021-1380

ARMC5 MODIFIES CELL REDOX STATE TO REGULATE ADRENOCORTICAL STEROIDOGENESIS

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Introduction: ARMC5 is a putative tumor suppressor gene that is frequently mutated in primary bilateral macronodular adrenal hyperplasia (PBMAH), a rare cause of Cushing's syndrome. The function of ARMC5 is poorly known, aside the fact that it regulates cell apoptosis and adrenal steroidogenesis in by mechanisms still unknown. Tumor suppressor genes play an important role in oxidative stress.

Objectives: To investigate the effects of ARMC5 on adrenocortical redox response.

Methods: In this study we used as model the adrenocortical carcinoma cell line H295R. In order to investigate ARMC5 response to stress, cells were treated with Menadione and reactive oxygen species (ROS) production was measured by CellroX assays with flow cytometry. Oxidative response genes and steroidogenic enzymes expression were investigated by qPCR, whereas p38 phosphorylation was investigated by western blotting.

Results: ARMC5 protein is differentially regulated in response to menadione-induced stress in H295R adrenocortical cells. Moreover, ARMC5 depletion increases total intracellular ROS production ($p < 0.05$) and causes an imbalanced transcription of pro and anti-oxidant genes leading to increased phosphorylation of p38 ($p < 0.05$). ROS production and p38 pathway activation alter steroidogenesis. These effects are partially reversed by the anti-oxidant compound N-acetylcysteine (NAC) or the p38 inhibitor (SB203580).

Conclusion: Altogether, this study describes a new function of ARMC5 as regulator of the redox homeostasis in adrenocortical cells.

Disclosure of Interest: None Declared

Adrenal

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BILATERAL PRIMARY ADRENAL LYMPHOMA: A SERIES OF CASES

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Introduction: Primary adrenal lymphoma (PAL) is a highly aggressive malignancy. It's extremely rare, representing <1% of extranodal lymphoma. PAL usually affects elderly males and is bilateral in about 70% of cases. In more than 50% of cases it presents with adrenal insufficiency (AI) secondary to bilateral adrenal infiltration. Our aim is to describe the clinical presentation, diagnostic and evolution of 3 patients with bilateral primary adrenal lymphoma (BPAL)

Case Description: Case 1 :A 71-year-old (yo) man with diabetes and anemia, showed anorexia and weight loss (15 kg in 6 months), vomits and unsteady gait. He had hypotension, hyponatremia and hyperkalemia, without hyperpigmentation. He received hydrocortisone replacement therapy (HRT) with symptomatic improvement, hypotension and ionogram alterations improved with the addition of fludrocortisone. Abdominal CT (CT-a) revealed bilateral adrenal nodules (BAN) with attenuation value >10HU. The adrenal needle biopsy puncture (ANB) reported a diffuse large B-cell lymphoma (DLBCL). The patient rapidly deteriorated and died 3 months later

Case 2 :A 56-yo woman with abdominal pain, night sweats, dyspnea at rest associated with hypotension and anorexia with a weight loss of 18 kg in 2 months, without hyperpigmentation. On CT-a, she presented 6cm BAN with 37UH and 2.3cm with 39 HU. She had elevated LDH, cortisol of 14.4ug/dl, and normal ACTH. 18FDG PET showed atypical hypermetabolic involvement of supra and infradiaphragmatic lymph nodes and bilateral adrenal glands. The ANB revealed a peripheral non-Hodgkin T Lymphoma. The initial treatment was chemotherapy. She achieved remission of the adrenal masses and adenopathies. She suffered a rapid recurrence with lymphomatous involvement in the CNS and died 6 months later

Case 3 :A 76-yo woman with epigastralgia, vomits and hyperpigmentation. On CT-a presented BAN of 8cm and 7cm, UFC of 2.2mcg/24h and ACTH 2700pg/ml. She received HRT with symptomatic improvement. The ANB was compatible with B small cell lymphoma

Clinical discussion: PAL is a very rare lymphoma. The most common type is DLBCL. It has very poor prognosis. Advanced age at diagnosis, large tumor size, increased LDH level, bilateral adrenal involvement, and AI at the time of presentation worsen the prognosis even more. It should be taken into account to rule out other causes of BAN, especially in elderly patients with AI. The ANB is a fundamental tool that must be performed without delay. Because of the rarity of PAL, its treatment has not been defined in detail.

Disclosure of Interest: None Declared

Adrenal

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CUSHING'S SYNDROME DUE TO INTRA-ADRENOCORTICAL ACTH IN A DOG

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Introduction: The production of intra-adrenocortical ACTH by steroidogenic cells in patients with primary bilateral macronodular adrenal hyperplasia (PBMAH) is an unusual cause of CS in humans.¹

Case Description: This abstract describes the case of a 12-year-old neutered male dog, with CS caused by primary bilateral adrenocortical hyperplasia. An initial diagnosis of ACTH-independent CS was reached based on clinical signs, elevated urinary cortisol/creatinine ratio, not suppressible post-dexamethasone cortisol, suppressed ACTH concentration and a left adrenal tumor. Remission of CS clinical signs occurred after oral treatment with trilostane, a competitive inhibitor of the enzyme 3beta-hydroxysteroid dehydrogenase (3b-HSD). Since episodes of agitation, nervousness and persistent systemic hypertension had been observed, a concurrent pheochromocytoma was confirmed through urinary vanillylmandelic acid/creatinine ratio. Post mortem, a pheochromocytoma in the left adrenal gland with positive immunostaining for synaptophysin and negative for 3b-HSD was confirmed. Primary bilateral adrenocortical hyperplasia (PBAH) was diagnosed on absence of hyperplasia-adenoma of the pituitary corticotrophic cells. No other neoplasms were found at necropsy. The ectopic production of ACTH by chromaffin cells of pheochromocytoma was ruled out as a cause of PBAH by immunohistochemistry. Surprisingly, a group of cells at the glomerular-fascicular junction and in multiple cell clusters with morphological steroidogenic characteristic distributed in the hyperplastic adrenal cortex were positive for ACTH but not for synaptophysin, dismissing the adrenomedullary origin. ACTH-positive cells were negative for 3b-HSD. Based on our findings, ACTH is abnormally expressed in adrenal cortices in dogs and associated with glucocorticoid excess.

Figure. A) Macroscopic appearance of the left adrenal gland. Pheochromocytoma (asterisk). B) Positive immunostaining for ACTH and negative for 3bHSD in cluster cells located in the hyperplastic adrenal cortex. C) Positive immunostaining for ACTH in adrenocortical cells at the glomerular-fascicular junction.

Clinical discussion: Due to high incidence of CS and adrenal anatomo-functional similarity, the dog could be an ideal study model for human CS by ACTH-intraadrenocortical.

Reference

Lefebvre H, Thomas M, Duparc C. et al. 2016. Role of ACTH in the interactive/paracrine regulation of adrenal steroid secretion in physiological conditions. *Front Endocrinol*, 7:98

Disclosure of Interest: None Declared

Adrenal

ICE2021-1477

ADRENAL-SPARING SURGERY IN PARAGANGLIOMA SYNDROME TYPE 1: CASE REPORT. LESS IS MORE?

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Introduction: Pheochromocytoma and paraganglioma are rare neuroendocrine tumors, with an incidence of 0.6 per 100 000 persons/year[i] and more than 40% of this patients carries a germline mutation.[ii] Up to 10% of hereditary pheochromocytomas are present in familial paraganglioma syndromes, due to a germline mutation of Succinate dehydrogenase gene (SHDx).

Total bilateral adrenalectomy has been used for treatment in pheochromocytoma in familial tumor syndromes[iii]. Since 1999, partial adrenalectomy was introduced into practice with the aim of preserving the adrenal cortex and thus reducing morbidity[iv].

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[ii] Neumann HP., Young W., Eng C. Pheochromocytoma and Paraganglioma. *N Engl J Med* 2019;381:552-65.

[iii] F Castinetti, D Taieb, J F Henry, et al. Outcome of adrenal sparing surgery in heritable pheochromocytoma. *Eur J Endocrinol*. DOI: 10.1530/EJE-15-0549.

[iv] Neumann HP, Bender BU, Reincke M, et al. Adrenal-sparing surgery for phaeochromocytoma. *Br J Surg* 1999;86:94-7.

Case Description: We describe the case of a 42 years old patient affected by familial paraganglioma syndrome type 1 with recurrent pheochromocytoma. She had surgery for retroperitoneal paraganglioma, total left adrenalectomy for noradrenaline producing pheochromocytoma, and left carotid paraganglioma. After 9 years she had recurrent right pheochromocytoma and laparoscopic partial adrenalectomy was done. The removal of the recurrent pheochromocytoma was successful with no recurrence or need for steroid replacement at 4 years of follow-up.

Clinical discussion: Given that to date there have been no reports of malignancy or mortality due to pheochromocytoma in familial paraganglioma syndrome type 1 and partial adrenalectomy, we transposed the concept and experience of the rest of the most inherited syndromes and their reports. Laparoscopic partial adrenalectomy should be considered a valid alternative in patients with synchronous o metachronous bilateral hereditary pheochromocytoma. We consider this report an example of successful partial adrenalectomy in recurrent pheochromocytoma with 4 years of follow-up in familial paraganglioma syndrome type 1.

Disclosure of Interest: None Declared

Adrenal

ICE2021-1507

ANALYSIS OF THE MUTATIONS OF TUMOR SUPPRESSOR GENE *ARMC5* IN A LARGE SERIES OF PRIMARY BILATERAL MACRONODULAR ADRENAL HYPERPLASIA (PBMAH): IDENTIFICATION OF CLINICAL PARAMETERS PREDICTIVE FOR *ARMC5* MUTATION

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Introduction: PBMAH is a rare but heterogeneous disease, characterized by multiple adrenal macronodules with variable levels of cortisol excess. In 2013, our team discovered germline inactivating mutations of *ARMC5*, acting as a tumor suppressor gene. *ARMC5* mutation rate is 50% in patients with PBMAH treated by adrenalectomy for severe hypercortisolism, 80% in familial cases and 20% in sporadic cases.

Objectives: Our purpose was to identify predictive criteria for *ARMC5* mutation.

Methods: Since 2014, 454 European index PBMAH cases have been genotyped for *ARMC5* in Cochin Institute or in Cochin Hospital. To date, among these 454 patients, we have reviewed the 264 consecutive index cases referred from five French endocrinology departments (COMETE network). A retrospective analysis of the clinical, radiological and biological data was done with a central review of the adrenal CT-scans.

Results: Sixty-five out of the 454 index cases (14.3%) present a germline inactivating *ARMC5* mutation. Similarly, 40 (15.2 %) out of the subgroup of the 264 reviewed patients had a germline *ARMC5* mutation. Patients with *ARMC5* mutations have a more severe disease than wild-type patients, in terms of cortisol excess (UFC 1.92 [0.2-12.1] vs 0.84 [0.08-10.1] fold ULN, respectively, $p=0.017$), adrenal morphology (10.8 [2-27] vs 3.4 [1-13] nodules, respectively, $p<0.001$) and complications (87.5 vs 68.3% of patients treated for hypertension, respectively, $p=0.013$). 100% of the mutated patients have bilateral adrenal nodules AND plasma cortisol after dexamethasone 1 mg suppression test above 50 nmol/L, only 61.6% of the non-mutated patients have these two associated criteria. Therefore, the 100% negative predictive value of the association of bilateral nodules and autonomous cortisol secretion allows to exclude *ARMC5* mutation when both are absent. Using more stringent criteria improved the specificity for *ARMC5* mutations : among the mutated patients, 75.9% had at least 4 and 65.5% had at least 6 adrenal nodules, vs 18.0 and 6.8% of wild-type patients respectively, improving the mutation rate to 37.3% and 57.6%, respectively. However by using these criteria some mutated patients would be missed (24.1 and 34.5%, respectively).

Conclusion: Restricting the indication of *ARMC5* sequencing to patients with bilateral adrenal nodules and a cortisol above 50 nmol/L after 1 mg dexamethasone suppression test could avoid useless genotyping in a third of patients, and would allow a cost and time economy and earlier results, without missing any mutated patient.

Disclosure of Interest: None Declared

Adrenal

ICE2021-1574

IDENTIFICATION OF A BLOOD METHYLOME SIGNATURE OF GLUCOCORTICOID EXCESS

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Introduction: The prolonged exposure to glucocorticoid excess (Cushing's syndrome - CS) associates with several comorbidities and complications. The diagnosis of CS relies on hormone assays. However, measured glucocorticoid levels don't reflect the individual consequences of glucocorticoid excess, since biological susceptibility varies among individuals, particularly in sub-clinical cases.

Objectives: To identify a specific molecular signature reflecting glucocorticoid levels, by evaluating the blood DNA methylation profile in CS patients.

Methods: Forty-seven patients with a confirmed diagnosis of CS were included. For each, blood samples were collected before and at least 3 months after CS correction (n=94 samples). Methylome was determined starting from leukocyte DNA using the Illumina methylation chip array (~850000 CpG sites).

Results: The variability of DNA methylation discriminated samples by their status of overt Cushing, mild Cushing/eucortisolism or adrenal insufficiency, reflecting glucocorticoid levels. Overt Cushing samples showed a signature of diffuse DNA hypomethylation compared to the others. This signature also reflected the blood count changes (increased neutrophils and decreased lymphocytes), combined to a specific glucocorticoid effect on DNA methylation. A set of 29 differentially methylated CpG sites optimally predicting the overt Cushing status were selected from a training sub-cohort (n=30 Cushing samples and n=30 non Cushing samples -either eucortisolism or adrenal insufficiency), using a penalized Lasso-regression procedure. These 29 CpG sites perfectly discriminated patients with overt Cushing on the training sub-cohort. The same 29 CpG sites also discriminated the majority of patients presenting overt Cushing on a validation sub-cohort of 34 samples.

Conclusion: Genome methylation is a potential biomarker of glucocorticoid excess. Future developments include the prediction performance in sub-clinical Cushing, the link with the different complications and the possibility to use this biomarker to develop specific targeted assays.

Disclosure of Interest: None Declared

Adrenal

ICE2021-1585

EFFECTS OF INHALED STEROIDS ON THE HYPOTHALAMO-PITUITARY ADRENAL AXIS: A HOSPITAL BASED STUDY

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Introduction: Synthetic Corticosteroids are important therapeutic agents prescribed in the treatment of allergic and inflammatory diseases. Complications of systemic steroids are well recognised however, there is increasing evidence that inhaled corticosteroids used in the treatment of Asthma and COPD may be associated with suppression of the hypothalamopituitary adrenal (HPA) axis resulting in adrenal insufficiency which may be insidious with nonspecific symptoms or lead to life threatening adrenal crisis.

Objectives: The aim of this study is to assess the HPA axis of patients on inhaled corticosteroids for the presence of adrenal suppression.

Methods: It was a hospital based cross sectional study conducted at two tertiary institutions in Nigeria involving adult subject age 18 to 70years. A low dose Synacthen test was carried out on forty-six subjects taking inhaled fluticasone propionate, thirty-four on inhaled budesonide and fifty healthy age and sex matched controls, to assess their HPA axes for adrenal suppression. Associated metabolic abnormalities in fasting blood glucose, electrolytes, urea, and creatinine were also assessed. Analysis was carried out using the IBM SPSS version 23. Chi square, Unpaired t-test, Mann Whitney U test, Logistic regression and linear regression were done. A p-value of <0.05 was taken as statistically significant.

Results: The proportion of adrenal insufficiency among subjects on ICS was higher (87.5%) compared to the proportion among controls (52%), p-value of <0.001. Post Synacthen cortisol levels were lower in subjects on ICS [475.7nmol/L (99.2)] compared to controls [625.8nmol/L (224)] with a p-value <0.001. Increasing age (OR 1.061 95% CI 1.004-1.121), longer duration of steroid use (p-value of 0.002) and the reported increased frequency of steroid use per week (OR 4.949 95% CI 1.140-12.628) were associated with an increased risk of adrenal insufficiency.

Conclusion: The use of inhaled steroids was associated with adrenal suppression. Increasing age, longer duration of ICS use and higher frequency of use per week were associated with an increased risk of adrenal suppression. This study identifies a group of topical steroid users who are at potential risk of adrenal insufficiency and may require stress doses in acute stressful situations.

Disclosure of Interest: None Declared

Adrenal

ICE2021-1589

NEW INSIGHTS INTO THE FUNCTIONAL HUMAN ADRENAL CORTEX ZONATION

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Introduction: The zonation of the human adrenal cortex has long been established morphologically and histologically as three distinct layers of cells. The outer zona glomerulosa (ZG) comprises densely packed cells arranged in clusters that produce aldosterone; the zona fasciculata (ZF) is composed of cells with large cytoplasm, containing lipid droplets arranged in radial columns that synthesize cortisol; and the zona reticularis is composed of compact and pigmented cells producing androgens.

Objectives: Our main objective was to study the expression of aldosterone synthase (CYP11B2 which catalyzes the last steps of aldosterone synthesis) and 11 β -hydroxylase (CYP11B1 which catalyzes the last step of cortisol synthesis) in normal adrenal glands to address issues regarding the zonation and the fate of the cells constitutive of each zone through the expression of Ki-67 and cleaved Caspase-3. We have also investigated the relevance of specific markers of the ZG.

Methods: Forty seven human adrenals (18 females, 29 males, ranging from 22 to 81 years old) were obtained from brain-dead organ donors. We have used immunohistochemical analyses to study CYP11B1 and CYP11B2 pattern of expression and investigate the remodeling of the adrenal cortex in relation to aging.

Results: As early as 22 years old, we found that the histological ZG (h-ZG) does not correspond to the functional ZG (f-ZF) expressing CYP11B2. Moreover, the h-ZG CYP11B2- cells were CYP11B1+ cells showing that these cells ascribed to the h-ZG are in fact cortisol producing cells. Our analysis also showed that the steroidogenic cells were either Cyp11B1 or Cyp11B2 positive. By immunofluorescence, we observed in 70% of our samples that isolated or clusters of CYP11B2+ cells located deeply in the h-ZF, in the medulla and in the vicinity of the central vasculature. Ki-67 expression was variable and observed throughout the whole cortex. It is interesting to note that some Ki-67+ cells located in the h-ZG were CYP11B1+. Apoptosis was extremely rare but detected in all zones;

Conclusion: Our data emphasize that mineralocorticoid- and glucocorticoid-producing cells are distributed between the histological ZG, ZF, ZR and medulla making the determination of the functional status of a cell or a group of cells a unique tool in deciphering the age-related changes in adrenal cortex. They also suggest that the functional zonation is not maintained by cell lineage conversion/migration and that steroidogenic cells are capable of migrating without changing their phenotype.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2020-1014

A LADY WITH ' PSYCHIATRIC OVERTONES'; PRIMARY HYPERPARATHYROIDISM DUE TO PARATHYROID CARCINOMA

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Introduction: In clinical medicine, hypercalcemia is considered a great masquerader which mimics diverse other ailments including psychological diseases. Neurobehavioral manifestations has been reported as a hypercalcemic presentation, mostly in primary hyperparathyroidism, even though the exact prevalence is not known due to the scarcity of research. The spectrum of symptoms span from mild anxiety to even coma. The pathology causing autonomous hypersecretion of parathyroid hormone (PTH) in primary hyperparathyroidism is either adenoma or hyperplasia in 99% of the occasions whereas parathyroid carcinoma which is the least common endocrine malignancy worldwide is the culprit in less than 1% of times.

Case Description: Here we present a rare case of a previously healthy middle aged lady who was admitted with psychotic symptoms of recent onset. The investigations unveiled severe hypercalcemia and extremely high PTH levels. Her Sestamibi parathyroid scan localized focal abnormal uptake in right superior pole of thyroid bed suggesting parathyroid adenoma but histology confirmed parathyroid carcinoma with positive vascular and capsular invasion. The initial medical management as for hypercalcemic crisis with IV hydration, IV furosemide and IV bisphosphonate plus oral calcimimetic-cinacalcet was futile in terms of sustained normalization of serum calcium. The subsequent curative parathyroidectomy brought down the PTH level to normal resulting in normocalcemia, rendering the patient symptomless.

Clinical discussion: We would like to point out that almost all the previous reported similar cases had been by virtue of parathyroid adenoma whereas this case elucidate an out of the common combination of psychosis with parathyroid carcinoma. Moreover the dramatic symptomatic response which occurred in parallel with the biochemical response following the surgery is also quite enticing.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2020-1100

CORRELATION OF BODY MASS INDEX AND AGE WITH OSTEOPOROSIS PROBABILITY IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

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Introduction: Currently there are no clinical or biochemical markers to predict the probability of osteoporosis in patients with primary hyperparathyroidism.

Objectives: We studied the relationship between various parameters and results of DXA scans, specifically T-scores, at four different sites (lumbar spine, forearm, femoral neck and total hip) in patients with primary hyperparathyroidism.

Methods: Retrospective review of data for 218 patients with primary hyperparathyroidism was performed. DXA results were categorized as osteoporosis (T-score ≤ -2.5 , n=60), osteopenia ($-2.4 \leq$ T-score ≤ -1.0 , n=89), and normal (T-score ≥ -0.9 , n=69). Age, BMI, serum total calcium, ionized calcium, intact PTH, albumin, alkaline phosphatase, phosphorus, 25-hydroxy vitamin D, 1,25-hydroxy vitamin D, 24-hour urinary calcium levels and parathyroid tumor weight were analyzed.

Two different statistical models- linear regression and multivariate linear logistic regression were performed at each of the four sites, where the former models the linear relationship between the T-score in the continuum of all possible negative values with the covariates and the latter models the likelihood of osteoporosis.

Results: At the lumbar spine, with the linear model, alkaline phosphatase ($p < 0.001$), BMI ($p < 0.001$) and ionized calcium ($p < 0.001$) significantly correlate with T-scores; whereas with the logistic model, BMI was the only variable predicting osteoporosis probability.

At the femoral neck, with the linear model, 25-OH vitamin D (< 0.001), BMI ($p = 0.022$), 1,25-OH vitamin D ($p = 0.034$) correlate with T-scores; whereas with the logistic model, both BMI ($p = 0.029$) and age ($p = 0.051$) were the significant variables that can predict osteoporosis.

At the total hip, with the linear model, BMI ($p = 0.001$) and age ($p = 0.001$) correlate with T-scores; whereas with the logistic model, only BMI ($p = 0.016$) can predict osteoporosis.

At the forearm, a model could not be generated as the cases were very few relative to the number of covariates.

Conclusion: In primary hyperparathyroidism, BMI seems strongly correlated with T-score using either the linear model or the logistic model and can predict probability of osteoporosis. Further studies with larger patient populations are needed.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2020-1105

CALCIFEDIOL SOFT GELATIN CAPSULES IS SUPERIOR TO CHOLECALCIFEROL FOR THE MANAGEMENT OF VITAMIN D DEFICIENCY IN POSTMENOPAUSAL WOMEN, INDEPENDENTLY OF BMI: A TREATMENT TO BE CONSIDERED IN THERAPEUTIC GUIDELINES

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Introduction: Vitamin D deficiency is a worldwide health issue. There is no consensus on the optimal dosing for treatment, however evidence suggests that overweight patients may have difficulty to achieve adequate vitamin D levels.

Objectives: To assess the efficacy of calcifediol compared with therapeutic guidelines dose recommended for cholecalciferol in the treatment of vitamin D deficiency in postmenopausal women, in terms of percentage of patients with 25(OH)D levels >30ng/mL. To assess these results according to BMI.

Methods: Phase III-IV, double blind, randomized, controlled, multicentre superiority clinical trial approved by Ethics Committees and Health Authorities. Postmenopausal women with baseline levels of 25(OH)D <20ng/mL were randomised to calcifediol 266 mcg/month for 4 or 12 months (standard and test regime), or to cholecalciferol 25000 IU/month (as per therapeutic guidelines) for 12 months.

Data was analysed upon completion of month 4 visit by 100% of evaluable patients and reported without unblinding subjects' study treatments. This phase lasted from March 2018 to December 2019. Both calcifediol groups are summarised for analysis.

Results: 298 women were included in the ITT analysis. When analysing per treatment group 13.5% and 35% of women in the calcifediol group reached 25(OH)D >30ng/mL at 1 and 4 months when compared to 0% and 8.2% respectively in the cholecalciferol group ($p<.0001$).

According to BMI, the distribution was: 41.3% obese, 32.6% overweight, 25.2% normal weight and 1% underweight (not considered for analysis).

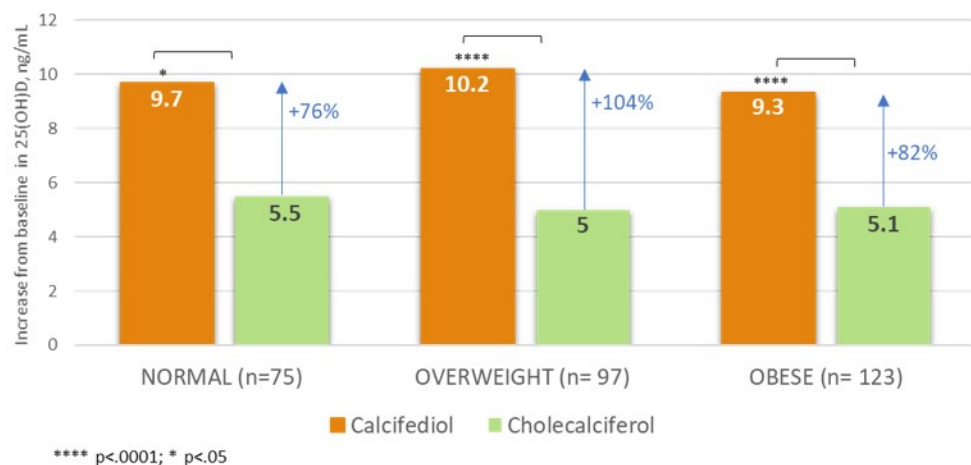
The increase from baseline of 25(OH)D was statistically significantly higher for calcifediol at both month 1 and month 4 in all BMI groups (Figure 1). The percentage of patients with 25(OH)D values >30ng/mL at month 4 for calcifediol was 25%, 33.9% and 51.7% vs 4.7%, 17.6% and 7.9% for cholecalciferol in obese, overweight and normal BMI groups, $p<.05$.

No relevant safety issues were reported.

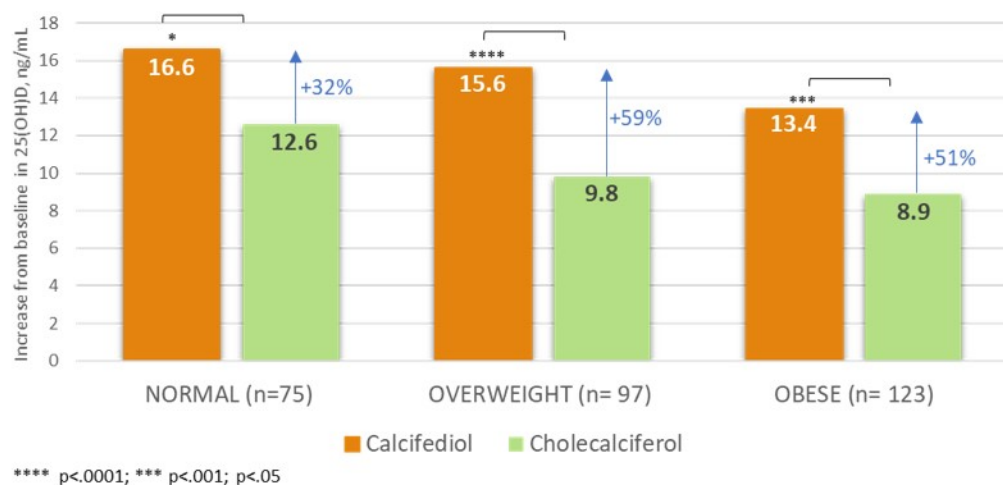
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Figure 1: Mean change from baseline in 25(OH)D levels by BMI

Month 1



Month 4



Conclusion: Calcifediol shows a greater efficacy than cholecalciferol for the treatment of vitamin D deficiency in postmenopausal women independently of their BMI. The increase of 25(OH)D levels from baseline are statistically significantly higher in calcifediol groups, regardless of BMI when compared to cholecalciferol. A significant percentage of patients on cholecalciferol group failed to reach recommended levels.

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Disclosure of Interest: E. Jódar Conflict with: Amgen, AstraZeneca, Faes Farma, GSK, Helios-Fresenius, Italfarmaco, Lilly, MSD, Mundipharma, Novo Nordisk, Shire, UCB, Conflict with: Amgen, AstraZeneca, Faes Farma, GSK, Helios-

Fresenius, Italfármaco, Lilly, MSD, Mundipharma, Novo Nordisk, Shire, UCB, Conflict with: Amgen, AstraZeneca, Boehringer, Faes Farma, Lilly, MSD, Mundipharma, Novartis, Novo Nordisk, UCB, J. L. Pérez-Castrillón Conflict with: Farmalider, Faes Farma, Pfizer, Conflict with: Farmalider, Faes Farma, Gedeon-Richter, Conflict with: Amgen, Faes Farma, Lilly, MSD, A. Dueñas-Laita Conflict with: Farmalider, Faes Farma, Conflict with: Faes Farma, Conflict with: Farmalider, G. Hernández-Herrero Conflict with: Faes Farma, S. P. Chinchilla Conflict with: Faes Farma, P. Arranz-Gutiérrez Conflict with: Faes Farma

Bone and Calcium

ICE2020-1110

INTRODUCTION TO A MULTINATIONAL, LONG-TERM, PROSPECTIVE OUTCOMES DISEASE MONITORING PROGRAM (DMP) IN PATIENTS WITH X-LINKED HYPOPHOSPHATEMIA

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Introduction: In X-linked hypophosphatemia (XLH), excess FGF23 causes hypophosphatemia, leading to chronic debilitating musculoskeletal impairments. XLH treatment options include a combination of oral phosphate and active vitamin D, or burosumab, a fully-human monoclonal antibody to FGF23 approved to treat patients with XLH.

Objectives: The XLH Disease Monitoring Program (XLH-DMP) is a prospective, multinational, outcomes study examining the longitudinal progression of clinical, radiographic, and biochemical features of XLH.

Methods: This 10-year study is collecting real-world safety and effectiveness data of both conventional therapy and burosumab and includes patients irrespective of age or treatment modality. Enrollment is targeted at ≥ 500 patients with a confirmed clinical diagnosis of XLH, of whom ≥ 200 will be children < 18 years.

Results: As of 29 February 2020, we have enrolled 566 patients (age range: 1 month to 76 years), including 334 adults and 232 pediatric patients. Of these, 34% (114/334) of adult patients and 36% (83/232) of pediatric patients completed the year 1 visit as of the analysis cutoff date. Overall, 28% of patients (89 adults, 67 children) had previously participated in burosumab clinical trials and were continuing this therapy (Group 1), 37% were non-trial patients (102 adults, 109 children) who initiated burosumab by prescription before or during the XLH-DMP (Group 2), and 35% of patients (143 adults, 56 children) never received burosumab (Group 3). At XLH-DMP enrollment, 53% (176/334) of adults reported a history of enthesopathy/bone spurs/osteophytes, and 22% (74/334) of adults reported spinal stenosis or cord compression. Bowing of the legs was reported in 79% (184/232) of pediatric patients. Burosumab-related adverse events were reported in 13% (25/191) of adult and 10% (17/176) of pediatric patients and were consistent with the known safety profile of burosumab. To date, there have been no burosumab-related serious adverse events. XLH-DMP enrollment is ongoing.

Conclusion: The XLH-DMP is establishing a comprehensive real-world dataset in one of the largest populations of this rare disease studied to date. Results from this ongoing 10-year study will improve understanding of the natural history of XLH. These results, and the added potential to link XLH-DMP outcomes with previous clinical trial assessments, will provide further insight into the long-term safety and effectiveness of XLH therapy.

Disclosure of Interest: H. Cassinelli Conflict with: Ultragenyx Pharmaceutical Inc, E. Imel Conflict with: Ultragenyx Pharmaceutical Inc, Conflict with: Ultragenyx Pharmaceutical Inc, L. Ward Conflict with: Ultragenyx Pharmaceutical Inc, Conflict with: Ultragenyx Pharmaceutical Inc, M. Lazaretti-Castro Conflict with: Ultragenyx Pharmaceutical Inc, A. Skrinar Conflict with: Ultragenyx Pharmaceutical Inc, Conflict with: Ultragenyx Pharmaceutical Inc, C. Wang Conflict with: Ultragenyx Pharmaceutical Inc, Conflict with: Ultragenyx Pharmaceutical Inc, L. Rees Conflict with: Ultragenyx Pharmaceutical Inc, Conflict with: Ultragenyx Pharmaceutical Inc, T. Carpenter Conflict with: Ultragenyx Pharmaceutical Inc, Nutricia, and Amgen, Conflict with: Ultragenyx Pharmaceutical Inc, Inozyme, and Regeneron

Bone and Calcium

ICE2020-1142

A RARE CASE OF REFRACTORY HYPOCALCAEMIA SECONDARY TO OSTEOBLASTIC BONE METASTASES FROM BLADDER CANCER.

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Introduction: Symptomatic hypocalcaemia is uncommon, occurring in < 2% in patients with malignancy. We report a case of refractory hypocalcemia in a patient with metastatic bladder cancer with extensive osteoblastic bone metastases and history of denosumab administration.

Case Description: A 64-year-old male was diagnosed with bladder carcinoma with metastases to the bone. He was treated with multiple rounds of chemotherapy with progression of his bone metastases. Denosumab 120mg was administered 3 months before admission for the prevention of skeletal related events.

He presented with symptomatic hypocalcemia with bilateral perioral paraesthesia but no muscle cramps and spasms. Serum calcium was 1.50 (2.09 – 2.46 mmol/L), albumin was 33 (40 – 51 g/L), serum phosphate was 0.89 (0.94 – 1.50 mmol/L), serum magnesium was 0.62 (0.74 – 0.97 mmol/L) and iPTH was 49.2 (0.9 – 6.2 pmol/L). Evaluation of the bone turnover markers revealed significantly elevated bone formation markers, P1NP 1348 (18.4 – 72.3 UG/L), alkaline phosphatase 1326 (39 - 99 U/L) but normal bone resorption markers, beta cross lap 0.34 (<0.58 UG/L). X-ray and computed tomography (CT) scans revealed extensive sclerotic bone metastases in the sacrum, pelvic bones, sternum, vertebrae and ribs.

He was treated aggressively with intravenous calcium gluconate boluses and was initiated on calcium carbonate, cholecalciferol, calcitriol and magnesium replacement. After 10 days of concomitant intravenous and oral calcium replacement, his calcium level reached a stable level of 1.8 to 1.9 mmol/L. He was eventually discharged with high doses of calcium replacement of 8.1g of elemental calcium (calcium carbonate 3.75g TDS, calcium lactogluconate 90mL BD), colecalciferol 20000u every fortnight and calcitriol 1mcg TDS.

Clinical discussion: Osteoblastic bone metastases lead to an increased influx of calcium and phosphate into the bone leading to hypocalcemia. The administration of denosumab might have aggravated the hypocalcemia even though it was given 3 months prior to admission. Severe hypocalcemia is unusual even in patients with osteoblastic bone metastases and is more commonly reported in prostate cancer and rarely in breast cancer. To our knowledge, no cases of hypocalcemia in bladder cancer with osteoblastic bone metastases have been reported. The possibility of osteoblastic metastasis should be considered in the differential of protracted and severe hypocalcemia.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2020-1150

COMPLETE ANDROGEN INSENSITIVITY SYNDROME AND EARLY OSTEOPOROSIS

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Introduction: Complete androgen insensitivity syndrome (CAIS) is a common cause of 46 XY disorders of sex development as well as primary amenorrhea, but its effect on bone mineral density (BMD) is singular and difficult to manage. Androgens are an important modulator of bone remodeling and health, and the androgen receptor (AR) is pivotal for signaling within the bone cells. CAIS results in a severely disrupted androgen receptor throughout the body, causing an elevated risk of early osteoporosis. Timing of gonadectomy and hormone replacement therapy protocols aren't established, creating a wide variety of treatment plans and BMD profiles. Our objective is to present a patient with CAIS status post gonadectomy that developed early osteoporosis despite prolonged hormone replacement therapy (HRT).

Case Description: A 44-year-old phenotypic woman with a history of CAIS status post bilateral orchiectomy at 4-years-old and osteochondritis dissecans of the right ankle status post multiple surgeries presents to follow up. Her CAIS diagnosis was presumptively made around the time of her orchiectomy. She was previously on conjugated estrogens tablets, Premarin®, at various doses from the age of 12 until her early 30s when her therapy became sporadic secondary to her up-tempo military career. In 2014, she was prescribed topical estrogen therapy, but discontinued soon after because of skin irritation. She had not been on any form of hormone replacement therapy (HRT) since that time. The physical examination during this appointment is significant for a stable height of 75 inches, weight of 244 lbs, BMI of 30.5, and normal cardiopulmonary and abdominal examination. DEXA revealed T-scores of -2.0 lumbar spine, -1.6 femoral neck, -1.1 total hip, -2.5 forearm, and -3.5 whole body. After being diagnosed with early osteoporosis via the WHO criteria, she was restarted on estradiol 1 mg oral tablet twice daily with a plan to repeat DEXA in 12-18 months to monitor interval changes.

Clinical discussion: This case emphasizes the importance of the timing of gonadectomy in relation to BMD in patients with CAIS as well as highlights how our HRT practices likely produce only modest results. While recent studies have helped establish postpubertal gonadectomy as the preferred practice to maintain BMD, there are still many questions on how to initiate HRT to prevent and treat osteoporosis in this patient population.

Disclosure of Interest: None Declared

Bone and Calcium

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EPIDEMIOLOGICAL PROFILE OF PATIENTS WITH OSTEOPOROSIS ATTENDED IN A SPECIALIZED AMBULATORY

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Introduction: Osteoporosis is an osteometabolic disease characterized by decreased bone mineral density (BMD), increased risk of fractures and impaired quality of life for affected individuals. Such morbidity affects more than 200 million people worldwide and is therefore a public health challenge.

Objectives: To characterize osteoporotic patients seen at Endocrinology and Rheumatology outpatient clinics at Hospital Universitário Alcides Carneiro (HUAC), Federal University of Campina Grande (UFCG), between August and October / 2019, regarding the epidemiological profile, risk of fractures, bone loss and predominant osteoporotic site.

Methods: This is a cross-sectional observational study, involving female individuals, diagnosed with osteoporosis and over 18 years of age. A questionnaire with clinical and epidemiological data was applied and weight, height, calf circumference (CC) and body mass index (BMI) measurements were performed. The study population was 483 patients and the valid sample was 42 patients. The data were compiled and analyzed using the Statistical Package for the Social Sciences version 25 program. For the analysis of concordance and graphs, Origin Pro version 8.0 was used.

Results: The average age was 66.8 years (+ - 7.57DP). Regarding ethnicity, 50% were brown. Five (12%) patients were smokers and 14 (33.3%) had fractures; the practice of physical activity more than 2x/week was associated with the incidence of 15% of fractures, while in the sedentary population this incidence was 54%. Regarding the use of medications, 11 (26%) used glucocorticoids and 10 (23.8%), sleep inducers / psychotropics. Regarding the osteoporotic site, 80% were in the lumbar spine (mean T-score: -3.14 SD) and 12% in the femoral neck (mean T-score: -3.00 SD). A 2.5-fold increase in the risk of fracture occurred in the face of a 1DP reduction in BMD. Lower CC measurements were related to significant bone loss, with an average CC value of 31.5 cm in the group with BMD between - 4.5 to -5.4 SD. Regarding weight, the majority (48%) had a normal BMI.

Conclusion: In the present study, there was a predominance of elderly population, with adequate weight, mixed race, non-alcoholic, with the lumbar spine being the most affected osteoporotic site. The use of glucocorticoids and psychotropics were relevant in the sample and physical activity was a protective factor for fractures.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2020-1216

STAT3 MUTATION IN PATIENT WITH MULTIPLE FRACTURES (AN UNUSUAL PRESENTATION)

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Introduction: Autosomal dominant Hyper Ig E syndrome (AD_HIES/Job's disease) is a Primary Immunodeficiency Syndrome, associated with connective tissue, skeletal, cerebral and vascular alterations. This rare disease is caused by heterozygous mutations of signal transducer and activator of transcription 3 (STAT3) gene, at 17q21.31, in approximately 70% of patients. STAT3 plays a key role in signal transduction from different cytokines. Fractures occurred in approximately 50% of patients but the exact pathophysiological mechanism of fractures is still unknown. Aim: to present a patient with multiple fractures (bone fragility) and STAT 3 mutation

Case Description: a 6 years old boy concurred to endocrinology because he had three non-traumatic fractures: clavicle, radio and ulna. He also had eczema, recurrent pneumonia, dental alterations and mitral prolapse. His father had two pathologic fractures. Physical examination showed very low weight (-2.5SD), normal height, conjunctival injection, joint hypermobility, dental alterations and bone pain. Multi-disciplinary evaluation detected bone alterations (low mineral density <2,5 SD and vitamin D deficiency, <5ng/ml), lung bilateral basal bronchiectasis, eczema and immunological evaluation showed low CD4 and TH17 normal/high levels with Ig E >1800 UI/ml. Firstly, panel study of most frequent mutations of STAT3 gene was negative. Because of high suspicion of Job's disease, gene sequencing was done and the result found a heterozygous mutation at p.His332Tyr in exon 10 of STAT3 gene.

Clinical discussion: Conclusion: Although the most frequent genetic cause of bone fragility is Osteogenesis Imperfecta, in this case the association of other symptoms like eczema and recurrent pneumonia were a key to think of another causative syndrome. In the present case, atopic symptoms were predominant, which is common within the pediatric practice. Interrogation and multi-disciplinary approach allowed us make a correct diagnosis. This rare genetic disease required a high degree of clinical suspicion. We recommend to consider the association between chronic dermatitis with torpid evolution, recurrent infections and bone fragility as a triad necessary to think in STAT3 mutations. As a multisystemic disease, a multi-disciplinary approach is needed in order to improve patient's quality of life.

Disclosure of Interest: None Declared

A STUDY ON THE GENETIC AND MOLECULAR BASIS OF HYPOPHOSPHATEMIC RICKETS (HR)

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Introduction: HR is a genetic disorder characterized by hypophosphatemia, defective intestinal calcium absorption, and vitamin D resistant rickets. X-linked HR due to *PHEX* mutation is the predominant type; autosomal dominant and recessive forms due to *FGF23*, *SLC34A1*, *DMP1*, *ENPP1* and *SLC34A3* mutations respectively are rare. Sporadic cases have also been reported. Fibroblast Growth Factor 23 (FGF23) is an important phosphate regulating hormone produced by osteocytes. It increases phosphate excretion and reduces renal phosphate reabsorption by inhibiting expression of genes (*SLC34A1* and *SLC34A3*) encoding sodium-phosphate cotransporters when serum phosphate levels are high. *PHEX*, *DMP1* and *ENPP1* regulate circulatory FGF23 levels and therefore play a major role in phosphate homeostasis.

Objectives: To screen for mutations in patients with HR and measure serum FGF23 levels by ELISA.

Methods: A total of 40 patients of HR were recruited in comparison to 100 healthy controls. Detailed clinical and family history was noted, and about seven milliliters of peripheral blood was withdrawn for DNA extraction and serum separation for measuring FGF23 levels. Whole Exome Sequencing (WES) was performed and data was analyzed using variant prioritization tools (QueryOR, Moon-Diploid, and Mutation Distiller) to identify mutations. The mutations were validated by Sanger sequencing.

Results: Forty patients (30 females; 10 males) had median disease onset at 2 years of age. They presented with hypophosphatemia, hypocalcemia, elevated parathormone and alkaline phosphatase, low-to-normal 25-OH vitamin D, growth retardation and predominantly lower limb deformities. WES revealed 24 *PHEX* (n=36; 90%), one *FGF23* (n=1; 2.5%), one *DMP1* (n=2; 5%) and two *ENPP1* (n=1; 2.5%) mutations, of which, 18 were novel and 10 were previously reported. The mutations were absent in the 100 controls and control databases such as 1000 genomes, dbSNP and gnomAD. Twenty three patients showed positive family history with 21 harboring *PHEX* mutations and the other two carrying *DMP1* mutations. Patients showed significantly higher serum intact FGF23 levels in comparison to controls (n=60) [P value <0.0001].

Conclusion: The present study suggested that *PHEX* mutations are mainly responsible for causing both familial and sporadic forms of HR in India. It also indicated that FGF23 could be used as a diagnostic marker for HR where genetic testing facilities are unavailable, especially in the developing countries. However, study on a large sample size is needed to confirm this.

Disclosure of Interest: None Declared

Bone and Calcium

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IMMOBILISATION RELATED HYPERCALCEMIA IN AN HIV-POSITIVE INDIVIDUAL

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Introduction: Hypercalcemia with suppressed PTH in a HIV +ve man might suggest malignancy (e.g. lymphoma) or infection (e.g. tuberculosis, cryptococcosis, CMV, HTLV1), granulomas (e.g. sarcoidosis, silicosis) or immobilization related. The hypercalcemia associated with lymphoma and granulomatous diseases are associated with raised 1,25 Di-OH Vit D due to extrarenal 1- α hydroxylase.

Case Description: 35-year-old man, previous IV drug user, HIV/HCV positive, previous tuberculosis, referred from genitourinary medicine clinic with hypercalcemia. He was started on HAART with Emtricitabine, Tenofovir, Darunavir and Ritonavir recently. He was not on calcium/vitamin D supplements. He had contracture of right hip secondary to right femoral artery pseudo-aneurysm surgery with significant tissue loss. He also had contracture of right knee with a deep overlying ulcer. He lived in 1st floor of a house with no stair-lift and his father had to lift him down for him to go outdoors in wheelchair, which had made him immobile for many months.

Calcium 3.65 mmol/l, phosphate 0.84 mmol/l, PTH 0.6 pmol/L, 25-OH vit D 19 nmol/L and 1,25 Di-OH Vit D <12 pmol/L and TSH 2.7 mU/L. ACE levels, protein electrophoresis, fungal antigens, QuantiFERON-TB Gold, blood/sputum cultures were negative. Whole body CT showed bilateral calcified lung granuloma with tiny pleural effusion with no evidence of malignancy.

Hypercalcaemia initially improved with IV fluids, but relapsed when fluids were stopped, requiring IV pamidronate. He was bedbound throughout hospitalisation. His HAART and PCP prophylaxis were continued. Started on colecalciferol 800 units for vitamin D deficiency. Tested extensively for infectious/granulomatous causes of hypercalcemia. Positive EBV viral load noted, which has 60-fold risk for Non-Hodgkin's lymphoma including primary CNS lymphoma in HIV. Bone marrow trephine biopsy ruled out lymphoma. Though pulmonologist wished to get a pleural fluid sample, interventional radiologist failed to get it.

Clinical discussion: Lymphoma, infections and granulomas are ruled out. Recent HAART initiation can cause immune reconstitution syndrome (IRS) as a cause of hypercalcemia. IRS will present as unmasking/paradoxical worsening of pre-existing infection or lymphoma once immune function is restored with HAART. As worsening of illness hasn't happened, it is not IRS. Final diagnosis was immobilisation related hypercalcemia (excessive bone resorption due to lack of mechanical stress) and is a diagnosis of exclusion. Bisphosphate can be used for this.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2020-1241

CO-EXISTENCE OF HYPERTHYROIDISM AND HYPERPARATHYROIDISM IN A PATIENT

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Introduction: Endocrine complications of lithium include hypothyroidism (5-15%), goitre (5-50%), hyperthyroidism (0.1-0.7%), nephrogenic DI (20-25%), and hyperparathyroidism (2.7%). Lithium can cause both hyperthyroidism and hyperparathyroidism. Apart from lithium, this combination can occur in nearly 1% of Graves' disease (with normal or raised PTH). Moreover, Graves' disease can cause hypercalcemia in nearly 22% of cases (with suppressed PTH).

Case Description: 60-year-old lady with bipolar disorder on stable dose of lithium 400mg daily for nearly 20 years underwent routine blood check-up and was referred as lithium toxicity. Patient was asymptomatic without gastrointestinal or visual disturbances, polyuria, tremor, or weakness. Systemic examination was normal with no goitre or thyrotoxicosis. ECG was unremarkable. Serum lithium 1.78 mmol/L, adjusted Calcium 2.62 mmol/l, phosphate 1.73 mmol/l, PTH 2.4 pmol/L, 25-OH vitamin D 19 nmol/L, TSH <0.01 mU/L, Free T4 33.4 pmol/L with TPO antibody 6.0 IU/mL. She was diagnosed as lithium toxicity with coexistent hyperparathyroidism and hyperthyroidism associated with severe hypovitaminosis D. Lithium was held and treatment with IV fluids, carbimazole 10mg, and colecalciferol (40,000 units weekly for 7 weeks, then 800 units daily) initiated, with strict fluid balance monitoring, to look for nephrogenic diabetes insipidus (DI). She was reviewed by mental health team who suggested to recheck lithium levels in 1-week time and to restart lithium 200mg once daily once lithium levels are < 0.5mmol/L and to titrate the dose up to 400mg if possible.

Clinical discussion: Lithium might cause exacerbation of pre-existing primary hyperparathyroidism or raise the threshold level of calcium needed to suppress PTH secretion, the latter leading to development of parathyroid adenoma or hyperplasia (solitary adenoma is common in lithium induced hyperparathyroidism than multiglandular hyperplasia). Various treatment options available are lithium discontinuation, surveillance, calcimimetics agents or parathyroidectomy. Clinically/sonologically detected goitre and hypothyroidism are the commonest lithium induced thyroid disorders. Lithium induced hyperthyroidism is rare and its mechanisms are uncertain. In most cases, it is due to transient painless thyroiditis caused by direct toxic effect of lithium on thyroid. The remaining are related to autoimmunity, by stimulating thyroid autoantibody production. Lithium augment activity of B lymphocytes and reduce suppressor/cytotoxic T cell ratio.

Disclosure of Interest: None Declared

Bone and Calcium

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HYPERPARATHYROIDISM CAUSED BY PARATHYROID CARCINOMA

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Introduction: Parathyroid carcinoma account for <1% of primary hyperparathyroidism (PHPT). It occurs equally in both sexes whereas parathyroid adenoma occur more commonly in females. Pancreatic carcinoma patients are younger by a decade and presents with extremely high PTH and calcium.

Case Description: 73-year-old lady admitted with constipation, abdominal pain, and weight loss of nearly 20 Kg. Bloods were suggestive PHPT, vitamin D deficiency with normal renal function: creatinine 58 µmol/L (45-84), eGFR >90 mL/min (90-200), corrected calcium 3.42 mmol/L (2.2-2.6), phosphate 0.55 mmol/L (0.80-1.50), PTH 47.8 pmol/L (1.6-6.9), and 25-OH vitamin D 17 nmol/L.

CT abdomen-pelvis did not show any sinister lesions. 24-hour urinary calcium was normal. Ultrasound neck showed a large 3 cm hypoechoic solid mass at the lower pole of right lobe of thyroid with appearances highly suggestive of a parathyroid adenoma. Renal ultrasound was unremarkable. Sestamibi scan showed an increased uptake overlying the inferior pole of right thyroid lobe that is highly active on 3-hour imaging, suggesting right lower pole parathyroid adenoma. She underwent right parathyroidectomy.

Bloods after surgery showed a corrected calcium 2.97 mmol/L, phosphate 0.51 mmol/L, and PTH 2.2 pmol/L. She developed new onset CKD with creatinine 124 µmol/L and eGFR 38 mL/min. Histology of surgical specimen showed features of parathyroid carcinoma. She underwent prophylactic right hemi thyroidectomy with neck dissection. Postoperative PET scan showed no signs of local recurrence. After thyroidectomy, the calcium levels were normalized, but PTH levels remained slightly high due to co-existing CKD (corrected calcium 2.28 mmol/L, and PTH 23.9 pmol/L).

Clinical discussion: Parathyroid carcinoma may occur sporadic or with genetic syndromes like MEN1, MEN2A, familial isolated hyperparathyroidism, or hyperparathyroidism-jaw tumour syndrome. Nearly 90% are hypersecretory, whereas 10% are non-functional, presenting with compressive symptoms. Lymph node metastasis occur in 6-30%.

Large, heterogenous and lobulated parathyroid lesions in ultrasound favour carcinoma. Preoperative diagnosis of carcinoma from adenoma is difficult due to similarities in endocrine secretion and symptoms. The diagnosis is often made post-operatively. Complete resection with clear margins offers the only opportunity for cure. Adjuvant chemotherapy or radiotherapy does not improve survival. Recurrence is common and is treated with surgery for resectable lesions and if not with calcimimetics.

Disclosure of Interest: None Declared

Bone and Calcium

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IDIOPATHIC HYPERCALCIURIA AND BONE IMPAIRMENT: REPORT OF A CASE

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Introduction: Idiopathic Hypercalciuria (IH) is an autosomal dominant disorder which affects equally both genders. It is associated with bone mass loss and decreased bone acquisition in children. It implies increased risk of osteoporosis and fragility fractures in adulthood. A case of a patient who suffered fractures due to minor trauma is reported. Based on anamnesis and complementary study, diagnosis of secondary osteoporosis due to Idiopathic Hypercalciuria is confirmed

Case Description: 61-year-old woman with history of falling from the same level in 2014. Lumbar Rx is taken, reveals: L1 fracture with depression of the upper vertebral platform. The study is completed with a CT of dorsal lumbar spine that shows: L1 fracture of the anterior aspect of the upper platform, with slight subsidence and minimal anterior displacement. Patient consulted later in 2016 due to pain on the left rib region after leaning on this area. A bone scintigram was requested, showing: Focal increase in osteoblastic activity in the left rib cage. Was referred to endocrinology for study with the following lab: Intact PTH: 85 pg / dl (NV: 11-67) calcium: 9.74 mg / dl, albumin: 4.7 mg / dl, phosphorus: 3.6 mg / dl Alkaline phosphatase: 74 IU / L (NV: 35 -104), CLU: 6.0 UG / 24 h, Vitamin D: 19 ng / ml. Urine Calcium: 510.4 mg / 24h, Ca / Cr index: 0.3, Hemogram, TSH, free T4, Plasma electrolytes: normal. Bone Densitometry: Lumbar spine T Score: -2.5 hip D.S Left hip: T Score - 1.8 D.S Right hip: - 2.0 D.S. Vitamin D and dietary calcium intake of 1200 mg per day was prescribed. Patient attends a new control with the following lab: PTH: 66 pg / dl - Vitamin D 38 ng / ml. Urine-Calcium 452.4 (mg / 24 h). After discontinuing vitamin D supplementation, hypercalciuria relapses. Because of this, treatment is resumed, and hydrochlorothiazide and bisphosphonates were added. 2 years later a new bone densitometry is performed: Spine L2-L4: T-score -2.0 D.S – Left Hip: T-Score -1.2 D.S – Right Hip: 1.8 D.S. Didn't present new fractures.

Clinical discussion: Idiopathic Hypercalciuria must be considered as a differential diagnosis of osteoporosis. The following findings in this patient are remarkable: High PTH, normal plasmatic calcium, low PTH with high urinary calcium excretion. In the context of a likely Secondary Hyperparathyroidism, treatment based on Vitamin D is entitled, correcting PTH levels. During treatment, bone densitometry shows a fast improvement, which may be associated with hydrochlorothiazide and bisphosphonates treatment.

Disclosure of Interest: None Declared

Bone and Calcium

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BEAVIS TYPE I AVULSION FRACTURE OF THE CALCANEUS IN A PATIENT WITH ESTABLISHED OSTEOPOROSIS

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Introduction: Tuberosity fractures account for 1% to 3% of all calcaneus fractures; they are more common in females in the seventh decade of life. The most commonly associated injury mechanisms are foot trauma in plantar flexion and vigorous, abrupt contraction of the soleus and gastrocnemius muscles. Normally this tension isn't enough to cause avulsion, but may occur in vulnerable bone due to osteoporosis. It can also occur in patients with peripheral neuropathy subject to repeated trauma or increased tension and stiffness of the plantar flexor. Treatment varies according to the avulsion fracture pattern (Beavis or Lee classification). This fracture pattern varies according to bone mineral density, injury mechanism, and force transmission.

Case Description: We present a case of a 67-year-old female patient observed in the emergency room with left foot trauma after tripping. She had personal history of Osteoporosis (T score >2.5) and High Blood Pressure. Imaging study revealed a fracture avulsion of the tuberosity (Beavis type I) and CT of the calcaneus showed the clear vertical direction of the fracture in the posterior third of the calcaneus, with multiple fragments, in which the largest would have about 30 x 33 x 14 mm. The insertion of the Achilles tendon was preserved, causing superior displacement of this fragment in about 13 mm. Osteosynthesis was performed with two cannulated cancellous screws with 2 rings and Achilles tendon reinforcement through minimal posterior incision. Postoperatively she was kept immobilized with a posterior splint for six weeks without load. At 8 weeks she started physiotherapy. Medication with biphosphonades was maintained. No complications were reported; 3 months post-op the patient presented without pain complaints, without mobility limitation, with an AOFAS score of 97% (American orthopedic foot & ankle score).

Clinical discussion: There are few guidelines for addressing this type of fracture or research on its etiology and vulnerability factors given the relative rarity of this type of injury. Osteoporosis has been proposed as a common entity in type I, so it can be considered a risk factor for this type of avulsion injury, which in turn should be considered a insufficiency fracture. Surgical treatment assumes a central position in the treatment; the complications are mainly related to soft tissues damage by the fracture itself or the surgical approach. Further studies should concentrate on establishing concise evidence on risk factors and the role of osteoporosis.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1313

THE RISK OF FRACTURES IN PRIMARY HYPERPARATHYROIDISM: A META-ANALYSIS

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Introduction: Primary hyperparathyroidism (PHPT) is a common metabolic bone disease with prevalence of 1% in adult population. Patients with PHPT have reduced bone mineral density (BMD) especially at the cortical bone. However, the magnitude of fracture risk is unknown and the related studies have shown contradictory results.

Objectives: The primary outcome of this meta-analysis was to determine risk of vertebral fracture (VF), non-vertebral fracture (NVF), hip fracture (HF), distal radius fracture (RF) and total fracture (TF) among patients with PHPT in comparison to the control population. We also assessed BMD at lumbar spine, femoral neck, total hip, and distal radius and possible predictors of VF as secondary outcomes.

Methods: We searched multiple databases from inception to March 2019. Seventeen studies analyzing fracture in patients with PHPT compared to a control population were eligible. We included a total of 3807 PHPT cases and 11908 controls in this meta-analysis.

Results: We found significantly increased risk of VF (risk ratio (RR) 2.57; 95 % CI 1.3-5.09; P= 0.007) and TF (RR 1.76; 95% CI 1.53-2.01; P<0.00001) in PHPT patients. There was significant decrease in BMD in PHPT patients versus controls at all sites except total hip. Older age, longer duration since menopause and lower BMD at lumbar spine and distal radius were predictors for VF.

Conclusion: PHPT patients are at significantly higher risk for VF and TF in comparison to controls.

Disclosure of Interest: None Declared

Bone and Calcium

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BONE MINERAL DENSITY IN LONG-LIVING PATIENTS WITH CORONARY ARTERY DISEASE

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Introduction: Limited data are available on osteoporosis in centenarians. Therefore, we evaluated bone mineral density in long-living patients with coronary artery disease (CAD).

Objectives: To evaluate bone mineral density in long-living patients with CAD and to assess relationships between bone mineral density and different clinical, laboratory and functional parameters.

Methods: 202 patients hospitalized with CAD were enrolled in this cross-sectional study. The patients' age ranged from 90 to 101 years. The majority of study participants (64.4%) were women. The main exclusion criteria: any disease or medication that can lead to the secondary osteoporosis. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry.

Results: Normal lumbar spine BMD was observed in 40.9%, osteoporosis – in 26.9%, osteopenia – in 32.2% of patients. Normal proximal femur BMD values was observed in 21.3%, osteoporosis – in 39.9%, and osteopenia – in 38.8% of patients. Normal femoral neck BMD was registered only in 10.4% of patients, osteoporosis was observed in 60.4%, osteopenia – in 29.2%. Significant positive correlation was found between all BMD values and body mass index of patients ($p < 0.001$). Positive correlation was registered between BMD values and serum uric acid ($p = 0.0005$). The likelihood of normal BMD values with hyperuricemia increased 3.8 times, compared to patients with normal uric acid, who often have osteoporosis (Odds Ratio=3.84; $p = 0.009$). Positive correlation was registered between all BMD values and body mass index ($p < 0.001$). Positive correlation between triglycerides levels and T-score ($p = 0.02$), but negative correlation between BMD and HDL-cholesterol ($p = 0.02$) were revealed. Negative correlation between frailty severity and BMD values ($p = 0.01$) was found. Positive correlation between BMD values and functional abilities of patients assessed using Barthel index ($r = 0.44$; $p = 0.000002$) and IADL scale ($r = 0.36$; $p = 0.00008$) was registered. Fractures in history were observed in 27.6% of patients.

Conclusion: The study results indicate some features of BMD in long-livers. In the study group significant relationships were found between bone mineral density on the one hand and patients' functional abilities on the other. It is advisable to further study the state of bone tissue in long-livers involving a large sample of patients.

Disclosure of Interest: None Declared

Bone and Calcium

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PRIMARY HYPERPARATHYROIDISM (PHPT): EXPERIENCE IN A SINGLE HIGH COMPLEXITY CENTER IN ARGENTINA OVER THE LAST 20 YEARS

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Introduction: In the past decades the clinical presentation of PHPT has shifted. As a referral center, we have a noteworthy series of cases in continuous follow up

Objectives: In a retrospective analysis assessing clinical, biochemical and histopathology phenotype we evaluated possible changes in these parameters over the past 20 yr

Methods: 136 patients with PHPT were divided into 2 groups, G1: 2000-2009 (n: 76) and G2: 2010-2019 (n: 60). Mean age 60 vs 58, F/M 4:1 vs 9:1, BMI 27.3 vs 26.9, and mean follow up 10.5 vs 3.5 yr for G1 vs G2 respectively. They all presented elevated intact PTH (iPTH) levels and serum calcium >10.2 mg/dl or inadequate levels of iPTH with serum calcium ≤10.2 mg/dl. Total (tCa) and ionized serum calcium (iCa), phosphate (P), magnesium (Mg), creatinine (Cr), iPTH, alkaline phosphatase (AP) and 25OHD were measured. Ca, P (tubular reabsorption of phosphate, TRP), Mg, and Cr clearance (CrCl) were measured in a 24-hr urine sample and, in 2-hr urine collection, Ca/Cr ratio. Bone mineral density (BMD) by DXA at lumbar spine (LS) and femoral neck (FN), classified according to OMS guidelines

Results:

Osteitis fibrosa cystica was found in 5.3 vs 3.3%, clinical and/or radiological fractures in 4 vs 13.3% and nephrolithiasis detected by ultrasound in 35.3 vs 37.5% of cases in G1 vs G2 respectively.

BMD LS T-Score (Median and range): G1 -2.1 (-0.3 to -5.1), G2 -2.3 (-0.2 to -5.5) (p ns, Mann-Whitney U test); BMD FN T-Score: G1 -2.2 (-0.28 to -5.71), G2 -2.25 (-0.2 to -5.5) (p ns).

Biochemical results (Median; Mann-Whitney U test):

| | tCa | iCa | P | Mg | Cr | 25OHD | AP | CrCl | uCa | uCa/Cr 2-hs | TRP % | uMg | iPTH |
|----|-------|-------|-------|------|------|-------|--------|-------|-----|----------------|-------|------|--------|
| G1 | 11.05 | 5.75 | 2.8 | 1.9 | 0.86 | 16 | 223.9 | 93.1 | 291 | 0.19 | 82.2 | 80 | 243 |
| G2 | 10.65 | 5.2 | 3 | 2.1 | 0.82 | 29 | 170 | 80.39 | 243 | 0.24 | 76.8 | 75.2 | 122.5 |
| p | ns | 0.015 | 0.026 | 0.01 | ns | 0.002 | 0.0034 | 0.03 | ns | 0.048 | ns | ns | 0.0001 |

PTx was performed in 82% of G1 and 52% of G2 cases. 82% vs 71% were adenomas, 18% vs 19% hyperplasia, and 0% vs 10% were carcinomas. After PTx: remission 92% vs 96%, persistence 8% vs 4%, inadequate PTH 14% vs 15% and hypoparathyroidism 5% vs 8%, in G1 and G2 respectively

Conclusion: Greater biochemical compromise was seen in G1; nonetheless, the clinical phenotype did not display significant changes between the 1st and 2nd decade. The smaller percentage of fractures in G1 can be explained by underdiagnosis of vertebral fractures during that period. We observed an important reduction of PTx in G2 probably due to the recent inclusion of mild and normocalcemic forms in the diagnosis of PHPT. This allows treatment in early stages avoiding the progression of complication

Disclosure of Interest: None Declared

ICE2021-1401

RECURRENT AND PERSISTENT PRIMARY HYPERPARATHYROIDISM DUE TO SECONDARY PARATHYROMATOSIS

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Introduction: Parathyromatosis is a potential cause of recurrent hyperparathyroidism, of rare etiology, described as multiple nodules of hyperfunctioning benign parathyroid tissue, it constitutes less than 1% of recurrent hyperparathyroidism cases and since its description in 1975, less than 40 cases have been reported worldwide. The presentation in primary hyperparathyroidism is extremely rare, with around 20 cases reported in the english literature.

Case Description: 43-year-old female patient, with a history of 18 years recurrent and persistent primary hyperparathyroidism due to secondary parathyromatosis that debuted with a brown cell tumor; currently with multiple spontaneous fractures, bone deformations and the debut of stage II chronic kidney disease secondary to bilateral nephrolithiasis and moderate right hydronephrosis. Parathyroidectomy of 6 glands was performed prior to the identification of the lesions by imaging studies, at four surgical times in a period of 18 years, associated with right hemithyroidectomy due to incidental finding of papillary thyroid carcinoma. In the last admission with serum parathyroid hormone of 1000 pg/mL, serum calcium of 3.9 mmol/L, serum phosphorus of 0.73 mmol/L. A radioguided left lower parathyroidectomy was performed. The pathological study reported oxyphilic cell proliferation with lesion limited to the capsule (*figure 1*). After the intervention, parathyroid hormone levels decreased by 40% (610 pg/mL) but remained high, with normalization of serum calcium and phosphorus. Patient continues her follow-up by outpatient consultation.

Clinical discussion: Parathyromatosis is a rare cause of recurrent and persistent hyperparathyroidism after parathyroidectomy. Preoperative diagnosis remains a challenge even with the advent of new imaging technologies, even 40 years after it was first described. Its pathophysiology continues to be studied and discussed today. Lack of knowledge about this entity can result in unsuccessful attempts to control and eradicate the disease. It should be considered especially in patients with persistent hyperparathyroidism despite having undergone successful surgical treatment.

Image:

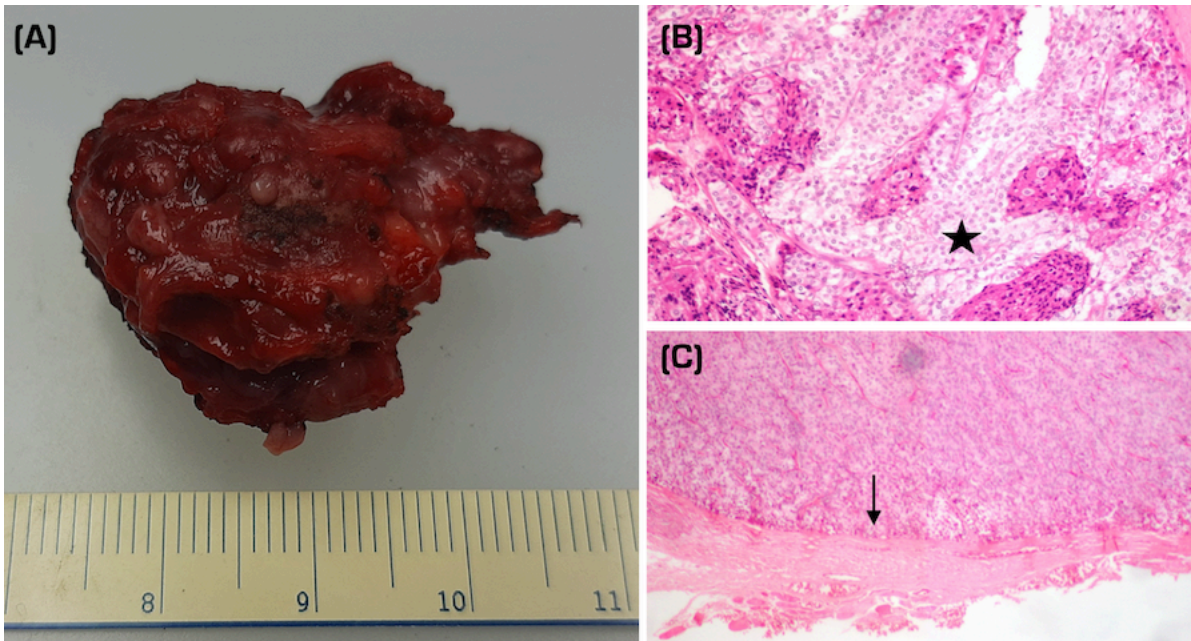


Figure 1. (A) Left inferior parathyroid adenoma removed. Dimensions 4.8 x 2.7 cm. Weight 6.1 grams.
(B) Parathyromatosis demonstrating hypercellularity with proliferation of oxyphilic cells (H&E x100).
(C) Presence of parathyroid tissue and capsule that limits the lesion. (H&E x200)

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1409

MULTIPLE OSTEOLYTIC LESIONS: BETWEEN HISTORY AND CURRENT PRACTICE

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Introduction: Osteolytic lesions in middle aged and elder patients are frequently caused by metastatic bone disease or multiple myeloma. Brown tumors represent the end stage of bone remodeling process in prolonged hyperparathyroidism and are a rare cause of radiologically lytic bone lesions.

Case Description: We report the case of a 66-year-old woman referred for generalized bone pain. Her personal history revealed a left nephrectomy for recurrent nephrolithiasis and a stage 4 chronic kidney disease with permanent right nephrostomy for pyonephrosis.

Clinical discussion: Thoracoabdominal CT scan revealed a right fragmented staghorn calculi and multiple osteolytic lesions suggesting bone metastasis without a primary tumor site localization. Whole body scintigraphy showed disseminated tissular and bone scintigraphic abnormalities suggestive of bone lesions from multiple myeloma, without the possibility to exclude other oncologic causes. 18F-FDG PET/CT scan provided evidence of multiple metabolic active osteolytic lesions, without the detection of a metabolic active primary tumor. Lab tests showed a mild hypercalcemia (11,2 mg/dl), anemia, elevated serum creatinine but biochemical diagnostic criteria for multiple myeloma were negative. A bone marrow biopsy was performed, and the pathological exam was suggestive of hyperparathyroidism. Serum PTH level was increased (1534 pg/ml). Neck ultrasound revealed a 2.34/1.8/1,15 cm hypoechoic lesion suggestive of a left inferior parathyroid adenoma.

Results: Thus, the patient was referred to the surgery department for left inferior parathyroidectomy.

Conclusion: Although in such cases the most frequent causes of osteolytic lesions must be first excluded, one should keep in mind that it is important to also look for rare causes and a PTH serum level should always be measured in patients with hypercalcemia, chronic kidney disease and multiple osteolytic lesions.

Keywords: multiple osteolytic lesions, metastatic bone disease, multiple myeloma, hyperparathyroidism, hypercalcemia, chronic kidney disease.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1411

A SINGLE-CENTRE EXPERIENCE RETROSPECTIVE OBSERVATIONAL REAL-WORLD STUDY OF OSTEOPOROSIS THERAPY IN MEN WITH DENOSUMAB (OSTEOPROM)

Diāna Pokšāne*, Marta Dubovska, Ingvars Rasa

Introduction: Despite increased attention on osteoporosis in men, clinicians still have less concern about osteoporosis in men. Pharmacologic therapy options for treating osteoporosis for men are limited.

Objectives: We studied the effectiveness of osteoporosis treatment with denosumab(Dmab). We analyze the efficacy of osteoporosis treatment on BMD and fractures in the men cohorts in a real-world clinical setting using a single-centre experience (OsteoProM).

Methods: The retrospective observational real-world study was provided in time August 2014–October 2020. Clinical University Hospital, Outpatient Clinic data were used to study over the past 6 yrs for the effectiveness of Dmab in men using total mean hip, spine BMD change after treatment start, and fracture incidence during treatment. We collected and analyzed risk factors, lab data, fractures, co-morbidities and medications used to treat pts, DXA and in some cases QCT data, DXA scans performed at the time of initial diagnosis; the analysis of BMD of the lumbar vertebrae L1-L4 and the total mean hip was performed using DXA.

Results: We analyzed a total of 34 men with an average age 62.7 ± 10.2 SD; the youngest was 44 yrs, and the oldest was 84 yrs. The average BMI(kg/m²) was 24.4 ± 3.7 SD. Spin and hip BMD analyzed DXA scans in 32 pts(94.1%) and QCT in 2 pts(5.9%). Men with idiopathic osteoporosis were 61.8%, glucocorticoid-induced osteoporosis was 32.4%, secondary osteoporosis were 5.9%. Dmab increased BMD at lumbar spine L1/L4 in 71.4% and total mean hip in 69.2% pts. Before study starts men with at least 1 fracture were 59.4%(63.2%% in spine, 10.5% hip, 10.5% forearm, 31.6% ribs, 26.3% other fractures). After study ends men with at least one fracture was 1(3%). Serum Ca, vitamin D and iPTH levels were analyzed before Dmab starts and after the study ends. Men with at least 1 co-morbidities were 97.1%. Most often used medication was rosuvastatin, which was used by 45.5% men.

Conclusion: Dmab is effective in increasing BMD at the lumbar spine, the total mean hip in men with osteoporosis. Studies indicate that Dmab is effective and safe. Dmab is an appropriate clinical option in men with intolerance or contraindications to bisphosphonates. However, long-term data and further research on fracture reduction rates in men should be explored. Dmab is also an appropriate first-line option for men with osteoporosis. We analyzed Dmab real-world data from a single-centre in Latvia for the first time.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1427

A CASE OF PRIMARY HYPERPARATHYROIDISM WITH RICKETS PRESENTED TO FRACTURE PREVENTION CLINIC, YANGON GENERAL HOSPITAL, MYANMAR

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Introduction: Rickets and osteomalacia are quite common among children. Primary hyperparathyroidism is rarely seen in children. Although vitamin D deficiency and secondary hyperparathyroidism is linked, primary hyperthyroidism simulating rickets or causing rickets is still puzzling.

Case Description: A 14 year old girl presented with gradual weakness of both legs over one year causing difficulty in walking. She got fracture with deformity at left forearm due to fall from bicycle at 13 year of age. Her family had no history of fracture and bone deformity. On examination, her height was 139 cm. She had pigeon chest deformity, deformity of left forearm, knock knee and waddling gait.

Imaging

- Lt forearm X ray – old healed fractures of radius and ulnar, periosteal reaction and callus present at fracture ulna, generalized osteopenia
- Rt, Lt knee X ray – old fracture with callus formation in upper 1/3 of fibula
- X ray both wrist joints – normal bony density, no fracture
- USG (abdomen), KUB, CT abdomen - NAD
- DXA scan - Z score spine -8.8, total hip -6.5.

Bone biochemistry revealed PTH dependent hypercalcemia, hypercalciuria, hypophosphatemia with severe vitamin D deficiency. **MIBI scan** showed parathyroid adenoma. **Rt superior and inferior parathyroidectomy** was done and benign parathyroid adenoma was found in Rt inferior parathyroid. Her postoperative period was uneventful with mild hypocalcemia.

| Date | Corrected Calcium (2.2-2.6 mmol/l) | Phosphate (0.8-1.5 mmol/l) | ALP (30-130 IU/l) | PTH (15-65 pg/ml) | Vitamin D (nmol/l) |
|------------------------------|--|-------------------------------|----------------------|----------------------|-----------------------|
| 25.4.2018 | 2.7 | 0.48 | 1645 | 1266 | 24.17 |
| 8.5.2018 | Parathyroidectomy | | | | |
| 9.5.18 (POD1) | 1.9 (symptomatic) | | | 60.5 | |
| 14.5.18 (POD6) | 1.8 | 0.53 | 1166 | | |
| 18.7.18 (2months post op) | 2.2 | 0.99 | 431 | 136.8 | 43.46 |
| 13.11.2018 (6 months) | Parathyroid scan. No scan evidence of parathyroid adenoma. | | | | |
| 30.12.2019 | 2.1 | 1.45 | 182 | 116.2 | |

After one year, she could walk without assistance again. Her knee deformity persisted and she has been on physiotherapy.

Clinical discussion: Vitamin D deficiency is not uncommonly seen in sunshine countries like Myanmar, mostly related to nutritional deprivation leading to rickets and skeletal deformity in children. Early bone biochemistry assessment is essential for finding rare coexisting primary hyperparathyroidism in order to get definitive treatment and prevention of deformity. Genetic causes of primary hyperparathyroidism must be searched. Multiple endocrine neoplasia should also be considered if there is accompanying problems.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1465

ONCOGENIC OSTEOMALACIA CAUSED BY AN FGF 23- SECRETING MESENCHYMAL TUMOR.

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Introduction: Oncogenic osteomalacia is a rare pathology characterized by hypophosphatemia, hyperphosphaturia, and osteomalacia. Benign tumors, predominantly of mesenchymal origin, secrete phosphaturic paraneoplastic factors that induce metabolic osteopathy.

Case Description: A 43 years old woman was referred for evaluation of severe generalized bone pain that compromised walking. During her last pregnancy, 2 years ago, she began with pain in the lumbar spine and ribs that worsened after delivery and lost 15 cm in height. Her medical record disclosed severe osteoporosis. She was on treatment with polypharmacy: calcium carbonate, Vitamin D3, biphosphonates, omeprazole, acetaminophen, and diclofenac. First physical exam, restricted for the wearing of a corset, showed BMI: 27; BP: 130/90 mmHg; 80 bpm; severe dorsal kyphosis and muscle atrophy in lower limbs. Relevant complementary methods: serum phosphorus 0.6 mg/dl (2.7-4.5), calcium correction 9 mg/dl (8.5-10.5), vitamin D3 30.4 mg/ml, PTH: 211 pg/ml (10-65), TSH: 1.17 µU/ml, uric acid 3.6 mg/dl, ESR 17 mm, creatinine: 0.57 mg/dl (0.6-1.20), Alkaline phosphatase: 450 U/L (46-116); Mg 2.2 mg/dl, urine calcium 54 mg/24 h, renal tubular phosphorus reabsorption 38% (85-100%). The X-ray showed generalized bone demineralization, salt and pepper lesions in the skull, multiple metacarpal fractures, and radiolucent areas were found in right ischiopubic branch. Phosphorous salts were prescribed but suspended due to digestive intolerance. During re-examination, a subcutaneous stony, painless, and mobile nodule was found in the left subcostal region that was excised. Biopsy disclosed bone trabecules, and osteoclast-like multinucleated giant cells. There were areas with hemangiopericytoid pattern and positive immunohistochemistry for fibroblastic growth factor 23 (FGF-23), compatible with a phosphaturic mesenchymal tumor. In the cervical region another small, stony, painless nodule, was excised, and biopsy disclosed a 3 mm bony tissue related to pilomatrixoma, with negative immunohistochemistry for FGF-23. A month after surgery the patient showed a significant clinical improvement, serum phosphorus was normal (3.3 mg/dl), uneventful walking.

Clinical discussion: Hyperphosphaturic tumors are of slow growth, hard to find, and probably underdiagnosed. In our case, clinical evaluation from severe hypophosphatemia accompanied with a full physical examination allowed us to find the tumor and resolve the clinical frame in two months.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1470

AUTOSOMAL DOMINANT HYPOCALCEMIA: DESCRIPTION OF CLINICAL AND BIOCHEMICAL FINDINGS IN A FAMILY WITH THE MISSENSE PATHOGENIC VARIANT P. PRO221LEU IN THE CASR GENE.

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Introduction: Gain-of-function heterozygous mutations in the gene encoding the calcium sensing receptor (*CASR*) result in autosomal dominant hypocalcemia type 1 (ADH1) which increase the sensitivity of *CASR* to extracellular ionized calcium. Patients present congenital hypoparathyroidism, it which can appear at different stages of life and have a variable degree of severity. Most activating mutations in the *CASR* gene are familial and usually there is a wide range of clinical presentation in the family members. We describe here the clinical and biochemical presentation in a family with ADH1.

Case Description: A 5-years-old female patient with moderate maturational delay presented with abdominal pain from perforated duodenal ulcer. Her laboratory results showed hypocalcemia of 7 mg/dl (normal 8.5–10.5), hyperphosphatemia of 6.6 mg/dl (normal 4.1–6.5), hypomagnesemia of 1.4 mg/dl, (normal 1.8–2.5), inappropriately low PTH levels <3 pg/ml and hypercalciuria relative to calcemic. At first, she required low doses of oral calcium and calcitriol supplements to maintain serum normal levels, but over the years she needed higher doses to maintain optimal values. During the follow up, she did not develop nephrolithiasis and had a normal growth (height -0.4 SDS). Her grandmother and father were diagnosed with hypoparathyroidism as adults, her grandmother from headaches and her father from screening tests. Both showed brain calcifications with mild hypocalcemia and hypomagnesemia. Her father had mild learning difficulties.

ADH1 was suspected and molecular analysis was performed by automated sequencing of the exons and flanking intronic regions of the *CASR* gene from genomic DNA, the presence of the missense pathogenic variant c.662C>T (p. Pro221Leu) was detected in heterozygous state in the patient and her father.

Clinical discussion: We describe the clinical and biochemical presentation of the members of a family with ADH1 due to the missense pathogenic variant c.662C>T (p. Pro221Leu) in the *CASR* gene, these variant was reported, but we found some phenotypic variables other than those described previously. Accurate diagnosis of the genetic cause in this family was essential for the follow up of the patients, the search for comorbidities and genetic counseling.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1479

ASSOCIATION BETWEEN BONE TURNOVER MARKERS AND ENDOCRINOPATHIES AMONG TRANSFUSION DEPENDENT THALASSEMIA PATIENTS

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Introduction: Osteopenia and osteoporosis are shown to be increasing among patients with thalassemia, partly due to improvement in treatment and survival rates. Bone turnover markers are potentially useful as non-invasive tests to assess bone remodelling in this high-risk population.

Objectives: The study aimed to detect abnormalities in bone turnover markers in adult transfusion-dependent thalassemia patients, and to evaluate its associations with vitamin D status and other hormonal deficiencies

Methods: This cross-sectional study involved transfusion-dependent thalassemia patients (n=40) from the adult haematology clinic. All participants underwent anthropometric measurements, pubertal assessment, blood investigations including renal function, liver function, ferritin, calcium, phosphate, 25-hydroxyvitamin D levels, bone turnover markers (s-CTX and s-P1NP), anterior pituitary hormone levels and glucagon stimulation testing.

Results: There were 47.5% female and 52.5% male subjects with mean age 27.5 ± 5.2 years. 63% of the patients had vitamin D deficiency ($<50\text{nmol/l}$), 90% had elevated serum ferritin ($>500\text{ug/l}$) and 95% were diagnosed with endocrinopathies. A significant negative correlation was found between vitamin D and s-P1NP ($r=-0.364$, $p=0.024$) and ferritin ($r=-0.444$, $p=0.005$). Abnormal bone turnover markers were detected in 27.5% of patients (n=11), with significantly high s-CTX seen among females ($p=0.018$). Hypogonadism was associated with high P1NP ($p=0.01$) despite sex hormone replacement therapy.

Conclusion: A quarter of transfusion-dependent thalassemia patients showed elevated levels of bone turnover markers, whereas endocrinopathies were seen in almost all patients. Bone resorption marker s-CTX was particularly high among females whilst high s-P1NP was associated with the presence of hypogonadism. There was also a notably high prevalence of Vitamin D deficiency, which was significantly associated with the bone markers and ferritin.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1503

AN AUDIT OF THE MANAGEMENT, FOLLOW-UP AND OUTCOMES OF HYPOPARATHYROIDISM AT THE DEPARTMENT OF ENDOCRINOLOGY AT THE UNIVERSITY HOSPITAL BRISTOL NHS TRUST, UK

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Introduction: Hypoparathyroidism is a rare condition characterised by low serum calcium and parathyroid hormone. Anterior neck surgery and autoimmune disease are responsible for the majority of cases. Standard treatment is activated vitamin D analogues and calcium supplementation. Patients may report symptoms of hypo and/or hypercalcaemia of various severities, depending on the adequacy of their replacement. Long-term complications include depression, chronic kidney disease, kidney stones, seizures, cataracts and intracerebral calcifications.

Objectives: The aim of this project was to evaluate the standard of care of patients with hypoparathyroidism of any cause under our care, against the standards set by the European Society of Endocrinology (2015)* in order to prevent complications and improve outcomes for patients.

Methods: The departmental database was searched using the criteria 'primary hypoparathyroidism' and 'hypocalcaemia'. 47 patients aged 18-85 were audited. Using electronic records, the data was collected, collated and analysed against standards proposed by the European guideline.

Results: 34 females and 13 males (2.6:1 ratio of women to men) were audited. 59% had post-surgical hypoparathyroidism, 21% were diagnosed with primary autoimmune hypoparathyroidism, 12% had a genetic cause, 8% of patients had no identified cause. 87% had annual monitoring of serum albumin adjusted calcium, 34% had annual measuring of serum phosphate, 40% had annual monitoring of serum magnesium and 79% of patients had annual monitoring of serum creatinine levels. Annual 24-hour urinary calcium was recorded in 23% of patients. 54% had serum albumin adjusted calcium, 75% had a serum phosphate and 68% of serum magnesium's were in target range at the last review. 91% of patients were being managed with activated vitamin D analogue only, 45% with activated vitamin D analogue and calcium, and 26% received the recommended therapy with activated vitamin D analogue, calcium and inactive vitamin D supplement.

Conclusion: Management of hypoparathyroidism in our centre is not reaching the desired standards in regards to regularity of patients' monitoring, achieving the desired level of metabolic control and preventing long term complications. Protocol driven (a 'check list') annual, virtual specialist endocrine nurse-led clinics were set up.

Reference:

*Bollerslev J. et al, "European Society of Endocrinology Clinical Guideline: Treatment of chronic hypoparathyroidism in adults", European Journal of Endocrinology (2015)

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1513

QUALITY OF LIFE ASSESSMENT IN TRANSFUSION DEPENDENT THALASSEMIA PATIENTS WITH MULTIPLE ENDOCRINOPATHIES AND ASSOCIATION WITH BONE TURNOVER MARKERS

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Introduction: As a result of improved treatment and longer life expectancy, thalassemia is now extending into adulthood. Although morbidity and mortality of patients have been reduced significantly, some aspects of the disease and its associated complications could influence diverse aspects of the patients' lives.

Objectives: This study aimed to assess the quality of life among adult transfusion dependent thalassemia patients and its association with bone turnover markers

Methods: This cross-sectional study involved transfusion dependent thalassemia patients (n=40) from the adult haematology clinic. Patients younger than 18 years, with liver disease, on anti-resorptive therapy or corticosteroids were excluded. All participants underwent anthropometric measurements, and biochemical investigations including anterior pituitary hormone and 25-hydroxyvitamin D levels, and bone turnover markers (s-CTX and s-P1NP). A self-administered 36-item Short Form (SF-36) health survey questionnaire was used to measure the patients' quality of life (QOL) in the form of scores ranging from 0 (for worse health) to 100 (best possible health).

Results: This study recruited a total of 40 patients consisting of 47.5% female and 52.5% male subjects with mean age 27.5 ± 5.2 years and mean body mass index (BMI) 19.4 ± 2.45 kg/m². A high prevalence of vitamin D deficiency (63%), elevated serum ferritin (90%) and endocrinopathies (95%) were found, while abnormal bone turnover markers were detected in 27.5% of patients. Majority of subjects had a physical and mental component summary score of more than 50 (87.5% and 90% of patients respectively). Among the eight SF-36 domains, vitality showed the highest percentage of patients (40%) with score below 50, followed by general health and role physical (37.5% each). Subjects' physical and mental health was not significantly associated with abnormal s-P1NP, s-CTX or vitamin D deficiency ($r=-0.119$, $p=0.466$; $r=-0.202$, $p=0.212$; $r=0.150$, $p=0.356$) for physical and ($r=-0.149$, $p=0.359$; $r=-0.243$, $p=0.131$; $r=0.188$, $p=0.246$) for mental health components of SF-36 respectively.

Conclusion: Majority of the patients had overall SF-36 health survey scores that trended towards good physical and mental health signalling satisfactory quality of life despite being largely affected by comorbidities and complications associated with thalassemia. Our results also indicated that the prevalence of abnormal bone turnover markers and vitamin D deficiency did not have a significant effect on the QOL of these patients.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1514

SIMILAR ACTIONS OF ESTRONE AT BONE AND VASCULAR LEVEL

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Introduction: It is known that during menopause, the decrease in estrogen levels has a negative impact on bone remodeling and vascular function. Although postmenopausal plasma levels of estradiol are considerably low, those of estrone (E_1) are sustained providing the major source of circulating estrogens. We previously reported that E_1 modulates bone cells growth, and at vascular level the estrogen stimulates cellular events involved in the early steps of atherosclerosis lesion progression such as, oxidative stress, and platelet and monocyte adhesion. The most advanced stage of atheroma involves vascular calcification (VCa) event triggered by vascular smooth muscle cell (VSMC) transdifferentiation into bone like cells.

Objectives: The aim of this work was to evaluate the effect of E_1 on VSMC transdifferentiation into osteoblasts (VSMC-OB) and to compare it with the E_1 action on murine calvarial osteoblasts (OB), focusing our attention on the modulation of cell maturation.

Methods: -

Results: E_1 showed a mitogenic effect on both cells type, stimulating VSMC-OB and OB proliferation, evaluated by the MTT conversion test (27; 39% a/C $p < 0.05$, respectively). These data was confirmed by cell counting (28; 41 % a/C, $p < 0.05$, respectively). Transdifferentiation model characterization showed that VSMC-OB exhibit similar differentiation profile to those of mature OB. On VSMC-OB, the estrogen increased alkaline phosphatase (ALP) activity (3.72 ± 0.25 vs 3.00 ± 0.14 ; E1 vs C, UI.10-2 / mg protein, $p < 0.001$), and enhanced the amount and size of calcification nodules of extracellular matrix (56% a/C, $p < 0.05$). In agreement with this result, we observed marked decreases in calcium content in culture medium (735.0 ± 30.5 vs 468.2 ± 21.1 C vs E1, μg calcium / mg protein, spectrophotometric measurement, $p < 0.001$). Using Sirius red staining, we showed that E1 elicited a significant increase in matrix collagen deposition in VSMC-OB (\leftarrow 19% a/C, $p < 0.05$). Similar results were obtained in native bone cells (OB). E_1 treatment stimulated ALP activity (4.64 ± 0.32 vs 3.37 ± 0.25 ; E1 vs C; IU.10-2 / mg protein, $p < 0.001$), calcium deposition (40, 2% a/C, $p < 0.05$) and collagen in extracellular matrix (\leftarrow 21% a/C, $p < 0.05$).

Conclusion: In conclusion, the results presented show similar action of E_1 in both cell systems. However, the physiological relevance of this evidence could be considered opposite: a beneficial action at bone level favoring osteoblastogenesis, and deleterious at vascular level promoting VCa.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1546

DISMOBILITY SYNDROME IN COMMUNITY-DWELLING OLDER WOMEN

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Introduction: Dismobility syndrome (DS) was recently described. Its identification can be used to prevent adverse health outcomes in adults at risk. It is characterized by three or more of the following criteria: osteoporosis, falls, low muscular mass, slow gait speed, low grip strength, and high fat mass.

Objectives: To assess the prevalence of DS in a population of women 60 years or older, and to determine if there is a relationship with osteoporotic fractures and falls.

Methods:

Cross sectional study design. A total of 250 women were recruited consecutively. Body composition and bone mineral density were assessed by DXA (Lunar Prodigy Advance). Falls questionnaire was conducted. Muscle strength was measured with hand dynamometry (JAMAR) and measures of physical performance (sit-stand and walking speed) were recorded. The diagnosis of DS was based on the criteria proposed by Binkley et al.

We defined baseline DS as having three or more of the following factors: appendicular lean mass/height <5.45 (kg/m²), high fat was defined as percentage values above 40%, lumbar spine or hip T-score value ≤ -2.5 ; gait speed with values below 1.0 m/sec and lower muscle strength (handgrip <20 kg)

Exclusion criteria:

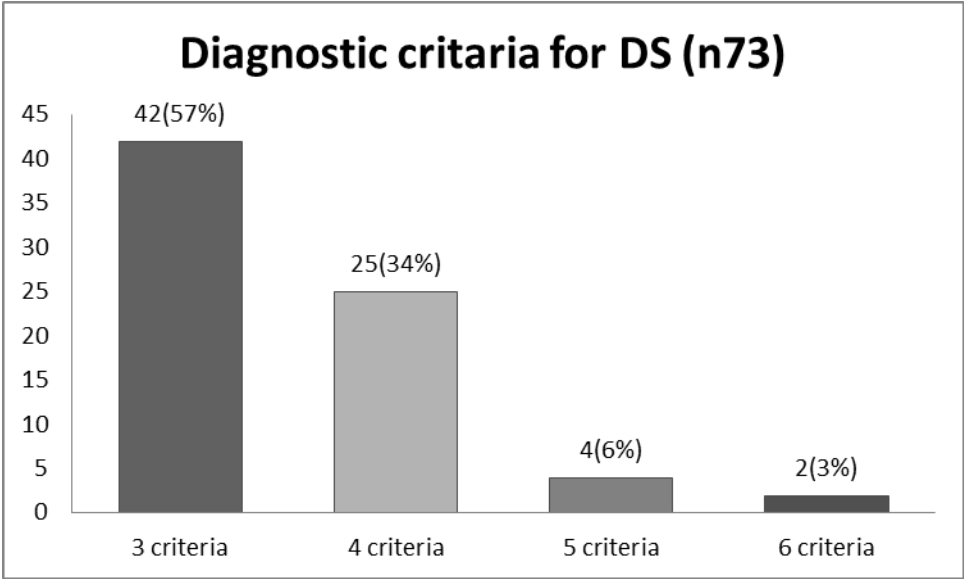
Women with diabetes, neurologic or oncologic conditions.

Statistics:

The samples with normal distribution were evaluated by Student's *t* and Wilcoxon tests for independent samples. Qualitative variables were analyzed using Chi-square. Statistical significance is considered with a $p < 0.05$. Statistical analyses were performed with the Statistix program.

Results: The average age of the population was 70.4 ± 7.7 years. Seventy three (29%) had DS. 57% met 3 criteria and 34% met 4 criteria. Women with DS were older (72 vs 69 years), had lower BMD at FN (0.728 vs 0.766 g/cm²) and TH (0.769 vs 0.801 g/cm²), lower muscle mass in arms and legs (IMME 5.6 vs. 5.95 kg/m²). The strength was 18.8 vs 23.8 kg and the physical performance tests were lower. All these differences were statistically significant. There was no difference in serum values of 25-hydroxyvitamin D (32.2 vs 30.4 ng/ml). Women with DS had a higher prevalence of osteoporotic fractures (42% vs 11%) and falls in the last year (60% vs 19%); $p < 0.0001$. DS was shown to be associated with recurrent falls (odds ratio [OR], 3.72; 95% CI, 2.64–6.91)

Image:



Conclusion: Women with DS reported a higher frequency of recurrent falls in the last year and a higher prevalence of osteoporotic fractures. The evaluation of these criteria is a useful tool to prevent adverse health events.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1549

PRIMARY HYPERPARATHYROIDISM; WHEN TO THINK ABOUT THE GENETICS?

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Introduction: 19 y/o female known primary hypothyroidism (on levothyroxine 50 mcg OD) referred by G.P to endocrine clinic for further evaluation of fatigue, tiredness and irregular periods. In clinic, retrospective review of her previous blood tests revealed persistent mild hypercalcaemia (2.61-2.77 mmol/L) since the age of 13.

Case Description: Patient confirmed having ongoing osmotic symptoms but didn't report any abdominal groans or painful bones. There was no significant PMH and no family history of calcium problems.

Repeat bloods showed mild hypercalcaemia (adj calcium 2.63 mmol/L) with raised parathyroid hormone levels (PTH 13.2 pmol/L) suggesting a biochemical diagnosis of primary hyperparathyroidism. She was vitamin D replete (71-83 nmol/L). Due to her hypercalcaemia being ongoing since the age of 13 years, genetic conditions were also considered as an underlying possibility.

Further workup showed low urinary calcium creatinine excretion ratio (0.002-0.009) suggestive of familial hypocalciuric hypercalcaemia (FHH) but fractional calcium excretion index (24.7) did not suggest FHH. 24 hours urinary calcium was also inconclusive (7.3). Ultrasound parathyroid showed bilateral parathyroid adenomas which raised the suspicion of MEN-1 and pituitary hormonal profile showed mildly raised prolactin (623 mU/L) and MRI pituitary picked up a 2 mm microadenoma in pituitary. Rest of pituitary hormonal profile was unremarkable with exception of gonadotrophins which were not interpretable due to hormonal implant for contraception.

She was discussed in endocrine MDT. She was offered genetic test and 4D CT scan of parathyroid glands to avoid an unnecessary parathyroid surgery.

The genetic tests were reported negative for MEN and FHH (MEN-1 and RET gene pathogenic variant not identified; AP2S1, CASR, CDC73, CDKN1A, CDKN1B, CDKN2B, CDKN2C, GNA11 genes pathogenic variant not identified). The 4D CT scan identified right side type D parathyroid adenoma. She underwent parathyroidectomy and histopathology confirmed parathyroid adenoma. Post-surgery PTH (2.8 pmol/L) & adj.Ca is 2.39 mmol/L are reverted back to normal.

Clinical discussion: This case highlights several learning points in assessment of hypercalcaemia. For young patients it is important to exclude genetic causes. The importance of using different modalities of investigations helps avoid unnecessary surgery but also prevents missing out the cases in need for surgical intervention.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1551

EVALUATION OF THE INCIDENCE OF FRACTURE IN AN OSTEOPOROTIC ELDERLY POPULATION ACCORDING TO THE PRESENCE OF DIABETES. ROLE OF SARCOPENIA ASSESSED USING THE SARC-F QUESTIONNAIRE.

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Introduction: Bone fragility has proven to be part of the cohort of complications of diabetes.

Objectives: To evaluate the incidence of fractures (Fx) in non-diabetic (non-D) osteoporotic (OP) patients compared with diabetic (D) OP and its relation with the incidence of sarcopenia evaluated by a validated questionnaire.

Methods: We evaluated retrospectively a population with diagnosis of OP registered since 2017, from an institution of tertiary care of older adults. We included those who responded to the SARC-F survey, considering sarcopenia a score ≥ 4 . We analyzed Ca, P, Mg, albumin, PTH, 25OHD, C-telopeptides, alkaline phosphatase, and HBA1C if the patient was D; and time of evolution of D (TOED) and use of metformin. Sarcopenia was evaluated through the SARC-F questionnaire. Parametric data were analyzed as mean and SD or median and interquartile range and χ^2 for non-parametric.

Results: 147 OP patients were considered, mean 74.42 ± 7.32 years, 136 (92.5%) women and 62 (42.17%) D. We found no differences in the risk of fracture (ROFx) in D or non-D. 48 patients had Fx, 33 (38%) in non-D and 15 (24%) in D ($p=0.06$, NS). However, 85.71% of D and 94.18% of non-D were under OP treatment. 25OHD levels in our population was 34.5 ± 2.12 in non-D and 37 ± 15.5 ng/ml in D. 11.62% of the non-D patients and 11.11% of D (NS) had sarcopenia and was not related to an increase in the incidence of fractures in any of the groups. Biochemically we only found significant differences in HbA1c in D with Fx vs non-Fx: 5.9% (5.7;6.1) in Fx vs 6.2 (5.9;6.8) in non-Fx ($p=0.015$). Neither the use of metformin nor TOED was associated with the ROFx in this population.

Conclusion: We did not find differences in the incidence of Fx in D vs non-D. However, practically all of the patients were under treatment for OP and were 25OHD sufficient. The percentage of sarcopenic patients in our population of older adults assessed by SARC-F questionnaire was 11% and it did not correlate with the incidence of fx. We consider that it is necessary to corroborate the results of SARC-F with functional tests or with the measurement of muscle mass. As no patient was treated with SGLT2i, the association between a lower HbA1c and a higher incidence of fx could be related to hypoglycemic episodes in elderly patients receiving antidiabetic treatment.

Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1570

SEVERE BONE MICROARCHITECTURE IMPAIRMENT IN PATIENTS WITH TUMOR-INDUCED OSTEOMALACIA AS ASSESSED BY HIGH-RESOLUTION PQCT.

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Introduction: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome characterized by persistent hypophosphatemia. Hypophosphatemia is caused by increased renal phosphate wasting consequent to elevated levels of circulating fibroblast growth factor 23 (FGF23).

Besides causing phosphaturia, FGF23 inhibits renal 1 α -hydroxylase, resulting in low levels of 1,25-dihydroxy vitamin D. Low levels of active vitamin D deter mineralization of the osteoid matrix causing bone pain, fragility fractures, muscle weakness and severe bone quality impairment. Deterioration of bone microarchitecture parameters in patients presenting osteomalacia has been described by histomorphometric analysis of bone biopsies samples

Objectives: The aim of this study was to assess the status of bone microarchitecture parameters in patients with TIO using high-resolution pQCT (HR-pQCT), a non-invasive procedure.

Methods: Bone microarchitecture parameters were assessed at the distal radius and tibia by HR-pQCT using Xtreme CT (Scanco Medical AG, Bassersdorf, Switzerland). Results were compared with a group of 16 healthy subjects (10 female, 6 male) obtained from our data base, paired by age and sex in a 2:1 ratio.

Results: We studied 10 patients (7 female, 3 male) consulting or referred to our bone clinic and diagnosed with TIO. Mean age was 47.4 \pm 12.6 (SD) years, range 28.5-64 years. Mean age of the control group was 47.3 \pm 12.2 (SD) years, range 28.8-68 years. The mean percent difference between the patients and controls groups was calculated and the results are depicted in Table 1.

Image:

| | Patients (n=10) | Controls (n=16) | Difference |
|--------------------------------|------------------------|------------------------|-------------------|
| | Mean ±SD | Mean ±SD | Mean % |
| Distal radius | | | |
| D100 (mg HA/cm ³) | 258.9 ± 85.7 | 338.5 ± 65.6 | -23,5 |
| Dcomp (mg HA/cm ³) | 795.6 ± 136.5 | 876.5 ± 57.8 | -9,2 |
| Ct. Th (mm) | 0.61 ± 0.28 | 0.81 ± 0.18 | -24,7 |
| Dtrab (mg HA/cm ³) | 128.4 ± 56.7 | 186.7 ± 53.6 | -31,2 |
| BV/TV (%) | 10.7 ± 4.7 | 15.6 ± 4.5 | -31,4 |
| Tb.N (1/mm) | 1.56 ± 0.49 | 2.02 ± 0.34 | -22,8 |
| Tb.Th (mm) | 0.067 ± 0.012 | 0.077 ± 0.015 | -13,0 |
| Tb.Sp (mm) | 0.640 ± 0.261 | 0.432 ± 0.087 | 48,1 |
| Tb.1/N.SD (1) | 0.354 ± 0.242 | 0.179 ± 0.041 | 97,8 |
| Distal tibia | | | |
| D100 (mg HA/cm ³) | 173.1 ± 97.9 | 306.0 ± 71.3 | -43,4 |
| Dcomp (mg HA/cm ³) | 780.7 ± 140.8 | 881.6 ± 54.2 | -11,4 |
| Ct. Th (mm) | 0.72 ± 0.42 | 1.22 ± 0.32 | -41,0 |
| Dtrab (mg HA/cm ³) | 83.0 ± 62.4 | 174.7 ± 50.5 | -52,5 |
| BV/TV (%) | 7.0 ± 5.2 | 14.5 ± 4.2 | -51,7 |
| Tb.N (1/mm) | 0.94 ± 0.56 | 1.98 ± 0.42 | -52,5 |
| Tb.Th (mm) | 0.064 ± 0.046 | 0.074 ± 0.017 | -13,5 |
| Tb.Sp (mm) | 1.565 ± 1.309 | 0.454 ± 0.125 | 244,7 |
| Tb.1/N.SD (1) | 1.220 ± 1.050 | 0.211 ± 0.078 | 478,2 |

Conclusion: The results confirm severe bone microarchitecture deterioration in patients with TIO. Deterioration of bone microarchitecture was more evident at the distal tibia, most probably due to impaired mobility as a result of muscle weakness.

HR-pQCT is a suitable method for the evaluation of bone microarchitecture in patients with TIO and can be a useful tool to evaluate the degree of deterioration and follow the response to treatment.

Disclosure of Interest: M. Zanchetta Conflict with: ultragenyx, F. Jercovich: None Declared, L. plantalech: None Declared, C. Balonga: None Declared, C. cohen: None Declared, S. nuñez: None Declared, Y. Mocarbel Conflict with: IDIM, A. Pignatta: None Declared, N. Elias: None Declared, A. Diaz: None Declared, C. Vigovich: None Declared, G. Mumbach: None Declared, S. Gonzalez: None Declared, J. M. Roganovich: None Declared, J. Zanchetta: None Declared

Bone and Calcium

ICE2021-1571

THERAPEUTIC CHALLENGES IN A PATIENT WITH AN UNUSUAL AND SEVERE CASE OF MCCUNE-ALBRIGHT SYNDROME AND POLYOSTOTIC FIBROUS DYSPLASIA.

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Introduction: McCune-Albright syndrome (MAS) is a rare multisystem disorder that classically was defined by the triad of polyostotic fibrous dysplasia of bone, café-au-lait skin pigmentation, and precocious puberty. The clinical phenotype of MAS is highly variable and no definite treatment is available.

Case Description: 24-year-old male diagnosed with McCune-Albright syndrome and polyostotic fibrous dysplasia (MAS / FD) at the age of 11 for progressive craniofacial deformity due to increased jaw size and head circumference, café-au-lait skin pigmentation and endocrine hyperfunction of the GH-IGF1-axis, Prolactin (PRL) and Parathormone (PTH), with normal puberty onset.

From the age of 11 through 18 years old, he received treatment with Cabergoline, Pamidronate EV every 6 months, Cholecalciferol, Calcium and Calcitriol. The patient evolved showing decrease in PTH, PRL and IGF-1. However, OGTT-GH did not inhibit.

At the age of 17, a complete surgical resection of a giant fibrous mass was performed in the lower jaw with placement of a titanium plate and a tracheostomy due to airway involvement. Anatomical pathology reported Fibrous Dysplasia.

The patient discontinued medical follow-up until the age of 22. He was referred to our institution for fast tumor grow in the left malar region. Physical examination revealed weight 65 kg, height 169 cm, BMI: 23.2 (family genetic height 174 +/- 5 cm.), craniofacial asymmetry, frontal prominence and lower jaw, with loss of lower teeth, gingival hypertrophy, genu valgus in lower limbs. Laboratory: (see table) normal thyroid profile and 24-H Urinary free Cortisol.

Octreotide LAR 30 mg every 28 days, Zoledronic acid 5 mg/month, Cabergoline 3 mg/week, Cholecalciferol and calcium were indicated.

During follow-up, he presented a spontaneous right subtrochanteric complete fracture of the right femur for which he required osteosynthesis.

Clinical discussion: The degree of severity, unusual presentation and the low incidence of MAS / DF motivated the communication of this case. Treatment was aimed at optimizing life quality and minimizing the morbidity associated with bone deformities, fractures and compromise of vital structures.

Image:

| Age/Before starting treatment | IGF-1 (120-338) ng/ml (SDS) | GH until 3(ng/ml) | PRL (2.5-17) ng/ml | PTH (12-87) pg/ml | VITD (30-100) ng/ml | CTX (16-584) pg/ml | FAL O (54-221) UI/l | Ca/P Ca: 8.5-10 P: 2.7-4.5 mg/dl |
|--|-----------------------------|-------------------|--------------------|-------------------|---------------------|--------------------|-----------------------|---|
| 11 years old Before starting treatment | 313 (0.49) | 6.9 | 152 | 111 | 36 | 2360 ng/l | 5330 | 10.1/3.1 |
| 15 years old Treatment using Cabergoline 4mg/w, Pamidronate, Cholecalciferol, calcium, calcitriol. | 130 (-2.26) | 6.6 | 2 | 76.6 | 31 | - | 1523 | 9.1/2.7 |
| 22 years old Treatment using Cabergoline 4mg/w, Cholecalciferol, calcium, calcitriol. Before starting with Zoledronic y Octreotide. | 405 (2.92) | 2.2 | <2 | 63.8 pg/ml | 38.5 | 3810 pg/ml | 318.4 (5.5-22.9) ug/L | 9.7/2.5 |
| 24 years old Being treated with Zoledronic, Octreotide. | 100 (-2.7) | 1.3 | 0,9 | 32 (4-39.4) pg/ml | 31.3 | 1950 pg/ml | 1298 | 10/2.6 |



Disclosure of Interest: None Declared

Bone and Calcium

ICE2021-1626

HYPOPHOSPHATEMIA AS A PRESENTING FEATURE OF PANIC RELATED HYPERVENTILATION

Mayuri Agarwal*, Cornelius James

Introduction: We describe a case of hypophosphatemia where it appeared that respiratory alkalosis induced by hyperventilation was the mechanism leading to severe symptomatic hypophosphatemia.

Case Description: 58-year-old male presented with paroxysmal episodes of feeling generally unwell and unsteadiness of feet for 4 months. There were no systemic symptoms. He is hypertensive, but not on diuretics. He had family history of Parkinson's disease, and the patient was anxious about getting this. His neurological examination was normal apart from 4/5 power in proximal muscle groups. During hospitalizations, bloods showed hypophosphatemia with normal calcium, magnesium, and electrolytes. On the first admission, his phosphate was 0.64mmol/L, (0.80-1.50) and was replaced with oral supplements. On a subsequent hospitalization, with phosphate of 0.25mmol/L, he received intravenous replacement. Endocrine review has not revealed any evidence of malabsorption, alcoholism, or drugs. PTH was repeatedly normal, 3.8 and 3.1 unit (1.6-6.9). 25-hydroxy vitamin D was 30 nmol/L for which he received vitamin D replacement. Neurology review and extensive investigations were normal. CT chest abdomen pelvis ruled out occult malignancy as a cause of recurrent hypophosphatemia. The urine phosphate level was normal, which ruled out renal phosphate loss. Presence of respiratory alkalosis with the third hospitalization raised the possibility of hyperventilation as a cause of hypophosphatemia. Phosphate replacement was delayed, and a repeat sample within few hours showed normal phosphate. A hyperventilation induction test was performed that revealed drop in phosphate levels to 0.72 mmol/L during hyperventilation and normalization to 1.15 mmol/L few hours later, concluding that his hypophosphatemia was secondary to anxiety related hyperventilation.

Clinical discussion: Hypophosphatemia, serum phosphate <0.8mmol/L, could be caused by three mechanisms including increased renal excretion, decreased intestinal absorption, and transcellular shifts. The transcellular shift occurs with insulin therapy, refeeding syndrome, and respiratory alkalosis. In panic related hypoventilation, the respiratory alkalosis stimulates phosphofructokinase enzyme, which consumes the intracellular phosphate causing hypophosphatemia causing skeletal muscle weakness, rhabdomyolysis, haemolysis, and mental status changes. Focus on treating the cause with careful replacement in sustained or severe hypophosphatemia.

Disclosure of Interest: None Declared

Cardiovascular

ICE2020-1041

SFLT-1, PLGF AND NT-PROBNP AS PREDICTORS OF MORTALITY IN A COHORT OF HEART FAILURE PATIENTS.

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Introduction: Soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF), members of the VEGF family, play key roles in angiogenesis.

Objectives: Since plasma levels of sFlt-1 and PlGF are reportedly elevated in coronary heart disease and heart failure (HF), our study aimed at investigating their utility as prognostic biomarkers in HF patients.

Methods: Assays for sFlt-1, PlGF and NTproBNP were performed in n=858 patients from a prospective multi-centre, observational study (PEOPLE study) of outcome among patients hospitalised for an episode of acute decompensated HF. sFlt-1 and PlGF were also assayed in n=200 heart healthy volunteers (HVOLs), age- and gender-matched to the PEOPLE cohort to compare plasma concentrations in healthy individuals. sFlt-1 and PlGF data were log₁₀-transformed to normalize distributions and the clinical endpoint was all-cause death. Patients were followed for a median of 2.60 (range 0.01-5.45) years.

Results: Mean plasma levels of both sFlt-1 and PlGF were significantly lower in the HVOLs compared to the PEOPLE cohort (sFlt-1 81.2±1.31 pg/mL in HVOLs versus 125±2.01 pg/ml in PEOPLE; PlGF 15.5±0.32 pg/mL in HVOLs versus 17.5±0.21 pg/ml in PEOPLE, both p<0.001). sFlt-1 was higher in patients with HF with reduced ejection fraction (HFrEF) (130±2.62 pg/ml, n=553) compared to those with HF with preserved EF (HFpEF) (117±3.59 pg/ml, n=305; p=0.005). sFlt-1 correlated with heart rate (r=0.148, p<0.001), and systolic blood pressure (r=-0.139, p<0.001). PlGF levels were weakly correlated with age (n=810, r=0.185, p<0.001), hsTnT (n=807, r=0.142, p<0.001), and negatively correlated with sFlt-1 (n=810, r=-0.104, p=0.003). sFlt-1 was a predictor of all-cause mortality (HR=5.88, p<0.001) in the PEOPLE cohort independent of age, NTproBNP, ischaemic aetiology, diabetes and beta-blocker therapy (n=843, 275 deaths), established predictors of mortality in the PEOPLE cohort. However, Cox proportional hazards modeling showed sFlt-1 levels and the ratio PlGF:sFlt-1 were similarly weighted but not independent predictors of all-cause death.

Conclusion: Baseline sFlt-1 levels have potential as a predictor of death; complementary to established prognostic biomarkers in heart failure.

Disclosure of Interest: None Declared

Cardiovascular

ICE2021-1376

REGULATION OF VASCULAR HOMEOSTASIS BY PLANT DERIVED ESTROGENS

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Introduction: Phytoestrogens (PE) such as genistein (Gen) are considered a natural therapy to counteract the risk of cardiovascular diseases in postmenopausal women. Atherosclerosis is a chronic inflammatory process that, in the later step of plaque generation could conduct to vascular calcification (VCa). Revascularization, mainly aided by angiogenesis, represents a survival mechanism for ischemic tissue.

Objectives: We have previously reported that Gen prevents cellular events involved in the early stages of plaque formation. In this work we study the effect of Gen on VCa and angiogenesis.

Methods: Aortic rings (AR); endothelial cells (EC) and vascular smooth muscle cells (VSMC) isolated from aortic explants of female Wistar rats were employed. Cells cultures (VSMC; EC) or AR were *in vitro* exposed to 1-100 nM of Gen.

Results: When the effect of Gen on VCa was assayed, intact aortas were cultured in procalcifying medium (10 mM β -glycerophosphate; 4 mM CaCl_2) for 14 days. A significant reduction in calcified areas, revealed by AgNO_3 staining, was detected after 10 nM Gen treatment. These results were confirmed by quantification of aortic tissue calcium content (552 ± 43 vs 235 ± 18 ug Ca/mg prot, C vs Gen, $p < 0.001$). Since VCa depends on VSMC transdifferentiation into osteoblast, VSMC cells were cultured for 21 days in procalcifying medium. Extracellular calcium content and alkaline phosphatase (ALP) activity were measured as osteoblastic differentiation markers. Gen induced 0,5 and 1-fold reduction in ALP activity ($p < 0.05$) and calcium deposition ($p < 0.05$) respectively, suggesting an inhibitory action on VSMC transdifferentiation into bone like cells. In view that angiogenesis involves EC proliferation, migration and VEGF synthesis; we studied the role of Gen on these events. Gen (4-96 h) stimulated EC proliferation at all concentrations tested (22-39% above C, $p < 0.05$, MTT assay), with higher effect at short time interval treatment. After 72 h of treatment, the PE enhanced EC migration (20% > 66% above C, 10-100 nM, $p < 0.01$; wound healing assay). Indeed, Gen increased VEGF synthesis (24.6-68.9 % above C, 1-10 nM Gen; ELISA assay). We confirmed that EC were able to proliferate after VEGF exposure. In order to evaluate new capillaries tube formation, AR were seeded on a collagen matrix and exposed to Gen for 15 d. Gen induced a 10-fold increase in tube formation around AR.

Conclusion: PE exhibits a potential beneficial effect on vascular homeostasis by reducing VCa and promoting angiogenesis.

Disclosure of Interest: None Declared

Cardiovascular

ICE2021-1382

RISK FACTORS OF ISCHEMIC HEART DISEASES IN TUNISIAN YOUNG ADULTS: DATA FROM NATIONAL HOUSEHOLD SURVEY, 2016

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Introduction: Ischemic heart diseases (IHDs) are ranking first among main causes of mortality in Tunisia, accounting for almost 27% of total deaths. High blood pressure (HBP), smoking, abdominal obesity and diabetes are common risk factors of IHDs leading the most to premature deaths and disability combined.

Objectives: We aimed to assess prevalence of IHDs' major risk factors in Tunisian young adults.

Methods: Data from 2016 Tunisian Health Examination Survey were used focusing on young adults aged 20 - 49 years. The blood testing device "Cardio Check" was used for diabetes and dyslipidemia screening [1]. Three measures of blood pressure were performed using automated recording device "Omron M6 Comfort" [2]. Diabetes and HBP were defined based on American Diabetes Association and WHO criteria, respectively [3,4]. Dyslipidemia was retained if total cholesterol level ≥ 240 mg/dl and/or triglyceride level ≥ 200 mg/dl, regardless of fasting duration. Abdominal obesity was defined by waist to height ratio ≥ 0.6 . The computer assisted approach was used for data entry and R software was used for data analysis.

Results: A total of 4625 participants were enrolled with a mean age of 36.8 ± 8.1 years and M/F sex-ratio equal to 0.8. Among participants, 15.5% [14.3-16.7] had HBP of which 82.8% were unaware of their disease, 8.5% [7.6-9.6] were diabetic of which 61.1% were unaware of their disease, and 37.5% [35.7-39.3] had dyslipidemia. Abdominal obesity was found among 22.6% [21.2-24.1] of surveyed young adults and more than fifth of participants were smokers (28.9%, [27.1-30.7]).

Conclusion: Our study highlighted high prevalence of IHDs major risk factors and alarming unawareness prevalence in Tunisian young adults. Reinforcement of IHDs' risk factors screening programs in frontline care besides of increasing awareness regarding healthy lifestyle commitment, are strongly recommended.

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Disclosure of Interest: None Declared

Cardiovascular

ICE2021-1476

PREDIABETES AND PHYSICAL ACTIVITY

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Introduction: The pre-diabetic (PDBT) is associated with insulin resistance, increased inflammatory markers, presence of risk factors (RF) for atherosclerosis, and increased risk of Cardiovascular Disease (RCVD). In people with PDBT suggest that risk reduction and its prevention may reduce the coronary heart disease epidemic. The objectives are to identify the risk for PDBT of sedentary individuals and with other CVD RF.

Objectives: Identify the risk for PDBT of sedentary individuals and with other CVD risk factors (RF).

Methods: 2754 patients (P) 59.4% women (W) and 40.6% men (M). 316 (11.4%) with confirmed DBT, who attended for pre-surgical exams with ages (AG) between 15 and 104 years. A Binary Logistic Regression (BRL) was performed. 70% as experimental group (EXG) and 30% for the control group (CG). The dependent variable (DV) PDBT [P who in self-report were identified as WITHOUT DBT or DON'T KNOW]. In the analysis (1), 3 independent V (IV) were incorporated: AG >= 45 years. BMI > 25. PA: SEDENTARY (P.SED) [without PA + with once/ W PA]; and ACTIVE (P. ACT) [with PA 3, 5, +5 times/ W and Active Work]. In a second step (2), Sex and Smoking Habit (SM) is incorporated.

Results: The IV chosen for the model predict DV, $X^2 = 941$ $p < 0.001$. The model correctly classifies 87% of the EXG and 85% of the CG. The pseudo $R^2 = 0.521$. The multivariate analysis stops at step 3 and Exp (B) rates the P.SED with 3.9, BMI > 25 3.2 and the AG >= 45 years 0.682. In 2, SM and SEX make the Exp (B) fall to 3.2 and 2.6 for the condition of P.SED and BMI > 25 respectively; and they increase it for SM 3.2 and for SEX M 1.6. Discussion. In BLR with categorical DV, it is not possible to calculate a single R^2 statistic as in linear regression with all its characteristics, and it is called pseudo R^2 , for the Nagelkerke test the model predicts PDBT in 52%, according to the risk conditions that some people would have to suffer from this disease. So far we can state that the P.SED condition and the BMI > 25 increase the probability of PDBT by 4 and 3 times. A higher AG decreases this risk by 0.7 times. The increase in IV only increased the RF in smokers and for sex M, decreasing for the condition of P.SED, AG and BMI > 25.

Conclusion: The increase in IV does not favor the classification and / or prediction capacity of the test. However, it reveals the negative factor of smoking and the greater predisposition of sex M and P.SED and BMI > 25, to suffer from PDBT.

Disclosure of Interest: None Declared

Cardiovascular

ICE2021-1482

PREDIABETES AND PHYSICAL ACTIVITY IN PATIENTS AGES UNDER 45 YEARS

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Introduction: Prediabetes (PDBT), typically defined as blood glucose levels above normal but below diabetes thresholds (DBT), is a risk state that defines a high probability of developing DBT. The diagnostic criteria for PDBT have changed over time and currently vary by institution but are primarily biochemical values. The term, itself, has been criticized on the grounds that many people with PDBT do not progress to DBT. In fact, the WHO used the term 'intermediate hyperglycemia' and an International Committee of Experts convened by the ADA described the 'high-risk state of developing DBT' instead of 'PDBT'. For simplicity, this term is used.

Objectives: Identify the risk for PDBT of sedentary individuals and with other RF of cardiovascular disease.

Methods: A cohort study was carried out 2754 patients (P) 59.4% women (W) and 40.6% men (M), 316 (11.4%) with confirmed DBT, who attended for pre-surgical examinations on 03/01/2020, with ages (AG) between 15 and 104 years. A Binary Logistic Regression (RLB) was performed. 70% as experimental group (EXG) and 30% for the control group (CG). The dependent variable (DV) PDBT [P who in self-report were identified as WITHOUT DBT or DON'T KNOW]. In the analysis (1), 4 independent V (VI) were incorporated: AG <45 years. BMI > 25. PA: SEDENTARY (SED P) [without PA + with once/W]; and ACTIVE (ACT P.) [with PA 3, 5, +5 time/ W and Active Work; and habit of smoking (SM)]. In (2) Sex, hypertension, COL yes and TG yes.

Results: The IV chosen for the model predict VD, $X^2 = 941$ p < 0.001. The model correctly classifies 89% of the EXG and 88% of the CG. The pseudo $R^2 = 0.678$. The multivariate analysis (1) the Exp (B) rates the SED P. with 1.9, BMI > 25 1.8 and AG <45 years 14.6. [the younger the age, the greater the risk]. SM 1.9. In (2) the pseudo $R^2 = 0.72$ the Exp (B): 12, 2.5, 2.3 and 2.4 for AG, SED P., BMI > 25 and SM respectively. COL yes 0.52 and TG yes 0.14. [are of very low value and negatively influence PDBT]. Between the multivariate analysis (1) and (2), the following were modified: the prediction of the Nagelkerke model 67.8% to 72%, SED P. from 1.9 to 2.5; BMI > 25 from 1.8 to 2.3 and SM from 1.9 to 2.4 times the probability of taking PDB. For AG decrease the risk factor from 14.6 to 12.

Conclusion: Age is a determining factor for the presence of PDBT. In SED P. <45 years, the increase in IV modifies the value of the Odds Ratio (relative risk) for SED P, BMI > 25 and SM, according to the risk conditions that some people would have to take PDBT.

Disclosure of Interest: None Declared

ICE2020-1040

SYNCYTIOTROPHOBLAST EXTRACELLULAR VESICLES KISSPEPTIN EXPRESSION IN GESTATIONAL DIABETES MELLITUS

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Introduction: Gestational diabetes mellitus (GDM) is reported to complicate up to 17% of pregnancies globally and 1 in 4 pregnancies in South Africa. More recent studies have challenged the theory which has suggested that insulin resistance in the later stages of normal pregnancies is due to placental hormones such as progesterone, oestrogen, human placental lactogen, and cortisol. Kisspeptin is largely produced by placental syncytiotrophoblasts with a consequent dramatic rise in circulatory levels in advanced pregnancy. Studies have shown that kisspeptin induces glucose-stimulated insulin secretion and has an inverse relationship with markers of insulin resistance. The role kisspeptin in the syncytiotrophoblast extracellular vesicles of pregnancies complicated by GDM is unknown.

Objectives: To determine the syncytiotrophoblast extracellular vesicles kisspeptin protein expression in GDM complicated pregnancies.

Methods: An exploratory experimental study was performed.

Eight archival placental lysates (GDM- 4, non GDM- 4) and 6 syncytiotrophoblast extracellular vesicles (STEVs) (GDM- 3, non GDM- 3) from University of Oxford Nuffield Department of Women's and Reproductive Health (Manu Lab) were used for the experiment.

STEVs were isolated by placental perfusion method using freshly delivered placentae of both GDM and normal pregnancies and stored at -80 degrees Celsius (all samples received ethical approval).

Western blotting, immunoprecipitation and immunohistochemistry were performed using anti kisspeptin 1 monoclonal antibody from Santa Cruz (Kiss-1(24Q): sc-101246), USA.

Results: The kisspeptin protein expression in the placental lysates was lower in GDM complicated pregnancies compared to normal pregnancies (p value= 0.5379).

Kisspeptin protein expression was lower in the STEVs of GDM complicated pregnancies than normal pregnancies (p value= 0.0831).

Co-expression of placental alkaline phosphatase (PLAP) and kisspeptin in the PLAP positive pulled out STEVs was found.

Image:

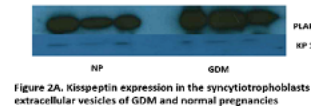
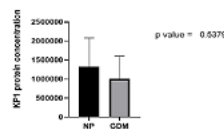
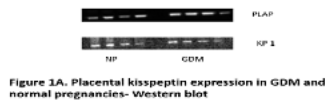
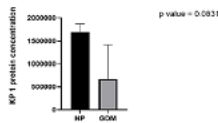
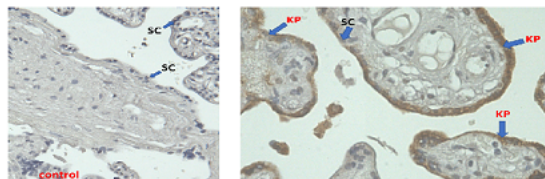


Figure 1B. Bar chart representing placental lysates kisspeptin 1 protein expression between NP and GDM



Immunohistochemistry



Conclusion: Kisspeptin protein expression is lower in both the placenta and STEVs of GDM complicated pregnancies compared to normal pregnancies. Findings suggest that in GDM pregnancies, lower STEVs kisspeptin levels are insufficient enough to stimulate insulin secretion by the pancreatic cells to counteract insulin resistance thereby leading to GDM.

Disclosure of Interest: None Declared

ICE2020-1044

A RARE CASE OF HYPERINSULINEMIC HYPOGLYCEMIA

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Introduction: Insulin autoimmune syndrome (IAS) is a rare endocrine disease characterized by repeated hypoglycemia – fasting/fed, with elevated serum insulin and positive anti insulin antibody .

Case Description: Here with we present this rare case of IAS with its clinical manifestations and treatment outcome .

Clinical discussion: Our patient, a 67 year old male, hypertensive since 15 years on telmisartan 40mg OD and metoprolol 25mg OD without any previous comorbidities like CAD/CKD presented with h/o repeated episodes of irrelevant behavior and decreased level of consciousness since 2 months, always GRBS <40mg/dl, corrected with IV 25% D.

Diagnosis: Serum islet cell antibody (ICA) and glutamic acid decarboxylase antibody (GADA) were negative, while insulin autoantibodies were positive. Serum insulin levels were significantly elevated. No abnormalities were found on enhanced CT of the pancreas, hence clinically diagnosed with IAS.

Interventions: An endoscopic ultrasound of the pancreas was planned, but due to non availability, the procedure was not done. Clinically, IAS , hence he was started on oral prednisolone 0.5mg/kg and was asked to take frequent carbohydrate rich diet, with self monitoring of blood glucose. Over the period of next 2 months, there were no new episodes of hypoglycemia.

Outcomes: At the 3-month follow-up visit, the hypoglycemic episodes had disappeared, serum insulin levels were significantly decreased, and insulin antibody (IA) levels were no longer detectable. For those patients with high insulin hypoglycemia, insulin auto anti bodies should be evaluated as a routine.

Therapeutically, a lower dose of glucocorticoids with small, frequent carbohydrate meals will yield better results.

Disclosure of Interest: None Declared

ICE2020-1050

A COMPARATIVE STUDY TO DETERMINE EFFICACY OF HYDROXYCHLOROQUINE AND CANAGLIFLOZIN ON GLYCAEMIC VARIABILITY IN INDIAN SUBJECTS WITH UNCONTROLLED TYPE 2 DIABETES MELLITUS ON COMBINATION OF VILDAGLIPTIN, METFORMIN AND INSULIN

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Introduction: Drugs Controller General of India (DCGI) has approved Hydroxychloroquine (HCQ) to be used as an add-on antidiabetic drug after metformin and sulphonylurea failure. But the effect on glycemic variability of HCQ is unknown.

Objectives: To determine the comparative effects of hydroxychloroquine and canagliflozin on glycemic variability (GV) using continuous glucose monitoring (CGM) as treatment adjuncts to insulin, vildagliptin plus metformin uncontrolled T2DM.

Methods: Twenty four Indian T2DM subjects (age: 57.6 ± 4.91 years, baseline HbA1c: $7.8 \pm 0.5\%$) who were on stable daily dose of Insulin (30.4 ± 7.2 IU plus vildagliptin 100 mg plus metformin 1000 mg) were enrolled for this prospective observational multicentric study. Subjects were divided into two equal groups and put on either HYQ 400 mg or canagliflozin 100 mg. Continuous blood glucose monitoring was done in participants using continuous glucose monitoring (CGM) (Free Style Libre Pro, Abbot) determined over a 6-day period (in order to obtain a continuous 72-hour reading) at baseline and after each active treatment.

Results: Both hydroxychloroquine and canagliflozin reduced postprandial glucose levels (16% vs. 15%) and measured plasma glucose (14% vs. 16%), both based on CGM data. Both the drug had showed similar lower glucose fluctuations as measured by mean amplitude of glycemic excursions (MAGE, $p = 0.1076$), standard deviation (SD) ($p = 0.1346$) of blood glucose rate of change but did not reach statistical significance attributed to the small sample size. Both the drug led to statistically significant lowering of the rate of change in the median curve (RCMC) and interquartile range (IQR) of glucose. Insulin dose was reduced to 28.5 ± 9.4 with HCQ group as compared to 29.58 ± 6.7 with canagliflozin group. There was no significant change in serum creatinine or eGFR in both the groups. Similar Hb1c reduction observed in both the groups (-0.89 ± 0.1 in HCQ group vs -0.91 ± 0.1 in canagliflozin group).

Image:

Table: Change from baseline to 8 week study end point with Hydroxychloroquine or Canagliflozin treatment.

| Characteristic | HCQ (N=13) | | | CANA (N=11) | | | P Value |
|--------------------------|------------|----------------------|-------------|-------------|----------------------|------------|---------|
| | Baseline | 8 th Week | Δ | Baseline | 8 th Week | Δ | |
| PPG (mg/dl) | 218±21 | 183±13 | 35±5 | 227±18 | 193±21 | 34±4 | 0.01 |
| HbA1c (%) | 7.7 ± 0.5 | 6.81± 0.5 | -0.89 ±0.1 | 7.9± 0.5 | 6.99± 0.5 | -0.91 ±0.1 | 0.01 |
| Insulin Dose (IU/Day) | 30.9 ± 7.8 | 28.5±9.4 | | 30.1 ± 6.9 | 29.58± 6.7 | | 0.001 |
| serum creatinine (mg/dl) | 0.65±0.2 | 0.64±0.2 | -0.01 ±0.01 | 0.58±0.1 | 0.59±0.1 | 0.02 ±0.01 | 0.789 |

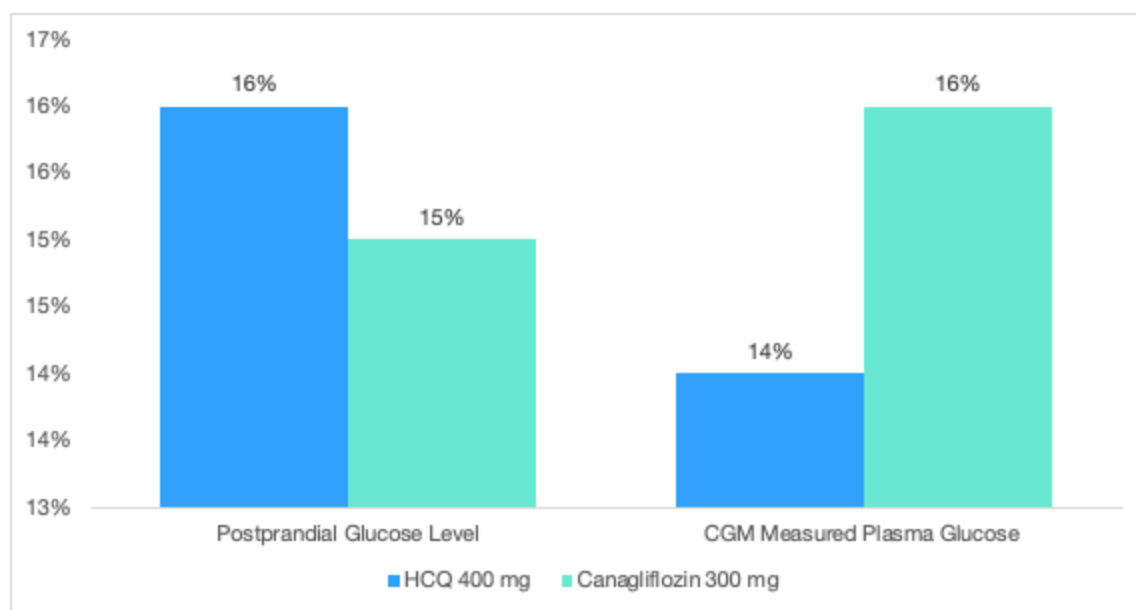


Figure 1: Both hydroxychloroquine and canagliflozin reduced postprandial glucose levels, and measured plasma glucose based on both CGM data

Conclusion: Hydroxychloroquine when compared with Canagliflozin bestowed similar effects on reduction of glycemic variability and achieving glycemic control in Indian T2DM subjects, but HCQ brought significant reduction in total daily dose of insulin requirement as compared to Canagliflozin.

Disclosure of Interest: None Declared

ICE2020-1070

WOLFRAM-LIKE SYNDROM: A RARE FAMILY GENEALOGY WITH HETEROZYGOUS MUTATION IN WFS1 GENE

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Introduction: Wolfram-like syndrome (WFSL) is a rare autosomal dominant disease characterised by congenital progressive hearing loss, diabetes mellitus, and optic atrophy. We aimed to investigate WFS gene sequences in a family with diabetes and nerve deafness.

Case Description: High-throughput sequencing in whole exon sequence was performed in the proband with diabetes and nerve deafness to reach the target region. Sanger sequencing technology was applied to the validation of candidate sites for the proband's two brothers and parents.

The proband and one of his brothers had non-insulin-dependent diabetes mellitus, cerebral demyelination and nerve deafness. Another brother and his mother had prediabetes. The proband's father had non-insulin-dependent diabetes mellitus. This pedigree, in which the proband had no specific mutations in mitochondrial genome, was found to have mutation in WFS1 gene (exon8: c.G2407A: p.V803M, chr4-6303929). This mutation in WFS1 gene was verified in the proband's two brothers and father, but not in his mother.

Clinical discussion: The mutation in WFS1 gene (c.G2407A: p.V803M, chr4-6303929) is associated with the occurrence of WFSL, of which clinical manifestations and progression are highly heterogeneous.

Disclosure of Interest: None Declared

ICE2020-1085

AUDIT ON INITIATION AND CONTINUATION OF FREESTYLE LIBRE IN TYPE 1 DIABETES PATIENTS AT THE ROYAL BERKSHIRE HOSPITAL

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Introduction: Freestyle Libre has been increasingly used in UK since the NHS long term plan announced that Type 1 Diabetes patients would benefit from flash glucose monitors from April 2019. However, there are criteria for initiation and continuation for these devices as below:

1. People with Type 1 diabetes requiring intensive monitoring >8 times daily,
2. Pregnant women with Type 1 Diabetes.
3. Any type of diabetes with special circumstances based on MDT assessment.
4. Previous self-funders of Freestyle libre with clinical improvement
5. Type 1 diabetes with recurrent severe hypoglycaemia or impaired awareness of hypoglycaemia.

Objectives: This audit aims to review whether Freestyle Libres were initiated according to criteria and whether it did help to improve clinical outcomes.

Methods: Retrospective study of randomly selected 50 patients in whom Freestyle Libre were initiated between May 2019 and June 2019. The above criteria was used and their HbA1C before and after initiation of freestyle libre and documentation on hypoglycaemia awareness and hypoglycaemia episodes were reviewed.

Results: All patients were initiated according to criteria; 19 patients requiring intensive monitoring, 25 patients with recurrent hypoglycaemia and impaired hypoglycaemia awareness, 4 patients recommended by specialist MDT outcome, 1 patient with T1DM and pregnancy and 1 self-funded patient with satisfactory diabetes care.

With rechecked HbA1C 3-6 months after initiation of Freestyle Libre in 19 patients requiring intensive monitoring, 7 patients had showed improvement in HbA1C, 3 patients had the same HbA1C, 6 patients had increased in HbA1C, and there was no data available in 3 patients.

Among 25 patients with recurrent hypoglycaemia and impaired hypoglycaemia awareness, 13 patients had improved hypoglycaemia awareness and reduced hypoglycaemia episode, 4 patients showed no improvement, 3 patients with no documentation on episode or awareness of hypoglycaemia, 4 patients was awaiting review in clinics and 1 patient had lost follow up. 4 patients had not only reduced in hypoglycaemia episode and improved awareness but also improvement in HbA1C.

Conclusion: Freestyle libre leads to the improvement in HbA1C of significant proportion of patients who required intensive monitoring. Similarly, better hypoglycemia awareness and reduction in hypoglycemia episodes were noted in patients with recurrent hypoglycemia. Lack of documentation of hypoglycemia awareness in a few patients was identified, and hence, a system to improve on this aspect would be set up.

Disclosure of Interest: None Declared

ICE2020-1092

FACTORS ASSOCIATED WITH A NEW DIAGNOSIS OF TYPE 2 DIABETES MELLITUS IN LATINO ADULTS IN THE SANGRE POR SALUD BIOBANK

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Introduction: In the United States (US), type 2 diabetes mellitus (T2DM) is more prevalent in Hispanics compared with non-Hispanic Whites. Despite this, the prevalence of risk factors associated with T2DM in Hispanics is incompletely described.

Objectives: To describe lifestyle, clinical and lipid risk factors associated with a new diagnosis of T2DM in Hispanic adults.

Methods: *Sangre Por Salud* is a prospective cohort of 3,733 self-identified Hispanic adults in Arizona, US, enrolled from 2013-2018. At enrollment, 434 adults had a prior diagnosis of T2DM (excluded from analysis), 280 were newly diagnosed with T2DM using ADA criteria and 3,019 were T2DM-free. Lifestyle factors (diet, physical activity, medical conditions) and anthropometric measures of obesity were obtained by trained interviewers. Blood samples were collected to measure lipid risk factors. The associations of lifestyle, clinical, and lipid risk factors with odds of newly diagnosed T2DM were analysed using logistic regression models.

Results: Among the 280 T2DM cases with a new T2DM diagnosis, 70% were women. Compared with T2DM-free adults, adults with T2DM had a higher prevalence of hypertension (14% vs. 27%) and obesity (46% vs. 64%). Compared with T2DM-free adults, those with T2DM had higher plasma concentrations of total cholesterol, LDL cholesterol, VLDL cholesterol, and triglycerides, but a lower concentration of HDL cholesterol. In models adjusted for age and gender, lifestyle factors such as consumption of regular soft drinks (≥ 3 drinks/day vs. lower) were associated with 1.8-fold higher T2DM risk, whereas consumption of vegetables (≥ 4 times/week vs. lower) and potato-based foods (≥ 4 times/week vs. lower) showed no association. Among clinical risk factors, adults with hypertension and obesity showed a 1.5-2.0 fold higher T2DM risk, compared to adults without these risk factors. Atherogenic lipid risk factors (per standard deviation increment) including total cholesterol, LDL cholesterol, VLDL cholesterol, and triglycerides were associated with a 1.2-1.7 fold higher T2DM risk, whereas HDL cholesterol was associated with lower risk. (Table)

Image:

Table: Factors associated with a new diagnosis of T2DM in Hispanic Adults in the Sangre Por Salud Biobank Cohort

| Risk factors | | No T2DM (n = 3019) | New T2DM (n = 280) | Adjusted model ^{###} odds ratio (95% CI) |
|--------------|---|-------------------------------------|-----------------------|--|
| Diet | Potato based foods ≥ 4 times/wk | 429 (16.3) | 28 (11.6) | 0.64 (0.41-0.95) [*] |
| | Vegetables ≥ 4 times/wk | 1503 (56.2) | 130 (52.9) | 0.78 (0.60-1.02) |
| | Regular soft drinks ≥ 3 /day | 229 (8.0) | 29 (11.2) | 1.82 (1.17-2.74) ^{**} |
| Exercise | Moderate/vigorous exercise ≥ 5 times/wk | 560 (19.6) | 40 (15.2) | 0.82 (0.57-1.15) |
| Clinical | Hypertension | 408 (14.3) ^{****} | 71 (26.8) | 1.47 (1.07-2.00) [*] |
| | Obesity (BMI ≥ 30 kg/m ²) | 1384 (46.3) ^{****} | 179 (63.9) | 2.00 (1.55-2.60) ^{****} |
| Lipids | Total cholesterol | 180.0 (157.0-205.0) ^{****} | 192.0 (170.0-221.5) | 1.26 (1.12-1.42) ^{**} |
| | HDL cholesterol | 48.0 (40.0-57.0) ^{****} | 44.0 (36.0-51.0) | 0.57 (0.49-0.67) ^{****} |
| | LDL cholesterol | 104.0 (85.0-125.0) ^{**} | 113.0 (90.0-135.0) | 1.16 (1.03-1.31) [*] |
| | VLDL cholesterol | 23.0 (16.0-32.0) ^{****} | 31.0 (23.0-41.0) | 1.65 (1.48-1.84) ^{****} |
| | Triglycerides | 114.0 (82.0-163.0) ^{****} | 159.5 (116.5-219.0) | 1.44 (1.30-1.59) ^{****} |

Data as median (interquartile range) for lipids and frequency (%) for others. Odds ratio for lipids is per SD increment
CI: confidence interval; ^{*}p<0.05; ^{**}p<0.01; ^{****}p<0.001; ^{###}adjusted for age and gender

Conclusion: A new diagnosis of T2DM in Hispanic adults is associated with a high burden of modifiable lifestyle, clinical and lipid risk factors. The low prevalence of a favourable cardiometabolic profile among T2DM-free adults identifies opportunities for T2DM preventive efforts.

Disclosure of Interest: None Declared

ENHANCEMENT OF TOTAL GLUCAGON-LIKE PEPTIDE-1 SECRETION IN TYPE 2 DIABETES MELLITUS PATIENTS IN MALAYSIA

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Introduction: Impaired secretion of glucagon-like peptide-1 (GLP-1) among Caucasians has been suggested to contribute to deficient incretin effect in patients with Type 2 diabetes mellitus (T2DM). Asian T2DM phenotypes have significant pancreatic β -cell dysfunction and lower insulin resistance, which may give rise to distinct GLP-1 secretory capacity compared to Caucasians.

Objectives: To compare total GLP-1 levels after oral glucose tolerance test (OGTT) in subjects with type 2 diabetes mellitus (T2DM), prediabetes and normal glucose tolerance (NGT).

Methods: In this cross sectional study, 171 Malaysian subjects age 22 to 75 years old were recruited. Subjects were divided into the NGT (n=57), prediabetes (n=54) and T2DM (n=60) after undergoing a 75g OGTT. Plasma total GLP-1 levels were measured at 0, 30 and 120 minutes during OGTT. Homeostasis model assessment of insulin resistance (HOMA-IR), HOMA of insulin sensitivity (HOMA-IS) and triglyceride glucose (TyG) index were calculated.

Results: Peak GLP-1 secretion occurred at 30 minutes during OGTT. T2DM showed a higher GLP-1 response to OGTT, as reflected by significantly higher plasma total GLP-1 levels at fasting and 30 minutes (26.75 ± 11.57 pmol/L; 50.22 ± 17.71 pmol/L) and AUC_{glp} (4654.05 ± 1568.36 pmol/L.min), compared to prediabetes (21.65 ± 11.57 pmol/L; 40.17 ± 15.64 pmol/L; 3750.71 ± 1490.91 pmol/L.min) and NGT (15.28 ± 8.86 pmol/L; 31.54 ± 22.78 pmol/L; 2925.17 ± 1845.05 pmol/L.min) ($p < 0.001$). This is associated with higher fasting insulin level in T2DM (18.41 ± 14.03 uU/ml) than prediabetes (16.32 ± 8.18 uU/ml) and NGT (10.83 ± 5.82 uU/ml) ($p < 0.001$). T2DM has significantly higher HOMA-IR and TyG but lower HOMA-IS than prediabetes and NGT. AUC_{glp} correlated positively with HOMA-IR ($r = 0.349$, $p < 0.001$) and TyG ($r = 0.419$, $p < 0.001$) but correlated negatively with HOMA-IS ($r = -0.351$; $p < 0.001$).

Conclusion: Increased total GLP-1 secretion was observed in T2DM patients. We hypothesise that an increased GLP response could possibly explain higher insulin levels in T2DM, which may initially help to overcome the insulin resistance in this patient group.

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Disclosure of Interest: None Declared

ICE2020-1096

USING DIFFERENT DIABETES RISK ASSESSMENT TOOLS REVEALS DISSIMILAR NUMBER OF RISK SCORE IN SAME POPULATION: A CROSS-SECTIONAL ANALYSIS IN A TERTIARY CARE HOSPITAL.

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Introduction: To identify individuals at high risk of developing type2 diabetes, use of a validated risk-assessment tool is currently recommended. A simple risk-assessment scoring system for early screening of type2 diabetes (T2DM) will be beneficial to identify the high-risk adults and thus taking adequate preventive measures in combating DM. It is under-reported, however, whether a different risk tool alters the predicted risk of an individual.

Objectives: The aim of this study was to examine if there were any differences between three commonly used validated risk-assessment tools when applied to the same population.

Methods: This cross-sectional analytical study was carried upon randomly sampled 602 non-diabetic adults visiting the outpatient department (OPD) of a tertiary care hospital in Dhaka, Bangladesh from January to December 2019. Subjects had previous history of high blood glucose during pregnancy or other health examination (i.e. gestational diabetes mellitus or impaired fasting glucose, impaired glucose tolerance) were also included. With written informed consent, the Indian Diabetes Risk Score (IDRS), American Diabetes (ADA) Risk Score and Finish Diabetes Risk Score (FINDRISC) questionnaires were used to collect the data including demographic-anthropometric and clinical characteristics, and different risk factors of an individual subject to calculate predicted risk score for developing T2DM within 10 years.

Results: Among 602 subjects, 55.0 % were female. The mean (\pm SD) age of the study subjects was 38.56 ± 1.13 years. Differences between the risk-assessment tools were apparent following cross-sectional analysis of individuals. IDRS categorized the highest proportion (38.2 %) of individuals at 'high risk' followed by ADA (22.4 %) and finally, the FINDRISC was the most conservative risk tool (8.6 %); [$p < 0.05$].

Conclusion: Differences were observed in predicted high risk individuals using different risk assessments tools, and therefore caution should be addressed when categorizing such individuals at high risk. This finding suggests that risk scores should not simply be expected to perform comparably well but rather may need to be validated within the population in which they are intended to be used.

Disclosure of Interest: None Declared

ICE2020-1109

SELECTED ADIPOKINES IN WOMEN WITH GESTATIONAL DIABETES AND TYPE 2 DIABETES

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Introduction: Adiponectin, adipocyte-fatty acid binding protein (A-FABP), and Wnt1 inducible signaling pathway protein-1 (WISP-1) are adipokines closely associated with insulin resistance.

Objectives: The aim of the study was to compare levels of adiponectin, A-FABP and Wnt1 in women with gestational diabetes (GDM), type 2 diabetes mellitus (T2DM) and healthy controls and determine their relation to metabolic parameters.

Methods: Women with GDM, T2DM and healthy women were included in this cross-sectional study. In addition to adipokines, anthropometric, lipid parameters, markers of insulin resistance and glucose control were assessed in all participants.

Results: Compared to healthy controls (n=35) significantly lower levels of adiponectin were detected in women with GDM (n=50), whereas in women with T2DM (n=50) higher levels of A-FABP and WISP-1 and lower levels of adiponectin were found. Women with T2DM had also lower levels of adiponectin and higher levels of A-FABP compared to women with GDM. A-FABP and adiponectin were independently associated with levels of triglycerides, HDL-cholesterol and C-peptide insulin resistance index. WISP-1 correlated only with waist circumference.

Conclusion: Adverse adipokines production reflecting dysfunctional fat tissue is less presented in women with GDM than in women with T2DM, but more expressed compared to healthy women.

Disclosure of Interest: D. Karásek Conflict with: AZV NV18-01-00139 (Czech health research council), V. Kubickova: None Declared, O. Krystynik: None Declared, D. Goldmannova: None Declared, L. Cibickova: None Declared, J. Schovaneck: None Declared, E. Karásková: None Declared

ICE2020-1119

GUT MICROBIOTA PATTERNS IN ROMANIAN PATIENTS WITH METABOLIC SYNDROME – PILOT STUDY

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Introduction: MetSyn has a worldwide prevalence ranging from < 10% to 84%, depending on geographical location, diagnosis criteria and characteristics of the studied population. As revealed by both animal and human studies, a pathogenic trigger affecting host metabolic balance is represented by the gut microbiota. The microbiota orchestrates several aspects crucial for host metabolic function including modulation of nutrition and energy harvest, gut motility, glucose and lipid metabolism, appetite, energy absorption, and hepatic fatty storage. Deciphering the microbiome patterns linked to metabolic syndrome could enable us for better disease management.

Objectives: Our pilot study aimed to investigate the microbiota patterns in Romanian metabolic syndrome patients.

Methods: Fecal samples were collected patients with metabolic syndrome (n=16) and healthy controls (n=10) and further used for bacterial DNA isolation. Using 16 rDNA qRT-PCR, we analyzed phyla abundance (Bacteroidetes, Firmicutes) as well as the relative abundance of specific bacterial groups (*Lactobacillus sp.*, Enterobacteriaceae, *Ruminococcus sp.*, *Faecalibacterium sp.*, *Clostridium coccooides*, *Clostridium leptum*).

Results: Among the 16 patients with metabolic syndrome investigated, 14 had impaired glucose tolerance or type 2 diabetes, 5 patients had grade I obesity, 1 grade II obesity and 4 had morbid obesity (grade III).

The microbiota of patients with metabolic syndrome was significantly enriched in Enterobacteriaceae, *Ruminococcus sp.*, *Turicibacter sp.*, and *Clostridium coccooides*. The microbiome of MetSyn patients was also characterized by significantly lower levels of *Butyricoccus sp.*, a bacterial population known to be an important producer of butyrate, a SCFA involved in host intestinal homeostasis. *Butyricoccus apartine de care Clostridium? De precizat mai sus.*

No significant differences were observed in the *Bacteroides sp.*, *Lactobacillus sp.*, *Faecalibacterium sp.* and *Clostridium leptum* relative abundance compared to the healthy control.

Short chain fatty acids (SCFAs) such as butyrate, propionate and acetate produced primarily from the microbial fermentation of dietary fibre directly modulate host health through tissue-specific mechanisms related to glucose homeostasis, gut barrier function, and immunity.

Conclusion: The pathogenesis of MetSyn is closely related to the intestinal microbiota. Hence, the basic MetSyn management begins with dietary therapy, which needs to be based on the knowledge of its influences on the gut microbiome.

Disclosure of Interest: None Declared

ICE2020-1121

EFFICACY AND SAFETY OF BASAL INSULIN SUPPORTED ORAL THERAPY IN TYPE 2 DIABETES PATIENTS INADEQUATELY CONTROLLED WITH COMBINATION THERAPY

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Introduction: Despite initiation of oral therapy, type 2 diabetes remains uncontrolled in a vast majority of patients in India. Early insulin initiation is thus warranted in this population

Objectives: To analyze the efficacy and safety of adding basal insulin (insulin glargine U100/U300) to existing oral therapy in type 2 diabetes patients uncontrolled on oral therapy alone.

Methods: A retrospective real-world analysis of laboratory reports of 485 type 2 diabetes patients attending three tertiary endocrine referral centers in India. Patients uncontrolled on combination oral therapy (in common practice metformin up to 1 g/day and glimepiride up to 4 mg/day, DPP-4 inhibitors and/or alpha-glucosidase inhibitors) were advised 0.18 u/kg basal insulin (insulin glargine u-100 or insulin glargine U-300) at baseline of the analysis. Fasting blood glucose (FBG), post-prandial glucose (PPG), glycated hemoglobin (HbA1c), episodes of hypoglycemia, lipid profile and blood pressure readings were analyzed at baseline (0 month) and at 6 months after addition of basal insulin to oral therapy using the paired t test.

Results: Fasting blood glucose decreased from 196.73 mg/dL to 146.73 mg/dL (n=140, SD 72.65; p< 0.001), while PPG decreased from 280.50 mg/dL to 222.50 mg/dL (n=136, SD 107.67; p<0.001). The HbA1c was reduced by 1.46% (9.78 at baseline and 8.32% at 6 months, n=157, SD 4.01; p<0.001). Mild episodes of hypoglycemia were reported by 102 patients on at least one occasion in the 6 months after initiation of basal insulin therapy. No episode of nocturnal hypoglycemia and severe hypoglycemia needing hospitalization was reported in this cohort. Weight gain was not significant in the analyzed cohort with a modest gain of 1.5 kg observed at 6 months' follow-up

Image:

Table 1: Analyzed Parameters at baseline and at 6 months

| Systolic blood pressure | N | Mean | SD | P value |
|----------------------------------|----------|-------------|-----------|----------------|
| Baseline | 469 | 128.27 | 15.44 | 0.844 |
| 6 months | 212 | 126.10 | 63.30 | |
| Diastolic blood pressure | | | | |
| Baseline | 468 | 80.14 | 8.35 | 0.708 |
| 6 months | 211 | 78.55 | 39.37 | |
| Fasting blood sugar | | | | |
| Baseline | 372 | 196.73 | 65.92 | < 0.001* |
| 6 months | 140 | 146.92 | 72.46 | |
| Post prandial blood sugar | | | | |
| Baseline | 366 | 280.50 | 87.35 | < 0.001* |
| 6 months | 136 | 222.15 | 107.67 | |
| Hba 1c | | | | |
| Baseline | 390 | 9.78 | 1.74 | < 0.001* |
| 6 months | 157 | 8.32 | 4.01 | |
| Serum creatinine | | | | |
| Baseline | 275 | 0.86 | 0.22 | 0.728 |
| 6 months | 87 | 0.92 | 0.37 | |

*Significant p-value

Note: P-values are based on paired T test.

Conclusion: Addition of basal insulins (insulin glargine u-100 or insulin glargine U-300) to oral therapy is efficacious and safe and resulted in significantly better glycemic control at 6 months. Basal insulin supported oral therapy should be considered early on in such patient profiles.

Disclosure of Interest: None Declared



ICE2020-1158

METABOLIC EFFECTS OF BARIATRIC SURGERY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND OBESITY

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Introduction: In type 2 diabetic and obese patients it is frequently difficult to achieve weight and metabolic control goals with lifestyle changes and pharmacotherapy and sometimes accomplished by bariatric surgery (BC).

Objectives: To evaluate metabolic effects of BC in a diabetic and obese population

Methods: 56 patients were evaluated preoperative and postoperative (BC). Personal background, anthropometric measurements, blood pressure, body mass index (BMI), hemogram, hepatogram, glycemia, lipid profile, HbA1c and renal function were analyzed. **Statistical analysis:** Student's and Mann-Whitney-Wilcoxon tests were applied. Spearman correlation coefficient was calculated. Values expressed in average \pm standard deviation. Significant $p < 0,05$

Results: The sample consisted of 35 female and 21 male with a mean age of $52 \pm 9,6$. One anastomosis gastric bypass (OAGB) was performed in 29 patients and laparoscopic Roux-en-Y gastric bypass (LRYGB) in 27. Pre and postoperative data was analyzed. Postoperative data with a time lapse between 3 to 79 months, average of 31.6. In the preoperative period 52% received insulin, 77% metformin, 23% IDPP4, 100% antihypertensive drugs and 69% lipid lowering therapies while in the postoperative group only 7% were still treated with insulin, 14% metformin, 11% IDPP4, 54% antihypertensive drugs and 31% lipid lowering therapies. During the follow up BMI decreased from $43,87 \pm 9,99$ kg/m² in preoperative period to $29,48 \pm 5,82$ kg/m² in postoperative period ($p < 0,0001$). There were not significant differences in blood pressure. Regarding metabolic parameters a significant difference was observed: Glycemia (mg/dl) 149 ± 58 vs 101 ± 21 ($p < 0,0001$); HbA1c $8,14 \pm 2,5\%$ vs $5,86 \pm 1,09$ ($p < 0,0001$); Triglycerides (TG) (mg/dl) 159 ± 68 vs 106 ± 60 ($p < 0,0001$); TG/HDL: $4,11 \pm 2$ vs $2,14 \pm 1,45$ ($p < 0,0001$); HDL(mg/dl) 41 ± 10 vs 53 ± 13 ($p < 0,0001$); no HDL(mg/dl) 140 ± 39 vs 122 ± 37 ($p 0,007$); uric acid $5,44 \pm 1,47$ vs $4,74 \pm 1,04$ ($p 0,0004$). There was significant correlation between time in months after surgery and TG ($r 0,27$ $p 0,04$) TG/HDL ($r 0,34$ $p 0,01$) levels. Statistical significant reduction was found in favor of OAGB vs LRYGB regard of BMI ($p 0,02$), TG ($p 0,01$), total cholesterol ($p 0,01$) y no HDL ($p 0,03$). Hypoglycemia was found in 3,5% post BC and anemia in 14,28%

Conclusion: As seen by other authors we found enhancement with BC in BMI, metabolic parameters and less use of medications. There were not significant differences in blood pressure levels

Disclosure of Interest: None Declared

ICE2020-1159

IMPACT OF BARIATRIC SURGERY ON BONE MINERAL METABOLISM IN PATIENTS WITH OBESITY AND TYPE 2 DIABETES MELLITUS

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Introduction: Bariatric surgery (BC) is a highly effective treatment for patients with type 2 diabetes and obesity but it has negative effects on bone mineral metabolism

Objectives: To evaluate bone mineral metabolism changes after BC in a diabetic and obese population

Methods: 56 patients were evaluated preoperative and postoperative (BC). Personal background, anthropometric measurements, body mass index (BMI), calcium, phosphorus, magnesium (mg/dl), creatinine, ionogram in plasma (mEq/L) and 24hs urine (mg/24hs, mEq/ 24hs), albumin (gr/dl), 25 OH vitamin D (ng/ml) were analyzed. **Statistical analysis:** Student's and Mann-Whitney-Wilcoxon tests were applied. Spearman correlation coefficient was calculated.

Values expressed in average \pm standard deviation. Significant $p < 0,05$

Results: The sample consisted of 35 female and 21 male with a mean age of $52 \pm 9,6$. One anastomosis gastric bypass (OAGB) was performed in 29 patients and laparoscopic Roux-en-Y gastric bypass (LRYGB) in 27. Pre and postoperative data was analyzed. Postoperative data with a time lapse between 3 to 79 months, average of 31.6. There was statistical significant reduction between pre BC and post BC levels for the following variables: calcemia $9,36 \pm 0,42$ vs $9,12 \pm 0,47$ ($p 0,02$); magnesemia $1,96 \pm 0,18$ vs $1,92 \pm 0,18$ ($p 0,03$); creatinine $0,81 \pm 0,23$ vs $0,77 \pm 0,23$ ($p 0,003$); natremia $139 \pm 2,62$ vs $138 \pm 2,93$ ($p 0,02$); and a statistical significant increased between pre BC and post BC levels for the following: phosphatemia $3,66 \pm 0,62$ vs $4,02 \pm 0,57$ ($p 0,002$); phosphaturia 48 ± 28 vs 70 ± 30 ($p 0,002$); creatininuria 1251 ± 422 vs 1456 ± 473 ($p 0,03$); vitamin D $23 \pm 8,8$ vs 29 ± 11 ($p 0,01$). We found negative significant correlation between time in months after surgery and urinary volume ($r -0,35$ $p 0,05$). Urinary calcium significantly differs ($p=0,03$) depending on the type of BC in favor of OAGB. Negative significant correlation was found between BMI and magnesemia $r -0,39$ ($p 0,03$)

Conclusion: The negative effects on bone mineral metabolism and BC are multifactorial, the decrease in calcemia, magnesemia, natremia and calciuria could be explained by the lower intestinal absorption after BC. Less urinary volume in post BC group can be attributed to less gastric volume. Knowing these consequences allows us to keep working in a better follow up treatment

Disclosure of Interest: None Declared

ICE2020-1170

IMPACT OF THE DIABETES MELLITUS IN THE CLINICAL AND RADIOLOGICAL PRESENTATION OF TUBERCULOSIS IN PATIENTS HOSPITALIZED IN 2 CENTERS IN PARAGUAY

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Introduction: Diabetes mellitus (DM) is a risk factor for the development of tuberculosis (TB); modifies the clinical characteristics and radiological involvement of TB, in different ways, in different populations.

Objectives: To establish the impact of the diagnosis of DM in the forms of clinical and radiological presentation of patients hospitalized with TB in 2 reference hospitals in Paraguay.

Methods: A cases controls study of patients with TB with and without DM admitted to 2 pneumology services, belonging to the Hospital Clinics and the National Institute of Respiratory Diseases, between the years 2015 and 2019.

Results: A total of 105 patients with the diagnosis of TB were included, of which 70.48% were male, whose mean age was 45.67 ± 17.38 years; 39% of them had DM. All with type 2 DM. The average blood glucose level of this group was 223.19 ± 112.67 mg/dl, with an average HbA1C value $10.26 \pm 2.94\%$ and an average BMI of 24.51 Kg/m². About pre-admission treatment, 58.5% of the patients were in treatment with oral antidiabetics, 21.9% with insulin and 14.6% were without treatment. Patients with DM had less extrapulmonary involvement than patients without DM 17% vs. 34% (OR: 0.36; p: 0.046). Bilateral and multilobar pulmonary involvement were not different between patients with DM vs. those without DM. The caverns were slightly more frequent in patients with DM than in those without DM 51.21% vs. 39% (OR: 1.63 p: 0.2) and especially those of lower location 43% vs. 16% (OR: 3.93; p: 0.002).

Conclusion: In our experience, patients with DM compared to patients without DM had less frequently extrapulmonary forms of TB and the pulmonary extension was not very different. The frequency of the caverns was slightly more frequent in patients with DM and especially in lower locations. The general practitioner must be alert to epidemiological and clinical variations and the scientific community continue their research to better understand the coexistence of these diseases.

Disclosure of Interest: None Declared

PREVALENCE OF MALNUTRITION IN DIABETIC AND NON-DIABETIC HOSPITALIZED PATIENTS

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Introduction: Malnutrition is a major problem in hospitalized patients, and is associated with increased morbidity and mortality, increased length of hospitalization and increased healthcare costs. A higher prevalence of malnutrition have been reported in patients with diabetes.

Objectives: The objective of the study was to assess the prevalence of malnutrition in diabetic and non-diabetic patients admitted in our Hospital.

Methods: We conducted a cross-sectional study among 82 adult patients admitted in our hospital during the period from July to August of 2019. Patients were classified as (1) well-nourished (WN), (2) mildly/moderately malnourished or being at risk malnutrition (MMN) or (3) malnourished or severely malnourished (SM) according to Subjective Global Assessment (SGA) and Mini Nutritional Assessment (MNA) for patients older than 65 years .

Results: The mean age of the population was 53.3 years (range 18-88). 58.5% were males. The average length of stay was 25 days (range, 2-185). Half (51.6 %) had BMI ≥ 25 kg/m², with 33% overweight and 18,6% obese. 19.5% had diagnosis of diabetes, 50% of them had diabetic retinopathy (DR), 43.7% diabetic nephropathy (DN) and 6.3% diabetic foot ulcers. Obesity was significantly more frequent in patient with diabetes ($p=0,0006$). In non-diabetic patients neoplasia and in diabetics surgical procedures were the most common reasons for hospital admission. Using SGA and MNA, 20.3% ($n=13$) and 58.8% ($n=10$), respectively, of the patients were classified at MM; and 3.1% ($n = 2$) and no patient, respectively, were assessed as SM. The prevalence of malnutrition (MMN and SM) was 30.5% in the total of patients and of 18.8% in those with diabetes. There was no significant association between the days of hospitalization and malnutrition ($p=0.35$), nor between the presence of diabetes and malnutrition ($p=0.17$). Diabetic patients with MMN where younger and with longer duration of diabetes. 50% of patients with DN had MMN, while only 14.3% of those with DR.

Conclusion: We found that one third of the inpatients are malnourished. Diabetes was not associated with higher rates of malnutrition, maybe due to small sample size. Patients with longer duration of diabetes should be monitored for malnutrition during hospitalization. More studies are warranted to assess nutritional status in inpatients and diabetics patients. The use of subjective scales (SGA and MNA) at the time of hospital admission can be a useful tool for nutritional assessment in inpatients.

Disclosure of Interest: None Declared

ICE2020-1174

GLOBAL ANALYSIS OF OBESITY AND PHYSICAL ACTIVITY RATES AND THEIR RELATION TO DIABETES RISK

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Introduction: Type 2 diabetes (T2D) rates vary significantly across geographic regions. These differences are sometimes assumed to be driven entirely by differences in environmental exposures between populations. However, there is limited data that support this view.

Objectives: Reanalyze publicly available data to unravel the relative contribution of obesity and insufficient physical activity (IPA) towards diabetes risk across different populations.

Methods: We used estimates from Non-Communicable Disease Risk Factor Collaboration (NCD-RisC) on rates and trends of diabetes (1975-2014) and obesity (1975-2016), in 200 countries. IPA rates were based on 2016 estimates across 168 countries in 2016. Countries were categorized into 9 regions according to NCD-RisC definition. Trends of obesity and diabetes were assessed for each region. Region-specific correlation of diabetes with obesity and IPA was assessed using Pearson correlation test. Joint effects of obesity and IPA on diabetes risk were assessed for 163 countries. All analyses were sex-specific.

Results: From 1975 to 2016, obesity rates increased across all populations, with the largest increases in rates observed in Oceania (men, 22.7%; women, 19.6%) and Central Asia Middle East and North Africa (CAMENA) (men, 17.5%; women, 9%) regions. Additionally, these two regions had the strongest correlation of obesity and diabetes in men (Oceania, $R^2=0.83$, $P<0.001$; CAMENA, $R^2 = 0.75$, $P<0.001$) and women (Oceania, $R^2 = 0.7$, $P<0.001$; CAMENA, $R^2 = 0.67$, $P<0.001$). On the other hand, other regions, including Latin America and Caribbean and Central and Eastern Europe, demonstrated a lack of correlation between obesity and diabetes. Similarly, the association of IPA with diabetes was not homogeneous amongst populations. Countries in various regions had very similar rates of diabetes, despite falling on opposite ends of IPA spectrum. The overall joint effect of obesity and IPA highlighted the larger impact of obesity on diabetes risk across populations (Figure 1). Despite that, some countries in various regions deviate from this overall observation, particularly in South Asia and High-income Western countries. Sex differences were observed across all our analyses.

Image:

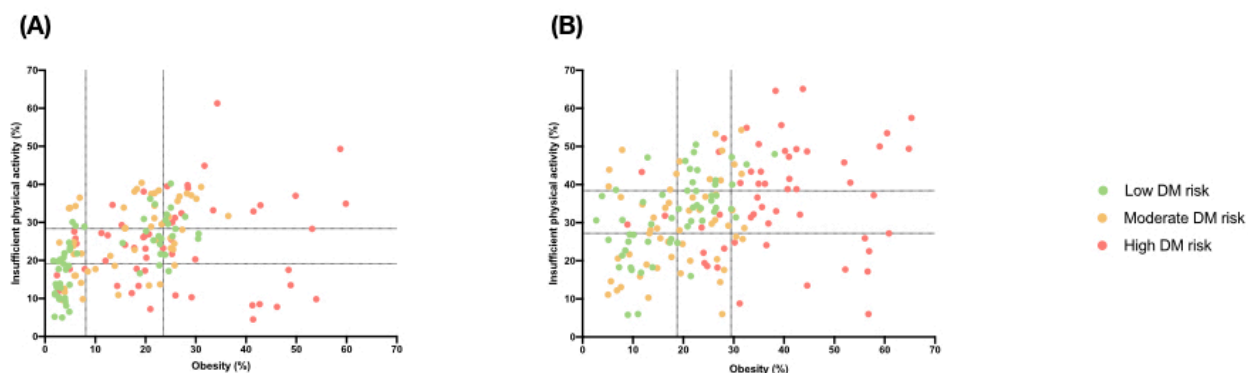


Figure 1. The joint relationship of obesity and insufficient physical activity (IPA) with diabetes risk in (A) males and (B) females. Diabetes and obesity rates were estimated by Non-Communicable Disease Risk Collaboration (NCD-RisC) group in 2014 and 2016, respectively. IPA rates were estimated by World Health Organization (WHO) in 2016. Scattergraphs represent distribution of age-standardized prevalence rates of obesity (x-axis) against IPA rates in 163 countries. Estimates of obesity, IPA, and diabetes were each grouped into three quantiles. Countries were color-coded based on diabetes rates quantiles; Low (green), Moderate (orange), and High (red) risk. Dotted vertical and horizontal lines represent the first and second quantiles of obesity and IPA rates, respectively.

Conclusion: These data indicate that different populations, while experiencing similar environmental shifts, are apparently differentially subject to diabetes risk. Sex-related differences observed suggest that men and women are either subject to different risk factor exposures or have different responses to them.

Disclosure of Interest: None Declared

ICE2020-1198

STRATIFICATION OF THE RISK OF DEVELOPMENT OF DIABETES MELLITUS TYPE 2 IN RIBEIRINHOS RESIDENTS IN THE BRAZILIAN AMAZON.

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Introduction: Type 2 diabetes mellitus (DM2) is an increasingly common public health problem in several countries around the world. Tracking individuals at risk of developing DM2 is important to plan health actions focusing on reducing harm and promoting a better quality of life.

Objectives: To identify the risk of developing type 2 diabetes mellitus in individuals living in riverside communities on the Tapajós and Cupari rivers, Pará, Brazil.

Methods: Cross-sectional, descriptive study composed of a sample of 270 riverside residents attended during voluntary health expedition. During the consultations, they were interviewed through a questionnaire composed of socioeconomic variables and, later, they responded to FINDRISC. This last instrument determines the risk of developing DM2 in the next 10 years and categorizes individuals at low risk (score <7), slightly elevated risk (scores between 7 and 11), moderate risk (scores between 12 and 14), high risk (scores between 15 and 20) and very high risk (score > 20). The analysis was descriptive and the variables expressed in simple frequencies.

Results: The global sample was composed predominantly of female individuals (54.8%), under the age of 45 years (53.7%), Catholics (55.1%), of mixed race (79.2%), married (44%), with a family income of up to 1 minimum wage (83.3%) and who studied on average 4 to 7 years (28.8%). Regarding the risk of developing DM2, most individuals scored in the slightly high-risk range (40.7%). Individuals with moderate, high and very high risk corresponded to 26.3% with rates of 15.5%, 9.3% and 1.5% respectively; while low risk was identified in 33% of patients.

Conclusion: Despite the cultural barrier present in riverside communities, FINDRISC proved to be an easy to use and low-cost instrument. Approximately 1 in 3 individuals in the sample was concentrated in the low risk range. This data suggests that actions in the scope of primary care, including risk stratification, periodic measurement of capillary blood glucose and health education aimed at modifiable risk factors established for DM2 should be considered in routine consultations. Socioeconomic indicators show that interventions of this nature are particularly special in remote locations and in situations of social vulnerability, as are the riverside populations of northern Brazil.

Disclosure of Interest: None Declared

ICE2020-1208

RISK OF HEPATIC CIRRHOSIS IN PATIENTS WITH NON-ALCOHOLIC HEPATIC STEATOSIS WITH AND WITHOUT DYSGLUCEMIA OF AN OBESITY UNIT

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is an entity of increasing interest related to obesity and other metabolic disorders. Liver cirrhosis is one of the complications of this disease. Risk assessment is important and can be done with the NAFLD score.

Objectives: To assess the risk of developing liver cirrhosis in obese patients with liver steatosis with and without dysglycemia.

Methods: Observational, analytical, cross-sectional design, where all the patients with hepatic steatosis diagnosed by ultrasound who attended an obesity unit were included. The risk of cirrhosis was assessed by the NAFLD fibrosis score.

Results: A total of 155 patients with the diagnosis of NAFLD were included, of whom 69% were female, whose mean age was 43.5 ± 12.14 years, with a mean weight of 128.99 ± 33.07 kg and an average BMI of 47.01 ± 9.21 kg / m². In this group of patients, 24.52% presented the diagnosis of DM2, 42.58% Pre DM and the rest were normoglycemic. Regarding the risk of developing liver cirrhosis, among the patients with diabetes 32.43% had a high risk, 18.92% a low risk and 48.65% an undetermined risk; in the group with Pre DM2, 41.53% presented high risk, 13.85% low risk and 44.62% undetermined risk; in the group of normoglycemic people, 11.76% presented high risk, 37.25% low risk and 50.98% indeterminate. A positive association was found between the presence of dysglycemia (Pre and / or DM2) and the high risk of developing liver cirrhosis compared to normoglycemic patients (OR: 4.45 CI: 1.73 - 11.41 p: 0, 0001)

Conclusion: In this study of patients with significant obesity, the group of patients with dysglycemia (Pre DM and / or DM2) had a higher risk of developing cirrhosis than patients with normoglycemia.

Disclosure of Interest: None Declared

ICE2020-1222

FACTORS ASSOCIATED WITH TYPE 2 DIABETES MELLITUS IN LATINO ADULTS IN THE UNITED STATES

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Introduction: Type 2 diabetes mellitus (T2DM) is more prevalent in Hispanics compared with non-Hispanic whites; however, the burden of factors associated with T2DM in Hispanic adults is incompletely described.

Objectives: The objectives were to describe factors associated with prevalent T2DM in Hispanics and to determine differences by gender.

Methods: In Sangre Por Salud, a prospective cohort of 3733 self-identified Hispanic adults in Phoenix AZ, we conducted a nested case-control study of T2DM using data at study enrollment. Participants with prevalent T2DM (cases) were matched 1:1 by age (± 5 yrs) and gender to T2DM-free participants (controls). The associations of lifestyle and clinical factors with odds of T2DM were analyzed using logistic regression models.

Results: Among 434 case control pairs, 65% were women. Compared with controls, participants with T2DM had lower consumption of alcohol (9% vs 4%) and potato based foods (20% vs 13%) with stronger associations in men. The consumption of vegetables (48% vs 51%) and frequency of exercise (12% vs 9%) was not associated with T2DM. Compared with controls, men and women with T2DM had higher prevalence of hyperlipidemia (26% vs 52%); higher prevalence of hypertension (29% vs 45%) and obesity (43% vs 55%) was found in women. In models adjusted for age and gender, the population attributable risk for T2DM was highest for obesity (21%). (Table)

Image:

Factors associated with prevalent T2DM (odds ratio [95% confidence interval])

| | T2DM cases vs controls | | Population Attributable Risk (%) (models adjusted for age and gender) |
|--|--------------------------------|--------------------------------|--|
| | Men n=154 pairs | Women n=280 pairs | |
| <i>Lifestyle factors, yes vs no</i> | | | |
| Alcohol ≥2 times/week | 0.41 (0.18–0.96)* | 0.45 (0.16–1.27) ^{NS} | |
| Potato based foods ≥4 times/week | 0.40 (0.17–0.99)* | 0.72 (0.43–1.21) ^{NS} | |
| Vegetables ≥4 times/week | 1.10 (0.64–1.89) ^{NS} | 1.14 (0.76–1.69) ^{NS} | |
| Exercise ≥5 times/week | 0.49 (0.21–1.15) ^{NS} | 0.94 (0.50–1.74) ^{NS} | |
| <i>Clinical factors, yes vs no</i> | | | |
| Hyperlipidemia | 3.48 (2.04–5.93) [#] | 2.78 (1.89–4.09) [#] | 10.2% |
| Hypertension | 1.44 (0.86–2.42) ^{NS} | 2.53 (1.71–3.72) [#] | 9.2% |
| Obesity | 1.47 (0.93–2.32) ^{NS} | 1.71 (1.22–2.39) [#] | 21.2% |

*p<.05; #p<.01; ^{NS}not significant

Conclusion: Modifiable lifestyle factors are associated with prevalent T2DM, especially in men. Future studies will examine lifestyle changes following a diagnosis of T2DM and if these changes can improve clinical factors.

Disclosure of Interest: None Declared

ICE2020-1231

INHIBITION OF VOLTAGE-GATED K⁺ CHANNELS MEDIATES DOCOSAHEXAENOIC ACID-STIMULATED INSULIN SECRETION IN RAT PANCREATIC B-CELLS

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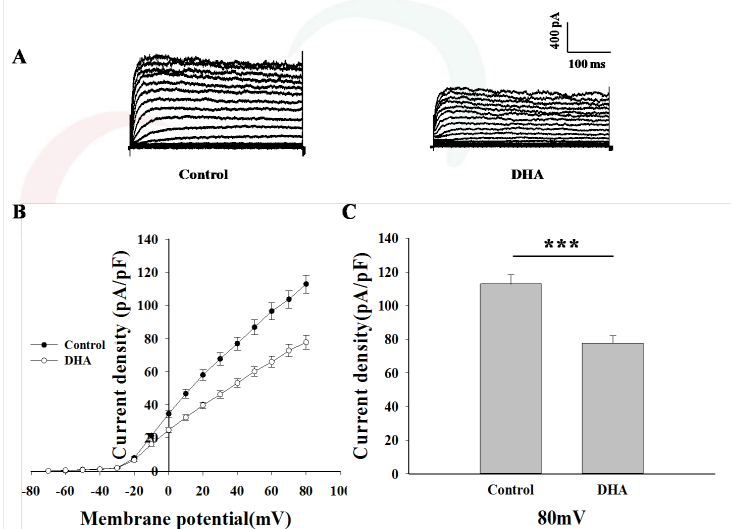
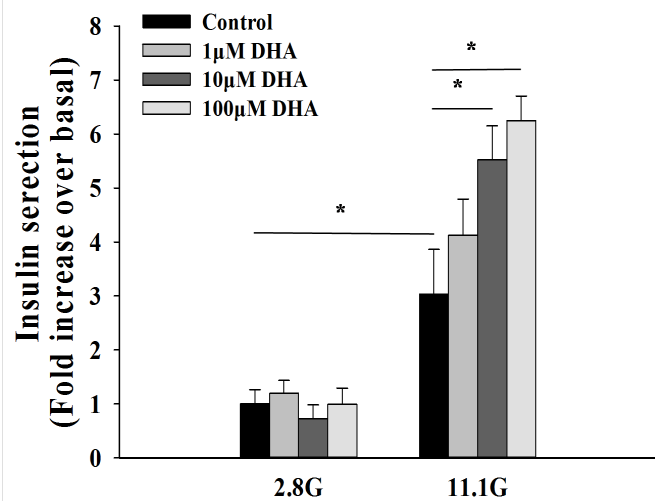
Introduction: Pancreatic β -cells are stimulus-secretion coupling cells, and insulin secretion from β -cells is regulated by a series of electrogenic events. During this process, K_v channels provide a negative regulatory effect on insulin release. Docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid, plays an important role in regulating glucose metabolism. However, the potential mechanism of DHA-modulated insulin secretion is still largely unknown.

Objectives: The aim of this study was to investigate the effect of DHA on insulin secretion and the underlying ion channels mechanism in rat pancreatic β -cells.

Methods: We performed insulin secretion experiments, calcium-imaging method and patch-clamp technology to gain insight into the effect of DHA on insulin secretion and the underlying ion channel mechanisms.

Results: The insulin secretion results illustrated that DHA promoted insulin secretion in a glucose-dependent manner. Calcium-imaging analysis indicated that DHA elevated intracellular Ca^{2+} concentration. Using patch-clamp technique, we found that DHA prolonged action potential duration (APD) and significantly inhibited voltage-dependent K^+ (K_v) channels, but did not act directly on voltage-gated Ca^{2+} channels. Further, our data demonstrate that the insulinotropic effect of DHA was mediated by G protein-coupled receptor 40 (GPR40) as well as adenylyl cyclase (AC) /cyclic adenosine monophosphate (cAMP) /phospholipase-C (PLC) signaling pathway.

Image:



Conclusion: These findings illustrate that K_v channels play a vital role in DHA-augmented insulin secretion through a mechanism whereby DHA blocks K_v channels via GPR40 and AC/cAMP/PLC signaling pathway in rat pancreatic β -cells.

Disclosure of Interest: None Declared

ICE2021-1264

EFFECT OF INTERMITTENT FASTING ON DIABETES MELLITUS IN PATIENTS WITH CARDIOVASCULAR DISEASES AND METABOLIC SYNDROME

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Introduction: Correction of eating behavior is one of the main ways to treat patients with type 2 diabetes mellitus (T2D). A common method is calorie restriction (CR), but this method requires daily restriction and patient compliance is low. Recently, the method of interval fasting (IF), which has several variations, is rapidly gaining popularity. This method allows patients to choose the most acceptable variant of fasting. There is currently no detailed information on the effects of IF on safety in patients with diabetes, metabolic syndrome (MS) and cardiovascular disease (CVD).

Objectives: To analyze and summarize available research data on the effects of IF on glycemic control, glucose, risk of hypoglycemia, body mass index (BMI), body fat, safety of IF in patients with T2D, metabolic syndrome and cardiovascular disease, over 18 years of age.

Methods: Systematic review was done. Electronic databases (MEDLINE, Web of Science, Scopus and Google Scholar) have been searched for the last 5 years (2015-2020) in English, Ukrainian, Russian and Bulgarian languages. Tools used in the analysis were the PRISMA protocol, JADAD scale, ROBINS-I and RoB 2 tools.

Results: Twenty-eight original articles were included in the analysis. All studies had a low risk of bias according to ROBINS-I and RoB 2 tools and from 2 to 6 points on the JADAD scale, and the data analyzed were statistically significant. Weight loss was found in 14 studies, 2 studies showed no serious changing in BMI. Reductions in Body fat — 2 studies; HbA1c- 2 studies; fasting glucose – 3 studies, were found. Three studies showed the same efficiency of IF and CR. A total of 8 studies indicated the safe use of various methods of interval fasting in patients with T2D. One study indicated an increase in the number of cases of hypoglycemia, but decreased significantly after therapeutic correction. Data on serious side effects and mortality were absent

Conclusion: IF is a safe and effective method for patient with T2D, CVD and MS to control glucose level, HbA1c and BMI. IF can be an alternate method of CR. Further long-term studies are needed to examine the effects of IF on mortality in patients with comorbid pathology.

Disclosure of Interest: None Declared

ICE2021-1265

THRIFTY-GENES POLYMORPHIC VARIANTS COMBINATION AND RISK OF DIABETES MELLITES

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Introduction: Identifying possible genetic factors combinations, which contribute to the development of diabetes mellitus, is highly important to work out an individualised prevention programmes.

Objectives: The aim of the study was to assess the possible association between different combinations of polymorphic variants of PPARG2(Pro12Ala), ADRB2 (Gln27Glu), ADRB2 (Agr16Gly), ADRB3 (Trp64Agr) and FABP2 (Thr54Ala) and risk of diabetes mellitus.

Methods: One hundred forty-two persons with mean age 37.1±5.1 y.o. without established cardiovascular disease and diabetes mellitus were included in the study. Blood pressure, body mass index, fat to muscular ratio (bioimpedance method, Body Composition Monitor BF511, Omron), blood lipids, glucose and HbA1c levels were assessed. Physical activity was assessed using «International Questionnaire on Physical Activity» (IPAQ) and pedometer (Walking style III, Omron). Genotyping of polymorphic sites of PPARG2(Pro12Ala), ADRB2 (Gln27Glu), ADRB2 (Agr16Gly), ADRB3 (Trp64Agr) and FABP2 (Thr54Ala) genes was done with real-time polymerase chain reaction. CFX Manager Software was used for alleles discrimination. FINDRISK calculator was used to assess risk of development of diabetes mellitus. Statistical processing of the obtained data was performed using the statistical package SPSS 17 (IBM).

Results: In studied population FINDRISK score varied from 0 to 30 and, in accordance with FINDRISK level, we divide the sample into quartiles. The first quartile is the group with a low FINDRISK from 0 to 6 (N1 = 35); the last quartile is the group with a high FINDRISK from 13 to 30 (N4 = 36); the FINDRISK median was 10. It was found out the odds ratio for high FINDRISK corresponds to 1.11 for PPARG2 (CC vs CG+GG); 1.32 for ADRB2 (CG vs CC+CG); 1.05 for ADRB2 (AG vs AA+AG); 2.0 for ADRB3 (TT vs CC) and 1.33 for FABP2 (GG vs AG+AA) (95% confidential interval). The odds ratio for combination of the polymorphic TC variant of the ADRB3 gene (Trp64Agr) and the GG variant of the FABP2 gene (Thr54Ala) in the groups with low level of FINFRISK was 2.33. Other combinations of genes and their polymorphic variants did not provide a reliable diagnostic criterion to predict FINDRISK.

Conclusion: Combination of the TC variant of the ADRB3 gene (Trp64Agr) and the AA variant of the ADRB2 gene (Agr16Gly) is reliable marker of a low level of FINDRISK.

Disclosure of Interest: None Declared

ICE2021-1267

EFFICACY AND SAFETY OF REMOGLIFLOZIN ADDED TO INSULIN WITH METFORMIN IN INDIAN T2DM PATIENTS

Anand Shankar*

Introduction: Other currently available SGLT2 inhibitors in India like canagliflozin, dapagliflozin and empagliflozin are highly priced. Remogliflozin which recently approved in India, demonstrated non-inferiority in achieving glycaemic goal and safety to existing SGLT2 inhibitor like dapagliflozin. Due to economical pricing as compare to other SGLT2i, remogliflozin gaining popularity in India.

Objectives: The aim of this prospective observational study was to evaluated the effect of 24 weeks of add-on remogliflozin (REMO) in Indian T2DM patients [A1C 7.5-10%] on stable insulin ± metformin (MET).

Methods: T2DM patients using insulin (bolus component < 30% of the total daily dose) with a MET (1000 to 2000 mg/day) were prescribed remogliflozin 100 mg BD. The primary efficacy end point was change in A1C from baseline and secondary end point was reduction in weight and insulin daily dose. Self-monitored blood glucose (SMBG) was performed using the patients' own BG meter, to detect hypoglycemia.

Results: In total, 108 patients received remogliflozin for 24 weeks. Baseline mean ± SD: age 58.4 ± 10.5 y; T2DM duration 5.9 ± 2.3 y; BMI 31.0 ± 6.7 kg/m²; Weight 93.7 ± 12.9 kg, A1C 8.2 ± 0.6%, FPG 156 ± 32.7 mg/dl, PPBG 231 ± 51.3 mg/dl. The overall changes in HbA1c, FPG, PPBG and body weight from baseline to EOT were 0.96% (p<0.001), 34.7 mg/dL (p<0.001), 59.3 mg/dL (p<0.001) and 1.37 kg (p<0.005), respectively. Insulin dose was significantly lower from baseline to EOT (-12.8±0.14 IU/D, p<0.001). Patients with <5 years duration of diabetes responded more (94.5%) compared to patients with a longer duration (5 years) of diabetes (85.2%). Despite the occurrence of hypoglycaemic episodes (18.5%), no episode was classified as severe and requiring assistance.

Conclusion: Long-term treatment with remogliflozin in insulin-treated Indian patients with T2DM is effective and there were no major or unexpected safety concerns with the combination. Body weight decreased over 24 weeks despite concomitant insulin therapy.

Disclosure of Interest: None Declared

ICE2021-1290

REAL-WORLD USE OF REMOGLIFLOZIN AS ADD-ON TO INSULIN THERAPY IN PATIENTS WITH TYPE 2 DIABETES

Ajay Sinha*

Introduction: While there are a number of randomized clinical trials (RCTs) that have shown improved clinical outcomes of remogliflozin as mono and add-on to oral therapy, there is paucity of real-world studies assessing similar outcomes as add-on to insulin therapy in type 2 diabetes (T2DM). Real-world studies (RWS) provide information on the effectiveness of treatment and since they have high generalizability, they add important information for clinicians in routine practice.

Objectives: The main objective of the study was to evaluate the efficacy and safety of remogliflozin as add on to stable insulin therapy in patients with type 2 diabetes mellitus

Methods: This 24 week retrospective cohort study examined data from a diabetes specific electronic medical record used in diabetes care settings in Patna to evaluate use of remogliflozin as add-on to insulin therapy under real-world conditions. Insulin dose adjustment aimed to achieve a self-monitored plasma glucose level $>70\text{mg/dL}$ and $\leq 130\text{mg/dL}$ without symptomatic hypoglycemia.

Results: A total of 92 patients [mean age 59.1 ± 8.1 years; mean BMI 26.2 ± 3.2 kg/m²; mean A1C 8.5 ± 0.7 %, mean insulin dose 38.7 ± 15.6 IU/day] who were prescribed remogliflozin 100 mg BD as add-on to insulin for at least 6 months between July 2019 and Feb 2020 were included. Furthermore, 32% of patients with suboptimal glycemic control (A1C $>7\%$) achieved a composite outcome consisting of improvement in A1C. Mean change in HbA1c at 6 months was $-1.01 \pm 1.12\%$ (95% confidence interval (CI): -1.20 ; -0.84) ($p < 0.001$). The mean change in fasting plasma glucose from baseline to end of treatment (LOCF method) was $17.03 (\pm 41.86)$ mg/dL (95% CI: -23.55 ; -10.52). Episodes of symptomatic hypoglycemia were reported by 22 patients (23.9%). Differences were found in: SBP -7.92 mmHg ($p < 0.0001$); DBP -3.67 mmHg ($p < 0.0001$); Weight -3.14 kg ($p < 0.0001$); BMI -1.07 kg/m² ($p < 0.0001$). There were 9 genital infections (9.8%, 3♂, 6♀, $p = 0.02$) and 3 urinary infections (3.3%); 1♂, 2♀ ($P = \text{NS}$).

Conclusion: Long-term treatment with remogliflozin in insulin-treated patients with T2DM is effective and there were no major or unexpected safety concerns with the combination. Body weight decreased over 24 weeks despite concomitant insulin therapy.

Disclosure of Interest: None Declared

Diabetes/Obesity/Dyslipidemia

ICE2021-1291

LONG TERM SAFETY AND EFFICACY OF SAROGLITAZAR ON DIABETIC DYSLIPIDEMIA WITH VERY HIGH TRIGLYCERIDE IN INDIAN SUBJECTS: REAL WORLD EVIDENCE

Amit K. Das*

Introduction: Diabetes and diabetic dyslipidemia with high triglycerides (TGs) are commonly associated. Saroglitazar is the first dual PPAR α/γ agonist approved in India for the management of diabetic dyslipidemia.

Objectives: The objective of this study was to evaluate the long-term safety and efficacy of Saroglitazar on diabetic dyslipidemia with very high triglyceride (>500 mg/dl) in real world clinical practice.

Methods: This is a real-world retrospective observational study. In this retrospective study, we identified 150 patients with diabetic dyslipidemia (type 2 diabetes) with triglycerides >500 mg/dL at baseline) and were treated with Saroglitazar 4 mg once daily and the follow-up data were available for 12 months after Saroglitazar treatment. At baseline, all patients were on stable dose of antidiabetic and statin therapy.

Results: Significant reduction of TG and LDL-cholesterol was observed from baseline to 12th weeks 669.93 ± 81.22 to 268.72 ± 82.32 mg/dl and from $167.68 \pm 10.$ to 118.88 ± 12 mg/dl ($p < 0.0001$ and < 0.001) respectively. The mean HbA1c was reduced from 8.02 ± 0.3 to $7.71 \pm 0.5\%$ (< 0.001) This reduction in lipid and glycemic parameters were continued till 52 weeks. At 52 weeks mean TG, LDL-cholesterol and HbA1c was reduced to 221.51 ± 61.81 mg/dl, 118.88 ± 12.16 mg/dl and $7.12 \pm 0.2\%$ ($p < 0.001$ for all). No major adverse event reported during the study period. CPK, liver enzymes and creatinine did not alter significantly.

Conclusion: The present study shows that Saroglitazar in addition to statins led to a significant improvement in all the lipid parameters. At 52 week there was a significant reduction in TG of 66.9%, LDL-C of 38.47%, total cholesterol of 44.84 % and non- HDL-C of 52.62 %. The addition of Saroglitazar in patients on existing baseline antidiabetic medications showed a significant 0.9% absolute reduction in HbA1c and significant improvement in fasting and post prandial plasma glucose. There were no serious adverse events or alteration in liver enzymes or serum creatinine and edema or weight gain reported in this study. Saroglitazar is a very effective therapeutic option in diabetic dyslipidemia with very high triglycerides level, not controlled by statins. It is very safe for long term use.

Disclosure of Interest: None Declared

ICE2021-1303

VITAMIN D DEFICIENCY AND ERECTILE DYSFUNCTION AMONG MEN WITH TYPE 2 DIABETES

Shahjada Selim*

Introduction: Background and aims: Several recent studies found out the association between vitamin D deficiency (VDD) and diabetes mellitus (DM). There is evidence of strong relationship of vitamin D deficiency with erectile dysfunction (ED) as well. Due to the growing epidemic of DM and VDD in Bangladesh, exploring the role of vitamin D in the prevention of DM is crucial. The morbidity of men with diabetes is also becoming more increasingly recognized which has been taken to have association again with VDD.

Objectives: Thus, the aim of this study was to determine the association between vitamin D status and ED Bangladeshi adult men with diabetes.

Methods: The nested case-control study included 2860 ED cases (between 30 to 69 years) with diabetes and 1195 age-sex matched controls with diabetes. Study subjects were recruited from six diabetes care centers of six administrative divisional cities in Bangladesh. Socio demographic, personal and family information were collected by face to face interview and disease specific data were recorded from the patient's record book. Fasting blood samples were collected, and serum levels of vitamin D, glucose, and free testosterone were measured. Body weight, height, waist circumference, hip circumference and blood pressure measurements were also recorded.

Results: The diabetes patients with ED has more severe vitamin D deficiency [(25 OH)D <10 ng/mL] than the controls (12% and 41%, respectively). The multivariate logistic regression analysis found that vitamin D deficiency [25(OH)D <20 ng/mL] to be associated with ED [OR 6.9 (95% CI: 2.9–15.8, p <0.001)]. Vitamin D level has positive linear association with glycemic control [OR 2.3 (95% CI: 1.7–5.9, p 0.003)] and with ED [3.6 (95% CI: 2.2–7.7, p 0.001)].

Conclusion: Vitamin D deficiency is an independent risk factor of ED in men with DM and severity of ED is linearly associated with the deficiency of vitamin D.

Disclosure of Interest: None Declared

ICE2021-1311

RELATIONSHIP BETWEEN BODY MASS INDEX AND 25-HYDROXYVITAMIN D IN MALE WITH TYPE 2 DIABETES

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Introduction: Although many therapeutic options are available, the increasing number of patients with diabetes and obesity has raised the need for innovative approaches to prevent the complications of metabolic disorders. The cluster of abnormal metabolic markers: hypertension, insulin resistance, proinflammatory processes, dyslipidemia, and vitamin D deficiency in patients with type 2 diabetes. Vitamin D status is inversely associated with the prevalence of obesity. The aim of this study was detect 25-hydroxyvitamin D level in male with type 2 diabetes depending on body mass index (BMI).

Objectives: A total of 62 male with type 2 diabetes have been examined and divided into IV groups according to their BMI: I group – 16 male with normal body weight (BMI 18.5-24.9 kg/m²), II group – 15 male with obesity class I (BMI 30.0-34.9 kg/m²), III group – 16 male with obesity class II (BMI 35.0-39.9 kg/m²) and IV group – 15 male with obesity class III (BMI ≥40 kg/m²). The participants were on average 65.8±8.4 years, type 2 diabetes duration of 8.3±5.2 years, mean value of glycated hemoglobin (HbA_{1c}) - 7.1±1.3%.

Methods: BMI was calculated by a ratio of body weight (in kilograms) and square of height (in meters), expressed in kg/m². Serum level of 25(OH)D was detected by electrochemiluminescent method (Roche Diagnostics, Germany) and cobas test system.

Results: Analysis of 25(OH)D level depending on BMI showed revealed the highest level 25(OH)D in male with normal body weight (30.2±6.2 ng/mL), while the lowest level were in male group II (20.6±10.3 ng/mL), group III (18.4±11.3 ng/mL), and group IV (15.3 ±2.4 ng/mL). Male with type 2 diabetes of group with normal body weight have a higher vitamin D level than patients with obesity of class III (30.2±6.2 vs 15.3±2.4; p=0.004). The highest correlation between the 25(OH)D levels and BMI was observed in patients with obesity class III (r=-0.22; p=0.0002).

Conclusion: In male with type 2 diabetes and obesity were detected significant influence BMI on the vitamin D. Vitamin D deficiency was found in 74.2% of male with type 2 diabetes and normal levels in 25.8%. 25(OH) D levels were significantly lower in men with obesity of class I (23.60±10.24 ng/ml) and obesity of class II (22.38±10.34 ng/ml), compared with patients who had normal body weight (29.8 ±6.2 ng/ml). The vitamin D deficiency negatively influenced obesity in male with type 2 diabetes.

Disclosure of Interest: None Declared

ICE2021-1320

THE RELATIONSHIP BETWEEN CARDIOVASCULAR AUTONOMIC NEUROPATHY AND BRAIN-DERIVED NEUROTROPHIC FACTOR IN PATIENTS WITH NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS

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Introduction: Cardiovascular autonomic neuropathy (CAN) is a serious risk factor for cardiovascular morbidity and mortality in patients with diabetes mellitus (DM) and prediabetes. On the other hand, gene brain-derived neurotrophic factor (*BDNF*) promotes synthesis of nerve growth factor. Degeneration of autonomic nerves is a common feature of autonomic neuropathy. However, an association between CAN and protein *BDNF* in newly diagnosed patients with DM type 2 was not fully investigated.

Objectives: The aim of this study was to investigate the relationship of CAN and gene encoding *BDNF* in patients with newly diagnosed type 2 DM.

Methods: We examined 52 patients with newly diagnosed type 2 DM, 16 males and 36 females (aged 60,9±1,55 years, HbA1c – 7,77±0,18 %) (data are presented everywhere as mean±SEM). All patients were performed cardiovascular autonomic reflex tests (CARTs) by Ewing and real-time PCR analysis for quantitative evaluation of *BDNF* gene. The diagnosis of CAN was confirmed in patients with 2 positive tests. The statistical analysis was performed using SPSS statistical package version 23.0 for Windows.

Results: CAN was diagnosed in 76,9 % patients. We found negative correlation between levels of *BDNF* gene and the total score of CARTs, ($r = -0,003$, $p < 0,05$), and positive correlation with presence CAN and *BDNF* gene in newly diagnosed type 2 DM ($r = 0,01$, $p < 0,05$).

Conclusion: We found some relationship between the presence of CAN, total score of CARTs and *BDNF* gene which could suggest the possible role of production of this protein in the development of CAN in patients with newly diagnosed type 2 DM.

Disclosure of Interest: None Declared

ICE2021-1321

HEME OXYGENASE 1 INDUCTION ALLEVIATES HEPATIC INSULIN RESISTANCE IN MALE WISTAR RATS

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Introduction: As the pandemic of obesity spreads, non-alcoholic fatty liver disease (NAFLD) has become one of the most prevalent liver diseases worldwide both in adults and children. NAFLD is the hepatic component of the metabolic syndrome and therefore is associated with the development of type 2 diabetes and cardiovascular disease. In our laboratory we focus on the heme oxygenase-1 (HO-1) system as a possible therapeutic target based on its antioxidant and cytoprotective activities.

Objectives: The main goal of the present study was to evaluate the effects of HO-1 induction in systemic and hepatic parameters of insulin resistance in an animal model of the disease generated by the administration of a sucrose rich diet (SRD).

Methods: Male Wistar rats were randomly distributed into control (C) and SRD groups (30% sucrose in the drinking water, for 12 weeks). Hemin treatment was administered for the last 2 weeks (15mg/kg/ip every 48hs, H and SRD+H groups).

Results: At the end of the treatments, liver HO-1 induction was confirmed after hemin administration via western blot. Animals of the SRD group presented hypertriglyceridemia ($p < 0.001$ vs. C), an effect that was significantly attenuated by hemin treatment ($p < 0.001$ vs. SRD, $p < 0.05$ vs. C). SRD treated rats showed lower insulin sensitivity than controls, as assessed by an insulin tolerance test (K_{ITT} , $p < 0.0001$ vs. C) but K_{ITT} was not affected by hemin treatment. Results from a pyruvate tolerance test, performed to determine hepatic insulin resistance showed an increased glucose output in SRD treated animals ($p < 0.05$ vs. C). In agreement, protein levels of PEPCK, a gluconeogenic enzyme, were also increased in this group ($p < 0.05$ vs. C). Insulin induced AKT phosphorylation (1IU/kg ip) was significantly decreased in the SRD group ($p < 0.001$ vs. C). Hemin treatment corrected all these parameters ($p < 0.05$ vs. SRD). Both mRNA and protein levels of PPARalpha were increased in the SRD+H group ($p < 0.001$ vs. C and $p < 0.05$ vs. SRD).

Conclusion: In summary, hemin treatment of IR-rats is associated with an improvement in insulin sensitivity in the liver, and a greater oxidation of fatty acids, while no changes in systemic insulin resistance were detected.

Disclosure of Interest: None Declared

Diabetes/Obesity/Dyslipidemia

ICE2021-1332

OBESITY, CARDIOVASCULAR RISK AND PHYSICAL ACTIVITY IN MEDICAL STUDENTS 3 UNIVERSITIES COLOMBIANAS- MULTICENTER STUDY.

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Introduction: A major change in public health that had the 21 century was the specter of increased body weight as a pandemic. In Colombia young and adultos one in three is overweight (37.7%), while one in five is obese (18.7%).

Objectives: Understanding that the central axis are cardiovascular and metabolic factors in child population and young adults that determine the development of fatal chronic diseases in adults, the research group has asObjective To assess the presence of obesity, cardiovascular risk and physical activity in medical students from 3 universities in Colombia, in order to know the local situation, and if applicable, in the future, designing strategies to promote healthy lifestyles in local and national university community

Methods: A multicenter cross-sectional descriptive study was performed. 3 Colombian universities participated. Data analysis Descriptive analysis for the variables of interest was performed. Classification and characterization were carried out using the values provided by the instruments.

Results: 233 medical students were selected. When analyzing BMI as many people were in a normal range with 75% followed by a 19, 9% classifies overweight. With respect to physical activity found that 46.7% of individuals carried a high level of physical activity, the 34, 2% perform moderate level of physical activity. Our study is consistent with the global reality, as the 19.9% are overweight. Physical activity where 58, 7% are sedentary evidenced by the time they remain sitting where 110 people remains between 6 and 10 hours.

Conclusion: Research on cardiovascular risk factors, obesity and metabolism increasingly focuses on start analyzing these variables since its inception, it is clearly necessary to continue being resolved on this issue and chart the future that leads to remission of this global pandemic.

Disclosure of Interest: None Declared

ICE2021-1340

LEPTIN IN VERY ELDERLY PATIENTS WITH CORONARY ARTERY DISEASE

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Introduction: Studies of leptin in old patients and centenarians are very few; therefore, we investigate leptin pathology in very elderly patients suffered from coronary artery disease (CAD).

Objectives: The main objective of this study was to determine the concentration of leptin and assess the relationships of this adipokine with obesity and a number of other pathological conditions in patients with coronary artery disease.

Methods: 110 very elderly patients were enrolled in the cross-sectional study: 90 patients with CAD – in the study group, 20 patients without CAD – in the control. Serum leptin concentrations were determined by enzyme-linked immunosorbent assay.

Results: Elevated serum leptin levels were found in 58%, low in 16.5%, and normal – in 25.5% of patients. In patients with CAD, mean leptin level reached 16.7 ng / ml, without CAD - 15.3 ng/ml ($p = 0.6$). Patients with heart failure had lower leptin levels ($p = 0.03$). In patients with obesity, mean leptin concentration was 28.5 ng/ml, without it – 12.2 ng/ml ($p < 0.001$). Significant correlation was found between leptin levels and body mass index ($p < 0.001$), and fat mass ($p = 0.000001$). Leptin levels positively correlated with serum total cholesterol ($p = 0.02$) and triglycerides ($p = 0.003$). In patients with diabetes mellitus higher leptin values were found (26.3 ng/ml vs 13.5 ng/ml in patients without diabetes; $p = < 0.001$). Significant correlation was found between serum leptin and glucose levels ($p < 0.001$). In patients with reduced leptin concentration lower values of bone mineral density were observed ($p < 0.001$).

Conclusion: Leptin pathology is common in very elderly patients (with or without coronary artery disease). Higher leptin levels are associated with various metabolic disorders. Lower leptin levels are associated with heart failure.

Disclosure of Interest: None Declared

ICE2021-1341

DIABETES MELLITUS IN VERY ELDERLY RUSSIAN PATIENTS WITH CORONARY ARTERY DISEASE

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Introduction: Conflicting data are available on prevalence and characteristics of diabetes mellitus in very elderly patients and centenarians; therefore, we evaluated features of this pathology in patients with coronary artery disease (CAD) over 75 years old.

Objectives: To study the characteristics of diabetes mellitus in patients with coronary artery disease over 75 years old and compare them with younger patients with coronary artery disease (CAD) and diabetes mellitus.

Methods: 580 patients with CAD over 75 years old were enrolled in the study on the prevalence of diabetes mellitus. 190 patients with CAD and diabetes mellitus were included in the cross-sectional study of the diabetes mellitus characteristics in old age: 153 very elderly patients (mean age – 85.7±4.7 years) – in the main group, 37 patients <70 years old – in the comparison group. To assess the condition of patients, standard clinical and laboratory methods for coronary artery disease and diabetes mellitus were used. 24-hour plasma glucose profile and hemoglobin A1c (HbA1c) level were evaluated in all patients with diabetes mellitus.

Results: Diabetes mellitus or impaired glucose tolerance was found in 22.2% of very elderly patients with CAD. Glucose levels in very elderly diabetic patients were lower at all time points than in patients <70 years old. The largest differences were recorded for the blood glucose concentration at 6 a.m. (p=0.00005). Glucosuria was registered in 29.7% of patients aged 51-69 years, while among elderly patients - in 11.1% (p=0.004). The mean levels of HbA1c were 7.3% and 8.7%, respectively (p=0.01). Correlation analysis revealed negative correlation between the age of patients and the glucose level (r= -0.4, p=0.00002 – for 6 AM glucose). The mean body mass index in very elderly patients was 30.8±5.8 kg/m², in patients <70 years old – 33.9±6.5 kg/m² (p=0.03). Significant differences between the groups of very elderly and younger patients were registered in terms of triglycerides (1.65 and 3.57 mmol/L, respectively, p<0.00001), HDL-cholesterol (1.16 and 0.87 mmol/L, respectively, p=0.03) and atherogenic index (3.45 and 6.73, respectively, p=0.002).

Conclusion: The study results indicate that diabetes mellitus is often diagnosed in very elderly patients with CAD. In very elderly patients, lower values of blood glucose, hemoglobin A1c and glucosuria are recorded, compared with younger patients with diabetes mellitus.

Disclosure of Interest: None Declared

ICE2021-1345

ALPHA-LINOLENIC ACID – RICH CHIA (*SALVIA HISPANICA* L.) SEED REDUCES BODY FAT EXPANSION AND PROMOTES MORPHOLOGICAL AND FUNCTIONAL CHANGES IN VISCERAL ADIPOSE TISSUE DEPOTS. STUDIES IN A DIET-INDUCED METABOLIC SYNDROME RAT MODEL.

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Introduction: Obesity has reached pandemic proportions worldwide. Since obesity, and more specifically visceral obesity, is strongly associated with metabolic dysregulation the increased obesity rates have had a deep impact on the prevalence patterns of the metabolic syndrome (MetS) and their associated complications. Changes in the food consumption patterns, are important strategies to address these major public health problems. *Salvia hispanica* L. (chia) seed is one of the richest botanical sources of α -linolenic acid (18:3 *n*-3). In previous studies we demonstrated that chia seed administration to sucrose-rich diet (SRD)- fed rats (an experimental model that mimics the phenotype of the human MetS) was able to reduce the increased visceral adiposity and improve the altered insulin sensitivity (IS) present in those animals.

Objectives: The aim of the present work was to analyze if changes in structural and/or metabolic characteristics of different visceral adipose tissue depots could be associated with the observed reduction of visceral adiposity.

Methods: Male Wistar rats were fed a SRD for 3 months. Half of the animals continued with the SRD until month 6, the other half was fed a SRD in which the fat source, corn oil (CO), was replaced by whole chia seed from month 3 to 6 (SRD+chia). Another group consumed a reference diet all the time. We analyzed: a- body weight gain (BW), body length, thoracic (TC) and abdominal circumference (AC), body mass index (BMI)- and energy intake; b- Carcass composition; c- visceral adiposity index (VAI), d. In epididymal (eAT) and retroperitoneal adipose tissues (rAT): fat cell size, number, distribution and lipid content in isolated adipocytes, total hormone sensitive lipase –tHSL- and tAKT protein mass levels (Western Blot), e-IS (euglycemic–hyperinsulinemic clamp) and serum levels of triglycerides, free fatty acids, glucose, insulin and leptin.

Results: The replacement of CO by chia seed in the SRD: a- significantly decreased ($p < 0.05$) the increased TC, AC, BMI, VAI and carcass fat content. BW and energy intake not change, b- reduced ($p < 0.05$) eAT and rAT fat cell sizes and lipid content, c-reduced ($p < 0.05$) the protein mass levels of tHSL. tAKT protein levels were similar in the three dietary groups. These changes were accompanied by a serum lipid-lowering effect, normalization of the IS, moderate hyperglycemia and hipoleptinemia.

Conclusion: These findings show that chia seeds could be a potential dietary strategy to prevent or improve visceral adiposity and related diseases.

Disclosure of Interest: None Declared

ICE2021-1349

SECONDARY CARE FOR DIABETES –DO WE MAKE ANY DIFFERENCE?

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Introduction: Diabetes is a growing challenge to National Health Services(NHS) in United Kingdom. Diabetes care in UK is managed in partnership between Primary and Secondary Care. Diabetes Health Care Specialists take a variety of referrals from primary care, requiring input in complex cases.

Objectives: The purpose of this study was to assess our care on the patients referred to our Adult Diabetes Clinic by using 9 care parameters(BMI, blood pressure, smoking, HbA1c, serum cholesterol, digital eye photography, laboratory urine microalbumin:creatinine ratio, serum creatinine, foot examination) and observing changes in three measurable targets(blood pressure, cholesterol, HbA1c) as set out in UK National Diabetes Audit 2017-2018, which reports on the quality of care for people with Diabetes in England.

Methods: In a retrospective longitudinal study we studied the source and reason for referrals to Secondary Care over 12 months. Each patient was followed over 18 month period and data was collected on documentation of 9 care processes. We analysed changes in three measurable targets and interventions involved.

Results: 446 patients were referred over the study period. 82.6% patients were referred by Primary Care Practitioners. Patients were referred for chiefly optimisation of glycaemia control(55%), with type 1 diabetes(35%), worsening complications (12%), Insulin or GLP-1 analogue start(0.5%) and young patients with type 2 diabetes(4.5%).

We evaluated care on 271 patients after excluding non-attenders. Demographic data was collected for age, gender and type of diabetes.

90% of patients had all 9 care processes documented. 72% patients had positive impact of our care in improvement of measurable targets. 74% of the patients were referred with HbA1c above the target(>7.5%) among which 52% showed an average improvement of 4.2% in their HbA1c. 72% patients were referred to at least one allied diabetes professional including diabetes nurses, dieticians, podiatry or hypertension nurse.

19% patients required referral to at least one other specialty clinic including renal, urology and bariatric clinics. 11% patients were referred to psychologist and structured diabetes education. 80% patient had changes made to their medications.

Conclusion: In times of economic austerity, with increasing numbers of diabetes patients, models of diabetes care are under great scrutiny to assess their impact. Our study proves the importance of secondary care, that patients with diabetes do require expert opinion and integrated approach to improve metabolic profiles.

Disclosure of Interest: None Declared

ICE2021-1351

DEHYDROEPIANDROSTERONE SUPPLEMENTATION IMPROVES CELLULAR AND BIOCHEMICAL MARKERS OF OBESITY

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Introduction: The obesity pandemic is a major worldwide health concern that predisposes to a higher risk of metabolic and cardiovascular diseases (CVD). In menopausal women the *decline of ovarian steroidogenesis* is associated to a high prevalence of CVD and obesity. Steroid hormones have a pivotal role in the regulation of angiogenesis. Vascularization of the adipose tissue modulates adipogenesis, lipids storage through a complex interplay not fully understood--.

According to intracrinology, DHEA can be converted into active sex steroids in peripheral tissues, avoiding their systemic exposure. DHEA supplementation is proposed as a low risk therapy for the prevention of postmenopausal diseases.

Objectives: The aim of this work was to study: a) the effect of DHEA administration on the metabolic profile and on oxidative stress markers related to obesity using using a murine model of obesity and hypoestrogenism; b) the role of DHEA on angiogenesis.

Methods: Ovariectomized Wistar rats feed with standard diet (ND) (4%fat) or high fat (HF) diet (27%fat) received daily injections of vehicle (C) or DHEA (1mg/kg.day) for 8 weeks. Angiogenic effect of DHEA was evaluated *in vitro* using primary cultures of endothelial cells (EC) and *ex vivo*, using the rat aortic ring assay.

Results: Caloric intake was 22% higher in HF vs ND groups, with an increase of body weight and adiposity index. No significative differences were detected in glucose, cholesterol, HDL-cholesterol and triglycerides levels (table). In contrast, DHEA induced a reduction of Cholesterol/HDL index in ND group, and of serum ROS (H2-DCFDA) both in NF and HF groups.

Nitric oxide production *ex vivo* by rat aortic rings was enhanced by DHEA in both ND and HF (130% and 138% vs C, $p < 0.01$), effect dependent on DHEA conversion to more active steroids since it was abolished in presence of a 3β -HSD inhibitor.

The angiogenic process requires ECs proliferation, migration and organization. In ECs *in vitro* treatment with DHEA increased cell proliferation (130% above C $p < 0.01$) and enhanced cell migration (15% above C $p < 0.05$). Indeed, DHEA stimulated capillary tube formation when ECs were cultured in a fibrin matrix. Consistently, *ex vivo* assays showed that DHEA (20 and 200nM) stimulated capillary tubes formation around aortic ring (8.5 vs 28.1, 29.2 μ m, C vs 20nM, 200nM-DHEA $p < 0.05$).

Image:

| | ND-Vehicle | ND-DHEA | HF-Vehicle | HF-DHEA |
|--------------------------|------------------|------------------|-------------------|---------------------------|
| Initial Weight (g) | 292.3 \pm 14.5 | 306.3 \pm 19.1 | 311.8 \pm 20.9 | 305.2 \pm 26.2 |
| Final Weight (g) | 334.7 \pm 17.1 | 342.6 \pm 15.7 | 368.9 \pm 25.5* | 366.1 \pm 24.5* |
| Adiposity index | 5.7 \pm 0.4 | 5.6 \pm 0.6 | 6.5 \pm 0.5* | 6.8 \pm 0.4* |
| Food intake (g/kg.day) | 53.7 \pm 5.1 | 52.9 \pm 5.6 | 41.8 \pm 4.0 | 42.0 \pm 6.0 |
| Caloric intake (Kcal/kg) | 166.5 \pm 15.8 | 164.1 \pm 17.4 | 200.8 \pm 19.2* | 201.4 \pm 28.8* |
| Liver (g) | 12.1 \pm 2.1 | 12.2 \pm 2.1 | 12.0 \pm 2.3 | 12.1 \pm 2.2 |
| Heart (g) | 1.1 \pm 0.1 | 1.2 \pm 0.1 | 1.2 \pm 0.1 | 1.2 \pm 0.1 |
| Abdominal White fat (g) | 10.0 \pm 1.1 | 11.2 \pm 1.3 | 18.1 \pm 3.3* | 17.6 \pm 3.1* |
| Brown fat (g) | 0.8 \pm 0.1 | 0.9 \pm 0.1 | 0.6 \pm 0.2 | 0.8 \pm 0.1 |
| Glucose (mg/dl) | 112 \pm 9 | 120 \pm 11 | 118 \pm 13 | 110 \pm 11 |
| Cholesterol (mg/dl) | 52 \pm 12 | 46 \pm 8 | 50 \pm 11 | 54 \pm 15 |
| HDL Cholesterol (mg/dl) | 11 \pm 3 | 13 \pm 3 | 9 \pm 1 | 12 \pm 4 |
| Cholesterol/HDL | 4.7 \pm 0.8 | 3.5 \pm 0.7* | 5.6 \pm 0.9 | 4.9 \pm 0.8 |
| Triglycerides (mg/dl) | 72 \pm 21 | 74 \pm 23 | 70 \pm 23 | 69 \pm 21 |
| ROS | 680 \pm 23 | 420 \pm 37* | 720 \pm 29 | 530 \pm 52 ^a |

Mean \pm SD of n=5 rats/group. * $p < 0,05$ vs. ND-Vehicle ^a $p < 0,05$ vs. HF Control

Conclusion: These results suggest that DHEA supplementation to hypoestrogenic rats would improve metabolic and inflammatory markers associated with obesity, and also promotes neovascularization.

Disclosure of Interest: None Declared

ICE2021-1355

RELATIONSHIP OF MICRONUTRIENT INTAKE AND NUTRITIONAL STATUS OF BRAZILIAN ADOLESCENTS (EVA-JF STUDY)

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Introduction: Food consumption in adolescence is marked by high intake of ultra-processed foods and low intake of fresh foods. Inadequate food consumption is an important risk factor for overweight and nutritional deficiencies, even in young age.

Objectives: To investigate the association between micronutrient intake and nutritional status of Brazilian adolescents

Methods: Total sample (n=794), from 14 to 18 years old, of both sexes, who participated in the EVA-JF survey, a cross-sectional study carried out in public schools of Brazilian medium-sized municipality, were evaluated. Food consumption was obtained through two 24-hour dietary recall assessments, in alternate days. To determine micronutrients intake, Table Brazilian Food Composition (TACO), United States Department of Agriculture (USDA) and food composition table proposed by the Brazilian Institute of Geography and Statistics (IBGE) were used. The usual intake of micronutrients was carried out using Multiple Source Method program (version 1.0.1), and later, adjusted by energy intake, according to residual adjustment method. To classify inadequate dietary intake of vitamins A, C, D, E, calcium, iron and zinc, *Estimative Average Requirement* (EAR) was used, and for sodium, *Tolerable Upper Intake Level* (UL), with cut off points recommended by Institute of Medicine. In addition, weight and height were collected and the body mass index (BMI) was calculated, classified according to the z-scores for age. Mann-Whitney tests and logistic regression were performed using the SPSS® software (version 20.0).

Results: The mean age was 16.1 ± 1.2 years, with 57.4% girls. Most had nutritional status considered adequate (69.8%) by BMI by age; however, there was a high prevalence of overweight (28.2%). For most of micronutrients (calcium, sodium, vitamins A, D and E), the intake averages were below the recommended values, in addition to having high prevalence of inadequate intake. It was found that only median calcium intake showed a difference according to nutritional status, with greater consumption among overweight adolescents (p <0.01). Overweight adolescents were 1.89 (OR) more likely to have adequate zinc consumption (β = 0.63; 95% CI = 1.19-2.99). No associations were found with other micronutrients.

Conclusion: There was a high inadequate dietary intake of micronutrients regardless of nutritional status among Brazilian adolescents in public schools. It is suggested that high consumption of ultra-processed foods may be contributing for this.

Disclosure of Interest: None Declared

Diabetes/Obesity/Dyslipidemia

ICE2021-1360

ASSESSMENT OF COVID-19 INFECTION IN PATIENTS WITH T2DM WHO WERE TAKING HYDROXYCHLOROQUINE AS AN GLUCOSE LOWERING DRUG

Ajay Sinha*

Introduction: Initial studies found Underlying uncontrolled diabetes mellitus can be considered risk factors for increased increased severity and mortality for COVID-19. HCQ already approved as anti diabetic and had established prophylactic action in COVID-19.

Objectives: To asses the Covid-19 infection in patients with T2DM who were taking Hydroxychloroquine as an glucose lowering drug

Methods: A total of 890 respondents who was taking HCQ as a glucose lowering therapy for more than 6 months, participated in this survey. All categorical variables were expressed as numbers and percentages using line charts and tables. This is a single-arm cohort study and does not involve a comparison of two groups or subgroup analysis. It was ensured that all respondents were undergone ophthalmology examination and present with no retinal abnormality.

Results: 780 respondents has confirmed that they didn't develop any symptoms like fever, sore throat, dry cough, Loss of smell and taste or breathlessness. 110 patients were tested positive in RT-PCR method. None of the patient experienced any episode of arrhythmia during HCQ treatment. Among this positive patients 33 (30%) belongs to containment zone as declared by the local authorities. Only 18 patients developed respiratory distressed 8 was managed at home quarantine and 10 were hospitalised. No death reported. Participants reported their glycemic parameters as HbA1c $7.2 \pm 0.8\%$, FBG 109 ± 11.7 mg/dl & PPBG 149 ± 22.6 mg/dl.

Conclusion: HCQ appears to be a safe anti diabetic option in people with diabetes during COVID 19 pandemic.

Disclosure of Interest: None Declared

ICE2021-1361

A STUDIES TO ASSES IN ACTIVE TUBERCULOSIS PATIENTS PREVALENCE OF DIABETES MELLITUS AND ITS PREDICTORS

Amit Kumar K. Das*

Introduction: World's leading public health issues includes Diabetes Mellitus (DM) and Tuberculosis (TB). The aim and objective of this study were to study to asses in active tuberculosis patients prevalence of Diabetes Mellitus and its Predictors.

Objectives: The aim and objective of this study were to study the prevalence of diabetes and its predictors among TB patients currently on treatment.

Methods: 212 patients who having tuberculosis and was on treatment were selected for this observational cross sectional study at tertiary diabetes care hospital in Bihar. Family history of TB, tobacco usage and self-reported information on diabetes was collected at the time of enrolment in the study. Frequency of getting blood sugar tested, type of treatment taken and daily drug adherence were also collected from diabetic tubercular patients during the study. Data were analysed by using statistical software.

Results: Among TB patients 13.1% was found to be the prevalence of diabetes. In which newly diagnosed diabetics was 4.0% and pre existing diabetics was 9.1%. current/former smokers was 25.5% and current/former smokeless tobacco users were 13.1%. Significant predictor for diabetes TB comorbidity was emerged as age 50 years and above. In all, 48 of the 212 study participants had a family history of TB (23%). The mean age at the diagnosis of "known diabetics" was 44.6 years (SD = 9.4). Regularly antidiabetic daily medication was consumed by 85%. The proportion of "known diabetic" who got their blood sugar tested daily, weekly, monthly, was 8%, 28%, and 64%, respectively. The proportion of "new diabetic" who got their blood glucose tested daily, weekly, and monthly was 18.2%, 27.2%, and 54.6%, respectively

Conclusion: In TB patients prevalent comorbidity is diabetes. Age more or equal to 50 years increases the chance of getting this two morbidity together.

Disclosure of Interest: None Declared

ICE2021-1362

STUDY TO CORRELATE GLYCEMIC CONTROL WITH HIGH SENSITIVE C REACTIVE PROTEIN AND CATALASE LEVELS IN PATIENTS WITH TYPE 2 DM WITHOUT NEPHROPATHY IN ESTERN INDIA

Shaibal Guha*

Introduction: Diabetic nephropathy is a serious chronic complication of Type 2 Diabetes Mellitus (T2DM) which impairs the quality of life, leading to increased morbidity and mortality. The high sensitivity C-reactive protein (hs-CRP) is an acute phase reactant which acts as a non-specific systemic marker of inflammation.

Objectives: To find out the relationship between serum hs-CRP and metabolic variables in Type 2 diabetic patients with and without nephropathy.

Methods: The study group consists of 116 subjects that include non-diabetic healthy controls, Type 2 diabetic patients without any complications and patients with diabetic nephropathy. The study group was composed of both genders, aged 31-70 years, who reported after 10-12 hours overnight fasting; then, venous blood and fresh urine samples were collected, in the morning from all the study subjects. Data were analysed using Statistical Package for the Social Sciences (SPSS). Independent t-test was used to compare between the groups and Chi square test was used to find out the relationship between serum hs-CRP and metabolic variables.

Results: The results showed a significantly ($p < 0.05$) increasing trend of serum hs-CRP with the degree of microalbumin excretion and the severity of nephropathy in Type 2 diabetic patients. The result showed a significant ($p < 0.05$) relationship between hs-CRP and the metabolic variables like Fasting Blood Glucose (FBG), Post Prandial Blood Glucose (PPBG), Total Cholesterol (TC), Triglycerides (TG), LDL-Cholesterol (LDL-C), TC:HDL-Cholesterol (HDL-C) ratio and estimated Glomerular Filtration Rate (eGFR) and no significance ($p > 0.05$) between hs-CRP and HDL-Cholesterol in both diabetic and diabetic nephropathy subjects. The study also showed a significant decrease ($p < 0.05$) in the mean level of eGFR in both diabetic and diabetic nephropathy subjects.

Conclusion: Hs-CRP was strongly associated with the metabolic variables and predictors of cardiovascular risk in Type 2 diabetes mellitus with and without nephropathy. The hs-CRP might be considered as a predictor or illness indicator for the development of nephropathy and cardiovascular risk in Type 2 diabetic patients. The study strongly suggests the importance of measuring the level of serum acute-phase proteins in the diagnosis and early detection of complications of Type 2 diabetes mellitus.

Disclosure of Interest: None Declared

ICE2021-1365

ASSOCIATION BETWEEN VISUAL ACUITY IMPAIRMENT AND SOCIAL DETERMINANTS OF HEALTH IN TUNISIAN DIABETIC ADULTS, 2016

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Introduction: In Tunisia, type 2 diabetes accounts for 4.4% of total disability adjusted life years (DALYs) related mainly to micro- and macro-angiopathic complications of the disease [1]. Nearly half of health outcomes are attributable to social determinants of health (SDH), defined as non-medical factors that influence a person's health status [2]

Objectives: We aimed to determine the prevalence of visual acuity impairment (VAI) in diabetic Tunisian adults and assess its association with SDH.

Methods: Data were obtained from 2016 Tunisian Health Examination Survey, a household survey, stratified at three degrees, focusing on adults aged 35-70 years previously diagnosed with diabetes. Distance vision acuity was tested using an e-health application integrated into tablets and WHO criteria were used to define VAI [3]. Based on the WHO framework, SDH introduced as independent variables were: profession, area of residence, medical insurance, households' standard of living and educational level [2]. Binary logistic regression model was used to assess associated factors to VAI after multivariable adjustments. Data analysis was performed with R software.

Results: A total of 705 participants were enrolled, with mean age of 56.6±8.4 and sex-ratio Male/Female equal to 0.9. Among participants, 12.8% had never had eyes examination before and more than half (68.2% [63.9-72.2]) had VAI. In multivariate analysis, we found that belonging to households with the lowest standard of living was significantly associated with VAI with Adjusted Odds Ratio equal to 1.6 [1.1-2.3].

Conclusion: High prevalence of VAI among Tunisian diabetic adults was highlighted. Thus, we need to promote mobile screening units based on e-Health technologies for diabetic retinopathy screening and raise healthcare providers' awareness in frontline care regarding SDH's impact on diabetic patient's quality of life.

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Key words

Visual Acuity, Social Determinants of Health, Diabetes, Tunisia

Disclosure of Interest: None Declared

ICE2021-1375

MODULATION OF THE IMMUNE STATUS IN THE SMALL INTESTINES OF DIABETIC DB/DB MICE

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Introduction: Intestinal permeability is affected by a complex interplay between inflammatory responses promoted by macrophages, dendritic cells (DC), regulatory T cells and, more recently recognised, eosinophils and the gut wall. Levels of immunoglobulin A (IgA) in the lamina propria and secreted into the lumen are important indicators of mucosal protection. Breakdown of the intestinal barrier leads to leaky gut syndrome and systemic lipopolysaccharide-induced endotoxemia, which have been implicated in the development of type 2 diabetes (T2D).

Objectives: To investigate (i) the intestinal immune status of leptin receptor deficient diabetic and obese (*db/db*) mice compared to lean (*db/+*) mice and (ii) whether a 16-week treatment with a green rooibos extract (Afriplex GRTTM), an indigenous South African fynbos plant with antidiabetic effects, and pioglitazone, a known antidiabetic drug, can modulate the intestinal immune system.

Methods: Four groups (n=8/group) of *db/+* and *db/db* mice received (i) control, (ii) low dose GRT (LD, 74 mg/kg/day), (iii) high dose GRT (HD, 740 mg/kg/day) and (iv) pioglitazone (PIO, 15 mg/kg/day) for 16 weeks. Body weights and oral glucose tolerance were assessed. Small intestinal tissue samples were processed into paraffin wax for the quantification of IgA expression using immunofluorescence. Immunophenotyping by flow cytometry of jejunal leukocyte populations included CD45-FITC (pan-leukocyte marker), F4/80-PerCP/Cy5.5 and CD11c-APC (macrophage/DCs) and SiglecF-PE (eosinophils) staining. Statistical significance was determined by 2-Way ANOVA.

Results: Pioglitazone improved glucose tolerance (p=0.004) and decreased HOMA-IR after 16 weeks in *db/db* mice while GRT did not affect glucose tolerance. Overall, immune cell populations SiglecF+ (p=0.0009), F4/80+ (p=0.0278) and CD11c+ (p=0.0655) were decreased in *db/db* mice compared to *db/+* regardless of treatments. Higher numbers of F4/80+ cells were found in mice treated with LD compared to PIO regardless of obesity status (p=0.0311). IgA expression tended to increase with the LD treatment in *db/+* mice (p=0.0704) compared to control.

Conclusion: The results suggested depletion of eosinophils and macrophages/DCs indicative of disturbances in small intestinal immune homeostasis in *db/db* mice, while GRT may exert immunomodulatory effects. Understanding how the intestinal immune system impacts on the development and progression of T2D may provide insights for treatment and prevention of T2D.

Disclosure of Interest: None Declared

ICE2021-1397

INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3 RELATES WITH GLUCOSE INTOLERANCE

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Introduction: The insulin-like growth factor (IGF)-system plays critical roles in the regulation of growth and cellular proliferation in the human body. Insulin is the primary regulator of glucose metabolism, but the growth hormone-IGF-IGF binding protein (IGFBP) axis also play a role in maintaining glucose homeostasis. However the IGF-independent role of IGFBP-3 is not poorly understood in glucose intolerance state.

Objectives: to investigate that serum IGF-I and IGFBP-3 levels are related with glycemic control and insulin resistance.

Methods: Children without known diabetes were checked an oral glucose tolerance test and collected the clinical and laboratory data. Serum IGF-I and IGFBP-3 concentrations, fasting plasma glucose, lipid profiles, insulin, c-peptide, homeostasis model assessment of insulin resistance (HOMA-IR) index and HbA1c were examined.

Results: Serum IGF-I and IGFBP-3 levels were significantly higher in individuals with impaired glucose tolerance (IGT) and diabetes (DM) than in those with normal glucose tolerance (NGT). Serum IGF-I and IGFBP-3 levels were correlated with age, HbA1c, c-peptide, insulin, and HOMA-IR in the NGT group. However, these relationships were disturbed in patients with glucose intolerance, especially in those with DM. In the DM group, serum IGF-I and IGFBP-3 levels were positively correlated with fasting plasma glucose level and HbA1c levels. In addition, IGFBP-3 levels were also positively correlated with total and LDL-cholesterol and IGF-I levels, but not with age or body mass index.

Conclusion: The IGF-I-IGFBP-3 axis, especially IGFBP-3, may play roles in the pathogenesis and metabolic control of glucose intolerance, especially in patients with type 2 diabetes.

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ICE2021-1398

IN HOSPITAL HYPOGLYCAEMIA - NOT A BENIGN CONDITION

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Introduction: Hypoglycaemia in hospital inpatients with diabetes (PWD) is associated with increased mortality. Limited studies have addressed inpatient hypoglycaemia in patients without diabetes (PWOD). However documented mortality rates are higher than in PWD. In this study we explored the associations between inpatient hypoglycaemia, mortality and other significant comorbidities in patients with and without diabetes in a tertiary referral hospital.

Objectives: To identify patients who experienced a hospital inpatient hypoglycaemic event (HE), their comorbidities and mortality rates.

Methods: The medical records of an Australian tertiary Hospital were searched via the coding system for inpatients who had an HE between May 2018 and July 2019. Exclusion criteria were infants, intentional insulin overdose or lack of documented capillary blood glucose level (BGL) ≤ 4 mmol/L. Data extracted included lowest recorded BGL, hypoglycaemic medications, renal function (KDIGO criteria), BMI, HbA1c, nutrition status (dietitian assessment) and patient mortality.

Results: 266 HEs were identified. 17 were excluded, 14 due to no BGL < 4 mmol/l. Of the 249 true HEs, 47.4% occurred in men, 52.6% in women. Median age was 69 years (Range:10-96) with mean BMI 28.7 and mean HbA1c 8.3%. Of the HEs, 200(80%) occurred in PW & 49 (20%) in PWOD.

In PWD, 44% were on insulin alone, 16% on oral agent(s) alone and 32.5% on insulin and oral agents. 20 patients (10%) were malnourished, 42(21%) had chronic kidney disease (CKD) and 14 (7%) had an acute kidney injury (AKI). 32 patients (16%) had an AKI on CKD and 11(6%) had an AKI, CKD and malnutrition.

In PWOD, 10 patients (21%) were malnourished, 4(8%) had CKD and 2(4%) had an AKI. 4 patients (8%) had an AKI on CKD and 6(13%) had an AKI, CKD and malnutrition.

44 patients (18%) died within 12 months of the event and 26(59%) of these died as inpatients. In PWD, 17(9%) died as inpatients, 10(5%) more died within 6 months. Every patient who died had at least one of: AKI, CKD, malnutrition or a combination of these.

In PWOD, 9(18%) died as inpatients, 5(10%) more died within 6 months and 3(6%) more died within 12 months. 2 patients (12%) had no AKI, CKD or malnutrition.

In PWD, the 12 month associated mortality rate after an in hospital HE was 13.5% and for PWOD 35%(p value $< 0.05\%$).

Conclusion: Our study confirmed a significant mortality rate associated with inpatient HE for both PWD and PWOD, with 12 month mortality rate for PWOD 35%, more than 2.6 fold higher than for PWD.

Disclosure of Interest: None Declared

Diabetes/Obesity/Dyslipidemia

ICE2021-1403

SATISFACTION WITH QUALITY OF CARE AMONG PATIENTS WITH DIABETES AT PRIMARY CARE CENTERS: RESULTS OF A MULTI-CENTRIC NATIONAL SURVEY.

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Introduction: Diabetes management is complex and it involves several stakeholders. It becomes increasingly evident that partnership with patients living with diabetes is integral to improving outcomes and quality of care. Obtaining patient satisfaction is crucial for this partnership to hold and achieve results.

Objectives: Our study aims to estimate the level of satisfaction among patients with diabetes who consult primary healthcare centers in Tunisia.

Methods: This is a retrospective cross-sectional study conducted as part of a multi-centric national survey to evaluate management of diabetes in Tunisia. The study systematically included all patients with diabetes aged 18 years or older who visited one of six randomly selected primary healthcare centers across the country during the month of November 2019. Participants answered a satisfaction questionnaire as a part of an interview with a trained investigator. Data analysis was carried out via the statistical analysis software SPSS 22.

Results: In this study, 376 patients with diabetes were surveyed. A slight female predominance (61%) was found. The mean age was 61.7 ± 10.7 years.

One-third (34.6%) of our study sample was either unsatisfied or slightly satisfied. Only one in seven patients (14.5%) was very satisfied with the delivery of public health services.

The difference in gender, age and education level had no statistically significant effect on satisfaction.

Four causes of dissatisfaction were most frequently reported: long wait time (42.1%), unavailable drugs (31.6%), lack of information (16.7%) and short consultation time (9.6%).

Conclusion: This study showed mixed satisfaction levels in our sample. Addressing dissatisfaction causes could help rectify the healthcare system's weaknesses and improve its efficiency. Some solutions could be fostering continuous education programs for primary care professionals, increasing the number of primary care centers, employing more staff and improving the availability of essential antidiabetic drugs.

Disclosure of Interest: None Declared

ICE2021-1419

EVALUATING SCREENING AND MANAGEMENT OF DIABETIC RETINOPATHY IN TUNISIA: RESULTS OF A MULTI-CENTRIC NATIONAL SURVEY.

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Introduction: Diabetic retinopathy (DR) is the most frequent complication of diabetes mellitus and the fifth leading cause of visual impairment worldwide.

Objectives: This study aims to evaluate guideline adherence in DR screening and management in Tunisia.

Methods: This is a cross-sectional descriptive study conducted as a part of a multi-centric national survey to prepare a national eye healthcare strategy. The study systematically included all patients with diabetes aged 18 years or older who visited one of twelve randomly selected primary healthcare centers or ophthalmology departments across the country during November 2019. Participants were interviewed by trained investigator. Data analysis was carried out via the statistical analysis software SPSS 22.

Results: In this study, 698 patients with diabetes were surveyed. A slight female predominance (57.8%) was found. Mean age was 61.7 ± 12 years.

Delay between the onset of diabetes and first ophthalmic examination was 6.2 years ± 7.3 in type 1 diabetes and 4.3 years ± 5.6 in type 2 diabetes.

Half participants (54.7%) had at least one ophthalmology visit in the past year. A significant regional difference was observed ($p < 0.001$).

Prevalence of DR was 29.9%. Patients with DR showed statistically significant difference in duration of diabetes compared to patients without DR ($p < 0.001$). This prevalence increased from 11.2% in patients with a duration of 5 years or less, to 60.3% in patients with 20 years or more.

A duration of 10 years was determined by ROC curve analysis as the threshold beyond which DR risk becomes greater (OR 4.3; 95% CI [2.98 - 6.21]).

More than a third (41.8%) of patients with DR have never had a Hemoglobin A1c (HbA1c) test. For the rest, the mean HbA1c level was $9.2\% \pm 1.8$. Only 9.3% met the recommended targets.

Patients reported three major obstacles to repeated ophthalmology visits: economical difficulties (32.2%), transport constraints (29.8%) and unpractical visit appointments (19.9%).

Conclusion: This study showed low guideline adherence in our sample. Patients with diabetes experienced many difficulties preventing them from receiving standard of care.

A revision of the national diabetes program is recommended along with the elaboration of a national eye healthcare strategy to address socioeconomic disparities.

Disclosure of Interest: None Declared

ICE2021-1420

DIABETES MANAGEMENT AND HEMOGLOBIN A1C TESTING IN TUNISIAN PRIMARY CARE CENTERS: RESULTS OF A MULTI-CENTRIC NATIONAL SURVEY.

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Introduction: Diabetes mellitus (DM) is currently the 8th leading cause of death for both sexes, with 1.5 million deaths worldwide. Assessing and improving how we manage of diabetes is essential to prevent complications and mortality.

Objectives: This study aims to evaluate guideline adherence in diabetes management in Tunisian primary care centers.

Methods: This is a cross-sectional descriptive study conducted as a part of a multi-centric national survey. The study systematically included all patients with diabetes aged 18 years or older who visited one of 6 randomly selected primary healthcare centers across the country during November 2019. Participants were interviewed by trained investigator. Data analysis was carried out via the statistical analysis software SPSS 22.

Results: In this study, 376 patients with diabetes were surveyed. A slight female predominance (61.7%) was found. Mean age was 61.7 ± 10.7 years. More than two-thirds of the sample studied does not have a functional glucometer at home. For diabetics without social security coverage, this rate is even higher (80%). Average wait time for appointments in primary care was 4 months ± 1 . Only 39.1% of patients with diabetes visited primary care centers at least four times in the last 12 months, while 93.6% visited at least twice in the same period. The yearly frequency of follow-up visits differed significantly in governorates ($p \leq 0.001$). More than half the sample (51.1%) had zero HbA1C tests in the last 12 months and only 1.9% of the patients were tested at least 3 times in the same period. Only 3 governorates were found where 50% of patients can get at least one HbA1C test yearly. Mean HbA1C was $8.31\% \pm 1.84$ (95% IC, [4-14.9]). Less than a quarter of the sample (23.8%) met the recommended HbA1C targets.

Conclusion: This study showed low guideline adherence in our sample. Over three quarters of the patients surveyed didn't achieve diabetes control. Revising the national diabetes program is strongly recommended to update guidelines and address socioeconomic and geographic disparities.

Disclosure of Interest: None Declared

ICE2021-1433

A RETROSPECTIVE STUDY ON PATIENT FACTORS IN THE CHOICE BETWEEN METFORMIN AND INSULIN FOR GESTATIONAL DIABETES

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Introduction: The use of metformin in the management of gestational diabetes mellitus (GDM) is increasing in Australia. After failing lifestyle therapy, women are often given the initial choice of metformin or insulin. We explore the characteristics of women who choose metformin compared to women who choose insulin therapy in a culturally and linguistically diverse population in Sydney, Australia.

Objectives: To investigate patient factors in the choice of metformin or insulin in gestational diabetes.

Methods: We conducted a retrospective study of singleton pregnancies delivered between 2016-2018 at Liverpool Hospital, Sydney, Australia that were complicated by gestational diabetes and who were unable to be managed on medical nutritional therapy alone. The women were given the choice of either metformin or insulin as initial pharmacologic management. Characteristics and pregnancy outcomes of each group were analysed using Chi-square and T-test.

Results: Six hundred and eighty-two women initially chose insulin compared to 263 who chose metformin. Of the 263 women who chose metformin, 75% (n=193) of them were younger than 35 years of age compared to 64% (n=432) of the insulin group (p<0.0001). In addition, women who chose insulin were more likely to have had GDM in the past (32.2% compared to 23.6%, p=0.01) and/or prior exposure to insulin therapy (20.5% compared to 9.1%, p<0.0001). There were no significant differences in the body mass index, ethnicity, gestational weight gain and pregnancy outcomes between the two groups. In particular, the risk of birthweight below 2000g was not significant between metformin or insulin (0.6% compared to 2.2%, p=0.561).

Conclusion: This study reflects real life clinical practice where women were given a choice in managing their gestational diabetes. The study helps characterise the women who are more likely to choose one therapy over the other with the metformin group more likely to be younger with no prior history of GDM or exposure to insulin administration. There were no significant differences in pregnancy outcomes between metformin or insulin, and the risk of birthweight below 2000g was not significantly different between the 2 groups.

Disclosure of Interest: None Declared

ICE2021-1437

BASED ON THE NLRP3-CASPASE-1-GSDMD PATHWAY MEDIATED CELL PYROPTOSIS TO EXPLORE THE EFFECT OF ARTESUNATE IN IMPROVING THE DAMAGE OF PANCREATIC B-CELLS

Jingya Yuan*, Hongwei jiang

Introduction: In recent years, new type of pancreatic β -cell death-cell pyroptosis has received widespread attention. The previous research of our laboratory confirmed that artemether can reduce The blood glucose level of db/db mice , increase the number of cells in the islets. This experiment intends to prove that artesunate improves pancreatic β -cell damage by inhibiting the pyroptosis pathway.

Objectives: Based on the NLRP3-Caspase-1-GSDMD pathway mediated cell pyroptosis to explore the effect of artesunate in improving the damage of pancreatic β -cells.

Methods: On day 0 , 7-week-old C57 mice were given a single intraperitoneal injection of STZ (streptozotocin) at a dose of 150 mg/kg. On the third day, blood was collected from the tail vein to measure fasting blood glucose. 18 mice with fasting blood glucose > 13.9mmol/L were selected into the experiment and randomly divided into STZ group (1ml of DMSO dissolved in 100ml of purified water, mice drink freely), 0.5 mg/ml artesunate (ART) group , 1.0mg/ml ART group ((50 mg or 100mg ART was dissolved in 1LDMSO and purified water was added to 100ml,mice drink freely), Another 6 C57 mice were injected with the same dose of 0.1mM sodium citrate buffer as a control group. ART intervention was started after blood glucose was measured on the 3rd day, and lasted for 18 days.

Results: The fasting blood glucose of the STZ group mice was significantly higher than that of the control group ($P < 0.05$). The blood glucose of the 0.5mg/ml ART group and 1.0mg/ml ART group was lower than that of the STZ group ($P < 0.05$, < 0.05). The weight of the mice in the STZ group continued to decrease. The weight of the mice in the 1.0mg/ml ART group increased compared with the STZ group . IPGTT was performed on the 18th day of ART intervention, the 1.0 mg/ml ART group had a statistically significant decrease in blood glucose values at each time point compared with the STZ group ($P < 0.05$). Compared with the control group, the fasting serum insulin of mice in the STZ group was significantly reduced ($P < 0.05$), the ART group was higher than that in the STZ group ($P < 0.05$). STZ increased the serum IL-18 levels in mice ($P < 0.05$), and the ART could reduce the serum IL-18 levels in mice ($P < 0.05$). ART can increase the islet area and the number of cells in the islets of STZ-induced diabetic mice, and reduce the expression levels of NLRP3, Caspase-1, and GSDMD in the pancreas of STZ-induced diabetic mice.

Conclusion: ART may protect pancreatic β -cells by inhibiting the activation of the pancreatic pyroptosis pathway.

Disclosure of Interest: None Declared

ICE2021-1444

COVID-19 LOCKDOWN AND EPISODES OF HYPOGLYCEMIA AMONG PATIENTS WITH DIABETES FASTING THE HOLY MONTH OF RAMADAN 2020

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Introduction: The holy month of Ramadan is the month when Muslims fast from sunrise to sunset. Patients with diabetes are targeted with Diabetes Education 8-10 weeks before Ramadan to have a safe fasting experience (1). In 2020 this timing has coincided with COVID 19 lockdown in Saudi Arabia when virtual clinics were implemented to secure the continuity of patient care (2,3).

Objectives: This study evaluated the episodes of hypoglycemia among patients with diabetes fasting in Ramadan 2020 during COVID-19 lockdown.

Methods: A cross sectional study was conducted after the holy month of Ramadan 2020 using self-administered online questionnaire and convenient sampling methods. Patients with diabetes, aged 14 years and older who are able to practice fasting in Ramadan were included in the study. Data analysis was performed using SPSS program version 20. Hypoglycemia rate in total and based on type of diabetes treatment among Participants' Ramadan 2019 and Ramadan 2020 were compared using McNemar test. Predictors of hypoglycemia during fasting Ramadan 2020 were estimated using logistic regression model.

Results: Out of 367 patients with diabetes aged 14 years and older, 326 (88.8%) participants had the ability to fast Ramadan and were included in the study. Comparing patients' experience in Ramadan 2019 and Ramadan 2020, participants reported lower episodes of hypoglycemia during Ramadan 2020 compared to Ramadan 2019, P-value 0.017. In sub-group analysis based on type of treatment, patients on non-insulin treatment had statistically significant lower episodes of hypoglycemia during Ramadan 2020 compared to Ramadan 2019 (P-value = 0.006). Patients on insulin treatment had less episodes of hypoglycemia during Ramadan 2020 compared to Ramadan 2019 but the difference was not statistically significant (P-value = 0.405). Probability of hypoglycemia during fasting Ramadan 2020 were higher among; younger age groups 14-30 years (OR 7.24, 95% CI 1.72-30.39) and 31-45 years (OR 7.18, 95% CI 1.97-26.19), patients with longer duration of diabetes (more than 10 years) (OR 2.30, 95% CI 1.01-5.26), and patients on insulin (OR 14.14, 95% CI 1.72-30.39).

Image:

Figure 1: Hypoglycemia during fasting Ramadan 2019 and 2020 among patients with diabetes based on type of diabetes treatment (n=326)

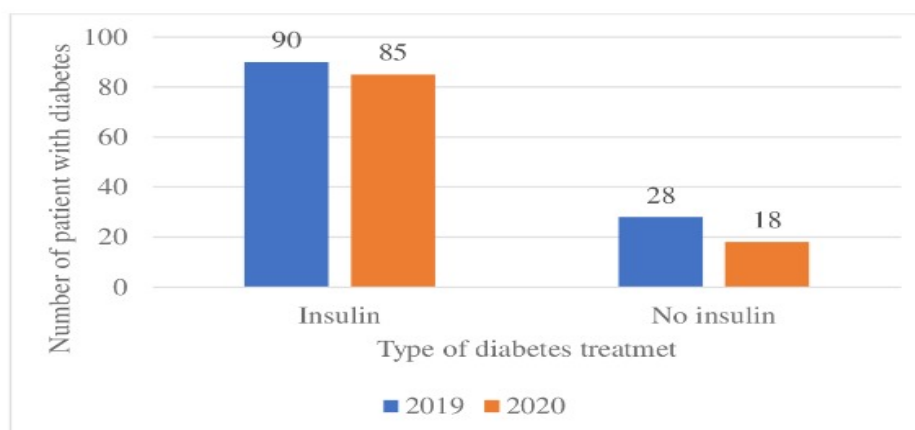


Table 1: Logistic regression for predictors of hypoglycemia during fasting Ramadan 2020 (n=326)

| Predictor | OR | 95% CI | P-value |
|--|-------|------------|---------|
| Age (reference: more than 60 years) | | | |
| 14-30 years | 7.24 | 1.72-30.39 | 0.007 |
| 31-45 years | 7.18 | 1.97-26.19 | 0.003 |
| 46-60 years | 2.78 | 0.86-8.99 | 0.088 |
| Sex (reference: female) | | | |
| Male | 1.21 | 0.60-2.42 | 0.593 |
| Duration of diabetes (reference: less than 5 years) | | | |
| From 6 to 10 years | 1.98 | 0.83-4.75 | 0.125 |
| More than 10 years | 2.30 | 1.01-5.26 | 0.048 |
| Type of diabetes management (reference: Oral hypoglycemic agents) | | | |
| Insulin | 14.14 | 5.70-35.12 | 0.001 |
| Oral hypoglycemic agents and Insulin | 4.68 | 1.95-11.27 | 0.001 |
| Diet | 0.93 | 0.24-3.59 | 0.913 |
| Consulting doctor 2-3 months before Ramadan (reference: No) | | | |
| Yes | 1.97 | 0.96-4.03 | 0.064 |
| Diabetes complication (reference: No) | | | |
| Yes | 0.74 | 0.37-1.47 | 0.391 |
| Comorbidities (reference: No) | | | |
| Yes | 1.51 | 0.74-3.08 | 0.257 |

Conclusion: During covid-19 lockdown, patients with diabetes experienced lower episodes of hypoglycemia this could be related to the implementation of telemedicine as a way of management and follow up. Further researches to evaluate telemedicine as a tool of care to patient with diabetes beyond the pandemic era is recommended.

Disclosure of Interest: None Declared



ICE2021-1446

ASSESSING DIABETIC POLYNEUROPATHY BY SIMPLE CLINICAL SCORING SYSTEMS

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Introduction: The diagnosis of diabetic polyneuropathy (DPN) relies on nerve conduction studies (NCS), which is costly, time consuming and usually not practically available. Three quarters of diabetes patients stay in low and middle-income countries where clinical measure of neuropathy would be of great benefit in practice.

Objectives: Three clinical scoring systems were selected and defined for its diagnostic value in detecting DPN compared to vibration perception threshold (VPT) using NCS as a golden standard

Methods: In the cross-sectional study, 177 diabetes patient were evaluated with Neuropathy Disability Score (NDS), Toronto Clinical Neuropathy Score (TCNS) and the examination part of Michigan Neuropathy Screening Instrument (MNSI-B). Participants were divided by electro-diagnostic tests (nerve conduction studies, NCS) and divided into groups of DPN and no DPN. Vibration perception threshold (VPT) was tested by Sensitometer.

Results: Using NCS criteria as golden standard, it proved MNSIB>2, NDS>2 and TCNS>7 with high specificity (93.2%, 72.2% and 88.6%) and low sensitivity (15.8%, 34.6% and 24.1%) which is comparable to that of VPT >25V (92.1%, 23.9%). Each neuropathy scoring system had shown a statistically significant increase in score with higher neuropathy severity group of VPT ($p<0.001$), and also demonstrated a moderate correlation with continuous scale of VPT ($p<0.001$); while TCNS presented with a stronger correlation coefficient ($r=0.369$) than NDS ($r=0.288$) and MNSIB ($r=0.310$). Receiver operating characteristic (ROC) curves analysis for abnormal nerve conduction studies criteria as the gold standard revealed NDS (0.572) had a smallest area under the curve (AUC) among the three scoring systems; while TCNS (0.619) had a comparable AUC with VPT (0.652), which is statistically significant. A cut off of NDS>1, TCNS>4, MNSIB>1 and VPT>15V had increased the sensitivity to 66.16%, 42.85%, 63.15% and 53.85%, respectively. While their specificity was reduced to 47.72% for NDS, 79.54% for TCNS, 54.54% for MNSIB and 81.57% for VPT.

Conclusion: The three clinical scoring system had comparable result to that of VPT in predicting DPN. Among the three scales, TCNS demonstrated the closest association and highest correlation with VPT result. Clinical measures can be used as alternatives to vibration test in case of low resource setting.

Disclosure of Interest: R. Thay: None Declared, V. Than Conflict with: Calmette Hospital, Z. Zhou: None Declared

ICE2021-1454

USE OF NON-REAL TIME CONTINUOUS GLUCOSE MONITORING SYSTEMS (CGMS) FOR GLUCOSE CONTROL ASSESSMENT IN PATIENTS WITH TYPE 2 DIABETES

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Introduction: Glycated hemoglobin (HbA1c) and pre- and postprandial blood glucose (BG) measurement are recommended for diabetes control assessment. Continuous Glucose Monitoring is often used for insulin dose adjustment usually in patients on multiple injections or receiving continuous subcutaneous insulin infusion. Some other goals could be achieved by using these devices.

Objectives: We assessed the Non-real Time Continuous Glucose Monitoring Systems (CGMs) as control assessment tool in patients with type 2 diabetes.

Methods: We studied 85 patients (50 men, 35 women; age 43.93 ± 10.87 years, mean disease duration 21.91 ± 6.07 years) with type 2 diabetes receiving different therapy (31 on oral therapy, 33 on insulin pre-mixed insulin, 21 on multiple insulin injections). Continuous glucose monitoring by using iPro™ (non-real time CGM) was performed for seven days, HbA1c was measured and derived data were assessed.

Results: High positive correlation was found between HbA1c ($7.46 \pm 1.19\%$) and average blood glucose level during CGM time (7.45 ± 1.57 mmol/l) ($r=0.73$), AUC above limit ($r=0.75$) and percentage of time spent with BG above 7.8 mmol/l ($38.26 \pm 26.38\%$, $p < 0.05$, $r=0.69$). There was similar but negative correlation between HbA1c and percentage of time within the limit ($56.07 \pm 24.28\%$, $p < 0.05$, $r=-0.63$). No correlation was found between HbA1c and number of excursions. These results stay the same in different treatment groups.

Conclusion: Based on our data we conclude that performing non-real time CGM in patients with type 2 diabetes could present the overall control and could be useful for treatment changes decision nevertheless short period of time reflected

Disclosure of Interest: None Declared

ICE2021-1488

NEXT-GENERATION SEQUENCING CUES FOR WFS1 GENE ASSOCIATED YOUNG ONSET DIABETES PHENOTYPES AND IDENTIFICATION OF A NOVEL FOUNDER MUTATION IN SOUTH INDIA.

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Introduction: Wolfram syndrome (WS) or DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness) syndrome is a rare autosomal-recessive disorder and is characterized by young onset diabetes along with progressive neurological abnormalities.

Objectives: To identify patients positive for WFS1 gene variants through comprehensive screening for syndromic forms of monogenic diabetes genes.

Methods: In house developed multiplex PCR based target enrichment for seventeen monogenic diabetes genes was carried out followed by Next-Generation Sequencing (NGS). The identified variants with clinical significance were confirmed by Sanger sequencing.

Results: In this study we have identified three unrelated families positive for a novel homozygous WFS1 gene mutation c.1107_1108insA(p.A370Sfs*173). These families on further investigation were found to be from the same community with a high rate of consanguineous marriages, suggesting a probable founder effect from southern part of India. The other WFS1 variants identified in this study include a recurrent homozygous mutation p.V412Sfs*29 in two unrelated patients, homozygous p.F883Lfs*56, p.W129X, p.S654X, p.C733G mutations each in four different patients, a heterozygous novel variant p.K178Afs*70 in one patient and a rare variant p.R558C in a patient with young onset diabetes.

Conclusion: NGS based parallel multigene testing strategy therefore may help in early diagnosis not only to identify the pathogenic variants in classical and non-classical form of WS but also heterozygous variants associated with young onset diabetes. To the best of our knowledge this is the first report of WFS1 founder mutation and heterozygous variants in young onset diabetes from South Asia.

Disclosure of Interest: None Declared

ICE2021-1494

A STUDY ON PREVALENCE AND RISK FACTORS OF DIABETIC NEPHROPATHY IN NEWLY DETECTED TYPE 2 DIABETIC PATIENTS

Pankaj Hans*

Introduction: Diabetes mellitus (DM) is a major health problem and causes considerable morbidity and mortality, primarily due to micro and macrovascular complications.

Objectives: This clinical study aimed to find out the prevalence of diabetic nephropathy in newly detected type 2 diabetic patients and also the risk factors associated with the development of the diabetic nephropathy.

Methods: A progressive kidney disease diabetic nephropathy involves damaging the capillaries in the kidneys' glomeruli. The study group comprised 350 subjects diagnosed with type 2 diabetes mellitus.

Results: Of the 350 total subjects involved in the study, 130 (37%) were men and 220 (63%) were women. The results showed that about 58% of the subjects had normal BMI, 32% were overweight, and 10% were obese. The mean age among the study population for diabetic nephropathy and non-nephropathy were found to be 52.53 ± 10.21 and 51.67 ± 11.19 years, respectively. The difference between the two groups was not significant ($P=0.821$). Among the 46 patients who were diagnosed to have diabetic nephropathy, 43 had microalbuminuria and 3 had macroalbuminuria. The mean serum creatinine value in non-nephropathy subjects was found to be 0.7 mg/dL, whereas in nephropathy group it was found to be 0.8 mg/dL. The prevalence found in this study was 13.14%. Incidence of nephropathy was higher in associated risk factors such as hypertension, obesity, and hypercholesterolemia. As for the GFR analysis, about 82 (23.4%) patients in the study group with 1% of nephropathy group were present with hyperfiltration. Among the remaining patients with nephropathy about 6% had a normal GFR, whereas the same percentage of the nephropathy subjects possessed a decreased GFR. Analysis of the prevalence of dyslipidemia in the study population showed that in TGL group about 161 of them had hypertriglyceridemia. Among these 161 subjects, 30 (18.6%) were diagnosed with nephropathy. The LDL group has witnessed the highest number of patients with 347 reported to have LDL-cholesterol dyslipidemia. Significant correlation between diabetic nephropathy and the following risk factors: male sex and BMI especially overweight and hypertension were observed.

Conclusion: Effective measures to create awareness among the people and educate them for a healthy life style are to be taken. The effective control of the risk factors in type 2 diabetic patients will prevent the development of nephropathy and also retard its progression.

Disclosure of Interest: None Declared

Diabetes/Obesity/Dyslipidemia

ICE2021-1497

ASSESSMENT OF CIRCULATING HIGH-SENSITIVITY C-REACTIVE (HSCRP) AS EARLY MARKER FOR DETECTION OF DIABETIC NEPHROPATHY (DN).

Pankaj Hans*

Introduction: Inflammation plays a very important role in progression of diabetic nephropathy and lead to chronic kidney disease.

Objectives: The main aim of this study is to evaluate the correlation between serum HsCRP levels with T2DM subject having high creatinine and microalbuminuria with T2DM subjects with normal creatinine and microalbuminuria.

Methods: This is a scribing trial conducted at single Center at Patna city. 489 T2DM subjects in which 242 having high creatinine and microalbuminuria (Gr A) and 247 normal creatinine and microalbuminuria (Gr B) were enrolled for the study. Blood samples collected from subjects to perform HbA1C, HsCRP, creatinine and urine for microalbuminuria.

Results: Both group has almost similar demographic characteristics (Avg mean duration of diabetes 10.7 ± 3.6 and 10.1 ± 3.2 and years, age 56 ± 5.8 and 54 ± 5.2 years and HbA1c 8.1 ± 0.5 % and 7.6 ± 0.5 % , respectively). It was observed that Hs-CRP was much higher (4.6 ± 1.3 mg/dl) in group A (Cre 1.67 ± 0.4 , Mic Albu 82.39 ± 9.26 mg/dl) as compared to Gr B (HsCRP $1.1 \pm .8$, Sr. Cre 0.86 ± 0.3 , Mic Albu 12.64 ± 9.47 mg/dl)(p value < 0.001). HsCRP was also correlated to high HbA1c level (p value < 0.05).

Conclusion: In T2DM subjects , high serum creatinine and microalbuminuria is accompanied by elevated HS-CRP, suggesting activation of inflammatory pathways in progression of renal disease. This observation has confirmed that hsCRP can be used as early marker for detection of diabetic nephropathy.

Disclosure of Interest: None Declared

ICE2021-1496

USE OF HYDROXYCHLOROQUINE IN COMBINATION WITH STATINS AS AN LDL LOWERING AGENT IN PATIENTS OF TYPE II DM WITH DIABETIC NEPHROPATHY

Pankaj Hans*

Introduction: Statins have established themselves as one of the best choice for lowering LDL levels, and have recently been proved efficacious for reducing albuminuria significantly. However, with the latest bar for target LDL levels set at 50 mg/dl, we definitely need to look for other ways of lowering LDL especially in population of Diabetics Nephropathy who are not only at high risk for CV mortality but also need dosage reduction due to impaired renal function. With the recent DGI approval of HCQS (hydroxychloroquine) for use as an antidiabetic drug, we decided to explore the effects of HCQS in combination with atorvastatin on Lipid profile of patients with Diabetic Nephropathy.

Objectives: Our study showed that combining HCQS with Atorvastatin results in even better control of LDL levels with favourable effect on other lipids as well.

Methods: This is a non-randomised controlled study. A total of 67 patients with Type II Diabetes Mellitus (in the age group of 30-80yrs, with clinical evidence of Diabetic Kidney Disease [DKD], HbA1c \geq 6.5) were selected and alternatively divided into two groups with one group taking Hydroxychloroquine (100mg b.i.d.) in addition to their regular medications. Both groups were then looked for any significant changes in their lipid profiles after 3 months.

Results: In our study, while triglyceride levels were reduced by 24.69% and 10.66% in the Hydroxychloroquine and Non-Hydroxychloroquine group respectively, both of which were statistically significant, Low density Lipid-cholesterol levels were reduced by 10.24 % in Hydroxychloroquine group while these levels continued to increase by 14%, in the NON-Hydroxychloroquine group, after a follow up of 3 months. Also although the total cholesterol declined in both the groups after 3 months but, decline was more with HCQS group. And while HDL increased significantly with the HCQS group after 3 months, it was not significant in the NON-HCQS group.

Conclusion: While the NON-HCQS group (On atorvastatin 20mg alone) observed decline in TGs and Cholesterol, their HDL did not rise and LDL continued to rise after 3 months of treatment. However, in the HCQS group (On combination of HCQS 100mg bd and atorvastatin 20mg h/s), HDL was seen increased with significant decline in LDL and TG after 3 months of treatment stating that the combination of HCQS with statins may be a better choice for lowering lipids in DKD patients than using statins alone.

Disclosure of Interest: None Declared

ICE2021-1500

GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY AND ITS EFFECTS ON GLYCOSYLATED HAEMOGLOBIN: DATA FROM AN EMIRATI COHORT

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Introduction: Glucose-6-phosphate dehydrogenase (G6PD) deficiency, the most common human enzyme defect, is an inherited X-linked recessive defect; affecting males more severely. The prevalence of G6PD deficiency in Abu Dhabi, UAE is reported to be around 11.6 % in male UAE nationals [1]. Diabetes is also a common condition globally, and in the UAE. Haemolytic anaemia is one of the major clinical manifestation of G6PD deficiency[2] and can affect glycosylated haemoglobin (HbA1c) which is used for monitoring and diagnosis of diabetes.

Objectives: In this retrospective study, we have compared HbA1C and haemoglobin(Hb) levels among male, individuals with type 2 diabetes and G6PD (Study group, SG) and G6PD normal (Control group, CG) subjects.

Methods: The study was conducted on male patients attending Imperial College London Diabetes Centre (ICLDC), Abu Dhabi, UAE. Information on patients tested for G6PD-deficient was retrieved from the ICLDC electronic database. Data for the SG and age-matched CG included: (1) age, (2) age at T2D diagnosis, (3) haemoglobin (Hb) levels and (4) HbA1C levels. Statistical analyses were performed using SPSS version 24. Data are presented as median (IQR) with statistical significance at p-value of 0.05.

Results: 794 G6PD-deficient males were identified; 171 (21.5%) also had T2D and composed the SG while 177 age-matched males with normal G6PD expression level composed the CG (Table 1). The majority of subjects were Emirati (88.0% for both SG and CG). There was no significant difference with the age of T2D diagnosis between the two groups ($p=0.961$). Haemoglobin and HbA1C were significantly lower in SG than in the CG (127 Vs 140 g/L, $p<0.001$ and 6.5 Vs 7%, $P<0.001$ respectively). Table 1. Comparison of anthropological and clinical parameters between the study (SG) and control groups (CG).

| Parameter | Group | N | Median | IQR | P-Value |
|------------------------------|-------|-----|--------|-------------|---------|
| Age (years) | SG | 171 | 56.7 | 49.0-66.5 | 0.879 |
| | CG | 177 | 57.0 | 51.7-64.7 | |
| Age at T2D Diagnosis (years) | SG | 171 | 44.0 | 36.0-53.0 | 0.961 |
| | CG | 177 | 44.3 | 35.0-51.6 | |
| HbA1C | SG | 171 | 6.5 | 5.7-7.3 | <0.001 |
| | CG | 177 | 7.0 | 6.3-8.0 | |
| Haemoglobin (g/L) | SG | 171 | 127.0 | 116.0-135.0 | <0.001 |
| | CG | 177 | 140 | 130.0 - 150 | |

Median values were compared using Mann Whitney U-test. T2D=Type 2 diabetes; SG=Study Group (G6PD-Deficient+T2D); CG=Control Group (G6PD-Normal+T2D); IQR=Interquartile Range

Conclusion: G6PD deficiency leads to a lowering of HbA1c; in the Arab population studied was around 0.5%. This effect needs to be considered in populations with a high prevalence of G6PD deficiency.

Disclosure of Interest: None Declared

ICE2021-1502

TRIPLE DRUG THERAPY FOR OPTIMAL GLYCEMIC CONTROL IN PATIENTS WITH T2DM IN COVID-19 TIMES: INDIAN CLINICIAN PERSPECTIVE

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Introduction: Background: Optimum glycemic control is pivotal to prevent complications and premature mortality, and improve quality of life in patients with type 2 diabetes mellitus (T2DM). Patients uncontrolled on mono- or dual- anti-diabetic therapy require triple drug therapy (TDT) to achieve optimal glycemic control.

Objectives: Objective: This survey was carried out to understand the clinical utilization of TDT in attaining durable glycemic control in patients with T2DM.

Methods: Methods: A structured objective questionnaire was used for the survey and responses were sought from 270 Healthcare practitioners (HCPs) across India during May 15 to May 30, 2020 via Google forms. The questionnaire consisted of questions related to proportion of patients with uncontrolled glycemia, role and choice of TDT in achieving durable glycemic control, importance of cost of therapy, etc. The responses were analyzed descriptively.

Results: Results: The respondent HCP pool comprised consulting physicians (47%), diabetologists (30%), endocrinologists (16%), and family physicians (7%).

More than 45% of HCPs agreed that 30-50% of their diabetes patients have HbA1c >8.5%, and uncontrolled fasting and postprandial blood glucose levels while 21% mentioned such uncontrolled glycemia in more than 50% of their patients.

Approx. 52% of the HCPs think that 50-70% of their patients can be brought under control with TDT, while a quarter of HCPs believe that more than 70% of their patients can be effectively managed with TDT.

72% of respondents aligned in their views that the cost of anti-diabetic therapy is an important parameter during Covid-19 pandemic.

In uncontrolled T2DM patients taking a combination of modern sulphonylurea and metformin, HCPs rated DPP-4 inhibitor, pioglitazone and voglibose as third line options for achieving durable glycemic control.

60% of the HCPs opined that triple drug therapy can delay the initiation of insulin therapy in patients with T2DM.

Almost two-thirds of the HCPs agreed that double and triple fixed dose OAD combinations have better pharmacy availability than insulin, enabling better patient accessibility.

Conclusion: Conclusion: A high proportion of patients have a suboptimal glycemic control during covid-19 pandemic, and TDT can control a majority of these patients. The survey also highlights the HCPs' opinion that the triple drug therapy has multiple patient-centric benefits like cost effectiveness, accessibility, delaying insulin usage.

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ICE2021-1511

FACTORS ASSOCIATED WITH POOR GLYCEMIC CONTROL AMONG CHILDREN WITH TYPE 1 DIABETES AT DORA NGINZA REGIONAL HOSPITAL, PORT ELIZABETH, SOUTH AFRICA

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Introduction: Type 1 diabetes (T1DM) is the commonest endocrine disease among children. It results from autoimmune destruction of beta cells leading to insulin deficiency with subsequent hyperglycemia. Poor adherence to treatment (mainly insulin), causes persistent hyperglycemia leading to acute and chronic complications. Strict glyceamic control is vital in delaying the onset and progression of T1DM related complications, thus it is important to identify causes of poor glyceamic control so as to optimize level of care by the health care team and by the patient. There is a paucity of studies reporting on glyceamic control of T1DM in South African children.

Objectives: The aim of this study was to assess glyceamic control and determine reasons for poor glyceamic among children and adolescents with T1DM at a regional hospital in Port Elizabeth, South Africa.

Methods: In a cross-sectional descriptive study patients aged ≤ 18 years, diagnosed with T1DM for more than 6 months attending the pediatric diabetic clinic were recruited after obtaining informed consent from their caregivers. A structured self-developed questionnaire was administered to assess adherence to diet, self-glucose monitoring and insulin injection technique and supervision by caregivers. Information on their insulin treatment and HbA1c levels was extracted from hospital files.

Results: In all, 43 children were recruited, their median age was 10 years (interquartile range; 8.2-11.8). There were 27 (63%) children with poor glyceamic control (HbA1c $\geq 9\%$) and 16 (37%) had fair or good glyceamic control (HbA1c $< 9\%$). Self-glucose monitoring was performed 4 or more times a day by 6 (14%) children, and 19 (44%) children were on twice a day biphasic insulin regimen. Insulin injections were administered by adults in 20 children, and among the 23 who were self-injecting, 9 (39%) were supervised by an adult. Poor glyceamic control was more frequent ($p < 0.05$) in children with poor adult supervision (78%), those monitoring self-glucose and injecting insulin less frequently i.e. $<$ thrice a day (79%), and those with lipohypertrophy (75%). Poor glyceamic was significantly associated ($p < 0.05$) with developing acute complications (80%) especially diabetic ketoacidosis.

Conclusion: Poor glyceamic control is common among children with T1DM attending the hospital's diabetic clinic. Lack of adult supervision, infrequent monitoring of glucose and of insulin injection and presence of lipohypertrophy were associated with poor glyceamic control.

Disclosure of Interest: None Declared

ICE2021-1516

BMI AND BODY FAT AND THEIR ASSOCIATION WITH CARDIOMETABOLIC ALTERATIONS IN ADOLESCENTS

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Introduction: Exposure to risk factors during adolescence may be responsible for the development of cardiovascular diseases in adulthood.

Objectives: To associate nutritional status with cardiometabolic alterations in adolescents from public schools in Juiz de Fora, MG, Brazil

Methods: This is a cross-sectional study with adolescents of both sexes, aged between 14 and 19 years old. Weight and height were measured and BMI was calculated, being classified in according Z score values for age $\geq +1$ as overweight. The percentage of body fat (%BF) was measured by bioelectrical impedance, boys with a fat percentage of $\geq 20.1\%$ and girls $\geq 25.1\%$ were classified as high. The individuals were grouped into: G1: adequate BMI and %BF, G2: adequate BMI and elevated %BF, G3: elevated BMI and adequate %BF and G4: elevated BMI and %BF. Total cholesterol (TC), triglycerides (TG) and fasting blood glucose were obtained by colorimetric enzymatic assay. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using a digital oscillometric device. Descriptive analyses were performed and the association between biochemical variables and BP was tested using the Kruskal Wallis test and post-hoc with Bonferroni correction. The analyses were performed using the Statistical Package for the Social Sciences® software (version 17.0), with a significance level of 5%.

Results: The sample consisted of 796 adolescents, 59.0% were female with a mean age 16.16 ± 1.21 years. Regarding nutritional status, 21.7% are overweight and 42.5% are elevated %BF. The variables SBP ($p < 0.001$), DBP ($p < 0.001$), TC ($p < 0.001$), TG ($p = 0.009$) and fasting blood glucose ($p = 0.027$) were different between groups. SBP differed between groups G1 and G3, G2 and G3, G2 and G4 and between G3 and G4 ($p < 0.001$ for all); the DBP between G1 and G4 and between G2 and G4 ($p < 0.001$ for both); the TC between G1 and G2 ($p < 0.001$) and G1 and G4 ($p = 0.001$); TG between G1 and G4 ($p = 0.001$) and fasting blood glucose between G1 and G2 ($p = 0.004$).

Conclusion: High prevalence of alterations in nutritional status and association with cardiometabolic alterations in adolescents were found. Because cardiovascular risk factors are identified in increasingly younger individuals, actions that encourage adolescents to lead a healthy lifestyle through proper nutrition and physical activities are necessary.

Disclosure of Interest: None Declared

ICE2021-1517

EXERCISE INTERVENTION INDUCES HYPERMETHYLATION OF FKBP5 IN OBESE SOUTH AFRICAN WOMEN

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Introduction: Obesity and insulin resistance are modifiable risk factors for type 2 diabetes. We previously identified altered *FK506-binding protein (FKBP5)* methylation in subcutaneous adipose tissue (SAT) from obese compared to normal-weight South African women, which associated with obesity and insulin resistance.

Objectives: This study aimed to investigate the effect of exercise training on *FKBP5* methylation and expression in SAT from obese South African women, as well as assess possible associations with adiposity, insulin sensitivity and cardiorespiratory fitness.

Methods: Study participants (n=19) underwent 12-weeks of aerobic and resistance training. *FKBP5* methylation was measured in SAT using bisulfite pyrosequencing. *FKBP5* expression and the rs1360780 polymorphism were assessed using quantitative real-time PCR. Associations between DNA methylation and metabolic parameters were evaluated using Pearson's and Spearman's correlation tests.

Results: Exercise training improved insulin sensitivity (p=0.003) and VO₂Peak (p=0.005), while it decreased waist circumference (p=0.001) and gynoid fat mass (p=0.007). Two *FKBP5* CpG dinucleotides were hypermethylated in response to exercise; of which only one was significant (CpG542: p=0.019). Increased CpG542 methylation positively associated with VO₂Peak (p=0.044); whereas CpG543 methylation negatively associated with waist circumference (p=0.001). While *FKBP5* expression decreased slightly in response to exercise, this was not significant. Women with the *FKBP5* rs1360780 CT polymorphism had higher CpG methylation after exercise (CpG542: p=0.027, CpG543 p=0.018) whereas no methylation changes were observed in CC carriers. On the other hand, individuals with the CC genotype exhibited increased VO₂Peak in response to exercise training, whilst no changes in VO₂Peak was observed in women with the CT genotype.

Conclusion: Exercise training induces genotype-dependent hypermethylation of *FKBP5* within SAT from obese South African women, which is associated with decreased adiposity and increased cardiorespiratory fitness. These findings highlight the potential of exercise to regulate epigenetic processes within a population at high-risk for metabolic disease.

Disclosure of Interest: None Declared

Diabetes/Obesity/Dyslipidemia

ICE2021-1520

COMPARING THE MORTALITY OF DIABETIC AND NON-DIABETIC PATIENTS WITH COVID-19 IN A UK DISTRICT GENERAL HOSPITAL

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Introduction: Initial reports during the first wave of the pandemic in the United Kingdom have shown that diabetic patients with COVID-19 often had a more severe infection with co-morbidities such as Hypertension (HTN) leading to a poorer prognosis. Males could also be at higher risk of death from COVID-19 as was demonstrated in one study. [1] SARS-CoV-2 has been theorised to trigger the increased secretion of glucocorticoids and catecholamine's due to stress conditions- increasing the frequency of acute hyperglycaemic events such as diabetic ketoacidosis in COVID-19 patients with diabetes. It has been suggested that SARS-CoV-2 enters into islets in the pancreas via angiotensin converting enzyme 2 as its receptor leading to acute beta-cell dysfunction. [2]

There is also some evidence to suggest that increased Body Mass Index (BMI) in diabetic patients with COVID-19 is linked with severity of the infection.

Objectives: We aim to investigate the impact of diabetes on mortality in patients with COVID-19, and to identify potential prognostic factors therein including body mass index (BMI), co-morbidities and gender.

Methods: We undertook a retrospective study of all patients aged ≥ 18 years during the first wave of the pandemic. All patients who had a confirmed diagnosis of COVID-19, via radiological and polymerase chain reaction testing, were included in the study. Data was collected using electronic patient records. Statistical analysis was performed using the Chi Squared Test for independence.

Results: 445 COVID-19 positive patients were included in the study, out of whom 127 (29%) were diabetic. Mortality in diabetic patients (61%) was found to be significantly higher than non-diabetics (48%) ($p=0.01$). There were no significant differences in mortality between diabetic and non-diabetic patient when grouped for BMI ≥ 25 ($p=0.4$), Male ($p=0.06$), Female (0.19) and hypertension ($p=0.12$).

Conclusion: Our study demonstrated how diabetic patients with COVID-19 had a significantly higher mortality rate compared to non-diabetics. This prompts the need to educate diabetic patients about hyperglycaemia arising from infection, the importance of sick day rules and compliance with social isolation measures. Further research is required to investigate the causes behind the raised mortality rate in diabetics.

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Disclosure of Interest: None Declared

ICE2021-1521

EXCESS ADIPOSITY AND SOCIO-ECONOMIC INEQUALITIES IN TUNISIAN ADULTS: RESULTS OF A NATIONAL SURVEY

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Introduction: The prevalence of excess adiposity (EA) is dramatically increasing worldwide at all ages [1]. Once seen as a problem specific to high-income countries, EA is now on the rise in low- and middle-income countries, particularly in urban areas. Tunisia does not seem to be spared from the phenomenon of EA. It is still one of the major challenges, in a context of nutritional and epidemiological transition.

Objectives: Our study aims to describe the national distribution of EA in relation to socio-economic determinants.

Methods: The Tunisian Health Examination Survey (THES) is a cross-sectional national household survey undertaken in 2016 targeting the population aged 15 years and older. For this work, we included only subjects aged 20 years and older. EA was defined as a waist circumference ≥ 80 cm in women, ≥ 94 cm in men and/or overweight: BMI ≥ 25 kg/m². Data analysis was carried out via SPSS 24 software. Associated factors were examined using Chi-square tests followed by multivariate logistic regression analysis.

Results: In this study, 7963 persons were surveyed. A slight masculine predominance (50,6%) was found. Overall prevalence of EA was 63%: 55.4% for men and 70.8% for women ($p < 10^{-3}$).

Prevalence varied according to age in both genders: it increased from 34.1% in patients aged 20 to 25 years to 72.8% in those aged 50 to 59 years ($p < 10^{-3}$). In multivariate logistic regression analysis, factors associated with higher risk of EA were: female sex [aOR(95%CI):1.94(1,68-2.23)], age ≥ 50 [aOR(95%CI):4.94(3.58-6.84)], urban area [aOR(95%CI):1.19(1.01-1.4)], having health insurance [aOR(95%CI):1.23(1-1.5)], primary education [aOR(95%CI):1.31(1.02-1.67)] and fourth standard of living quintile [aOR(95%CI):2.46(1.58-3.82)].

Conclusion: This study showed a high prevalence of EA among Tunisian adults. Gender and socioeconomic inequalities were among the most important risk factors. Hence the urgency of developing a comprehensive national plan taking into consideration both these determinants of EA.

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Disclosure of Interest: None Declared

ICE2021-1524

ADIPOCYTOKINES (CHEMERIN, VISFATIN AND RETINOL BINDING PROTEIN 4) AND DIABETIC FOOT

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Introduction: Diabetic foot is an advanced complication of diabetes mellitus, which is associated with severe invalidization and high mortality rate among affected people. Many factors are involved in its pathogenesis but not all of them are fully elucidated.

Objectives: Adipose tissue and its hormones – adipokines, are proved factors in diabetic complications and cardiovascular diseases. Until now, there is no data on their role in diabetic foot. The aim of this cross-sectional study is to determine the levels of some adipocytokines in people with and without diabetic foot and to look for their potential involvement in the evolution of this complication.

Methods: Eighty patients with diabetes (type 1 and 2) and mean age of $60,8 \pm 10,5$ years were included in this study and were divided into two groups –with established diabetic foot ($n=36$) and without diabetic foot ($n=44$). The standard antropometric measurements and body composition analysis with device based on bioelectrical impedance method (Tanita TBF-215 GS Body Composition Analyzer) were made. The plasma levels of the adipokines – Chemerin, Visfatin and Retinol binding protein-4 (RBP-4) were tested using ELISA method.

Results: It was found that the plasma levels of Chemerin are significantly lower among people with diabetic foot ($521,26 \pm 189,94$ ng/ml), compared to the other group ($592,82 \pm 125,43$ ng/ml). Chemerin levels correlated positively with BMI ($r = 0,400$), fat mass ($r = 0,320$) and hip circumference ($r = 0,409$). The mean values of Visfatin ($1,825 \pm 1,309$ vs $1,873 \pm 1,473$ ng/ml) and RBP-4 ($23,12 \pm 23,70$ vs $21,04 \pm 23,13$ ng/ml) showed no significant difference between subjects with diabetic foot and without diabetic foot, respectively.

Conclusion: Adipokines, and particularly lower levels of Chemerin, in diabetic foot patients might be included with different aspects in the pathogenesis of this multifactorial complication. Further prospective trials over larger population are needed to elucidate the potential mechanisms, underlying the observed association.

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ICE2021-1527

CORRELATION BETWEEN THE GLYCATED HEMOGLOBIN AND HOMA INDICES IN TYPE 2 DIABETES MELLITUS: IMPACT OF WHOLE-BODY DIGITAL TWIN TECHNOLOGY ENABLED PRECISION NUTRITION

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Introduction: The glycemic control is efficiently expressed as the changes in the glycated hemoglobin (HbA1c). HbA1c is known to be correlated with insulin resistance parameter (HOMA IR) and with the measure of the functionality of the beta cells as (HOMA B), through the conventional pharmacological modalities of management of T2DM

Objectives: We explored for the impact of intervention through technological enabled platform, the Twin Precision Nutrition (TPN) Program, which utilises a whole-body digital twin technology, powered by artificial intelligence and Internet of Things, for the change in the glycemic change (HbA1c), insulin resistance (HOMA2 IR) and improvement in the insulin secretory capacity of beta cells (HOMA2 B)

Methods: 381 subjects (287 males, 94 females) were evaluated in this longitudinal study for a period of three months. Descriptive statistics, correlation matrix and chi-square tests were used for statistical analysis.

Results: The mean age (years) was 49 (± 10 , minimum 25, maximum 79, range 54, 95% CI 48 to 50). The mean duration of diabetes (years) was 8.1 (± 7.1 , minimum 0, maximum 35, range 35, 95% CI 7.4 to 8.9). There was a statistically significant improvement in HbA1c (%) 8.8 (± 1.9 , 95% CI 8.6 to 9) reduced to 6.9 (± 0.94 , 95% CI 6.8 to 7; $p < 0.0001$), HOMA2-IR 2.7 (± 8.6 , 95% CI 1.8 to 3.5) reduced to 1.5 ($\pm 0.1.5$, 95% CI 1.4 to 1.6; $p = 0.0094$). There was a numerically superior improvement in the HOMA2-B, 59 (± 47 , 95% CI 54 to 64) increased to 64 (± 38 , 95% CI 60 to 68; $p = 0.1103$ NS). The change in the HbA1c showed positive correlation with the change in HOMA2-IR ($r = 0.077$, 95% CI -0.02 to 0.17, $p = 0.13$ NS) and negatively correlated with HOMA2-B ($r = -0.391$, 95% CI -0.47 to -0.30, $p < 0.0001$), respectively. At 90 days, 227 (60%) of T2DM were exclusively on the TPN program, without any ongoing medication and 69 (18%) were on TPN and metformin only.

Conclusion: Technology enabled precision nutrition, a combination of macro, micro and biota nutrients, with physician led adoption and technology driven intervention had positive implications for the improvements in the indices for the insulin sensitivity and beta cell function, with clinically meaningful glycemic control. The TPN intervention appears to have the potential to for reverse diabetes with drug free remission. The sustainability of these findings need corroboration with long term continuous evaluation.

Disclosure of Interest: None Declared

ICE2021-1528

DOUBLE BURDEN OF MALNUTRITION AND SOCIO-ECONOMIC INEQUALITIES IN TUNISIAN ADULTS: RESULTS OF A NATIONAL SURVEY.

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Introduction: Malnutrition, referring to both nutritional deficits and excess adiposity (EA), currently affects one third of the world population. A new paradox of modern societies, linking undernutrition to overweight, puts poverty at the center of malnutrition problems [1]. In Tunisia, nutritional deficits are still major challenges in a context of epidemiological transition.

Objectives: Our study aims to describe the national distribution of the double burden of malnutrition (DBM) in relation to socio-economic determinants.

Methods: Tunisian Health Examination Survey (THES) is a cross-sectional national household survey undertaken in 2016. This study included subjects aged 20 years and over. DBM was defined as the association of EA and anemia. EA was defined as waist circumference ≥ 80 cm in women, ≥ 94 cm in men and /or overweight: BMI ≥ 25 kg/m². Anemia was defined as hemoglobin (Hb) < 13 g/L in men and < 12 g/L in women. Data analysis was carried out via SPSS24 software. Associated factors were examined using Chi-square tests followed by multivariate logistic regression analysis.

Results: The sample size was 7963 persons. A slight masculine predominance was found (50,6%).

Two thirds (63%) of our population had EA and one third (33.2%) had anemia. Prevalence of anemia in patients with EA was 59.2%. Overall prevalence of DBM was 20%: 23.4% for women and 16.7% for men ($p < 10^{-3}$). An age gradient was identified: prevalence increased from 6.9% in those aged 20-25 years to 29.9% in those aged 70 years and older ($p < 10^{-3}$). In multivariate logistic regression analysis, factors associated with higher risk of DBM were: female sex [aOR(95%CI):1.51(1.3-1.75)], age ≥ 70 [aOR(95%CI):3.6(2.21-5.91)], marriage [aOR(95%CI):1.88(1.39-2.56)], having health insurance [aOR(95%CI):1.59(1.24-2.01)], and fourth standard of living quintile [aOR(95%CI):1.53(1.18-1.98)].

Conclusion: This study highlighted the alarming prevalence of DBM in Tunisian adults and the existence of socio-demographic inequalities. Middle to high-socioeconomic classes were the most affected suggesting that Tunisia has entered the fourth stage of nutritional transition. A national plan addressing regional, socioeconomic and gender-related disparities is needed. It should take into consideration the high prevalence of nutritional deficits such as anemia in people with EA.

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Disclosure of Interest: None Declared

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ASSESSMENT OF FOOD ENVIRONMENT AROUND SCHOOLS AND PREVALENCE OF OVERWEIGHT AMONG ADOLESCENTS

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Introduction: The food environment around schools, especially the density of establishments such as cafeterias, convenience stores and grocery stores, has been associated with the occurrence of overweight and obesity in adolescents.

Objectives: Evaluate the food environment around schools and its correlation with the prevalence of overweight in adolescents in a medium-sized Brazilian municipality.

Methods: Cross-sectional study in which the weight, height and BMI-for-age of adolescents and the school food environment were evaluated. By obtaining the Taxpayer Registration worksheet, a database of establishments selling food was constructed, which were classified according to the proposal of the *Câmara Interministerial de Segurança Alimentar e Nutricional* – CAISAN, which classifies the establishments according with the categories of the Brazilian Dietary Guidelines. The coordinates of the schools addresses and establishments were obtained and their distribution was verified on the map of the urban area of the municipality. Subsequently, buffers with radii of 500 meters were drawn around the schools using the QGis 2.10.1 – Pisa Program. The prevalence of overweight in schools and the characterization of school buffers were presented through frequencies. Linear regression was performed between the prevalence of overweight and availability of establishments in the buffers of each school. Statistical analyzes were performed using SPSS software, with a 5% significance level.

Results: 787 adolescents from 29 public schools have participated in the study. The prevalence of overweight, according to schools, was $28.21 \pm 10.82\%$. Evaluating the establishments in the buffers, it was found that $61.03 \pm 6.79\%$ of these were classified as unhealthy; $26.47 \pm 7.36\%$ of the mixed type and only $10.82 \pm 5.38\%$ healthy. No significant correlations were found between the prevalence of overweight and the frequencies of unhealthy establishments ($R^2 = 0.002$, $\beta = 0.043$, $p = 0.826$); mixed establishments ($R^2 = 0.003$, $\beta = 0.053$, $p = 0.785$) and healthy establishments ($R^2 = 0.000$, $\beta = -0.011$, $p = 0.953$).

Conclusion: High availability of establishments that sell unhealthy foods around schools was identified. Although no significant correlations were found with excess weight, this result is alarming.

Disclosure of Interest: None Declared

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DIABETIC KETOACIDOSIS ASSOCIATED ISCHEMIC STROKE

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Introduction: DKA is a state of severe insulin deficiency, either absolute or relative, resulting in hyperglycemia, ketonemia, acidemia, and systemic inflammation. The most common complication of DKA is cerebral edema, which resulted in the death of 21 to 25% of affected patients, and significant morbidity in a further 10 to 35%. Less common, and perhaps underappreciated is the risk of acute ischemic or hemorrhagic stroke during the acute DKA episode. Although diabetic ketoacidosis associated stroke is observed more in the pediatric population, our case was a 46-year-old male with type 1 diabetes who presented with DKA to the hospital and subsequently developed global ischemic brain injury involving the entire territories of the right and left internal carotid arteries.

Case Description: 46-year-old male with past medical history of Uncontrolled Type 1 Diabetes Mellitus with Hyperglycemia presented to the hospital with altered mental status. Patient has had multiple admissions in the past for DKA in setting of insulin non-compliance. Upon arrival to Emergency room, patient was lethargic but was following verbal commands. CT head on admission revealed no signs of cerebral edema and no acute hemorrhage or mass was present. Patient was managed per DKA protocol. Day 2 patient was obtunded but responded to noxious stimuli. On Day 3 of hospital course, patient was noted to not having a pupil or gag reflex. To our surprise, repeat CT Head showed Extensive hypoxic ischemic brain injury involving the entire territories of the right and left internal carotid arteries. CTA head/neck with perfusion revealed occlusion of the left and right internal carotid artery. Otherwise, the anterior and middle cerebral arteries were not opacified with contrast, consistent with occlusion.

Clinical discussion: Type 1 diabetes is a common autoimmune condition that often represents in childhood and may be complicated by episodes of diabetic ketoacidosis(DKA). DKA is associated with systemic inflammatory response characterized by vascular endothelial injury and coagulopathy. Stroke in DKA is very rare but life threatening. Since the presentation of cerebral edema and primary stroke in DKA can overlap, clinicians should have a high index of suspicion for stroke, hence early imaging for any patient with neurological deterioration is often required. Magnetic resonance imaging with perfusion has a sensitivity nearing 100 % for identification of ischemia associated with stroke.

Disclosure of Interest: None Declared

ICE2021-1553

RISK OF TYPE 2 DIABETES MELLITUS IN NUTRITION AND DIETETICS STUDENTS FROM COLOMBIAN UNIVERSITIES.

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Introduction: Diabetes is a chronic disease in which the pancreas does not produce enough insulin or the body does not use it effectively.

Objectives: To determine the risk of presenting type 2 diabetes mellitus (DM2) in young university students from the Metropolitan Universities (MU) and Antioquia (AU) in Colombia.

Methods: Observational, descriptive, cross-sectional study carried out in 220 Nutrition and Dietetics students without DM2, 51.8% of the MU (114) and 48.2% of AU (106). A questionnaire was applied that investigated sociodemographic variables, lifestyles and the risk of developing DM2 was determined using the Findrisc test, which measures the global risk in 10 years, assigning scores to the related variables. Weight and height were measured to determine BMI and waist circumference. Statistical analysis was performed in SPSS software.

Results: The mean global risk score for DM2 was 4.1 ± 2.9 , The high and medium risk was higher in the UM population; 58.4% of the participants were from the middle socioeconomic stratum and 37.57% from the low stratum; the risk factors most related to the risk of DM2 were physical activity, 53.8%, daily consumption of fruits and vegetables in 52.2%, and a family history of DM2 in 46.5%.

According to the confidence intervals for the prevalence ratio, the association strength and statistically significant relationship with the presence of DM2 risk ($p = 0.0000$) were observed for the practice of physical activity, low consumption of fruits and vegetables; family history of DM2, overweight and obesity according to BMI ($p = 0.03$). When they were analyzed in the population of each university, a similar behavior was observed ($p = 0.0000$). The variables waist circumference, a history of hyperglycemia and the consumption of drugs for arterial hypertension did not present a statistically significant relationship with the risk of developing DM2, since 100% of the population was under 45 years of age, in this case it was a factor protector.

Image:

Table 1. Classification of the Risk of DM2 according to the Findrisk test in Young University Women

| Classification of the Risk of MD2 | Metropolitan Un | | Antioquia Un | | Total | |
|-----------------------------------|-----------------|----------------|--------------|----------------|------------|---------------|
| | n | % | n | % | | |
| Sin riesgo | 8 | 7,02% | 12 | 11,32% | 20 | 9,1% |
| Riesgo bajo | 73 | 64,04% | 77 | 72,64% | 150 | 68,2% |
| Riesgo medio | 29 | 25,44% | 16 | 15,09% | 45 | 20,5% |
| Riesgo alto | 4 | 3,51% | 1 | 0,94% | 5 | 2,3% |
| Total | 114 | 100,00% | 106 | 100,00% | 220 | 100,0% |

Source: Study Data

Conclusion: Research on university students is relevant; it is constituted in a group of young population that allows to inquire about the presence of risk factors for DM2, the results of this study confirm the importance of carrying out actions of early identification of risk, especially because an important influence of the presence of family inherited factors of MD2 risk.

Disclosure of Interest: None Declared

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GLYCAEMIC IMPACT OF AN E-LEARNING DIABETES EDUCATION MODULE ON TYPE 2 DIABETES MELLITUS PATIENTS IN MALAYSIA

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Introduction: Diabetes education is important as it increases health literacy which leads to improvement in control of diabetes mellitus. Diabetes education modules have shown benefits in several aspects of diabetic care including glycaemic control. We assessed the effect of an e-learning diabetes education module on short term glycaemic parameter (HbA1c) in type 2 diabetes (T2DM) patients in an urban tertiary hospital in Malaysia.

Objectives: To assess the effectiveness of a specific e-learning diabetes education module on glycaemic control in T2DM patients.

Methods: Adult T2DM patients were recruited from endocrinology clinic and randomized to control and intervention groups, with a study duration of six months. Participants in the intervention group were required to complete an education module utilizing a computer aided learning programme with interactive quiz elements and immediate feedback designed specifically for this study. This dual-language (English and Malay) timed quiz comprising of questions on nutrition, physical activity, medications, and complications was administered to participants in the intervention group in two different modules every 3 months. Glycaemic parameter (HbA1c) was assessed in all subjects at recruitment and at the end of the 6-month study period.

Results: 54 patients completed the module, compared to 55 in the control group (Total N = 109). Median age was 55 +/- 11.3 years. Mean weight was 82 +/- 18.1 kg and mean body mass index (BMI) was 31 +/- 6.9 kg/m². Mean HbA1c in the intervention group was 8.1 +/- 1.8 % while the control group was 8.2 +/- 1.5 %. Six months post intervention, there was a non-significant reduction in HbA1c of 0.3% (p=0.55) in the intervention group compared to 0.1% (p=0.82) in the control group. There was no statistically significant difference between the two groups (p=0.7).

Conclusion: The use of an e-learning diabetes education module showed a trend in improvement of diabetes control over a 6 months' period. Continued education may be required to enable behaviour change which can lead to improved glycaemic parameters in the future.

Disclosure of Interest: None Declared

ICE2021-1556

HYPERTRIGLYCERIDEMIA ASSOCIATED ACUTE PANCREATITIS AND DKA IN A PATIENT WITH NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS AND TYPE IIB HYPERLIPOPROTEINAEMIA

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Introduction: Hypertriglyceridemic pancreatitis is the 3rd common cause after cholelithiasis and alcoholism. Severe (11.29-22.58mmol/L) and very severe hypertriglyceridemia (>22.59 mmol/L) could cause pancreatitis by 5% and 10-20%, respectively.

Case Description: A 28-year-old morbidly obese male with BMI of 41kg/m² admitted with abdominal pain and vomiting. He had no past medical history of note. On arrival his VBG showed hyperglycaemia (18.8mmol/l) with borderline ketonemia (2.1mmol/l), but without acidosis. His initial bloods were lipaemic and not analysable, except lipid profile (total-cholesterol: 28.6mmol/l, HDL-cholesterol: 0.4mmol/l, non-HDL cholesterol: 28.2mmol/l, and triglyceride: 145.6mmol/l). CT abdomen demonstrated acute pancreatitis and he was commenced on conservative management. Few hours later, he developed diabetes ketoacidosis (pH: 7.28, bicarbonate: 14.4mmol/l, glucose: 24mmol/l, capillary ketone: 3.4mmol/l). After initiating fixed rate intravenous insulin infusion for DKA, the lipaemic serum started clearing so that amylase was measurable (151U/L) nearly 24 hours after admission. The was euthyroid and his HBA1C was 113 mmol/mol. Possible hypertriglyceridemia induced acute pancreatitis leading to DKA was considered. He has had generalized eruptive xanthomas.

After resolution of DKA, we have continued him on variable rate intravenous insulin infusion until his triglycerides were normalised. Islet antibodies (GAD65, ZnT8, & IA-2) were negative. ApoA1 was 71mg/dl (104-202), ApoB was 172mg/dl (66-133). Lipoprotein electrophoresis revealed Fredrickson type IIb hyperlipoproteinaemia. Molecular genetics showed absence of mutation in LPL and its cofactors (APOC2, APOA5, GPIHBP1, LMF1 and G3PDH1). Patients was established on basal-bolus insulin, low fat diet, high dose statins and fenofibrate. However, we lost his follow-up.

Clinical discussion: Though hypertriglyceridemia associated acute pancreatitis is classically described in type I, IV, and V primary hyperlipoproteinemias, it is also described with type IIb and type III subtypes. Among the primary hyperlipoproteinemias, IIb and IV have the highest occurrence (40% and 45% respectively). Secondary hypertriglyceridemia and polygenic diseases like type 2b, by themselves, will not cause pancreatitis as they have only moderately triglyceride elevation. However, when type 2b is combined with secondary conditions severe hypertriglyceridemia and thereby acute pancreatitis can occur.

Disclosure of Interest: None Declared

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CHALLENGES IN IMPLEMENTING INTEGRATED E-HEALTHCARE SERVICES FOR DIABETES MELLITUS PATIENTS DURING THE PANDEMIC IN INDONESIA

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Introduction: Diabetes mellitus is a degenerative disease that requires patients to receive continuous healthcare services. During a pandemic situation, all access to healthcare facilities become limited. A web-based integrated e-healthcare system was used to overcome this problem. This study was aimed to describe patients' ability to access and to understand this web-based application.

Case Description: A total of 29 outpatients with diabetes mellitus participated in this study. These patients belonged to local community-based diabetes mellitus. This study took place in Muara Tebo – Indonesia, during 2020. Only adult patients that accustomed to using smartphones were invited to participate in this study. All participants were taught to access the web-based application through video recordings. They were asked to fill the form regarding their ability to understand the web-based integrated e-healthcare application. This form was sent online.

Clinical discussion: A significant result was found in the level of education (OR 0.021) and job type (OR 0.001). The higher the level of education, the more access and understanding of this web-based application. Interestingly participants who do not have a permanent job were easier to use and utilize this application. Other sociodemographic data were found not to be significant, including age, gender, and duration of having diabetes mellitus. **Conclusion:** Participants' condition in this study reflects the general condition of outpatients. The ability of these participants to access an internet-based application was related to their education level. This condition becomes a challenge for policymakers to improve local human resource next to increase their health literacy.

Disclosure of Interest: None Declared

ICE2021-1577

DIABET MELLITUS AND COVID 19.HOW TO MANAGE IN OUTPATIENT

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Introduction: Diabetics are more susceptible to developing severe inflammatory response to Covid 19. Optimal glycemic control improves prognosis in people with diabetes and COVID-19. In general, hyperglycemia is associated with an increased risk of various infections, including viral ones. Hyperglycemia impairs neutrophil chemotaxis, phagocytosis, opsonization, vascular endothelial adhesion, and intracellular bacterial activity. The presence of diabetic complications, such as vascular insufficiency and peripheral neuropathy may also predispose to infections. Moreover, poor glycemic control contributes to this increased risk of infections in people with diabetes. Diabetes and obesity are associated with a low-grade chronic subclinical inflammation due to increased secretion of adipose tissue hormones and cytokines that contribute to the development of insulin resistance. Chronic low-grade inflammation along with hypercoagulation state in diabetes can trigger cytokine storm, a severe COVID-19 complication characterized by excessive production of inflammatory cytokines (IL-6, IL-10 and TNF)

Case Description: Case 1 M.Sh 37 years old Covid 19 pozitiv, No Diabetic, afebrile. Prandial glycemia 185, postprandial glycemia 220, HbA1c 5.58, Pcr 20, ferritinemia 670, D dimer 300, leukocytes 8000, Hb 12, erythrocytes 4500000, sediment 40, BMI 40 oxygen saturation 92-93%. Anti Covid 19 treatment + Diet + Metformin 850 2 × 1 after 10 days of medication, improvement of the condition and decrease of glycemias. Case 2 T.B 70 years old Covid 19 Positive , CT positive. Diabetic patient treated with oral metformin and glibenglamide. Second Day of the beginning of the disease temperature 39 grade celsius, prandial glycemia 450 , HbA1c 11.9 Pcr 50, ferritinemia 1650, sediment 120, leukocytes 4000, Hb 11, erythrocytes 4000000, D dimer 5000 oxygen saturation 85% Treatment (increase insulin +AntiCovid medicamentation. Normalization of glycemia after 3 weeks. Case 3 L.M 75 years old Covid 19 Positive. Treated with insulin therapy. Leukocit 20 000, sentiment 70, hb 17, glycemia 459, Pcr 48.9 creatinine 1.58, azotemia 93 ferritinemia 580.14, D dimer 10,000, oxigen saturation 76%. Treatment antiCovid medicamentation + insulin therapy) the patient makes exitus after 5 days of treatment

Clinical discussion: Covid 19 and Diabetic patients we can treat in home in order to controll their glicemia. Optimal glycemic controll improves prognosis in people with diabet.

Disclosure of Interest: None Declared

ICE2021-1584

PLASMATIC LEPTIN AND ENDOTHELIN-1 LEVELS IN A GROUP OF PATIENTS WITH DIABETIC RETINOPATHY

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Introduction: Diabetic retinopathy (DR) is a degenerative ocular pathology and a leading cause of visual disability worldwide. Markers of retinal injury are microaneurysms, hemorrhages, exudates, macular edema and neovascularization (1). Molecules such as leptin (LEP) and endothelin-1 (ET-1) have been detected in the plasma of patients with DR. LEP plays a significant role in the regulation of body weight, energy homeostasis, and angiogenesis; it has been found in high levels in severe forms of DR (2). ET-1, a potent vasoconstrictor plays a role in the development of vascular diseases as DR, in the retina. It has been shown to mediate decreased retinal blood flow during hyperglycemia (3).

Objectives: To determine the plasmatic levels of leptin and endothelin-1 and to evaluate their correlation with DR.

Methods: Case-control study. Two groups were evaluated, one group of patients with DR (DRG)(n=37) and a control group (CG)(n=37). Eligibility criteria: voluntary adults of 18 years and older who signed informed consent, in the DRG, with diagnostic of DR. A sociodemographic survey was applied, anthropometric parameters and blood samples were taken. LEP and ET-1 were determined by ELISA.

Results: The media of age was higher for DRG. For leptin levels, it was found higher significant differences in CG versus DRG (p=0.002); LEP values were higher between females of 40-59 years of CG vs DRG (p=0.010). The other age groups did not have differences. For ET-1, there were no significant differences between GC and RDG (p=0.324). When compared group, sex, and age it was found ET-1 significant higher levels between the male patients of DRG of > 60 years respect to 10-39 and 40-59 years (p=0.043; p=0.036 respectively). There is a correlation between age and ET-1 in GRD. Glucose levels were significantly higher in DRG of 40-59 years.

Conclusion: For this study, in ages of 40-59 years were obtained higher LEP values, in the CG females, remarkably LEP values in DRG had an opposite trend decrease with the age increase in females, and for males with a highest spike for 40-59 years. This characteristic could be associated with well glucose regulation in CG, and in DRG probably could be related to leptin resistance.

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Disclosure of Interest: None Declared

Diabetes/Obesity/Dyslipidemia

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DYSLIPIDEMIA ASSOCIATED WITH MORBIMORTALITY IN COVID-19 PATIENTS HOSPITALIZED IN PARAÍBA

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Introduction: COVID-19 is a disease caused by the SARS-CoV-2 virus, an emerging global public health issue. Although the epidemiology has been widely studied, many aspects of the disease are still unknown, such as risk factors as dyslipidemia. This study aimed to evaluate the correlation between lipid fractions and morbimortality of hospitalized patients.

Objectives: Correlate lipids fractions - the levels of low-density lipoprotein (LDL-c), high-density lipoprotein (HDL-c), total cholesterol (CT), and triglyceride - and biochemical markers of the COVID-19 severity outcome.

Methods: A retrospective study was carried out, from June 1st to August 15th of 2020, with hospitalized COVID-19 patients in a referral hospital in João Pessoa city, Paraíba. We measure serum levels of LDL-c, HDL-c, CT, and triglycerides in patients with COVID-19. The demographic data, past medical history, and hospital course were collected from the medical record and analyzed. Later, a multivariate logistic regression and Spearman's correlation were performed to evaluate the association between dyslipidemia and severity outcomes.

Results: We collected data from 253 patients. Then, split the patients into two groups: critical ill (24.9%) and non-critical ill (76.1%). We noticed that the critical patients had significantly lower LDL-c levels ($P = 0.0156$) and lower HDL-c/LDL-c ratio ($P = 0.0315$) compared to non-critical. Further, the CT and triglyceride values were also lower in critical patients, although there was no statistical significance ($P = 0.0827$ and $P = 0.7150$, respectively).

Conclusion: Our findings confirm previous evidence, suggesting that high lipid fraction is a protective factor against COVID-19 infection.

Disclosure of Interest: None Declared

ICE2021-1591

QUANTITATIVE ANALYSIS OF SERUM INTERLEUKIN-6 LEVEL IN DIAGNOSIS OF TYPE 2 DIABETES MELLITUS IN NORTH INDIAN POPULATION: A CASE CONTROL STUDY

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Introduction: Type 2 Diabetes Mellitus (T2DM) is a chronic inflammatory condition and associated with increased in serum level of various inflammatory markers.

Objectives: Objective of this study is to estimate the serum Interleukin-6 (IL-6) in diagnosis of Type 2 Diabetes Mellitus (T2DM).

Methods: This was age sex matched 1:1 case control study. A total of 60 subjects with age range 18-60 years were enrolled in the study, which included 30 newly diagnosed T2DM patients and 30 healthy controls. The serum IL-6 was measured by Enzyme-linked immunosorbant assay (ELISA). Receiver operating characteristics curve (ROC) analysis was used to determine the diagnostic utility of serum IL-6. The Youden index was used to select the optimum cut point to discriminate T2DM patients from healthy controls.

Results: The serum IL-6 were significantly higher in T2DM patients as compared to controls. The Area Under Curve (95% CI) for IL-6 were 0.792 (0.678-0.906) ($P < 0.001$) Serum IL-6 level above 5.80 pg/ml was diagnostic of T2DM with 73.33% (95% CI: 55.55-85.82%) sensitivity and 80% specificity (95% CI: 62.69-90.49%). In binary logistic regression analysis, T2DM occurrence increased with increasing concentration of IL-6 with an odds ratio (OR) of 1.348 (95% CI: 1.145–1.587; $P < 0.001$). In multiple linear regression analysis, body mass index and serum triglyceride are independent predictor of serum IL-6 level.

Conclusion: The serum IL-6 may be utilized as a surrogate marker for diagnosis of T2DM. A cut-off value of 5.8 pg/mL was shown to be significantly diagnostic of T2DM.

Disclosure of Interest: None Declared

ICE2021-1593

SECONDARY CARE FOR DIABETES –DO WE MAKE ANY DIFFERENCE?

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Introduction: Diabetes is a growing challenge to National Health Services(NHS) in United Kingdom. Diabetes care in UK is managed in partnership between Primary and Secondary Care. Diabetes Health Care Specialists take a variety of referrals from primary care, requiring input in complex cases.

Objectives: The purpose of this study was to assess our care on the patients referred to our Adult Diabetes Clinic by using 9 care parameters(BMI, blood pressure, smoking, HbA1c, serum cholesterol, digital eye photography, laboratory urine microalbumin:creatinine ratio, serum creatinine, foot examination) and observing changes in three measurable targets(blood pressure, cholesterol, HbA1c) as set out in UK National Diabetes Audit 2017-2018, which reports on the quality of care for people with Diabetes in England.

Methods: In a retrospective longitudinal study we studied the source and reason for referrals to Secondary Care over 12 months. Each patient was followed over 18 month period and data was collected on documentation of 9 care processes. We analysed changes in three measurable targets and interventions involved.

Results: 446 patients were referred over the study period. 82.6% patients were referred by Primary Care Practitioners. Patients were referred for chiefly optimisation of glycaemia control(55%), with type 1 diabetes(35%), worsening complications (12%), Insulin or GLP-1 analogue start(0.5%) and young patients with type 2 diabetes(4.5%).

We evaluated care on 271 patients after excluding non-attenders. Demographic data was collected for age, gender and type of diabetes.

90% of patients had all 9 care processes documented. 72% patients had positive impact of our care in improvement of measurable targets. 74% of the patients were referred with HbA1c above the target(>7.5%) among which 52% showed an average improvement of 4.2% in their HbA1c. 72% patients were referred to at least one allied diabetes professional including diabetes nurses, dieticians, podiatry or hypertension nurse.

19% patients required referral to at least one other specialty clinic including renal, urology and bariatric clinics. 11% patients were referred to psychologist and structured diabetes education. 80% patient had changes made to their medications.

Conclusion: In times of economic austerity, with increasing numbers of diabetes patients, models of diabetes care are under great scrutiny to assess their impact. Our study proves the importance of secondary care, that patients with diabetes do require expert opinion and integrated approach to improve metabolic profiles.

Disclosure of Interest: None Declared

ICE2021-1597

PATTERNS OF UNHEALTHY FOOD GROUPS INTAKE AND OBESITY AMONG URBAN CHILDREN IN ECUADOR: A CROSS-SECTIONAL STUDY

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Introduction: In the last decade, obesity prevalence has increased worldwide regardless of the population's socioeconomic status, age, or sex. Unhealthy eating in childhood is an important risk factor for obesity and non-communicable diseases.

Objectives: To identify patterns of unhealthy food groups intake and evaluate associations between BMI z-scores with unhealthy food groups intake.

Methods: A cross-sectional study involving 1028 children aged 9 to 12 years old was conducted from October 2018 until May 2019 in Cuenca-Ecuador. We collected anthropometry data and evaluated food intake using a food frequency questionnaire. Multiple correspondence analysis was used to identify patterns of unhealthy food groups intake (fast food, pastry products, processed and ultra-processed salty snacks, sweets and soft drinks). A multinomial logistic regression model was applied to identify associations between unhealthy food groups with BMI z-scores

Results: The children showed BMI z-score mean values of 0.54 ± 1.17 (male 0.54 ± 1.23 , female 0.54 ± 1.11). Our study identified three unhealthy food patterns ("Healthy", "Fair" and "Unhealthy"). The first pattern was named "Healthy," and was associated with those children who do not consume fast food, processed and ultra-processed salty snacks, sweets and confiture, pastry products and soft drinks. The second pattern was called "Fair" and was associated those children who consume fast food, processed and ultra-processed salty snacks, sweets and confiture, pastry products once a week and once a day for soft drinks. The last pattern was named "Unhealthy," and was associated with those children who consume more than twice a week fast food, processed and ultra-processed salty snacks, sweets and confiture, pastry products and more than twice a day for soft drinks. Most of the children were located in the "fair" (40,5%) and "unhealthy" (39.3%) cluster, and 20.2% of the participants belonged to the "healthy" one. Finally, BMI z-score was not associated with the food patterns.

Conclusion: We identified three groups of eating patterns ("Healthy", "Fair" and "Unhealthy"), according unhealthy food intake. If these patterns are maintained, the Ecuadorian children are at risk of non-communicable diseases

Disclosure of Interest: None Declared

ICE2021-1601

NON-ALCOHOLIC FATTY LIVER DISEASE IN HIV INFECTED PATIENTS – THE INFLUENCE OF ANTHROPOMETRIC PARAMETERS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is recognized as an important metabolic disturbance and has a great socioeconomic impact. The existing data points towards a greater prevalence of NAFLD in patients infected by HIV-1 (30 to 40%), comparing to the general population. Several hypotheses try to explain this association. It is thought that both metabolic comorbidities (such as obesity and insulin resistance) as well as factors related to the infection itself (associated inflammation and drugs used) are possible contributors.

Objectives: To evaluate the association between the occurrence NAFLD and anthropometric parameters in HIV-1 infected patients.

Methods: Cross-sectional study. We evaluated 354 HIV-1 infected patients followed in Endocrinology appointment in *Centro Hospitalar e Universitário de São João*. We assessed the association between the occurrence of NAFLD (evaluating hepatic biochemical profile and the indexes FLI, *Fatty Liver Index*, predictor of hepatic steatosis, and BARD, *BMI, AST/ALT ratio and diabetes*, predictor of hepatic fibrosis) and anthropometric parameters (body mass index, BMI, waist and hip circumferences and hip circumference/ waist circumference ratio).

Results: The study sample had an average age of 45.6 (SD 11.0) years, with a median of HIV-1 infection duration of 9.0 [IQR 6.0] years and 30.2% of women. Our results point towards a positive association between the occurrence of hepatic steatosis (FLI index) and BMI IMC ($\beta=0.699$, $p<0.01$), waist circumference ($\beta=0.778$, $p<0.01$) and hip circumference/ waist circumference ratio ($\beta=0.604$, $p<0.01$). There was no significant association between the occurrence of hepatic fibrosis and anthropometric parameters.

Conclusion: Our results corroborate the importance of the metabolic factors to the greater prevalence of NAFLD in HIV-1 infected patients, particularly in the initial stages of the disease (steatosis).

Disclosure of Interest: None Declared

ICE2021-1604

URIC ACID AND SERUM FERRITIN LEVELS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA: A CROSS-SECTIONAL, RETROSPECTIVE STUDY

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Introduction: Obstructive Sleep Apnea (OSA) is defined by episodic sleep state-dependent collapse of the upper airway, following periodic reductions or cessations in ventilation, with consequent hypoxia, hypercapnia, or arousals. OSA is a highly prevalent but underdiagnosed disease. May cause endocrine-metabolic alterations, culminating in additional cardiovascular risk, neurocognitive impairment, high morbidity, and worse quality of life. Obesity is OSA well-known risk factor, and it occurs in around 50% of these patients. Both conditions lead to a chronic inflammatory process and can correlate with the rise of inflammatory biomarkers. Then, the biochemical parameters can be useful in clinical practice to measure the severity of the disease outcome.

Objectives: Evaluate the relationship between uric acid and ferritin levels with the severity of OSA.

Methods: Cross-sectional, retrospective, quantitative study conducted in patients with OSA. It occurred between January 2011 and October 2016 in an endocrinology and diabetes center. We evaluate 103 cases, 30 male (29.13%) and 73 female (70.87%), and the mean age was 52.33 years. We split the patients into three groups based on the outcome of OSA: mild (25,24%), moderate (48.54%), and severe (27.22%). Then, we use a multivariate logistic regression and a Spearman's correlation to measure the association between OSA with ferritin and uric acid level

Results: To measure the apnea-hypopnea index (AHI), we use polysomnography, and the mean found was 23.78 events per hour. The mean level of Ferritin in the groups were: 89.9 ng/ml (mild), 175.3 ng/ml (moderate), and 250 ng/ml (severe). Further, we found a significant difference between the three groups ($P = 0.0007$), between mild and severe ($p \leq 0.0001$), and between moderate and severe ($P = 0.0391$). The mean uric acid level were: 4.09 (mild), 4.62 (moderate) 5.51 (severe). We found a significant difference between the three groups ($P = 0.0235$), between mild and severe ($p \leq 0.0006$), and between moderate and severe ($P = 0.0159$).

Conclusion: There is a close relationship between AHI with ferritin and uric acid levels. It can be use as a practical and low-cost way to predict the severity of the disease.

Disclosure of Interest: None Declared

ICE2021-1608

LINK CONTROVERSIES BETWEEN COVID-19 AND DIABETES MELLITUS TYPE II IN PARAIBA

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Introduction: The state of art says that the Diabetes Mellitus (DM) type II is a risk factor for 2019 coronavirus infection. But, nowadays, we find some evidence that does not agree with this hypothesis.

Objectives: We aim to evaluate the correlation between DM, biomarkers of mortality (D-dimer, PCR, and ferritin), and COVID-19 outcomes.

Methods: We conducted a cohort, observational, longitudinal, and prospective study between June 1 to August 15, 2020, in Joao Pessoa city. We collected demographic data, medical history, and hospital course from 200 patients. Then, we used Spearman's correlation and multivariate logistic regression to measure correlations.

Results: In our sample, 88 (44%) patients had diabetes diagnosis. Further, 121 (61.5%) had glycated hemoglobin over 6.5% during hospitalization. In the multivariate logistic regression analysis, the previous diagnosis of DM showed no significant difference (adjusted OR: 1.833; 95% CI: 0.82-4.19, $p = 0.202$). Glycated hemoglobin had a median of 8.07% in surviving patients and 8.72% in non-surviving patients. And there was no significant difference between them ($P = 0.39$). Also, in univariate logistic regression, decompensated DM ($HG > 7.5\%$) showed no significant difference to mortality (adjusted OR: 1.317; 95% CI: 0.588 - 3.017; $P = 0.56$) or disease severity outcome (OR adjusted: 1.157; 95% CI: 0.604 - 2.226; $P = 0.70$). In Pearson's correlation, glycated hemoglobin showed a positive correlation with the PCR ($R = 0.164$, $P = 0.033$) and with the D-dimer ($R = -0.158$, $P = 0.032$); and negative with the TGO enzymes ($R = -0.182$, $P = 0.013$), TGP ($R = -0.159$, $P = 0.031$) and with the DHL ($R = -0.168$, $P = 0.024$).

Conclusion: The diagnosis of type 2 diabetes mellitus, previously recognized or not, was quite prevalent in the studied population. We did not found the DM as a significant risk factor for COVID-19 outcomes.

Disclosure of Interest: None Declared

ICE2021-1611

DEPRESSION AMONG PATIENTS WITH DIABETES: A COMMUNITY-BASED STUDY IN BIHAR, INDIA

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Introduction: Depression is one of the more common mental health conditions found among people suffering from chronic diseases. Its presence in patients with type 2 diabetes could hinder the adherence to and effectiveness of treatment. Most studies on depression among patients with diabetes are hospital-based suggesting the need for a community-based study to assess the correlates of depression among patients with diabetes.

Objectives: This study aimed to estimate the prevalence and to identify the factors influencing depression among patients with type 2 diabetes in Patna, Bihar in eastern India.

Methods: This study recruited 230 patients with type 2 diabetes from both rural and urban areas. Demographic, clinical, and diabetes-related information were collected using a semi-structured questionnaire. Depression was assessed using Patient Health Questionnaire-9; a standardized questionnaire developed in the United States of America and validated in the Indian population.

Results: The prevalence of depression among patients with diabetes in the community was found to be 37.5%. Most frequently, depression was mild (49, 21%) in nature with severe depression (11, 4.8%) seen the least. The statistically significantly associated variables include female gender ($P < 0.01$), marital status ($P < 0.01$), rural residence ($P < 0.05$), and unemployment ($P < 0.01$). The presence of diabetic complications and other chronic diseases such as hypertension and obesity also were found to be associated with depression. More than half (137, 59.6%) of the participants were shown to bear extra burden of other chronic conditions with hypertension (106, 46%) being the most common comorbid condition.

Conclusion: Depression was found to be particularly high among the study population. Since depression could significantly hinder patient's adherence to treatment, there is an urgent need for early diagnosis and treatment. This calls for the integration of mental health care into the management of diabetes.

Disclosure of Interest: None Declared

ICE2021-1612

A STUDY OF BLADDER DYSFUNCTION IN WOMEN WITH TYPE 2 DIABETES MELLITUS

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Introduction: Diabetes mellitus has been associated with an earlier onset and increased severity of urologic diseases that often result in debilitating urologic complications. Diabetic bladder dysfunction refers to a group of bladder symptoms occurring in patients with diabetes mellitus ranging from bladder over activity to impaired bladder contractility.

Objectives: Bladder dysfunction is an under evaluated issue in women with diabetes. Aim of our study was to investigate prevalence of bladder dysfunction and its relation with other chronic complications of diabetes in women with type 2 diabetes.

Methods: In a hospital-based cross sectional study, a cohort of women with type 2 diabetes mellitus who had lower urinary tract symptoms (LUTS) were enrolled. We used the American Urological Association Symptom Index (AUA-SI) to assess the severity of LUTS and the Indevus Urgency Severity Scale (IUSS) to assess presence of overactive bladder (OAB). Age-BMI- matched controls that did not have diabetes but had lower urinary tract symptoms were also studied and compared with women with type 2 diabetes. Urodynamic evaluation was done in willing patients.

Results: LUTS attributable to bladder dysfunction were reported in 67% of women with type 2 diabetes after exclusion of other causes. Out of them, 36% had moderate to severe LUTS (total AUA-SI score >7). Prevalence of OAB was 53%. Among the chronic complications of diabetes, peripheral neuropathy, nephropathy, and presence of metabolic syndrome were significantly associated with moderate to severe LUTS and OAB. In the present study, 102/153 (67%) women had LUTS attributable to bladder dysfunction secondary to diabetes. Out of them, 36% of women with type 2 diabetes were considered to have moderate to severe LUTS (total AUA-SI score >7) as compared to 11% in control group. The storage and voiding symptom scores were significantly higher in women with diabetes than controls. The prevalence of OAB, as defined by an IUSS score of 2 or greater, was 53% in women with diabetes, which was significantly higher than in age- and BMI-matched controls. The overall prevalence of stress urinary incontinence and urge urinary incontinence in diabetic women was 19% and 23%, respectively.

Conclusion: Bladder dysfunction is a highly prevalent complication in women with diabetes. Chronic complications of diabetes especially neuropathy, nephropathy, and presence of metabolic syndrome are important predictors of bladder dysfunction.

Disclosure of Interest: None Declared

ICE2021-1613

TREATMENT AND CONTROL OF DIABETES IN ELDERLY PEOPLE: A STUDY IN CENTRAL REGION OF BRAZIL

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Introduction: The age group with the highest proportion of people with DM is the elderly, and 6.1 million of the total diabetics in Brazil are elderly. Diabetes Mellitus control is complex and consists of lifestyle changes and pharmacological treatment. Lack of control results in severe complications (IDF 2019).

Objectives: The objective of this study was to estimate the rate of treatment and glycemic control of elderly people with type 2 diabetes mellitus.

The objective of this study was to estimate the rate of treatment and glycemic control of elderly people with type 2 diabetes mellitus.

Methods: Cross-sectional study with a probabilistic sample of 221 elderly users of SUS in Goiânia, in the State of Goiás, central region of Brazil. Diabetes *mellitus* was defined by self-report, use of an antidiabetic, fasting glucose ≥ 126 mg/dL and/or glycated hemoglobin (HbA1c) $\geq 6.5\%$. Treatment was determined by the use of the oral or injectable antidiabetic drug. The control rate defined by HbA1c levels $\leq 7.5\%$ (ADA, 2019). The data were analyzed in STATA 12.0, using descriptive statistics and Pearson's chi-square comparison test. The project was approved by the Research Ethics Committee.

Results: The prevalence of DM was 39.4% and the treatment rate was 71.3%. Of these 88.8% approximately use some oral antidiabetic, 27% injectables and 15.9% used both. The average consumption of antidiabetics was 1.6, varying from 1 to 4. The control rate was 76%, 26% of which did not reach the adequate glycemic objective for the elderly (≤ 7.5 mg/dL), being associated with the female gender and age 80 ($p < 0.05$).

Conclusion: Although Brazil is a developing country, in comparison to other emerging countries, the rate of treatment and control for diabetes performs better, justified by public policies that include the Family Health Strategy, and the National Health Policy Pharmaceutical Assistance (MONTEIRO et al, 2018). The prevalence of DM was high, and although the rate of treatment and control was high, a portion of approximately 20% of the elderly did not reach therapeutic targets. Considering the complications and difficulties in the management of other diseases, which the presence of DM can bring to the elderly, it is important strategies that promote greater accessibility and quality of them, in order to guarantee a higher rate of treatment and glycemic control, well as reduced access to high complexity services due to complications.

Disclosure of Interest: None Declared

ICE2021-1614

THE IMPACT OF COVID-19 LOCKDOWN ON THE GLYCEMIC CONTROL AND BODY WEIGHT IN TYPE 2 DIABETES MELLITUS ASSESSED DURING THE PROGRESSIVE UNLOCKING PHASE IN URBAN INDIAN SETTING

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Introduction: There is limited, yet varied evidence for the impact of the change of the metabolic parameters in T2DM during the COVID-19 lockdown. The impact of previous pandemics and natural disasters on metabolic derangements may not be replicated with COVID-19.

Objectives: To assess the impact of lockdown on glycemic control and body weight

Methods: We evaluated the change in body weight and HbA1c for patients (n=357) following up regularly, post the unlocking period in India (1st June 2020) with at least one visit in last one year before lockdown and on stable medications since last visit.

Results: The mean age (years) was 60 (± 12 , minimum 19, maximum 89, range 70, 95% CI 59 to 62). The mean HbA1c (%) before the lockdown was 7.4 (± 1.3 , minimum 5.2, maximum 14, range 8.8, 95% CI 7.3 to 7.6) which reduced by 0.29% at the follow up with mean HbA1c 7.2 (± 1.1 , minimum 5.1, maximum 11, range 6.3, 95% CI 7 to 7.3). The reduction was statistically significant ($p=0.0012$). The mean body weight (kg) before the lockdown was 75 (± 15 , minimum 44, maximum 131, range 87, 95% CI 73 to 76) which reduced by 0.9 kg at the follow up with mean body weight 74 (± 14 , minimum 42, maximum 129, range 87, 95% CI 72 to 75) ($p=0.40$ NS). 215 out of 357 patients (60.2%) achieved reduction in HbA1c. Out of 215 patients, 150 achieved HbA1c < 7%. Out of 215 patients, 152 also achieved weight loss. 233 patients out of 357 achieved weight loss. There was a significant positive correlation between the difference of HbA1c and the difference in the weight loss ($r=0.088$, $p=0.098$, 95% CI -0.016 to 0.190). The mean change in the HbA1c (-0.29%, $p=0.96$ NS) was similar in both the age groups, of age group ≤ 60 years ($n=159$) and age group > 60 years ($n=198$). Higher proportion of age group >60 years as compared to ≤ 60 years achieved HbA1c < 7, (53% Vs 47%, Odds ratio [OR] 1.28, $p=0.2839$ NS).

Conclusion: The reduction in the HbA1c was more prominent than the weight loss achieved during the lockdown phase, with greater number of elderly patients achieving good glycemic control than the younger patients. We attribute the virtual and in person consultations, as part of the diabetes continuity care program that enabled

the patients maintain the metabolic health and mitigate the potential detrimental effect of lockdown.

Disclosure of Interest: None Declared



ICE2021-1619

**EFFECTIVENESS AND DURABILITY OF EXTENDED RELEASE GLICLAZIDE
IN THE TREATMENT OF TYPE 2 DIABETES- A REAL WORLD PERSPECTIVE**

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Introduction: Modern sulfonylureas including extended Gliclazide are acceptable standard of care in the management of diabetes

Objectives: To assess the control rates and periods until the initiation of insulin from the onset of diabetes (durability) and from the time of initiation of the treatment of diabetes, through an open label observational study

Methods: We conducted a retrospective analysis (n=300, 159 male, 141 female), of the dataset to evaluate the patients who were under a longitudinal follow up adherent to our guideline directed treatment protocol. The study was conducted in the year 2018, at a dedicated, institutional diabetes care clinic providing comprehensive care in a multi-specialty hospital. The patients, with duration of diabetes of more than five years, adherent to modern sulfonylurea-based regimen (gliclazide extended release) with standard care of approach since the year 2000, were evaluated. Structured patient education for lifestyle management was provided during each follow up visit. Descriptive statistics was utilized for analysis

Results: The mean age (years) and mean HbA1c (%) was 55.14 (± 8) and 7.1 (± 0.6), ($p < 0.001$), respectively. 82% of patients achieved target range of HbA1c $< 7\%$. 18.7% (56/300) patients had diabetes for ≥ 20 years. The mean duration of treatment for the regimen of gliclazide extended release plus metformin was 12.81 (± 6) years. 1% (n=3) patients reported episodes of confirmed hypoglycaemia but were self-managed. 16.3% (49/300) patients in due course required insulin. The number of patients with BMI (kg/m²) ≤ 25 , 26-30, 31-34, > 40 were 150 (50%), 124 (41.4%), 19 (6.4%) and 5 (1.6%), respectively. The number of patients with duration of diabetes (years) 5-9, 10-14, 15-19, ≥ 20 were 103 (34.3%), 87 (29%), 54 (18%), 56 (18.7%), respectively. Insulin initiation was at mean HbA1c $> 8\%$

Conclusion: We observed a sustained glucose lowering attributed to gliclazide-based approach demonstrated by majority of patients, which enabled to postpone insulin initiation despite a long duration of diabetes. Overall, the patients achieved a glycemic level close to the target values of < 7 . Our findings support sustained glycemic control for durability with potential to postpone insulin initiation attributed to extended release Gliclazide, a modern sulfonylurea

Disclosure of Interest: None Declared

ICE2021-1636

NEW ONSET DIABETES WITHOUT THE HISTORY OF USAGE OF CORTICOSTEROIDS: A METABOLIC PARADOX AS A COMPLICATION OF COVID-19

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Introduction: It is now known that poorly controlled diabetes is associated with high mortality rate, in COVID-19. However, there is paucity of evidence for the COVID-19 induced diabetes, without the history of usage of steroid. There are only few isolated reports for new onset of diabetes in individuals with COVID-19, which is attributed for the potential of SARS-CoV-2 for direct and indirect cytotoxicity to pancreatic islet β cells. This is due to the binding and entry of SARS-CoV-2 into β cells via co-expression of its entry factors, angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2)

Objectives: To assess the correlation between the fasting blood glucose and C-peptide levels in new onset diabetes due to COVID-19

Methods: We identified six new cases of new onset of diabetes post COVID-19, who had recovered without the therapeutic intervention with corticosteroids and without the history of use corticosteroids

Results: The mean age was 42 years (± 13 , minimum 23, maximum 58, 95% CI 29 to 55). The mean BMI was 26 kg/m² (± 2 , minimum 25, maximum 30, 95% CI 24 to 28). Only one case who had BMI 30 kg/m², no urinary ketone, had positive family history of diabetes. The mean fasting blood glucose and HbA1c was 292 mg/dL (± 112 , minimum 142, maximum 485, range 343, 95% CI 175 to 410), 12 % (± 3.1 , minimum 8, maximum 16, range 8, 95% CI 8.2 to 15). The mean C-peptide was 15 ng/mL (± 4.2 , minimum 9, maximum 21, range 12, 95% CI 11 to 20). Urinary ketone was detected positive in five cases. Initial management with insulin was followed with OHA.

Conclusion: We observed markedly elevated fasting blood glucose levels and a remarkable degree of elevated C-peptide levels with the presence of ketone bodies, which suggests pancreatic islet β -cell dysfunction or apoptosis, with cellular shift to alternate fatty acid metabolism. The corroboration for the urinary ketone and the C-peptide levels, in relatively lean individuals, appears to be potential biomarkers for detection of COVID-19 induced diabetes. The results provide insights into perturbed mechanisms, that activate metabolic pathways inducing new onset diabetes, during evolution of COVID-19, translating as a complication of COVID-19. The metabolic paradox of ketone bodies with high C-peptide levels, need corroboration for the emerging evidence from other centres across the world

Disclosure of Interest: None Declared

ICE2021-1637

COMPARISON BETWEEN DIFFERENT METABOLIC SYNDROME CRITERIA IN PEDIATRIC PATIENTS WITH NORMAL WEIGHT, OVERWEIGHT AND OBESITY.

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Introduction: Metabolic syndrome is composed by factors that increase atherosclerosis, diabetes mellitus and cardiovascular disease. The International Diabetes Federation (IDF), in 2005, defined in adults three of five criteria: central obesity, hyperglycemia, hypertriglyceridemia, and high density lipoprotein cholesterol, and hypertension. There are more than 40 definitions created for pediatric population, with different cut-off values, making diagnosis difficult, and prevalence vary from 0.2% to 38.9%.

Objectives: Compare metabolic syndrome prevalence according to normal weight, overweight, and obesity, criteria, and maturation stages.

Methods: In an observational, transversal, comparative study we included patients from 6 to 16 years. The sample size was calculated based on program G power for the difference of prevalences with χ^2 with a size of effect 0.5, alfa error 5% and 95% potency. We excluded patients with diabetes mellitus, thyroid pathology, with use of glucocorticoids, lipid regulating drugs, oral hypoglycemic drugs, antihypertensive drugs one month prior to the study.

Results: 80 patients were included, with ages 10.6 ± 2.8 years. According to nutritional stage normal weight (12.5%), overweight(26.3%) and overweight(61.8%). Prepuberal stage was the most common (43.8%) followed by continuous maturation(41.3%). Prevalences varied from Cook(30%), Cruz and Gorán(30%), Ferranti(40%), Zimmet(IDF)(25%), Ahrens (32.5%). Ferranti had the highest prevalence in obesity(44.9%), Ferranti and Zimmet with overweight population(38.1%). The strongest concordance was between Cook and Cruz y Gorán ($\kappa=0.881$). Dyslipidemia is present in all nutritional stages.

Image:

Comparison between different authors and criteria

| | Romero-Velarde | Peña-Espinoza | Agudelo | Guilherme | Gianni | Reuter | This study |
|-----------------------------|---|-------------------|---------------------|---------------------------------|---|-----------------------------|--|
| | % | % | % | % | % | % | % |
| Criteria | IDF (Zimmet) | Cook 13.8 | Cook 3.8 | Cook 3.3 | IDF 26.6 | Cook 1.9 | Cook 30 |
| | OMS | IDF 15.4 | IDF 0.9 | IDF 1.7 | NCEP-ATPIII 40.4 | IDF 1.7 | IDF 25 |
| | ATP III | Ferranti 45.9 | Ferranti 11.4 | Ferranti 12.6-22.3 | (Ferranti) | Ferranti 17.4 | Ferranti 40 |
| | | NCEP-ATP III 21.1 | Ford 4.1 | | | | Cruz y Gorán 30 |
| | | Weiss 2.4 | Agudelo 10.5 | | | | Ahrens 32.5 |
| Population (years) | 10 ± 2.7 N=120 | 9-13 N=507 | 10-18 N=851 | 7-24 N=4540 | 10 - 18 N=106 | 12 - 17 N=1200 | 6 - 16 Mean: 10.5±2.9 N=80 |
| Distinction | HOMA-IR Dyslipidemia Divided by sex Birth Weight | HOMA- IR | Prepuberal 20.4% | C-HDL 10-14>obesity 28.7% | MS≥ Obese HDLc, waist circumference | Continuos maturation 66% | MS≥ Obese TAG↑ Prepuberal 43.8% |
| Concordance | No realizada | HOMA- IR | | | | | |
| Cook- IDF | | k=0.7 | k=0.39 | k=0.95 | | k=0.532 | k= <0.2 |
| Ferranti- IDF | | K=0.353 | k= 0.14 | k=0.67 | k=0.48 | k=0.382 | k= <0.2 |
| Cook-Ferranti | | k=0.37 | k=0.45 | k=0.72 | | k= 0.542 | k= 0.511 |
| Cook- Cruz y Gorán | | | | | | | k= 0.88 |
| IDF- Ahrens | | | | | | | k= <0.2 |
| Cruz y Gorán- Ahrens | | | | | | | k= 0.826 |
| Ahrens- Cook | | | | | | | |
| Agudelo- IDF | | | k=0.15 | | | | |
| Ferranti- Agudelo | | | k=0.64 | | | | |
| NCEP- Cook | | k=0.736 | | | | | |
| Ferranti- Weiss | | k=0.056 | | | | | |

IDF:(International Diabetes Federation:Zimmet).MS=Metabolic Syndrome. N= population number, HDLc= High Density Lipoprotein cholesterol WHO: World Health Organization. Concordance TAG: Trilglycerides HOMA- IR: (Insulin resistance Index) interpretation (Kappa value): <0,2 (poor), 0,21-0,4 (weak); 0,41-0,6 (moderate); 0,61-0,8 (strong); 0,81-1 (very strong)

Conclusion: There is a difference in prevalence of metabolic síndrome according to diferent deffinitions. Ferranti was the most prevalent. For a population from 6 to 10 years old, Ahrens was the most prevalent. Dyslipidemia is present in all nutritional stages.

Key words: obesity, metabolic síndrome, nutritional stages, sex maturation stages.

Disclosure of Interest: None Declared

ICE2021-1638

DIAGNOSIS OF METABOLIC SYNDROME IN PATIENTS WITH TYPE 2 DIABETES MELLITUS, TO OPTIMIZE TREATMENT AND REDUCE THE RISK OF COMPLICATIONS.

Izabela De Oliveira*, Gabriella de Souza, Vilmar Baldissera

Introduction: Type 2 diabetes mellitus (DM2) is a metabolic condition in which lack of control triggers organic complications, resulting in tissue damage, loss of function and failure of several organs. While the metabolic syndrome (MS) is defined by associated factors: increased blood pressure, disorders of the metabolism of glucose, lipids and being overweight. Cardiovascular disease is the leading cause of mortality in individuals with DM2, and MS increases the risk of mortality from cardiovascular causes by 2.5 times.

Objectives: Establish the diagnosis of MS among patients with DM2 to optimize care and prevent complications resulting from the association between MS and DM2.

Methods: An observational, retrospective study, based on the analysis of the medical records of 60 patients with DM2 over the age of 40, made available in basic health units (BHU) in Rio Claro-SP. Of the data collected, 38 patients are women and 22 men, the average age is 63.6 years, 56 patients attend the BHU at least once a year. When analyzing the 56 patients undergoing continuous monitoring, 77.3% are hypertensive, 92.4% are overweight and do not eating balanced 86.7% are sedentary, and 83% have dyslipidemia. All patients with decompensated DM2 - glycated hemoglobin (h1ac) greater than 7%, have at least 3 of the 5 diagnostic criteria for MS. 20 patients had some type of complication associated with DM2.

Results: All patients with decompensated DM2 were classified with MS and overweight. 20 patients presented some complication. In view of the results, it is notable that the high prevalence of physical inactivity, obesity, irregular eating habits and hypertension, are factors that are related, aggravate the individual's health and configure MS. In addition, a sedentary lifestyle prevents the uptake of glucose in the muscles, which could be obtained from physical activity, obesity contributes to the accumulation of glycogen in the adipose tissue, and finally, eating habits, rich in carbohydrates, sugars and fats contribute to elevate glycemic, triglyceride and cholesterol levels. Therefore, they are attenuating factors for the high rates of h1ac and DM2 decompensation.

Conclusion: The appearance of complications related to DM2 has a close relationship with MS, which helps to increase the rates of h1ac, which, when altered, trigger tissue damage or organ failure. The data demonstrate that the care of these patients must address concomitant MS and DM2 for a better prognosis and prevention of the complications mentioned.

Disclosure of Interest: None Declared

ICE2021-1366

CUTANEOUS MANIFESTATIONS OF DIABETES MELLITUS: CLINICAL ANALYSIS OF 109 VIETNAMESE PATIENTS

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Introduction: Skin diseases are among common injuries in diabetes. Skin changes play a role as an early manifestation as well as a reflection of glucose metabolic control and chronic complication management of diabetes.

Objectives: To evaluate clinical and laboratory features of diabetic patients with skin manifestations and the relation between common skin diseases and chronic diabetic related characteristics.

Methods: 109 patients with type 1 and type 2 diabetes having skin injury hospitalized in our hospital from August 2019 to August 2020

Results: The prevalence of male and female patients in the study were 52,3% and 47,7% respectively, with the mean age of $60,46 \pm 15,27$. There were 4,6% patients with DM type 1 and 95,4% with DM type 2, the mean duration of DM was $7,71 \pm 7,78$ năm years. The most prevalent cutaneous findings were xerosis (59,6%), bacterial infection (22%), fungal infection (15,6%), onychodystrophy (19,3%), diabetic dermopathy (7,3%). Majority of patients (57,8%) had more than one type of skin injury. Of 109 patients, 33% had nephropathy, 27,5% had rentinopathy, 29,8% had neuropathy; the prevalence of stroke, coronary artery disease and peripheral artery disease was 12,8%, 9,2% and 6,4% respectively. There was a statistically significant relationship between some common skin manifestations and duration of diabetes and microvascular complication, however, similar correlation had not been found regarding such skin lesions and macrovascular diseases.

Conclusion: The most frequent cutaneous manifestation in patients with diabetes were xerosis, bacterial infection, fungal infection, onychodystrophy and diabetic dermopathy. Skin disorders may hint the existence of microvascular complication of diabetes.

Disclosure of Interest: None Declared

ICE2020-1112

ESTROGEN RECEPTOR-DEPENDENT AND PI3K/AKT PATHWAYS WERE INVOLVED IN BREAST CANCER MIGRATION AND ANGIOGENESIS BY A PESTICIDE, FENHEXAMID

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Introduction: A fungicide, fenhexamid (Fen), is used to treat the gray mold of fruits and vegetables. In particular, in wine, its residue concentration was detected more than other fungicide of similar effects such as cyprodinil, azoxystrobin and boscalid.

Objectives: In this study, to examine the effects of Fen on breast cancer progression, the ER positive-MCF-7 breast cancer cells and the ER negative-MDA-MB-231 breast cancer cells were employed.

Methods: The cells were treated with 0.1% DMSO (control), 17 β -estradiol (E2; 1x10⁻⁹ M) and Fen (10⁻⁵-10⁻⁷ M) in the absence or presence of ICI 182,780 (ICI, ER antagonist, 10⁻⁸ M) or Pictilisib (Pic, PI3K inhibitor, 10⁻⁷ M). To confirm the migration of MCF-7 by Fen compared to E2 as a control, wound-healing assay was conducted.

Results: In similar, when they were observed by live cell imaging incubator system for 72 h, the scratch area of MCF-7 cells was decreased by E2 or Fen in a time-dependent manner. In migration assay used insert chamber with fibronectin, the MCF-7 cells migrated to the opposite side from the inside of chamber by E2 or Fen at 72 h. The cell migration induced by E2 or Fen was inhibited partially or completely by co-treated with Pic or ICI. In immunofluorescent, E2 and Fen promoted the decrease of E-cadherin (cell adhesion protein), and increase of N-cadherin (cell-cell adhesion protein) in MCF-7 cell at 72 h. In addition, in Western blot, E2 and Fen induced the decrease of cell adhesion related proteins such as E-cadherin and Occludin, while expression of cell migration regulating proteins was not observed in MDA-MB-231 cells. In an angiogenesis assay, E2 and Fen promoted the vessel formation than control for 4 h in HUVEC cells. When HUVEC cells were incubated in conditioned HUVEC media for 4 h, which was incubated in MCF-7 cells treated with the E2 or Fen for 24h, E2 or Fen directly increased the vessel formation in HUVEC cells. In tumor spheroid formation assay, E2 and Fen promoted larger and higher density of the formation of spheroid than the control. These effects were reversed in partially or completely in the presence of Pic or/and ICI.

Conclusion: These results imply that Fen may induce breast cancer progression by increasing cell migration and angiogenesis via an ER-dependent and PI3K/AKT pathways.

Disclosure of Interest: None Declared

Endocrine Disruptors

ICE2020-1114

PROLIFERATION AND SURVIVAL OF BREAST CANCER CELLS WERE ENHANCED BY A PESTICIDE, FENHEXAMID, VIA AN ESTROGEN RECEPTOR-DEPENDENT AND PI3K/AKT PATHWAYS

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Introduction: Fenhexamid (Fen) is a fungicide used to treat the gray mold of fruits and vegetables. This pesticide may play a role as endocrine disrupting chemicals in the progression of estrogen receptor (ER) expressing breast cancer.

Objectives: In this study, the ER positive-MCF-7 and ER negative-MDA-MB-231 breast cancer cells were used to examine the effects of Fen on breast cancer progression.

Methods: The cells were cultured with 0.1% DMSO (control), 17 β -estradiol (E2; 1x10⁻⁹ M) and Fen (10⁻⁵-10⁻⁷ M) in the absence or presence of ICI 182,780 (ICI, ER antagonist, 10⁻⁸ M) or Pictilisib (Pic, PI3K inhibitor, 10⁻⁷ M).

Results: In MTT assay, Fen increased MCF-7 viability about 2.5 times compared to a control as E2 did (about 3 times). When co-treated with Pic or ICI, the cell viability increased by E2 or Fen was inhibited partially or completely. The cell viability increased by E2 or Fen was more inhibited by co-treatment with Pic and ICI than a single co-treatment of Pic or ICI. Likewise, E2 and Fen increased the ratio of MCF-7 cells that entered the S-phase of cell cycle, but co-treatment of Pic and ICI increased the cell ratio in the G0/G1-phase. But Fen could not induce the change of cell proliferation or cell cycle by ER or/and PI3K inhibitor in ER-negative MDA-MB-231 cells. In Western blot assay to support this, E2 and Fen promoted the cell cycle related proteins, i.e., Cyclin D1 and E1 and inhibited the expression of p27, a cell cycle inhibitory protein in MCF-7 cells. In co-treated with Pic or ICI, cell cycle related proteins were altered to the direction of inhibiting the cell cycle. In the colony formation assay, colony area and number of MCF-7 cells were increased by E2 and Fen, while it was, in part, reversed in the presence of Pic or ICI and completely reversed by co-treatment with Pic and ICI. In JC-1 dye assay to confirm apoptosis, the apoptotic cells were decreased by E2 and Fen in MCF-7 breast cancer cells, while the apoptotic cells were reversed by Pic or/and ICI. In Western blot assay, E2 and Fen induced the expressions of Survivin, a cell survival promoting protein, and PCNA protein, a cell proliferation promoting protein.

Conclusion: Taken together, these results indicate that Fen, a pesticide, may induce cancer progression by increasing cell viability and survival via an ER dependent and PI3K/AKT pathways.

Disclosure of Interest: None Declared

Endocrine Disruptors

ICE2020-1177

CHANGES IN RESTING METABOLIC RATE (RMR) AND BODY COMPOSITION: A UAE RAMADAN STUDY

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Introduction: Both eating and drinking is restricted during Ramadan fasting days (~30 days) marked by two main meals; one at sunset (*Iftar*) and one at dawn (*Suhour*). Our previous work indicated changes in feeding patterns, glucose variability energy metabolism, expenditure and physical activity during Ramadan.

Objectives: To investigate differences in resting metabolic rate (RMR) and various parameters of body composition via bioelectric impedance analysis (BIA) pre-, during and post-Ramadan.

Methods: Healthy participants attended Imperial College London Diabetes Centre (ICLDC) were assessed for RMR (COSMED-Quark RMR indirect calorimetry machine) and BIA. (SECA mBCA machine) Of the 35 consented participants initially recruited who fasted Ramadan, 14 patients were included for data analysis. Strict exclusion criteria included full record of fasting days, no chronic or metabolic conditions and/or medication that may affect either measurements or the ability to fast. Changes in RMR, body mass index (BMI), weight (WT), fat free mass (FFM), fat free mass index (FFMI) and total body water (TBW) were assessed at: (1) Pre-Ramadan (Pre-R), (2) during Ramadan (R), (3) end of Ramadan (End-R) and (4) Post-Ramadan (Post-R). Data analysis was carried out using (STATA -v15.0). Repeated measures of ANOVA with Greenhouse-Geisser correction, was used with tukey post-hoc pairwise comparison with statistical significance at $P \geq 0.05$.

Results: Of all the parameters measured at all the time points, statistically significant changes were observed between: (1) RMR: increased by 156.36 kcal/day between R and Post-R, (2) BMI: decreased by 0.37 kg/m² between Pre-R and End-R and (3) all the other parameters decreased between Pre-R and Post-R; weight (-0.98kg), fat free mass (-0.74 kg), fat free mass index (describing the amount of muscle mass in relation to height and weight) (-0.26 kg) and total body water (as a percentage of body weight) (-0.59 kg) (**Table1**).

Image:

Table 1. RMR and BIA changes pre-, during and post-Ramadan fast.

| Parameter | Time Point 1 | Point 1 Mean | Time Point 2 | Point 2 Mean | Mean Difference | Std. Err. | P-value | ANOVA | G-G |
|----------------------------|--------------|--------------|--------------|--------------|-----------------|-----------|---------|-------|------|
| RMR (Kcal/day) | R | 1530.00 | Post-R | 1686.36 | 156.36 | 48.79 | 0.01 | 0.01 | 0.02 |
| BMI (Kg/m ²) | Pre-R | 26.03 | End-R | 25.66 | -0.37 | 0.09 | 0.00 | 0.00 | 0.01 |
| Weight (Kg) | Pre-R | 74.04 | Post-R | 73.06 | -0.98 | 0.27 | 0.01 | 0.01 | 0.02 |
| Fat Free Mass (FFM) (Kg) | Pre-R | 50.43 | Post-R | 49.69 | -0.74 | 0.27 | 0.05 | 0.04 | 0.04 |
| Fat Free Mass Index (FFMI) | Pre-R | 17.64 | Post-R | 17.37 | -0.26 | 0.09 | 0.03 | 0.01 | 0.01 |
| Total Body Water (TBW) | Pre-R | 36.76 | Post-R | 36.17 | -0.59 | 0.20 | 0.03 | 0.02 | 0.03 |

Table 1. RMR and BIA changes pre-, during and post-Ramadan fast. Changes in various parameters were measured Pre-Ramadan (Pre-R), during Ramadan (R), end of Ramadan (End-R) and Post-Ramadan (Post-R) for fourteen healthy participants attending ICLDC health facility. Statistical significance ($p \leq 0.05$) was tested using repeated measures ANOVA on STATA (v15).

Conclusion: All parameters assessed were significantly modulated by Ramadan fasting. Our data show that changes in RMR and BMI are not limited to decreases in fat mass and water (often associated with restricted eating and drinking during Ramadan fasting hours), but extend to changes in other parameters such as muscle mass. Moreover, the noted difference in timeline of these observed changes merits a closer look into the implicated physiology. Ongoing work is elucidating these changes and other related parameters in a larger cohort.

Disclosure of Interest: None Declared

Endocrine Disruptors

ICE2021-1330

SEVERE HYPONATRAEMIA IN AN ELDERLY PATIENT SECONDARY TO EMPTY SELLA SYNDROME

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Introduction: 68 years old Patient admitted with recurrent episodes of generalized weakness and dizziness

Case Description: On examination, patient was lethargic and has low blood pressure. Investigations showed low sodium, low cortisol and low anterior pituitary hormones with abnormal short synactin test. CT scan and MRI brain confirm the empty sella syndrome. Management plan include treatment with hydration, electrolyte replacement, hydrocortisone and thyroxine. The patient responded to treatment and sent home thereafter. Regular follow-up arranged in endocrine clinic.

Clinical discussion: Empty sella syndrome (ESS) can be primary with unknown etiology or secondary due to radiation and surgery. Most of the cases are asymptomatic [1]. ESS can cause secondary adrenal insufficiency leading to euvolumic hyponatraemia. Diagnosis needs confirmation by assesment of adrenal axis functions.

References :

1. Chiloiro S, Giampietro A, Bianchi A, Tartaglione T, Capobianco A, et al. (2017) Diagnosis of Endocrine disease: Primary empty sella: A comprehensive review. Eur J Endocrinol 177: 275-285.

Disclosure of Interest: None Declared

Endocrine Disruptors

ICE2021-1370

ENDOCRINE-DISRUPTING CHEMICALS AND OBESITY

Hassan M. Heshmati*

Introduction: Endocrine-disrupting chemicals (EDCs) represent a heterogeneous group of exogenous chemicals or chemical mixtures that interfere with the action of hormones and consequently cause adverse effects to humans. Humans are constantly exposed to hundreds of EDCs mainly through air, water, and food. Obesity is a worldwide pandemic responsible for increased morbidity/mortality and high cost for the society.

Objectives: The aim of this presentation is to discuss the role of EDCs in the current obesity pandemic.

Methods: A systematic search of literature was conducted using the search terms EDCs, obesogens, weight gain, obesity, and pandemic.

Results: The number of EDCs has exponentially increased over the past 60 years. Approximately 1,000 agents have been characterized. This increase coincides with the obesity pandemic. Some EDCs are able to impair regulation of adipose tissue and food intake, reduce basal metabolic rate, and predispose to weight gain and obesity despite normal diet and exercise. They can also cause resistance to weight loss if subjects are on anti-obesity diet and/or drug. These EDCs are called obesogens. Approximately 50 chemicals have been identified (e.g., monosodium glutamate, nicotine, bisphenol A, phthalates, parabens, and tributyltin). White adipose tissue is an important reservoir of lipophilic obesogens (several obesogens are lipophilic chemicals). Obesogens have several target tissues including adipose tissue, brain, liver, stomach, and pancreas. At the level of adipose tissue, obesogens promote obesity by inducing an increase in the number of adipocytes (by activating nuclear receptor signaling pathways critical for adipogenesis) and storage of fat. The metabolic programming of obesity risk may be linked to *in utero* or lifetime exposure to obesogens. Perinatal exposure to obesogens is associated with overweight and obesity in children. Some obesogens (e.g., bisphenol A and tributyltin) are able to induce heritable changes that are propagated through multiple generations without any new exposure (transgenerational inheritance).

Conclusion: The obesity pandemic is associated with increased exposure to some EDCs called obesogens. Obesogens alter metabolic processes and predispose some subjects to weight gain and obesity despite normal diet and exercise. The dramatic increase in the prevalence of obesity, especially among children, shows that intervention actions are needed urgently. It is important to reduce or avoid exposure to obesogens especially in fetus and neonate.

Disclosure of Interest: None Declared

Endocrine Disruptors

ICE2021-1386

CEREBRAL VENOUS THROMBOSIS WITH HYPERTHYROIDISM – A CASE REPORT

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Introduction: While the aetiology of Cerebral Venous Thrombosis (CVT) is multifactorial, its association with hyperthyroidism as a possible cause is rare as compared with other thrombotic state as seen in 85% cases, which include genetic and acquired, haematological, hormonal inflammatory or immunological, infection and cancer. Idiopathic causes accounts for about 15%.

This is a case of CVT caused by thyrotoxicosis due to autoimmune hyperthyroidism with goitre, exophthalmos, muscle weakness, tachycardia and symptoms of CVT.

Case Description: A 34 years old male, non-smoker, with known history of hyperthyroidism on alternative therapy was admitted with neurological symptoms. Prior to this, patient had been developing symptoms of hyperthyroidism, worsening despite alternative therapy.

He was admitted in HDU due to neurological deficit, altered sensorium, transient hemiparesis and headache.

Clinical discussion: MRI showed acute venous thrombosis left transverse straight sinuses and cortical veins. There is also a small infarct in the right cerebellar hemisphere. He was treated with anticoagulants. With history of hyperthyroidism, he was started on thionamide, carbimazole 10mg BD and beta blockers for adrenergic symptoms. ECG showed sinus tachycardia at a rate of 122/min.

Echo showed mild to moderate MR, mild PAH with mild TR.

Thyroid Function Test:

| PARAMETER | OBSERVED VALUE | REFERENCE VALUE |
|----------------|----------------|-----------------|
| TSH | < 0.015 | 0.5-4.5 mIU/L |
| FT4 | > 6.99 | 0.78-2.19 ng/dl |
| FT3 | > 22.8 | 2.7-5.27 pg/ml |
| TPO Antibodies | > 2000 | < 5.61IU/ml |

The investigations such as Prothrombin, Protein C and S, Anti-phospholipid Antibodies, Homocysteine were estimated and found to be normal.

Several studies have shown increase in incidence of venous thromboembolic events, for eg, DVT and pulmonary embolism in association with hyperthyroidism. In addition to increased fibrinogen, Von Willebrand factor, plasminogen activator I and coagulation factors VIII, IX and X are associated with hypercoagulability and decreased fibrinolysis in the hyperthyroidism.

CVT may be caused by multiple factors with hyperthyroidism being one. Hyperthyroidism can cause coagulation abnormalities and lead to thrombotic events. MRI becomes an important investigation modality for those with hyperthyroidism developing severe headache, neurological deficit suspecting CVT. Blood screening for coagulation abnormalities is also mandated. In patients with CVT, Thyroid Function Test has to be made a routine investigation.

Disclosure of Interest: None Declared

Endocrine Disruptors

ICE2021-1492

1. THYROID DYSFUNCTION AMONG TYPE 2 DIABETIC PATIENTS SEEN IN THE IDENTIFIED OUTPATIENT CLINICS IN A TERTIARY HOSPITAL A DESCRIPTIVE BASELINE STUDY

Ivarrene E. Cahinde*, Joyce Rosario Matoza-Serna, Salvacion Sible

Introduction: This study was conducted to determine the thyroid dysfunction among type 2 diabetic patients seen in OPD of Divine Word Hospital, Tacloban City, Leyte.

Case Description: A cross-sectional descriptive design was used in study wherein samples collected were patients seen from identified OPD at Divine Word Hospital from June 2018 - June 2019. A sample was 19 years old and above patient diagnosed with type 2 diabetes based on the American Diabetes Association (ADA) criteria with no previous thyroid dysfunction irrespective of treatment either oral or on insulin regimen antidiabetic agents. About 56 type 2 diabetic patients were included in the study. A standard questionnaire was utilized to collect demographic profile and clinical data. To assess the thyroid function, patients underwent with consent thyroid function test specifically Total Free Thyroxine (FT4), and Thyroid-Stimulating Hormone (TSH). Moreover, Glycosylated haemoglobin (HbA1c) result was also determined among these patients.

Clinical discussion: There were 56 type 2 diabetic patients included in the study. Majority (73.2%) were female (41) and the mean age was 54 years. Based on the thyroid function test, there were 40 (71.4%) type 2 diabetic patients with normal thyroid function, about 12 (21.4%) had some type of thyroid dysfunctions and 2 (7.2%) has abnormal thyroid test but needs further evaluation to confirm for secondary hypothyroidism or hyperthyroidism. For those patients with thyroid dysfunction, 6 (50%) has hyperthyroidism, while 4 (33%) has subclinical hyperthyroidism and 2 (17%) with subclinical hypothyroidism. Of the 56 patients, 31 (55%) had glycosylated haemoglobin (HbA1C) of more than 7.5%. The BMI based on the Asia Pacific Guidelines, majority (57%) of these samples were obese with a BMI 25 and above, while 10 (18%) were overweight with BMI of 23-24.9 kg/m².

In this study, thyroid dysfunction was observed in type 2 diabetic patients upon determination through thyroid function test. Subjects were predominantly female (73%). Fifty-two percent (52%) of the studied subjects belong to the age group of 41 to 60 years old. Among

The 56 diabetic patients seen from the identified OPD clinics at Divine Word Hospital, 21.4% had thyroid dysfunction. The most common thyroid dysfunction was hyperthyroidism, followed by subclinical hyperthyroidism. Therefore, it is recommended that thyroid function should be tested routinely in diabetic patients to reduce the complications of these two endocrine disorders.

Disclosure of Interest: None Declared

Endocrine Disruptors

ICE2021-1506

THE INFLUENCE OF RAMADAN FASTING ON THE THERMIC EFFECT OF FOOD (TEF): A UAE STUDY

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Introduction: Ramadan fasting is an annual form of intermittent fasting with daily food and drink restriction between dawn and sunset. We previously demonstrated that Ramadan fasting induces changes in feeding patterns and energy metabolism and expenditure. However, comparisons in changes of thermic effect of food (TEF) during Ramadan and non-Ramadan periods require detailed exploration.

Objectives: To investigate the influence of Ramadan fasting on TEF in healthy participants.

Methods: Healthy participants (9) attended ICLDC and fasted Ramadan were assessed for TEF changes in (1) Ramadan, (2) post-Ramadan (Day) and (3) post-Ramadan (Night). COSMED-Quark RMR was used to measure metabolic rate. Exclusion criteria was: incomplete fasting record, chronic/metabolic conditions and/or medication affecting measurements or fasting ability. Each meal was 843kcal; 43.5% carbohydrate, 24 % fat and 32.5% protein. Leftovers were recorded to ensure food consumption consistency. Initial baseline measurement was first taken at rest pre-meal (T-30min) for 15 minutes, after which the meal was provided (T-15min). Thereafter, five sequential measurements were taken (every 15 mins, 15 mins each) with a total of 30 minutes between readings (T0, T30, T60, T90 and finally T120min). Area under the curve (AUC) on Energy Expenditure/Time was an indicator of TEF. Statistical analyses was carried out on STATA (v15.0). Paired t-test compared difference in area under the curve between Ramadan and post-Ramadan day. Mean and standard deviations are presented.

Results: In total, nine subjects completed Ramadan assessments, seven and five completed post-Ramadan day and night measurements respectively. Pairwise comparisons were only computed for Ramadan and post-Ramadan day for seven subjects. Area under the curve (AUC), peak energy expenditure (Cmax) and time to reach peak energy expenditure (Tomc) were higher in post-Ramadan day as compared to Ramadan but not statistically significant Table 1.

Image:

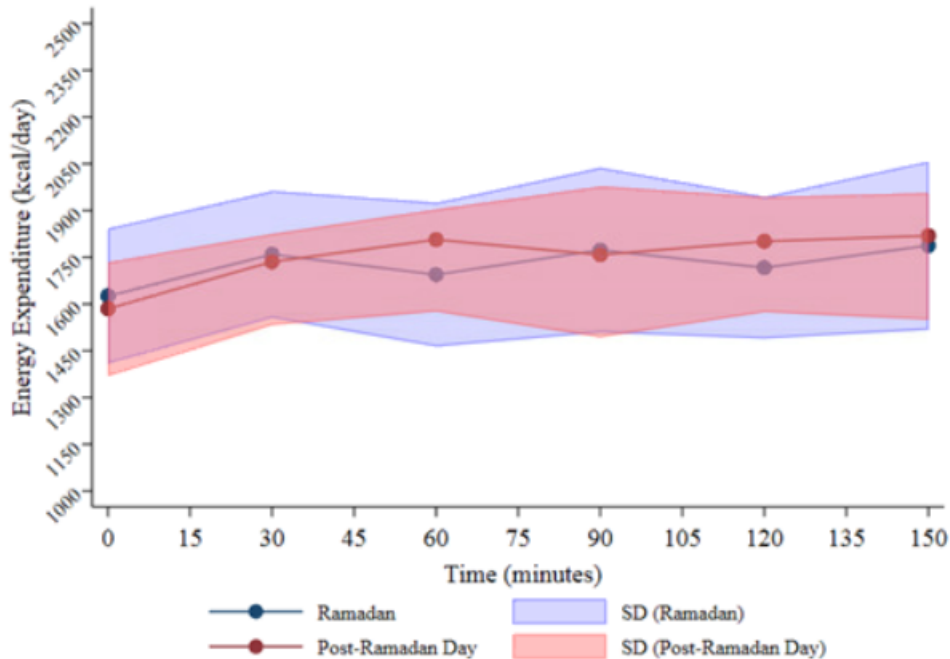


Figure 1: Energy Expenditure during Ramadan (blue) and post-Ramadan Day (red) with repeated measurements (N=7).

| Variable | Mean | Standard Deviation | 95% Confidence Interval | | P value |
|---------------------------------------|----------------------|---------------------|-------------------------|----------------------|---------|
| AUC Ramadan (0-150) | 2595.2×10^2 | 320.8×10^2 | 2298.5×10^2 | 2891.9×10^2 | 0.628 |
| AUC Post-Ramadan Day (0-150) | 2641.1×10^2 | 174.7×10^2 | 2479.5×10^2 | 2802.7×10^2 | |
| C_{max} Ramadan (kcal/day) | 1852.0 | 260.5 | 1611.0 | 2093.0 | 0.934 |
| C_{max} Post-Ramadan Day (kcal/day) | 1859.1 | 130.1 | 1738.8 | 1979.5 | 0.509 |
| T_{max} Ramadan (min) | 102.9 | 48.5 | 58.0 | 147.8 | |
| T_{max} Post-Ramadan Day (min) | 115.7 | 36.4 | 82.0 | 149.4 | |

Table 1. Change in AUC (Area under the curve, kcal/day.minutes), C_{max} (peak energy expenditure, kcal/day), T_{max} (time to reach peak energy expenditure, minutes) between Ramadan (N=7) and Post-Ramadan Day (N=7). Paired t-test indicates a statistically non-significant increase in AUC, C_{max} , T_{max} in post-Ramadan day as compared to Ramadan.

Conclusion: We report no significant differences in TEF between Ramadan and post-Ramadan Day. We previously demonstrated that energy expenditure (TEF, RMR and physical activity) and energy intake (food consumption) change patterns during Ramadan with small variance. It is likely that any changes observed e.g. in weight are due to the timing, quality and quantity of food consumed in Ramadan; often high-energy dense foods. Ongoing work with larger participant numbers, endeavors to elucidate implicated mechanisms.

Disclosure of Interest: None Declared

ICE2021-1622

INTRAUTERINE EXPOSURE TO PERCHLORATE DISRUPTS THE HYPOTHALAMUS-PITUITARY-THYROID AXIS OF MALE OFFSPRING AT BIRTH AND DURING ADULTHOOD

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Introduction: Perchlorate inhibits NIS-mediated iodide uptake in thyrocytes, interfering in the synthesis of thyroid hormones. However, the effects of perchlorate exposure at critical stages of development are still poorly described. It is known that intrauterine period plays an important role in the gene expression programming of different tissues, controlling the susceptibility of the progeny to develop several diseases during the adulthood.

Objectives: This study aimed to evaluate the effects of maternal exposure to perchlorate during pregnancy on the hypothalamus-pituitary-thyroid (HPT) axis of male offspring at birth and during adulthood.

Methods: Pregnant Wistar rats were treated or not with NaClO₄ dissolved in drinking water (0.3 or 1 ppm) during the pregnancy. The euthanasia of male offspring occurred at gestational day 20 (GD20) or postnatal day 90 (PND90). The gene/protein expression of hypothalamus, pituitary and thyroid were evaluated by Real-Time PCR and Western Blotting. Histological analysis of the thyroid gland was also performed.

Results: The intrauterine exposure to perchlorate increased the gene/protein expression of Pax8, Nkx2.1, Nis, Tshr, Tg, Tpo in the thyroid of male offspring at GD20. There was a reduction in the expression of DNA methyltransferases and histone deacetylase (Hdac), and increased expression of histone acetylase (Hat) in this tissue, results that are consistent with the increased gene expression in the thyroid. At PND90, there was a reduction in the protein content of TRH in the hypothalamus and of TSHb in the pituitary, suggesting increased hormonal secretion. This was confirmed by increased TSH serum levels in perchlorate-exposed animals. The gene/protein expression of Pax8, Nkx2.1, Nis, Tshr, Tg, Tpo was increased in the thyroid of the exposed adult animals. In addition, the expression of Hdac was decreased and the Hat expression was increased in the thyroid of these animals. Additionally, the acetylation of histone H3 was increased and the methylation status of this histone was decreased. These results are consistent with increased gene expression in the thyroid. Finally, the thyroid of animals exposed to perchlorate had larger follicles filled with high amounts of colloid in comparison to the control group.

Conclusion: The intrauterine exposure to perchlorate interferes with the embryological development of the thyroid and potentially programs and disrupts the HPT axis of the offspring rats, increasing their susceptibility to develop of thyroid diseases during adulthood.

Disclosure of Interest: None Declared

Miscellaneous

ICE2020-1111

THE PROGRESSION OF PROSTATE CANCER CELLS WAS HINDERED BY A PHENOLIC ACID, GALLIC ACID, VIA THE REGULATION OF ANDROGEN RECEPTOR SIGNALING PATHWAY AND THE EXPRESSIONS OF HISTONE DEACETYLASE 1 AND 2

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Introduction: Gallic acid (GA) is known to possess diverse biological activities, including anti-cancer. Histone deacetylase (HDACs) are controlled by tumor suppressor gene transcription and are overexpressed in various tumors, resulting in tumor development, progression and poor prognosis. The class I HDACs (HDAC1, 2 and 3) are known to be highly expressed in prostate cancer (PCa), and their upregulation is strongly associated with PCa progression.

Objectives: This study aims to demonstrate the effect of GA on inhibition of PCa progression by modulating the expression of HDAC1 and 2 in PCa cell lines, namely, LNCaP and PC-3 cells.

Methods: To prove our research rationale, we have used diverse experimental methods such as cell viability assay, colony formation assay, tumor spheroid formation assay, cell cycle analysis, mitochondrial membrane potential (MMP, $\Delta\Psi_m$) assay, Annexin V assay, TUNEL assay, Western blot analysis, xenograft mice model and histological analysis.

Results: We demonstrate that GA decreases the cell viability of only PCa cell lines and not normal cells (contrary to another HDAC inhibitor SAHA), and also inhibits colony and tumor spheroid formation. Exposure to GA decreases the MMP ($\Delta\Psi_m$), increases the number of cells in apoptotic stages, and induces DNA fragmentation. Western blot analysis reveals downregulated expressions of HDAC1 and 2, leading to upregulation of acetyl-p53 expression at the protein level, subsequent to downregulating the expression of cell cycle related genes such as PCNA, Cyclin D1 and E1, upregulating the expression of cell cycle arrest gene, p21, and regulating the expression of apoptosis intrinsic pathway related genes, such as Bax, Bcl-2, cleaved-Caspase-3 and PARP-1, in both PCa cell lines.

Conclusion: Furthermore, oral administration of GA for 8 weeks on PC-3 cells derived tumor xenograft mice model decreases the tumor size, damages the tumor structure, and downregulates the expression of HDAC1, 2 and PCNA in tumor mass, as confirmed by histological analysis.

Disclosure of Interest: None Declared

Miscellaneous

ICE2020-1199

TISSULAR AND MOLECULAR EFFECTS ON MAMMARY GLAND OF GH/IGF-I UP-REGULATION.

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Introduction: Breast cancer is the most frequently occurring cancer in women and the second most common cancer in general, worldwide. There are various types of therapies for breast tumors but, regrettably, the heterogeneity and complexity of tumors often result in resistance and long-term ineffectiveness of those clinical approaches, which highlights the importance of identifying new therapeutic targets.

Growth hormone (GH) and insulin growth factor-I (IGF-I) are essential for normal mammary growth and development. However, there is evidence, in animal models and humans, relating their upregulation with tumorigenic processes of the breast. Consequently, GH and IGF-I receptor have been suggested as possible therapeutic targets for the treatment of breast cancer. However, the pro-oncogenic effects of GH and IGF-I over mammary tissue at the tissular and molecular level have not been fully elucidated.

Objectives: The aim of this work was to ascertain, at the tissular and molecular levels, how elevated concentrations of GH and IGF-I could promote or facilitate mammary tissue oncogenic transformation.

Methods: The mammary tissue from 15-week old transgenic virgin female mice overexpressing GH (GH-Tg) and their normal siblings were studied. Whole mounting, and hematoxylin and eosin staining of the gland were performed. Besides, expression of several receptors, signaling mediators and transcription factors linked with development, proliferation and survival as well as with oncogenic processes in breast tissue were evaluated by Western blotting and RT-qPCR.

Results: Morphological and histological studies showed significantly less duct and alveolar structures, but major proportion of terminal ends buds (TEBs), in the mammary tissue from transgenic. The receptors of IGF-I, epidermal growth factor and estrogen were increased in the transgenic animals. Besides, GH and IGF-I mRNA levels were augmented in GH-Tg breast tissue as well as the expression of the proto-oncogene c-fos. However, the activation of Akt and Src were lower in GH-Tg compared to control animals, while the activation of p38 was increased.

Conclusion: The upregulation of GH/IGF-I induces morphological alterations in the mammary gland and increased expression of receptors associated to mitogenic processes, which affect normal breast development. While these effects are non-tumorigenic *per se*, they might predispose to oncogenic transformation.

Disclosure of Interest: None Declared

Miscellaneous

ICE2020-1213

ACUTE SEVERE HYPONATREMIA IN PATIENT ON TERLIPRESSIN FOR RECURRENT VARICEAL BLEEDING

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Introduction: Terlipressin is a vasopressin agonist used in acute variceal bleeding due to its effect on vasopressin V1 receptors, causing splanchnic vasoconstriction. Although it has good safety profile, it has been shown to act as partial agonist of V2 receptors but its effects on serum sodium concentration can be variable.

Case Description: 58 year old lady was admitted after banding for variceal bleed found at routine screening. She was started on terlipressin, antibiotics and admitted for monitoring. Hemoglobin continued to dropped and she was scoped again and found a bleeding varix and was banded. On day 3, her sodium level started dropping , coming down to 128 mmol/L from 140 mmol/L at admission. Over next 48 hours, it further dropped to 116mmol/L despite halving the dose of terlipressin. She was euvolemic on examination with a urinary sodium of 209, urinary osmolarity 598 and serum osmolarity 252. She became symptomatic, was given hypertonic saline, and started on fluid restriction. Terlipressin was withdrawn with sodium level returning back to 135 mmol/L over next 48 hours. She was observed as an inpatient for sodium level and further bleeding for 2 days and then discharged after remaining stable during the observation period.

Clinical discussion: Acute hyponatremia can develop during treatment with terlipressin for portal-hypertensive bleeding, can develop rapidly and usually reversible with cessation of therapy.

Disclosure of Interest: None Declared

Miscellaneous

ICE2020-1240

CAN WE IGNORE EMPTY SELLA IN PATIENTS WITHOUT ENDOCRINE DYSFUNCTION? ARE HEADACHE AND VISUAL SYMPTOMS IMPORTANT IN THESE PATIENTS?

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Introduction: Empty sella (ES) which is characterised by herniated subarachnoid space within sella could be secondary ES: due to surgery, radiotherapy, drug therapy, brain trauma, spontaneous necrosis, and infectious or autoimmune pituitary process, or primary ES (PES): which is of unknown cause. In majority of cases, PES is an asymptomatic radiological finding, but when symptomatic with headache, visual or endocrine symptoms, it is known as PES syndrome (PESS).

Case Description: 41-year-old lady presented with severe persistent left sided headache associated with blurred vision. Neurological examination was normal. CT brain showed empty sella without hydrocephalous. MRI brain confirmed empty sella with normal ventricular system. In dedicated pituitary MRI, pituitary gland was along the sellar floor with normal signal changes and normal contrast enhancement without adenoma. Pituitary stalk was in midline with unremarkable chiasma, cavernous sinuses, internal carotid arteries, suprasellar/parasellar regions. MR venography showed evidence of mild hypoplastic left transverse and sigmoid sinuses without cerebral venous sinus thrombosis. CSF opening pressure was 25 cm of water. Subarachnoid haemorrhage and meningeal infections were ruled out. Ophthalmologist ruled out papilloedema. Though imaging findings of empty sella and narrowed transverse sinus raised the possibility of idiopathic intracranial hypertension (IIH), neurologist ruled out this possibility. Anterior pituitary profile showed prolactin 541 mIU/L (102-496), FSH 5.9 IU/L, LH 12.0 IU/L, IGF-1 14.4 nmol/L, TSH 1.1 mU/L, Free T4 14.9 pmol/L, and 17 β estradiol 982 pmol/L. As initial cortisol was low (125 nmol/L), short synacthen test was done which ruled out adrenal insufficiency (Pre 317, Post 549).

Clinical discussion: Primary ES is possibly due to diaphragm sella incompetence +/- raised intracranial tension (ICT) or change in pituitary volume. Pituitary volume increases with pregnancy, and primary hormone deficiencies, and decreases after hypophysitis, and at menopausal age. Headache and blurred vision can occur in PESS even with high normal ICT of 14-24 cm of water. Endocrine dysfunctions occur in 19% and headache in 84-88% of PESS. Though PES is a feature in 70-94% of IIH, only 8-15% of PES patients develop IIH, as raised ICT can be intermittent in early IIH. Patients with PES need a multidisciplinary evaluation. PESS patients need frequent follow-up, whereas PES patients require follow-up every 2-3 year for possible IIH.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1298

BIOLOGICAL POTENTIAL OF CEPHAELINE FOR THE TREATMENT OF HUMAN DISORDERS: MEDICINAL IMPORTANCE THROUGH SCIENTIFIC DATABASES ANALYSIS OF CURRENT SCIENTIFIC RESEARCH WORK

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Introduction: Plant chemical are important phytochemicals found to be present in the various vegetables, fruits and medicinal plants. Plant pure phytochemical have important role in the medicine and nutraceuticals filed. Medicinal importance and therapeutic benefit of Ipecac plant and their pure phytoconstituents have numerous applications in the medicine and other allied science. Pharmacological activities such as expectorant, amebicide and vomitive properties of Ipecac have been well known in the medicine.

Objectives: In order to develop better molecule for the treatment of various human disorders from cephaeline.

Methods: In the present investigation different literature databases have been searched and collected all the needed scientific information. Biological importances of cephaeline in the medicine for the treatment of human disorders have been investigated through literature data analysis of current scientific research work. Medicinal importance of cephaeline was assessed for their potential role against various types of enzymes in the present investigation through literature data analysis of different scientific research work.

Results: Literature data analysis revealed the biological importance of cephaeline in the medicine for the treatment of numerous human health disorders. Literature databases analysis revealed their medicine importance against on gastrointestinal tract cardiovascular system disorders however it therapeutic potential have been also proven in some scientific research work against Zika virus, Ebola virus, leishmania and malaria. The molecular study signified the biological role of cephaeline on various enzyme systems which signified their importance in the different field of science.

Conclusion: Literature data analysis of current scientific research work revealed the medicinal importance and therapeutic potential of cephaeline in medicine.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1299

BIOLOGICAL POTENTIAL OF FLAVONOID PECTOLINARIN IN THE MANAGEMENT OF LIVER DISORDERS: SCIENTIFIC DATABASE ANALYSIS WITH MOLECULAR MECHANISM

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Introduction: Flavonoidal compounds are important class of phytochemical founds in different attractive coloured plant material and their derived products. Flavonoids are naturally occurring polyphenolic compounds abundant in food plants which can use as nutraceuticals in the human diet due to their significant antioxidant potential. *Cirsium japonicum* is a well know medicinal plant of Korea and Japan contain significant amount of pectolinarin.

Objectives: In order to know the biological potential of pectolinarin in the scientific field for the treatment of liver disorders.

Methods: Here in the present investigation numerous scientific data have been searched and collected from literature source of scientific field. Medicinal importance and pharmacological potential of pectolinarin have been searched and analyzed through different literature work. Biological importance of alanine transaminase (ALT), super oxide dismutase (SOD), aspartate transaminase (AST) and catalase in the medicine for the antioxidant potential of pectolinarin have been also analyzed through different literature work. However biological importance of antioxidant in the liver disorders has been also investigated through literature data analysis of various scientific works.

Results: From the literature databases analysis it was found that pectolinarin have beneficial potential in the medicine as it showed beneficial effects on human liver disorder through their protective action against H₂O₂-induced cell death and inhibited ROS generation. Dala analysis of literature signified that pectolinarin inhibited phosphorylation of MAPK and revealed the hepatoprotective activity. Molecular study revealed the biological importance of ALT, AST, SOD and catalase in the medicine for the treatment of numerous human helath complications. Molecular study highlighted the key role of biological interaction of pectolinarin with different enzymes in the scientific research work.

Conclusion: Scientific data analysis reported the beneficial effects of pectolinarin in liver disorders through interaction with various types of liver enzymes.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1390

PRELIMINARY EVALUATION OF PSA AS A POTENTIALLY USEFUL ANDROGENIZATION MARKER IN TRANSGENDER MEN: PROOF OF CONCEPT WITH FOUR CASES IN A SINGLE CENTRE STUDY.

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Introduction: The identification of an adequate laboratory marker to better monitor the hormonal treatment in transgender men (female to male) is a challenge in clinical practice. Testosterone is commonly used for this purpose, but with important limitations, such as its wide normality range based on healthy young men. Hence, in the effort to improve the protocol for the evaluation of the process of androgenization, it would be helpful to identify a better marker. Prostate-specific antigen (PSA) might be a candidate, since it has been shown that periurethral Skene's glands in women, and to a lesser extent the breast, are able to produce it when faced with an androgenic stimulus.

Objectives: Preliminary study of the evolution of PSA vs. testosterone as androgenic markers in 4 patients following our transgender men androgenization protocol.

Methods: After confirming the condition of transsexualism, a clinical study is carried out to discard any associated pathology. Subsequently, treatment with low doses (25 mg) of injectable testosterone cypionate is administered every 30 days. After three months, it is re-evaluated and the dose of testosterone is increased by 25 mg at each visit, approximately every 3 months.

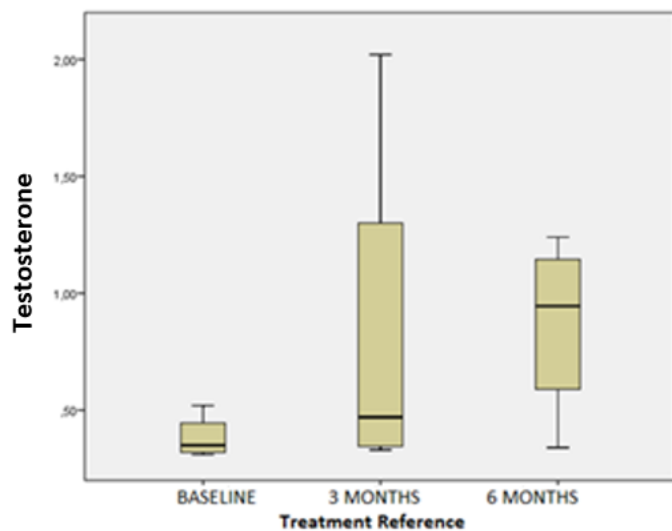
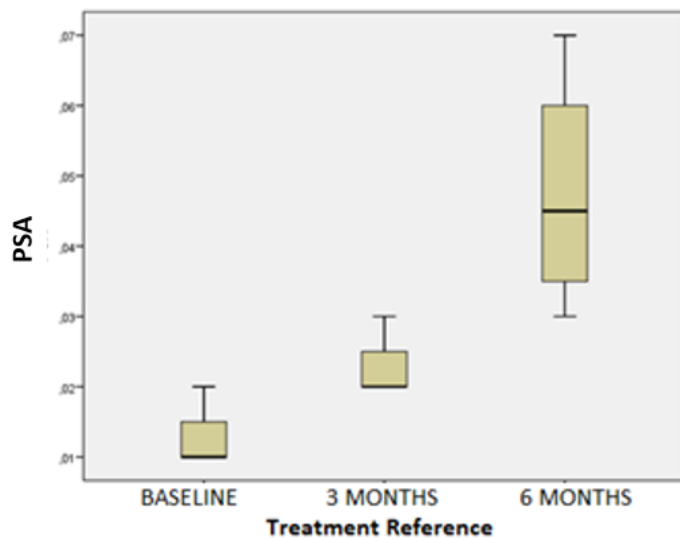
Testosterone and PSA levels were evaluated at baseline, 3, and 6 months during this protocol in four transgender men. Testosterone and PSA were determined by direct chemiluminescence in the Atellica Solution® IM autoanalyzer and statistical analysis of the data was performed with SPSS Statistics® software v20.

Results: *Table. Statistic analysis*

| | | Baseline | 3 months | 6 months |
|--------------|---------|---------------|----------------|---------------|
| Testosterone | Average | 0,3825 | 0,8225 | 0,8675 |
| | IC95% | 0,2313-0,5337 | -0,4601-2,1051 | 0,2505-1,4845 |
| | Median | 0,3500 | 0,4700 | 0,9450 |
| | SD | 0,0950 | 0,8061 | 0,3878 |
| PSA | Average | 0,0125 | 0,0225 | 0,0475 |
| | IC95% | 0,0045-0,0205 | 0,0145-0,0305 | 0,0203-0,0747 |
| | Median | 0,0100 | 0,0200 | 0,0450 |
| | SD | 0,0050 | 0,0050 | 0,0171 |

PSA showed significant differences in Kruskal Wallis test among baseline, 3 and 6 months ($p < 0,05$). Testosterone levels increased significantly at both times too but showed a greater variability as compared to PSA, as well as lack of statistical significance ($p > 0,05$).

Image:



Conclusion: Testosterone is widely used in the evaluation of the effectiveness of transgender men androgenization protocols, although it has limitations. Changes in PSA levels in response to androgen therapy seem to be significant and more robust than testosterone in this preliminary analysis. Therefore, we propose PSA as a candidate to be further studied as a useful marker in the evaluation of androgenization in transgender men.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1408

BIOLOGICAL IMPORTANCE OF HYPERIN IN THE MEDICINE FOR THE TREATMENT OF HUMAN HEALTH COMPLICATIONS

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Introduction: Herbs have important role in the human civilization as they were used for different purpose such as beverages, perfumery, medicine, nutraceuticals, fragrances and cosmetics industry. Plants are valuable source of natural products for the development of new molecule and medicines against disorders, including development of some of the important industrial products too. Presence of flavonoidal compounds in the nature are well known as flavonoidal compounds are widespread in the plant kingdom and Hyperin is one of the best examples of flavonoidal class plant chemical found to be present in the *Hypericum perforatum*.

Objectives: Here in the present investigation, scientific data of medicinal importance and therapeutic benefit of Hyperin for the treatment of various forms of health complications have been collected from numerous literature databases and analyzed.

Methods: Detailed medicinal importance and biological activities of hyperin have been collected from various scientific research work of the literature and analyzed for their effectiveness in the medicine. Literature database analysis of various scientific research works have been done to know the biological potential of hyperin with their suitable mode of actions.

Results: Literature data analysis of various scientific research works revealed the biological importance and therapeutic significance of hyperin in the medicine and other research fields. Detailed pharmacological investigation signified their biological importance in the medicine for the treatment of numerous health complications. Scientific data analysis signified the biological importance of hyperin in the medicine due to their free radical scavenging properties.

Conclusion: In the present investigation, scientific data analysis of various research works revealed the biological importance of hyperin for the treatment of various form of human disorders.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1415

PERIPARTUM HYPONATREMIA; CASE REVIEWS AND VIGILANCE IN MANAGEMENT

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Introduction: Peripartum hyponatremia is a common electrolyte disorder which may result in severe maternal and neonatal sequelae. We present three cases of peripartum hyponatremia with hypervolemic hyponatremia and water overload as a risk factor. All cases reverted to normal serum Na⁺ levels post-delivery.

Case Description: Case 1: 33 years old primigravida, went into spontaneous labour at home at 40 weeks of gestation. She required transfer to hospital because of exhaustion and slow progress in labour and had normal vaginal delivery. Her bloods revealed serum Na⁺ of 116mmol/L. Baby was born in good condition with cord blood Na⁺ level of 111mmol/L. Following a multi-disciplinary review, fluid restriction to 1.5L /day instituted. Retrospective enquiry revealed 8L fluid intake at home.

Case 2: 32 years old primigravida, presented in spontaneous labour at 40⁺² weeks gestation. Initial blood results showed serum Na⁺ of 132mmol/L. She had poor urine output with positive balance of 2,625mls hence had repeat bloods with serum Na⁺ of 126mmol/L. Fluid restriction was commenced at 80ml/hr. She had forceps delivery with neonatal cord Na⁺ of 125mmol/L.

Case 3: 39 years old primigravida with past history of nephrotic syndrome, normal renal function and blood pressure in pregnancy underwent induction of labour at 41 weeks of gestation. During labour, her serum Na⁺ was 126mmol/L with normal creatinine at a positive balance of 999mls. Fluid restriction to 80ml/hr was commenced. Due to further drop in her Na⁺ level to 124mmol/L and symptomatic with twitching of head and neck, medical and anaesthetic team were involved and further fluid restriction commenced to 30ml/hr.

Clinical discussion: Peripartum hyponatremia is mostly dilutional or hypotonic. Pregnant women are more at risk because of physiological changes in pregnancy. Oxytocin has a similar chemical structure to ADH and increases the risk of fluid retention. Incidence increases with increased fluid intake, 1% in 1L versus 26% with >2.5L in labour. Early symptoms are non-specific and may be attributed to pregnancy and labour. It leads to risk of neonatal hyponatremia because of fluid and electrolyte equilibrium across placenta. A strict fluid balance should be maintained during induction and in established labour. All maternity units should create a local guidance apart from a need of a national guideline to increase awareness of fluid management in labour and peripartum hyponatremia to avoid serious complication for women and neonates.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1436

INFLUENCE OF VITAMIN D LEVELS ON THE CLINICAL COURSE IN PATIENTS WITH COVID 19: AN ARGENTINE PILOT AND MULTICENTER REAL-LIFE STUDY

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Introduction: Vitamin D (VD) plays a role in immune response. Its benefits on respiratory diseases induced by viruses have been previously described and recent data shows that low levels of VD could worsen COVID-19 outcomes

Objectives: To establish association between VD blood levels among COVID-19 patients with their clinical outcomes and biochemical inflammatory markers.

Methods: Prospective, multicentric, cohort study. COVID-19 patients were recruited consecutively and grouped as ambulatory or hospitalized, being followed until discharge, transfer to other centers, intensive care unit (ICU) admission or death. The variables evaluated were: age, gender, oxygen mask requirement (O2r), mechanical ventilation (MV), pre-existing comorbidities, inflammatory markers, severity of COVID-19 by News Score. VD levels were classified as: sufficient: >30 ng/ml (VDS), insufficient: 20-30 ng/ml (VDI), deficient: <20 ng/ml (VDD). Parametric test, linear multivariate, logistic and cox regressions adjusted by confounders (comorbidities, age) plus survival analysis and long rank were performed.

Results: 287 patients were recruited; 243 (85%) were hospitalized, showing significant differences in VD levels against ambulatory patients (18±10ng/ml - 24,3±13ng/ml respectively p<0,01). Group classification according to VD and characteristics are expressed in Table1.

COVID-19 severe forms and VD levels were negatively associated (p:0,009). VDI and VDD had higher risks for moderate (OR:3,2 95CI:1,1-9 p:0,03) and severe (OR:3 95%CI:1,09-8 p:0,03) disease. VD has also shown correlation with baseline markers as ferritin and LDH (p:0,019 -0,03 respectively).

O2r risk was increased between VDI (OR:3,4 95%CI:1,2-9 p:0,016) and VDD (OR:2,74 95%CI:1,1-6,8 p:0,03) noticing a higher risk in presence of comorbidities, multiplying the odds in 3,39 or 3,6 in presence of 1 or more comorbidities respectively.

Lower calcium levels correlated with ICU admission (p:0,02), and noticeably presented itself as a risk factor for mortality (OR: 7,9 95%CI:1,7-36,3 p:0,008).

Image:

| | VDS n= 37 | VDI n= 70 | VDD n= 174 | p |
|--|--------------|--------------|---------------|-------|
| Age (years) | 48, 8 ±17 | 52,9 ±17 | 53,5 ±16 | 0,62 |
| Male gender (%) | 18 (49%) | 50 (71%) | 93 (53%) | 0,019 |
| Days of hospitalization | 10,9 ± 6,5 | 10,7± 5,5 | 13,4 ± 13 | 0,09 |
| O2r | 7 (19%) | 33 (47%) | 69(40%) | 0,02 |
| Comorbidities (hipertension,diabetes,obesity, chronic lung disease, cardiovascular disease,smoking,immunosuppression) | 18 (48%) | 42 (60%) | 99 (57%) | 0,5 |
| Hospitalization requirement | 24 (41%) | 61 (82%) | 152 (82,4%) | <0,01 |
| Ferritin (ng/ml) | 473±533 | 806±735 | 842±919 | 0,049 |
| LDH (U/l) | 321±173 | 467±275 | 438±226 | 0,01 |

Conclusion: This study shows that among COVID-19 hospitalized patients, vitamin level was significantly lower, besides its association with O2r, severity and baseline inflammatory markers. Calcium also plays a role in the evolution of this disease and further studies are needed to emphasize the importance of adequate levels of VD and supplementation as an effort to improve COVID-19 outcomes.

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Miscellaneous

ICE2021-1458

AGGRESSIVE CRANIOPHARYNGIOMAS

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Introduction: Craniopharyngiomas (CP) are rare tumors that may be locally aggressive. The presence of functional estrogen receptors (ER) has been reported in CP and might be related to risk of recurrence.

Objectives: To ascertain if the expression estrogen and progesterone receptor (PR) might be associated with to recurrence in CP.

Methods: Descriptive retrospective observational study of patients with confirmed histology of CP and tissue sample available admitted to Virgen Del Rocio University Hospital (Seville, Spain) from January 1967 to October 2020 were included. Estrogen and progesterone receptor expression was analyzed by Immunohistochemistry. Ki-67 levels were also analyzed. Two CP groups were considered according to Ki67 levels: Group A (Ki67<10%) and group B (Ki67>10%). As all variables followed a non-parametric distribution, U Mann Whitney, Chi-Square, and Z-test with Benjamini-Hochberg correction were used when needed.

Results: Our study population includes 80 patients (46 male and 34 female), with a median age at diagnosis of 34 years [10-50.00]. Twenty-six patients were under 18 years old (children) with a median age of 7 years [4.5-10.00], and 54 were adults (aged 18 and above) with a median age of 45 years [33-58.50]. Our data shows higher recurrence rates when Ki67 levels staining were higher than 10%: 8/14 (57.2%) in comparison with Ki67<10% (6/14, 42.9%, p=0.018). In children we found 6 samples with Ki67<10% and 6 samples with Ki67 >10%; recurrences were observed in 2/6 (33,3%) in the first group and in 6/6 (100%) in the second, respectively (p= 0,199). In adults, we found 9 and 3 patients for high and low Ki67 levels, respectively. Recurrences were observed in 4/9 (44,4%) in the group A and in 2/3 (66,7%) in the group B, respectively (p= 0,28). There were no differences between age groups. In patients with positive ER, we observed an increased rate of recurrence: 12/23 (52.17%) versus 2/13 (15,38%) in patients with negative ER stain but it was no significant. (p=0,21). No association between PR and recurrence was observed.

Conclusion: In our series, patients with CP with high Ki67 levels are more likely to recur. No clear association between ER, PR expression and recurrence was observed. These findings support the use of Ki67 as a marker of recurrence in CP.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1480

BIOLOGICAL IMPORTANCE OF KAEMPFERITRIN IN THE MEDICINE FOR THE TREATMENT OF VARIOUS FORMS OF INFLAMMATORY DISORDERS

Dinesh Kumar Patel*

Introduction: Flavonoids are secondary metabolites present in plant sources and scientifically proven for their potential health benefits in the human diet. Pharmacological activities of flavonoidal compounds are mainly due to interaction with enzymes, structural proteins, transport and cellular mechanism. Kaempferitrin is a flavonoid glycoside found to be present in the *Hedyotis verticillata*.

Objectives: In order to know the biological importance of kaempferitrin in the medicine, numerous scientific research data have been collected and analyzed in the present investigation.

Methods: Medicinal importance and pharmacological potential of kaempferitrin have been searched in the literature databases and collected all the needed information for their therapeutic benefit in the medicine. Detailed pharmacological activities of kaempferitrin have been analyzed and presented in the present investigation to know their biological importance.

Results: Literature data analysis revealed the biological importance and therapeutic benefit of kaempferitrin in the medicine. Scientific data analysis signified that kaempferitrin have numerous health beneficial aspects as it showed therapeutic benefit on bone mass and have anti-inflammatory activity. Literature data analysis signified their biological potential against various form of inflammatory disorders in the medicine and health sectors.

Conclusion: Scientific data analysis revealed the therapeutic benefit of kaempferitrin in the medicine for their better biological activity against various form of human disorders.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1481

MEDICINAL IMPORTANCE AND THERAPEUTIC BENEFIT OF VISNAGIN IN THE MEDICINE: BIOLOGICAL POTENTIAL AND PHYSIOLOGICAL ROLE IN OXIDATIVE STRESS INDUCED DISORDERS

Dinesh Kumar Patel*

Introduction: Plants have been used by the human being for the treatment of various health complications including various types of neurological disorders. Plant belongs to the different family are well known for their rich source of pure plant chemical called phytoconstituents. Visnagin is the main active phytoconstituents of *Ammi visnaga* belongs to the furanochromone class plant chemical.

Objectives: Medicinal importance and therapeutic benefit of visnagin for the treatment of various forms of human disorders have been investigated through literature data analysis of various scientific research works.

Methods: Biological importance of visnagin for the treatment of human disorders has been investigated in the present investigation through literature data analysis of various scientific research works. Pharmacological activities of visnagin for their effectiveness against oxidative stress have been investigated in the present investigations through literature data analysis. Literature data analysis of the numerous scientific research works for their biological importance of and health beneficial potential of visnagin in the medicine have been also carried out.

Results: Literature data analysis of various scientific research works revealed the biological importance of visnagin in the medicine and other allied health sectors which have physiological functions against oxidative stress and neurodegenerative disorders. Literature data analysis in the present investigation revealed the biological importance of visnagin in the neuroinflammation. Literature data analysis revealed the medicinal importance of visnagin on cell injury associated with various form of human complication.

Conclusion: Literature data analysis of various scientific research works signified the biological potential of visnagin in the medicine for the treatment of various form of human disorders including oxidative stress induced disorders.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1485

AUTOIMMUNE POLYGLANDULAR SYNDROME IN A POSTMENOPAUSAL WOMAN AFTER COVID-19 INFECTION

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Introduction: There has been growing evidence that coronavirus disease 2019 (COVID-19) patients present with dysregulated immune response that could lead to autoimmune and autoinflammatory diseases affecting multiple organs or systems. Several reports suggest possible long-term endocrine-metabolic complications in COVID-19 patients.

Case Description: A 52-year-old Caucasian healthy woman with no known previous diseases or medications was diagnosed with COVID-19 respiratory infection in March 2020. She spent 2 weeks in hospital and was discharged after two negative swabs. During the following weeks had persistently high temperature, weakness, fatigue, anorexia and high inflammatory markers such as leucocytes, ferritin and C-reactive protein. Her complaints progressed over time and eventually she ended in the emergency department with vomiting, hypotonia, hyponatremia, hyperkalemia and impending renal failure. Considering the clinical manifestations and the laboratory findings she was found to have Addison crisis caused by primary adrenal failure. In addition, she had very high titre of thyroid peroxidase antibodies and thyroid function tests revealed subclinical hypothyroidism suggesting the development of autoimmune polyglandular syndrome type 2. She was also tested for anti-glutamic acid decarboxylase antibodies, anti-nuclear antibodies, anti-extractable nuclear antigens antibodies, anti-transglutaminase antibodies, which were negative, but anti-parietal cell antibodies titre was positive. After managing the acute decompensation oral replacement therapy with cortisone acetate was initiated, levothyroxine sodium added in the following weeks. Three months later she needed adjustment of the replacement therapy according to the laboratory results and was left under close monitoring due to the possibility of another autoimmune disorder development.

Clinical discussion: COVID-19 infection may trigger chronic autoimmune endocrine dysfunction presumably due to the complex immune dysregulation although the intimate mechanisms are not yet elucidated. The clinical features of adrenal insufficiency overlap with the recently described "long COVID" syndrome making the differential diagnosis challenging. It is of utmost importance to recognize the potential adrenal involvement as if left untreated may lead to serious health complications and be life-threatening.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1504

EFFECT OF POMEGRANATE (*PUNICA GRANATUM L.*) PEEL EXTRACT ON HEAD DIAMETER, SPINAL CURVATURE, SENSORY, MOTORIC RESPONSE, HATCHING AND SURVIVAL RATE OF ZEBRAFISH (*DANIO RERIO*) EMBRYO EXPOSED TO CAFFEINE IN VITRO

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Introduction: Child congenital disability may be caused by many aspects, including hormonal and nutrition. Caffeine (1,3,7-trimethyl xanthine) can cause morphological abnormalities in one of them is spinal abnormalities that can affect the quality of life of the fetus. Caffeine is a psychoactive substance that can act as a free radical that can damage the body at the cellular level through the mechanism of oxidative stress. Pomegranate peel extract (PPE) is known to contain potent antioxidant compounds of around 92 per cent. Antioxidants will inhibit the oxidative stress process.

Objectives: This study aims to prove the effect of pomegranate skin extract on the head diameter, spinal curvature, sensory, motoric response, hatching and survival rate in zebrafish larvae exposed to caffeine.

Methods: Zebrafish embryos were divided into nine groups consisting of one control group, two negative control groups (Caffeine 100 ppm and PPE 0,70 ppm), one positive control group (Vitamin C 30 ppm), and five treatment groups namely caffeine 100 ppm and PPE 0,14, 0,28, 0,42, 0,56 and 0,70 ppm. Head diameter and spinal curvature examination using microscope measured by Image J Software, sensory motoric response, hatching and survival rate observed by microscope.

Results: PPE administration significantly inhibits the reduction of head diameter ($p < 0.05$), lower the spinal curvature ($p < 0.05$), did not affect the sensory, motoric response as well as hatching rate and the survival rate in caffeine-exposed zebrafish larvae ($p > 0.05$).

Conclusion: PPE is potential to treat embryonic and larval zebrafish abnormalities, but further research is needed to explore dosages including the cellular mechanisms involved

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1564

WHAT EVERY INTERNIST SHOULD KNOW ABOUT RARE GENETIC SYNDROMES IN ORDER TO PREVENT NEEDLESS DIAGNOSTICS, MISSED DIAGNOSES AND MEDICAL COMPLICATIONS: FIVE-YEAR EXPERIENCE OF INTERNAL MEDICINE FOR COMPLEX RARE GENETIC SYNDROMES

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Introduction: Patients with complex rare genetic syndromes (CRGS) have, by definition, combined medical problems affecting multiple organ systems. Intellectual disability (ID) is often part of the syndrome. During childhood, most patients with CRGS receive multidisciplinary (MD) and specialized pediatric care in tertiary centers. As improvement of medical care has improved life expectancy, more patients are now reaching adult age. While the complexity of the syndromes persists into adulthood, adequate MD syndrome-specific care is rarely available for adults. Although internal organs and endocrine tissues are often affected, internists or endocrinologists are rarely involved. Pediatricians have expressed the urgent need for adequate, syndrome-specific, MD tertiary healthcare for adults with CRGS.

Objectives: To provide an overview of the special needs of CRGS adults and the medical pitfalls.

Methods: All CRGS patients who visited the center for adults with CRGS at the Endocrinology unit between 2015 and 2020 filled out a medical questionnaire and underwent a systematic health screening (followed by treatment, if indicated). For the current study, we collected data on physical complaints, medication use and missed diagnoses.

Results: Between 2015 and 2020, 726 adults (256 M, 470 F) with over 60 syndromes visited our center. The main differences from the general internal medicine population were ID, polypharmacy and use of psychotropic drugs. Missed diagnoses were common and many patients had undergone extensive diagnostic tests for symptoms that could actually be explained by their syndrome. Fatigue (52%), abdominal discomfort (23%) and hypertension (10%) were among the most frequent reasons for referral to Internal Medicine. Based on the literature and our clinical findings, 73% of the syndromes was associated with endocrine problems. We provide an algorithm for the clinical approach to CRGS adults, in order to prevent unnecessary diagnostics as well as missed diagnoses.

Conclusion: Our overview shows that missed diagnosed and needless invasive tests are common in CRGS adults. As more CRGS patients are now reaching adult age and transfer to Internal Medicine, internists and endocrinologists should be aware of the special needs of CRGS adults and of the medical pitfalls. Knowledge about syndrome-specific health problems and MD expert care is crucial to prevent the personal and financial burden of unnecessary diagnostics and under- and overtreatment.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1583

SIDE EFFECTS OF HORMONE THERAPY IN TRANSGENDER COMMUNITY

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Introduction: Hormone therapy (HT) aims to suppress the characteristics associated with the biological sex, and promote the appearance of traits associated with gender. It is a physiological and anatomical adequacy. As with any treatment, it has advantages and risks. In trans women, treatment has “feminizing” effects. In transgender men it suppresses the secondary female characteristics and promote the appearance of male ones. The transition experienced by transgender people is a process that requires monitoring by a multidisciplinary team.

Objectives: Through the analysis of several studies that involve hormone therapy in transgender adults, this study aims to assess its side effects, both physiological and psychological.

Methods: This is a review with a descriptive character, seeking to assess, qualify and quantify the most recurrent side effects of the HT. Were selected 23 articles, of which 7 were discarded because they did not include information associated with the central theme of the study.

Results: Estrogen is the central substance in female HT, whereas for transgender men, it is based on the use of testosterone ester drugs. Side effects are associated with a high risk of cerebrovascular disease and myocardial infarctions, elevated glucose rates, deterioration of pre-existing psycho-emotional conditions, osteopenia and decreased or increased sexual desire. Cardiovascular risks and increased bone mineral density (BMD) in trans women are the most evident factors. For the success of HT, in addition to clinical and psychological monitoring, it is important to reduce habits that can increase the risks. Therefore, hormone therapy, when performed by qualified professionals, is safe for transgender adults.

Conclusion: Hormone therapy plays a major role in the transition process, being associated, in most cases, with positive results for patients. The advantages outweigh the risks. In addition, serum BMD measurement should be performed in patients treated with testosterone and assessment of patients' metabolic parameters to prevent cardiovascular diseases. The education of patients and the team that performs the treatment is essential.

Disclosure of Interest: None Declared

Miscellaneous

ICE2021-1600

ASSOCIATION OF HYPONATREMIA AND CLINICAL OUTCOMES IN HOSPITALIZED PATIENTS WITH HIV/AIDS IN A TEACHING HOSPITAL FROM COLOMBIA

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Introduction: Hyponatremia is the most frequent electrolyte disorder in hospitalized patients with HIV infection (about 40%). It appears to be in correspondence, mostly, to pulmonary and central nervous system opportunistic infections and gastrointestinal loss¹. The SIADH is the main pathogenic mechanism in pulmonary and central nervous system opportunistic infections. Also, loss of effective gastrointestinal solutes, contributes to depletion of the circulating volume and ends up stimulating the secretion of ADH², leading to hyponatremia. Retrospective analytical studies in HIV infected patients and hyponatremia had reported an association with unfavorable outcomes^{3,4}. In Latin America the lack of information in regard of this matter led us to conduct this study.

Objectives: To determine the association between hyponatremia and mortality and length of hospital stay.

Methods: An observational, analytic, retrospective, case-control study was executed since March 2020 in a teaching hospital from Colombia. The entire protocol was reviewed and approved by the institutional ethics committee. Hospitalized patients in the Internal Medicine service, aged 18 years or older, with a history or recent diagnosis of HIV infection, hospitalized for AIDS-defining illnesses, from 2013 to 2018, were included. Patients with heart failure, cirrhosis or death not related to AIDS, were excluded. A sample of 122 patients was calculated. Patients who died during hospitalization secondary to AIDS-defining illnesses were taken as cases, whereas controls were the ones alive at hospital discharge.

Results: Up to this date, 81 patients met the inclusion and exclusion criteria, which is equivalent to 66% of the total calculated sample. Of these, 54 patients are in the control's and 27 in case's group, for a 2:1 ratio. 59% were male, with an average age of 40 and 39 years for case's and control's groups, respectively. The mean CD4 lymphocyte count in the group of cases was 78.2 cells/mm³, while in the control group it was 129.8 cells/mm³. The length of hospital stay was 22,4 days for case's group and 24,1 days for control's group. The prevalence of hyponatremia in case's group was 70% while in control's group was 32%. So far it has not been founded hypernatremia at the admission (See Table 2).

Image:

Table 1. Sample size for unpaired case-control studies

| | |
|--|-------|
| Confidence interval two sided (1 – alpha) | 95 |
| Statistical power | 80 |
| Ratio of controls per case | 2 |
| Hypothetical proportion of controls with exposure | 50 |
| Hypothetical proportion of cases with exposure | 77.78 |
| Less extreme odds ratios to be detected | 3.50 |

| | | | |
|----------|--------|--------|----------------|
| | Kelsey | Fleiss | Fleiss with CC |
| Cases | 37 | 35 | 41 |
| Controls | 74 | 70 | 81 |
| Sample | 111 | 105 | 122 |

Source: Kelsey et al, *Metodos en Epidemiologia Observacional 2da Edicion*, Tabla 12 – 15, Fleiss, *Metodos Estadisticos para Relaciones y Proporciones*, formulas 3,18 y 3,19.

Table 2. Prevalence of hyponatremia.

| | Cases (%) | Controls (%) | Total |
|----------------------------|------------------|---------------------|--------------|
| Normal serum sodium | 8 (30) | 37 (38) | 45 |
| Low serum sodium | 19 (70) | 17 (32) | 36 |
| Total | 27 | 54 | 81 |

Source: author

Conclusion: The length of hospital stay was similar in both groups, and the proportion of patients with hyponatremia showed a twofold increased in case's group.

Disclosure of Interest: None Declared



ICE2020-1075

SPECTRUM OF CLINICAL, BIOCHEMICAL AND MRI IMAGING FINDINGS IN A COHORT OF IDIOPATHIC HYPOGONADOTROPIC HYPOGONADISM IN A TERTIARY CARE HOSPITAL IN EASTERN INDIA

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Introduction: Idiopathic Hypogonadotropic Hypogonadism (IHH) is an uncommon disorder. Approximately 1/3rd and 2/3rd of cases are normosmic IHH and hypo/anosmic IHH (Kallmann syndrome) respectively. Although there are overlapping features, differentiation between the two conditions can usually be made, based on specific imaging findings and relevant clinical information. MRI allows precise depiction of the olfactory bulb and olfactory tract, and very sensitive detection of even very little damage to the central projection areas of the sense of smell.

Objectives: Evaluation of the spectrum of morphological abnormalities of olfactory system & pituitary gland in patients of IHH. And evaluation of the usefulness of MRI in confirming the diagnosis of Kallmann syndrome and differentiating it from normosmic IHH.

Methods: This cross-sectional observational study was conducted for the period of December 2014-August 2019. A total of 55 cases of IHH presenting to the department of endocrinology clinic were included into the study. We first established the diagnosis of IHH biochemically. Then we subjected the patients for MRI to define the olfactory system pathology.

Results: Out of these 55 cases, 45 (81.8%) were normosmic IHH and only 10 (18.2%) cases were Kallmann Syndrome (**Table 1**). Age of presentation of normosmic IHH & Kallmann group was similar in both the groups. Male predominance was seen in both the groups. All patients in Kallmann syndrome group were male. Kallmann syndrome subjects had reduced gonadal, axillary hair & pubic hair development. Normosmic IHH subjects had significantly higher serum testosterone level than Kallmann. However, no significant difference of serum FSH & LH could be found out between normosmic IHH & Kallmann group. Patients with normosmic IHH have normal olfactory bulb or olfactory tract whereas out of 10 Kallmann patients, 5 (50%) had completely absent and 5 (50%) had hypoplasia (**Table 2**). Among the 10 patients with Kallmann syndrome, 5 (50%) patients had hypoplasia of olfactory sulcus & 5 (50%) had complete aplasia of olfactory sulcus (**Table 3**).

Image:

Table 1

| Smell abnormalities in <u>normosmic Idiopathic Hypogonadotropic Hypogonadism vs Kallmann Syndrome</u> | | | | | | | |
|---|-----------------|-------|---------|----------|--------|--------|--------|
| | | | Smell | | | Total | P |
| | | | Anosmia | Hyposmia | Normal | | |
| Idiopathic Hypogonadotropic Hypogonadism | <u>nIHH</u> | Count | 0 | 0 | 45 | 45 | <0.001 |
| | | % | 0.0% | 0.0% | 100.0% | 100.0% | |
| | <u>Kallmann</u> | Count | 5 | 5 | 0 | 10 | |
| | | % | 50.0% | 50.0% | 0.0% | 100.0% | |
| Total | | Count | 5 | 5 | 0 | 55 | |
| | | % | 9.1% | 9.1% | 81.8% | 100.0% | |

Table 2

| Olfactory Bulbs / Tracts development in Idiopathic Hypogonadotropic Hypogonadism | | | | | | | |
|--|-----------------|-------|--------------------------|------------|--------|--------|--------|
| | | | Olfactory Bulbs / Tracts | | | Total | p |
| | | | Aplasia | Hypoplasia | Normal | | |
| Idiopathic Hypogonadotropic Hypogonadism Type | <u>nIHH</u> | Count | 0 | 0 | 45 | 45 | <0.001 |
| | | % | 0.0% | 0.0% | 100.0% | 100.0% | |
| | <u>Kallmann</u> | Count | 5 | 5 | 0 | 10 | |
| | | % | 50.0% | 50.0% | 0.0% | 100.0% | |
| Total | | Count | 5 | 5 | 45 | 55 | |
| | | % | 9.1% | 9.1% | 81.8% | 100.0% | |

Table 3

| Olfactory Sulci Development in <u>normosmic Idiopathic Hypogonadotropic Hypogonadism vs Kallmann Syndrome</u> | | | | | | | |
|---|-----------------|-------|-----------------|------------|--------|--------|--------|
| | | | Olfactory Sulci | | | Total | P |
| | | | Aplasia | Hypoplasia | Normal | | |
| Idiopathic Hypogonadotropic Hypogonadism Type | <u>nIHH</u> | Count | 0 | 0 | 45 | 45 | <0.001 |
| | | % | 0.0% | 0.0% | 100.0% | 100.0% | |
| | <u>Kallmann</u> | Count | 5 | 5 | 0 | 10 | |
| | | % | 50.0% | 50.0% | 0.0% | 100.0% | |
| Total | | Count | 5 | 5 | 45 | 55 | |
| | | % | 9.1% | 9.1% | 81.8% | 100.0% | |

Conclusion: Normosmic hypogonadotropic hypogonadism is the most common type of IHH in our study. Hyposmia & anosmia are related to anatomical abnormalities of olfactory bulbs / tracts in 100% patients of Kallmann Syndrome. MRI is a useful tool to demonstrate abnormalities of olfactory system and to differentiate Kallmann Syndrome from normosmic IHH.

Disclosure of Interest: None Declared

ICE2020-1095

EFFICACY AND SAFETY OF THE FIRST 6-MONTH SUBCUTANEOUS LEUPROLIDE ACETATE FOR TREATMENT OF CENTRAL PRECOCIOUS PUBERTY

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Introduction: Gonadotropin-releasing hormone (GnRH) agonists, such as intramuscular leuprolide acetate, triptorelin and subcutaneous implants of histrelin, are standard treatment for central precocious puberty (CPP). Implants require surgery and sometimes anesthesia, while frequent intramuscular injections can be painful and lead to suboptimal compliance.¹ A shift to longer acting-formulations and subcutaneous injections has been proposed.² Treatments with convenient administration, prolonged duration of action and favorable safety profile may be beneficial, improving patient adherence.

Objectives: This pivotal Phase III study evaluated the efficacy and safety of the first small volume (0.375 mL) 6-month subcutaneous injectable in situ gel leuprolide acetate for CPP.

Methods: Sixty-two children (60 girls, 2 boys) with CPP (naïve to treatment) received 2 doses of 45 mg subcutaneous leuprolide acetate at 24-week intervals, constituting the intent-to-treat population. GnRH stimulated peak luteinizing hormone (LH), estradiol (E₂) or testosterone (T), and follicle stimulating hormone (FSH) levels were measured pre-treatment and at Weeks 12, 24, 36 and 48. The primary endpoint was rate of LH<4 IU/L at Week 24. Safety outcomes were measured.

Results: Mean age at onset of treatment was 7.5 ± 0.9 (SD) (range 4-9) years. 87% (54/62) of subjects achieved stimulated LH suppression to <4 IU/L by Week 24 and 85% at all assessed timepoints. 97% (58/60) of girls achieved E₂ suppression <20 pg/mL at Week 24 and over 97% remained suppressed at Week 48. Both boys had T <29 ng/dL at Weeks 12, 24 and 36. At Week 48, one boy was above target at 43.2 ng/dL. 66% (41/62) met the criterion for suppression of FSH (<2.5 IU/L) at Week 24 and 55% at Week 48. 52/53 treatment emergent adverse events were mild or moderate.

Conclusion: Six-month 45 mg subcutaneous leuprolide acetate is a promising addition to existing treatment options for CPP. It effectively suppressed LH, sex steroids, and clinical signs of pubertal progression, and demonstrated a good safety profile. It also has the beneficial features of subcutaneous administration, small injection volume and twice a year dosing, that may improve dosing adherence and clinical outcomes for children with CPP.

Disclosure of Interest: None Declared

ICE2020-1106

INFLUENCE OF DISEASE ACTIVITY AND BODY COMPOSITION PARAMETERS ON CROSS-SECTIONAL AREA OF THE MEDIAN NERVE IN ACROMEGALIC PATIENTS

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Introduction: Carpal tunnel syndrome (CTS) is neuropathy that occurs due to compression of median nerve in the carpal tunnel. Acromegaly is one of the important causes of CTS

Objectives: The aim of this study was to examine median nerve with ultrasound in acromegalic patients and assess the relationship with activity, duration of disease, anthropometric and body composition parameters.

Methods: We prospectively examined the cross sectional area (CSA) of median nerve with high-resolution ultrasound in 107 acromegalic patients (70 females and 37 males). Body composition parameters were assessed by dual – energy X-ray absorptiometry (DXA). The t-student tests and Pearson correlation were used for data analysis

Results: The cross sectional area of median nerve in patients was 0.12 ± 0.05 cm² (0.11 ± 0.05 cm² in women and 0.13 ± 0.05 cm² in men, $P = 0.043$). Positive correlation was found between the levels of IGF-1 and CSA in whole study group ($R = 0.400$, $P < 0.001$) and female population ($R = 0.466$, $P < 0.001$). In male population our results did not reach statistical significance ($P = 0.07$). Relationship between CSA and duration of disease in both genders was not confirmed. BMI correlated with the CSA in whole study group ($R = 0.294$, $P = 0.002$) and also in subgroup of women ($R = 0.375$, $P < 0.001$). No correlation was observed between fat mass, FMI (total body fat mass/ height) and CSA of median nerve in all study subgroups. Lean mass and LMI (total body lean mass/ height) positively correlated with CSA in whole study group ($R = 0.340$, $P < 0.001$; $R = 0.424$, $P < 0.001$) and also in subgroup of female ($R = 0.491$, $P < 0.001$; $R = 0.491$, $P < 0.001$).

Conclusion: We confirmed positive correlation between the levels of IGF-1 and CSA of median nerve and according to our findings CSA is independent on the duration of the disease. We also confirmed positive correlation between CSA of median nerve and body composition parameters BMI and lean mass, we did not describe any correlation with fat mass.

Disclosure of Interest: None Declared

ICE2020-1141

ASSOCIATION OF PRL-3 AND P21 IN EXPERIMENTAL PITUITARY TUMORAL MODEL: A POSSIBLE NEW TUMOR GROWTH REGULATION

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Introduction: PRL-3 is a subclass of a protein tyrosine phosphatase super family which is expressed in a wide range of epithelial neoplasms. However, up to now, PRL-3 has not been described in the pituitary.

Objectives: Our aim was to evaluate PRL-3 expression. p53, p21, Ki67 were also analyzed.

Methods: Fisher male rats treated with estradiol benzoate (EB) during 10, 20 and 30 d (n: 9) were used. Rat normal pituitaries (n:3) were used as control (C). Analysis of PRL-3, p21, p53 and Ki67 expression was performed by Immunohistochemistry at photonic and electronic level and Western Blot. Statistical analysis: Anova-Fisher and Pearson's correlation.

Results: P21 was increased in the experimental model, reaching the highest values at 30 EB (adenomatous state) compared to C ($p < 0.05$). On the other hand, p53 exhibited a marked and significant increase from 10 to 30 d compared to C ($p < 0.05$). Ki67 index reached the highest values at 20 EB. PRL-3 was immunodetected in pituitary tumoral cells after EB stimulus at both, cytoplasmic and nuclear compartments. Cells were immunolabeled with 10 nm gold particles, showing a clear association with the cytoplasmic side of the plasma membrane and in vacuole-like of the early endosome. PRL-3 protein levels reached the highest value at 20 EB compared to the other experimental groups ($p < 0.05$ vs C, 10d EB and 30d EB), decreasing at 30d EB ($p < 0.05$ vs 10d EB and 20d EB). PRL-3 showed a linear correlation with p21 (Pearson coefficient = 0.57; $p < 0.05$).

Conclusion: These findings lead us to hypothesize that the mechanism of action of p21 in the hyperplastic/adenomatous gland could be regulated by PRL-3 by inactivating p21 and accumulating in the cytoplasm, thus favoring tumor growth regardless p53 regulation.

Disclosure of Interest: None Declared

ICE2020-1168

REGULATION OF FGF2-INDUCED CELL PROLIFERATION BY INHIBITORY GPCR IN NORMAL PITUITARY CELL

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Introduction: The growth factors effects may be regulated by the inhibitory G protein-coupled receptors (GPCR-G_{ai}) activation, thus modifying the metabolic activity of pituitary gland.

Objectives: Considering that intracellular communications are essential; the aim was to evaluate whether GPCR-G_{ai} regulates the basic fibroblast growth factor (FGF2) proliferative activity in normal pituitary cell populations.

Methods: Anterior pituitary primary cell cultures from Wistar female rats were treated with FGF2 (10ng/mL) or somatostatin analogue (OCT, 100nM) alone or co-incubated with or without an inhibitor of GPCR-G_{ai}, pertussis toxin (PTX, 500nM) or MEK inhibitor (U0126, 100μM).

Results: The BrdU uptake shows that the basal lactotroph and somatotroph mitosis cells was 6.9% and 3.34%, respectively. The FGF2 increased and OCT decreased the lactotroph and somatotroph BrdU positive cells respect to control group ($p < 0.05$), whereas the FGF2-induced cell proliferation was prevented by OCT co-incubation in both cell types. This effect was reverted by PTX or U0126 pre-incubation. The inhibition of lactotroph and somatotroph mitosis was associated with a downregulation of c-Jun expression by a decrease of phosphorylated (p) ERK, p-AKT, p-PS6 and an increase of p-JNK observed by western blot. The SSTR2 and 5 expression and the percentage of TUNEL positive cells did not show any significant variation. Furthermore, the OCT inhibition on proliferative effect induced by FGF2 was evidenced for an increase in the number of cells in the G₀/G₁ phase with a concomitant reduction in the number of cells in the S and G₂/M phases ($p < 0.05$). This effect was related to a decrease of cyclin D1 gen and protein expression with an increase in the cell cycle inhibitors p27 and p21 expression. The cyclin E1 and CDK4 did not show any variation.

Conclusion: These results show that the FGF2 and OCT combined treatment induced a decreased of prolactin and somatotroph population associated with G₁-phase arrest, modulating key proteins in the early phases (transition from G₀/G₁ to the S-phase) of cell cycle progression and proteins involved in the cell proliferation. This regulatory effect, mediated for GPCR-G_{ai}, could participate in the homeostasis of lactotroph and somatotroph in physiological conditions.

Disclosure of Interest: None Declared

ICE2020-1169

CHOLANGIOCARCINOMA INVOLVING THE PITUITARY GLAND

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Introduction: Pituitary Metastasis is a rare disease, with a total of approximately 289 reported cases in the literature. Breast and lung cancer constitute the most frequent primary origin. We present the first case in the literature of pituitary metastasis due to a primary cholangiocarcinoma.

Case Description: A 34 y/o female with no past medical history presented to the ED with 1-month history of headache and double vision in the setting of a right 6th cranial nerve palsy. MRI of the brain revealed a pituitary mass (2.5x2.6cm) that was extending into the sphenoid sinus, with abutment of the bilateral cavernous sinuses but no involvement of the optic chiasm. The pituitary stalk was thickened and deviated to the left (3.8mm) She underwent gross total transsphenoidal tumorectomy revealing a moderately differentiated adenocarcinoma. Immunohistochemistry was performed, but was unable to determine the primary malignancy (negative for TTF1, GCDFP-15, PAX8, GATA-3, glypican-3, CDX2, S-100). Next generation sequencing identified a FGRF2-BICC1 gene fusion which has been reported in a molecular subtype of cholangiocarcinoma. A surveillance PET scan showed a large hypermetabolic partially necrotic mass within the right hepatic lobe extending to the caudate lobe, a hypermetabolic left hepatic lobe mass (SUV 12.9) and a hypermetabolic portocaval lymph node, suspicious for metastasis (SUV 3.9). A liver biopsy confirmed the diagnosis.

Clinical discussion: Pituitary metastasis of gastrointestinal tract is extremely rare and most commonly related to colon cancer. We report the first case of metastatic cholangiocarcinoma involving the pituitary gland. Moreover, we report the use of next-generation sequencing coupled with imaging surveillance as a tool to identify the primary tumor in patients with pituitary metastases of unknown origin. Cancer of unknown primary (CUP) is a distinct clinicopathological entity with poor prognosis. Gene expression profiling could complement standard pathologic diagnostic workup in determining the organ of origin in patients with CUP, particularly when immunohistochemistry is inconclusive. The majority of tumors have identifiable mutations that can be targeted by the current approved novel therapies, which broadens the diagnostic and therapeutic horizon in this group of patients.

Disclosure of Interest: None Declared

ICE2020-1191

PREVALENCE OF ANEMIA IN A BRAZILIAN COHORT OF MEN AND WOMEN WITH PITUITARY ADENOMAS

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Introduction: Reports on the prevalence of anemia in pituitary tumors are rare and, in general, related to male hypogonadism.

Objectives: This study aimed to establish the prevalence of anemia in a cohort of patients with acromegaly, non-secretory pituitary adenomas (NFA), and prolactinomas.

Methods: Clinical and hematological data at diagnosis were reviewed in the medical records of patients diagnosed with pituitary adenomas treated at a Brazilian neuroendocrinology referral center, excluding those diagnosed with acute or chronic infections, hematopoietic diseases, renal failure and submitted to radiotherapy. Of the 342 cases eligible for the study, 96 were acromegalics (mean age 50.5±14 years old, 58.3% women), 166 patients had NFA (mean age 64.6±13.2 years old, 44.2% women) and 80 had prolactinomas (mean age 52.1±17 years old, 60.8% women). Among acromegalics, 74% had macroadenomas, and in those with NFA and prolactinomas all were macroadenomas.

Results: Anemia was diagnosed in 22/96 (22.9%) of acromegalics, with average hemoglobin (Hb) of 11.85 and a mean age of 47 years old; 29/166 (17.5%) of NFA (average Hb: 11.62; mean age: 62.41 years old) and 17/80 (21.2%) of those with prolactinomas (average Hb: 11.56; mean age 60.41 years old), anemia cases constituting 19.9% of the total sample. Classifying by severity, most cases had mild anemia (86.76%), the remainder being classified as moderate anemia (WHO criteria). In this last subgroup, 7 of the 9 patients were women. Regarding the classification according to the values of MCV and MCHC, 59 (87%) had normocytic and normochromic anemia, 6 suffered from microcytic and normochromic, and the others, one of each following classification: normocytic and hypochromic, microcytic and hyperchromic, and macrocytic and normochromic. In all anemic subgroups, it was found a predominance of male patients (68% in acromegalics, 66% in NFA, 65% of prolactinomas).

Conclusion: The found values are twice the prevalence found in the adult Brazilian population, which is 9.9%. These results improve knowledge of the epidemiological profile of pituitary adenomas patients in terms of hematimetric parameters; and suggest the need to expand studies in the area with the assessment of clinical and hormonal variables with a possible impact on the establishment of anemia.

Disclosure of Interest: None Declared

ICE2020-1197

NEUTROPHIL-TO-LYMPHOCYTE AND PLATELET-TO-LYMPHOCYTE RATIOS IN PITUITARY ADENOMAS

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Introduction: The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are used as markers of subclinical inflammation in various clinical situations.

Objectives: This study aims to evaluate these ratios in patients with GH-secreting, PRL-secreting, and non-functioning pituitary adenomas and, in acromegaly, to correlate them with clinical variables.

Methods: Clinical features, hematological and hormonal data were reviewed in the medical records of patients diagnosed with pituitary adenomas treated at a Brazilian neuroendocrinology referral center. The sample comprises 338 patients, 52.1% female, aged 57.7 ± 15.9 years. Of these, 96 had a somatotropic adenoma, of which 74% were macroadenomas; 163 had non-secreting macroadenomas (NFA) and 79 had macroprolactinomas. A second complete blood count test was appraised during the evolution of 54 acromegalics. NLR and PLR were interpreted according to the threshold available in the literature.

Results: The value of NLR ranged from 0.3 to 17.5. The NLR and PLR did not differ significantly between groups. The NLR was significantly higher in the subgroup of giant prolactinomas than in the non-giant ones. In acromegalics patients, there was no correlation between NLR and PLR with GH in the presentation, biochemical control of the disease, tumor volume or invasiveness, and the presence of diabetes mellitus. The ratios were higher in 15 individuals than the levels commonly used as poor prognosis in cancer patients.

Conclusion: This study evaluated, for the first time to the knowledge of the authors, the behavior of inflammatory markers in the composition of the complete blood count test in patients with prolactinomas and NFA, and extended the evaluation of these markers in acromegalics, subject of rare reports in the literature. The significance of high individual NLR and/or PLR rates in patients with pituitary adenomas requires new and extended analysis to establish their clinical relevance.

Disclosure of Interest: None Declared

ICE2020-1204

SEVERE SECONDARY ERECTILE DYSFUNCTION CAUSED BY GIANT MACROPROLACTINOMA

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Introduction: Giant prolactinomas are less often seen currently, due to a greater availability of access to health care and image exams.

Case Description: JBP, a 30 years old male, sales person, evangelic, sought medical assistance due to a severe erectile dysfunction. Married for 9 years with report of never being able to perform satisfactory sexual intercourse due to the severity of erectile dysfunction. Obese, with grade III, BMI 48, absence of facial or trunk hair, bilateral gynecomastia, hypotrophic testicles (volume 15ml), hypodeveloped phallus, depressed and introverted humor. In the initial propaedeutic evaluation it was found: LH 0,12mUI/ml, FSH 1,0mUI/ml, Total Testosterone 37,4ng/dl, Free Testosterone 0,90pg/ml TSH 2,8mU/L, Prolactin 6.300,06ng/ml. During subsequent propedeutica it was observed by MRI, massive lesion in the sella turcica with invasion and infiltration of adjacent structures with 5,0x4,1x3cm, suggestive of pituitary macroadenoma. We opted for the use of cabergoline with a progressive increase till 0,5mg 3 x week, but he tolerated the maximum dose of 1mg weekly. After 6 weeks he developed prolactin normalization (12,2ng/ml), although without significant improvement of testosterone (63,5ng/ml). In an attempt to reestablish the gonadotrophic axis, clomiphene was introduced 25mg/daily. After 2 months, there was an expressive improvement in self-esteem, libido, satisfactory sex life, mood, weight loss of 10kg. (Prolactin 14,59ng/ml, total testosterone 610ng/ml, free 15,38pg/ml, basal cortisol 19,14µg/dl).

Clinical discussion: The macroprolactinoma can present varying intensities of hypogonadotrophic hypogonadism. Religious conviction regarding sexuality may postpone seeking medical assistance causing worsening of the clinical picture with profound repercussions regarding the patient's biopsychosocial impairment. The correct diagnosis and treatment of severe hyperprolactinemia, even if late, may restore the gonadotrophic axis rescuing the well-being and sexuality of the affected patient. Giant macroprolactinomas with intense production of prolactin can show desirable response to relatively low doses of cabergoline.

Disclosure of Interest: None Declared

ICE2021-1288

PITUITARY MACROADENOMA: A CASE OF BALANCED DEFICIENCIES

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Introduction: Diabetes insipidus (DI) rarely occurs in pituitary tumors although some patients may develop DI following pituitary tumor resection. However DI is known to occur in patients with tumors metastatic to the pituitary or in infiltrative disorders of the pituitary gland. We are reporting a patient with a 2cm pituitary macroadenoma whose DI was unmasked by glucocorticoid therapy.

Case Description: A 61-year-old male with a history of non-functioning pituitary macroadenoma, incidentally discovered on imaging in 2015 and stable at 1.6cm for 4 years, was referred to endocrinology for interval enlargement of macroadenoma. He presented with new headache during exercise, but denied vision loss, fatigue, decreased libido, weight loss, or urinary frequency. Repeat MRI indicated growth to 2.1cm in the suprasellar component, no cavernous sinus involvement, and abutting the optic chiasm. Laboratory results: central hypothyroidism (FT4 0.21 ng/dL, T3 68 ng/dL and TSH 1.61 mIU/L), central hypogonadism (testosterone free 1.3 pg/mL) and adrenal insufficiency (serum cortisol 4.4 mcg/dL). He was empirically started on hydrocortisone, and after 3 days instructed to begin low-dose levothyroxine. At close followup, patient revealed that he developed new hourly nocturia causing significant distress. An overnight water deprivation test yielded a serum sodium 152 mmol/L with a urine osmolality 191 mOsm/kg, copeptin 4.6 pmol/L. Symptoms rapidly improve with desmopressin.

Clinical discussion: Diabetes insipidus occurring in pituitary tumors including macroadenomas is extremely rare. Secretion of AVP occurs in the hypothalamic osmoreceptors, supraoptic or paraventricular nuclei, and the superior portion of supraopticohypophyseal tract. AVP deficiency is most commonly due to damage to these areas either through neurosurgery or trauma, and more rarely tumors or infiltrative disease. However, glucocorticoid and thyroid replacement each may precipitate the development of diabetes insipidus by impairing free water excretion. Low cortisol stimulates release of antidiuretic hormone, but this secretion is then inhibited by exogenous steroid replacement. Cortisol interferes with AVP signaling through unclear mechanisms either at the V2 receptor or post-receptor level, decreasing translocation of type 2 aquaporins and therefore reducing free water reabsorption. It is important to recognize that CDI can be unmasked after glucocorticoid or thyroid hormone replacement.

Disclosure of Interest: None Declared

ICE2021-1294

MUSCLE DYSFUNCTION IS ASSOCIATED WITH POOR QUALITY OF LIFE IN PATIENTS WITH ACROMEGALY WITH LONG-TERM CONTROL

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Introduction: Residual morbidity in patients with controlled acromegaly (ACRO) significantly affects Quality of Life (QoL). While sustained muscle weakness is a frequent complaint in these patients, the impact of muscle dysfunction on their psychophysical wellbeing is currently unknown.

Objectives: To assess the relationship between QoL and muscle strength and performance tests in patients with controlled ACRO

Methods: Thirty-six acromegalic patients [20 females and 16 males, mean (\pm SD) age, 53 \pm 9 years, BMI 27 \pm 4 Kg/m² and duration of control 92 \pm 58 months], and 36 age, gender and BMI-matched controls were studied. QoL was assessed using both generic (SF-36) and disease-specific (AcroQoL) questionnaires. Muscle function was assessed using the following tests: gait speed velocity (GS), timed up and go (TUG), 30-second chair stand and hand grip strength (HGS) measured by a manual dynamometer in both hands.

Results: The mean (\pm SD) AcroQoL total score was 55 \pm 21. Duration of TUG was negatively associated with total score, and both physical and psychological subscales of AcroQoL (p <0.05). TUG was also associated with several items of SF-36 (physical function, role physical, body pain, vitality, role emotional and mental health) in patients (p <0.05), but not in controls.

HGS was associated with both total score and physical and personal relations subscales of AcroQoL; p <0.05. HGS was also associated with all the items of SF-36 (physical function, role physical, body pain, general health, vitality, social functioning, role emotional and mental health).

In patients, GS was associated with physical functioning on SF-36; p <0.05; 30-second chair stand was associated with general health on SF-36; p <0.05.

In a multiple linear regression model, duration of TUG negatively predicted total AcroQoL score, regardless of age, gender and length of acromegaly control (β -0.48, p =0.022).

Image:

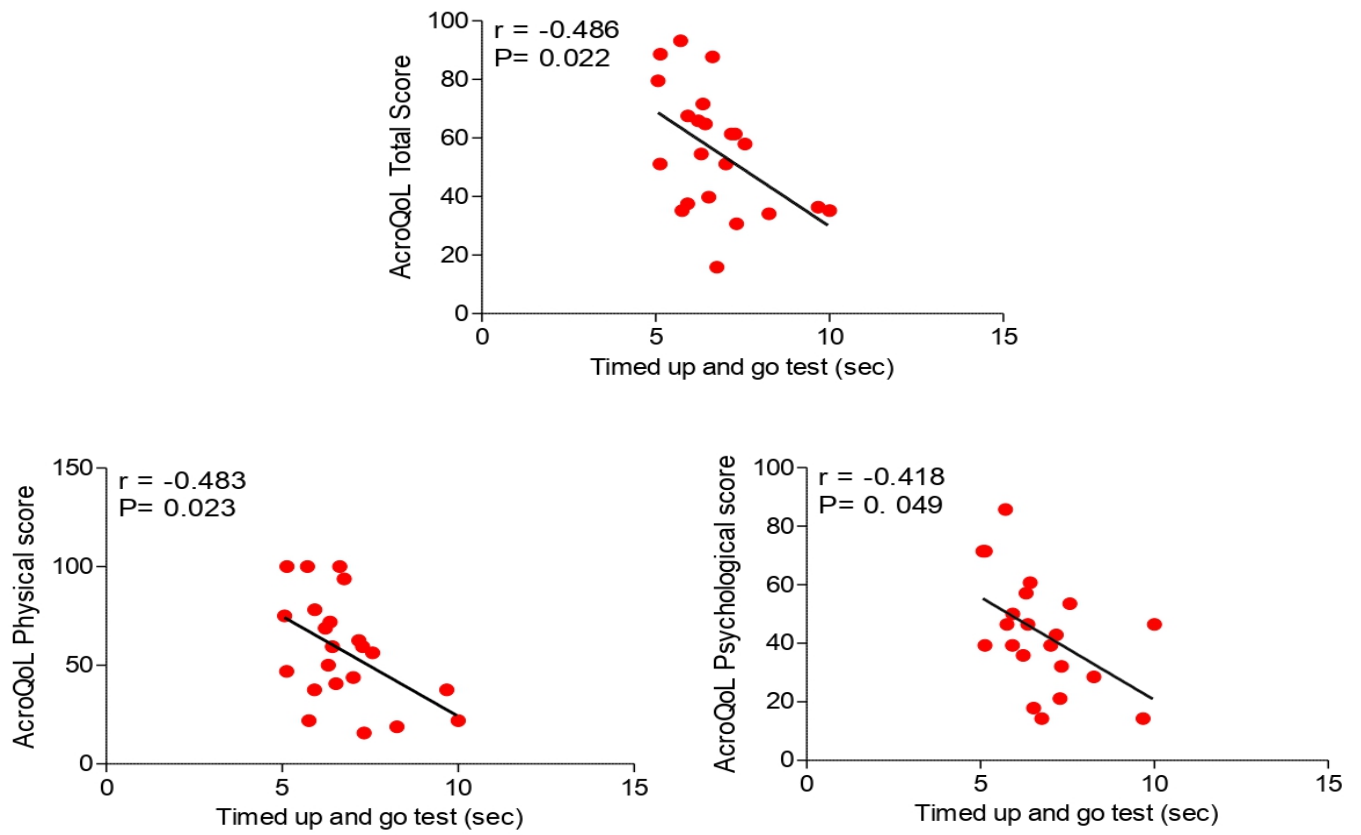


Figure 1. Relationship between Timed up and go test and AcroQoL Total Score, physical and psychological subscales.

Conclusion: Muscle dysfunction is associated with impaired quality of life in patients with long-term controlled acromegaly.

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Disclosure of Interest: None Declared

ICE2021-1317

RSUME TIGHT CONTROL OF PTTG PROTEIN LEVELS BY POST-TRANSLATIONAL MODIFICATIONS

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Introduction: Pituitary tumor transforming gene (PTTG), vertebrate securin, is a sister chromatid separation inhibitor¹. On the onset of anaphase, PTTG is ubiquitinated by the APC/C complex² and degraded rapidly allowing cell division. Increased expression of PTTG is associated with enhanced tumor cell growth, aneuploidy and malignant status. Recently, we reported a protein increase and stabilization of PTTG by RWD-containing SUMOylation enhancer (RSUME)³ in pituitary tumor cells⁴. As a consequence, RSUME enhances PTTG transcription factor and securin activities. Both proteins were cloned from lactosomatroph pituitary tumor lines^{3,5}.

¹ Zou 1999 *Science*

² Zur 2001 *EMBO J*

³ Carbia-Nagashima 2007 *Cell*

⁴ Fuertes 2018 *Endocr Relat Cancer*

⁵ Pei 1997 *Mol Endocrinol*

Objectives: We explore the mechanism of stabilization of PTTG focusing in post-translational modifications by Ubiquitin and SUMO.

Methods: We investigated PTTG post-translational modification in COS-7 cells transfected with His-Ub or HA-SUMO1 vector, by immunoprecipitation (IP) assay purifying Ubiquitinated or SUMOylated proteins and posterior western blot with specific PTTG-antibody. RSUME knockdown was achieved using a specific short hairpin RNA. Endogenous SUMOylation was performed in rat tumor pituitary lactosomatroph GH4 cells. For *in vitro* SUMO assay we used a commercial kit. To inhibited the proteasome system, we used 10µM MG-132; while an expression vector of Gam1, a viral enzyme, was used to block SUMOylation.

Results: By IP we observed that both RSUME and SUMO-1 promote a decrease on Ub conjugation to PTTG, stepping up its protein abundance. RSUME knockdown increases PTTG ubiquitination but had no effect on PTTG stability when the proteasome degradation is inhibited by MG-132. Adding Gam1 we restored PTTG ubiquitination levels by preventing SUMOylation, even in the presence of RSUME.

We observed that RSUME mutant which loses its activity as SUMO-enhancer, YAPA, showed a decreased action on PTTG stability. Accordingly, we found diminished protein levels of PTTG in the presence of Gam1, although RSUME was present. By IP we found that PTTG was conjugated to SUMO-1 and RSUME enhanced this SUMOylation. We validated PTTG SUMOylation by *in vitro* SUMO assay and also at endogenous level in GH4 cells.

Conclusion: We found that RSUME-regulated PTTG is conjugated to SUMO, promoting an increase in protein levels and stability, in addition to a falling on PTTG degradation by proteasome, contributing by this mechanism to the abundance of PTTG in tumor cells.

Disclosure of Interest: None Declared

ICE2021-1352

ERDHEIM-CHESTER DISEASE: A RARE HISTIOCYTOSIS WITH OUTSTANDING RESPONSE TO COBIMETINIB

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Introduction: Erdheim-Chester disease (ECD) is a rare form of histiocytosis, characterized by xanthogranulomatous infiltration of multiple organs by lipid-laden histiocytes. It is considered a myeloid inflammatory clonal disorder and it's been recently classified by the Histiocyte Society in the "L" Group along with the Langerhans-cells histiocytosis, given the fact that they both share the same mutations in more than 80% of cases. It mainly affects men with a mean age of 55 years and the most frequent manifestations are bilateral osteosclerotic involvement of the knees, perinephric fat infiltration and circumferential sheathing of the thoracic and abdominal aorta.

Case Description: We present the case of a 65-year-old caucasian man who consulted our Endocrinology Unit because of polyuria and polydipsia of 4 months of evolution, diagnosing central diabetes insipidus associated with panhypophysitis on nuclear magnetic resonance imaging (MRI). Physical examination showed skin lesions he has had for 7 years, that were papules-nodules in the anterior chest and xanthelasmas in the face and neck. He presented a normal lipid profile, with elevated eritrosedimentation rate and reactive c protein (PCR). Hormonal tests results showed a panhypopituitarism and the skin biopsy was compatible with non-Langerhans histiocytosis.

Clinical discussion: Given the suspicion of ECD, and considering the lack of presentation of the most frequent and typical clinical manifestations, we performed the genetic study of the skin biopsy that showed the absence of a mutation in BRAF V600 but the presence of a mutation in MAP2K1, confirming the diagnosis.

The patient started treatment with interferon alpha, but after 10 months he showed a frank progression of skin lesions, with a poor quality of life related to interferon injections. For instance, given the mutation found, we changed his treatment to cobimetinib, a potent and selective inhibitor of MEK1 and MEK2 tyrosine threonine kinases, with disappearance of the skin lesions and a great improvement in his quality of life after eight months of therapy.

Disclosure of Interest: None Declared

ICE2021-1353

PREOPERATIVE LOW CORTISOL AND THYROXINE IN PITUITARY MACROADENOMA: DOES TUMOR SIZE MATTER?

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Introduction: Anterior pituitary dysfunction is one of the commonest mass-effect related features of pituitary macroadenoma and it is imperative to evaluate adrenocortical and thyroid status before surgery to initiate appropriate hormonal replacement. However, tumor size may not correlate with involvement of different hormonal axes to same extent.

Objectives: To observe the correlation of basal cortisol and thyroxine with maximal tumor diameter (as observed in preoperative magnetic resonance imaging) in pituitary macroadenoma patients excluding those with autonomous secretion of ACTH or TSH.

Methods: In this cross-sectional study, 56 patients [median age 33.5, IQR 26.5-40.0 years; 33 (59%) female] with pituitary tumor [non-functional 30 (53.6%), functional 26 (46.4%)] awaiting surgery at the department of neurosurgery, National Institute of Neurosciences and Hospital, Dhaka were included purposively from July 2018 to October 2020. Clinical information was obtained through direct history and examination. Laboratory and imaging records were evaluated for anterior pituitary hormonal axes and characteristics of tumor. Preoperative morning serum cortisol $<5 \mu\text{g/dL}$ with low/normal ACTH was taken as evidence of secondary hypoadrenalism and low free thyroxine (FT4) with low/normal TSH as secondary hypothyroidism.

Results: Among the participants, secondary hypoadrenalism was present in 20 (35.7%) and secondary hypothyroidism in 8 (14.3%) with similar frequencies in functional and non-functional tumor ($p>0.05$). Preoperative FT4 level had significant negative correlation with maximal tumor diameter ($r=-0.366$, $p=0.006$); every 1 cm increase in diameter increased 1.9 (CI 1.03-3.59, $p=0.040$) fold risk of secondary hypothyroidism. On the other hand, basal cortisol had no significant correlation with maximal tumor diameter ($r=-0.030$, $p=0.824$), neither there was increased risk of secondary hypoadrenalism with increase of tumor size (OR 0.91; 95% CI 0.60-1.38; $p=0.650$). The median maximal tumor diameter of participants with secondary hypoadrenalism was 3.0 cm (range 1.0-6.3 cm) and with secondary hypothyroidism 4.5 cm (range 2.6-5.9 cm). Maximal tumor diameter <2.5 cm was observed in 16 patients; of them none had hypothyroidism, while 6 had hypoadrenalism.

Conclusion: Tumor size correlated well with thyroxine but not with cortisol in patients with pituitary macroadenoma. Secondary hypoadrenalism was observed even in patients with smaller tumor mass.

Disclosure of Interest: None Declared

ICE2021-1371

RESISTANCE TO FIRST GENERATION SOMATOSTATIN RECEPTOR LIGANDS DOES NOT IMPAIR THE RESULTS OF GAMMA KNIFE IN ACROMEGALY

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Introduction: The goals of the treatment of acromegaly are control of tumor mass, clinical symptoms, decrease GH and IGF-I. Surgery is the first-line treatment, but remission rate is variable. Somatostatin receptor ligands (SRL) therapy control GH and IGF-I excess in 50–60% of patients. Gamma knife radiosurgery (GKRS) has proven to be an attractive therapy to achieve goals of treatment. There are no data on the effect of the resistance to SRL on the outcome of GKRS, however it is commonly thought that SRL resistant patients may represent a subset of patients with a worse long-term outcome.

Objectives: The aim of our study was to investigate if the resistance to SRL affected the probability to obtain remission of disease after GKRS.

Methods: Ninety-six patients were included. The cumulative probability of normalization of IGF-1 levels after GKRS was assessed by the Kaplan-Meier method. The association of several clinical characteristics, with GKRS outcome was explored with the use of a Cox proportional-hazard model with the relative hazard ratio (HR) and 95% confidence interval (CI).

Results: Resistance to SRL occurred in 39 of the 96 patients (40.6%). The median duration of SRL treatment was 12 months (IQR 8-24 months, range 6-60 months). After GKRS, patients resistant to SRL had a 5- and 10-yr probability of remission of 40.7% (95% CI, 23.7 - 57.7%) and 75.9% (95% CI, 57.9 - 93.9%), respectively. Patients responder to SRL had a 5- and 10-yr probability of remission of 46.8% (95% CI, 32.2 - 61.4%) and 58.1% (95% CI, 41.5 - 74.7%), respectively. The difference was not significant ($p = 0.48$ by the Log-Rank test). Multivariate analysis confirmed that the only independent variables associated with GKRS outcome were basal GH ($P = 0.001$) and IGF-1 mULN levels ($P = 0.013$).

Conclusion: We demonstrated for the first time that resistance to SRL therapy had no effect on the probability to obtain remission of acromegaly after GKRS. GH and IGF-1 levels before GKRS were the only characteristics associated with GKRS outcome. These data permit to focus the attention on the tumoral characteristic to decide the follow up therapy for acromegalic patients after surgery, and to individualize the choice in the perspective of a personalized medicine.

Disclosure of Interest: None Declared

ICE2021-1416

CEREBRAL INFARCTION IN CHILDHOOD-ONSET CRANIOPHARYNGIOMA PATIENTS – RESULTS OF KRANIOPHARYNGEOM 2007

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Introduction: Cerebral infarction (CI) is a known vascular complication following treatment of suprasellar tumors.

Objectives: Risk factors for CI, incidence rate, and long-term prognosis are unknown for patients with childhood-onset craniopharyngioma (CP).

Methods: MRI of 244 CP patients, recruited 2007-2019 in KRANIOPHARYNGEOM 2007, were reviewed for CI. Risk factors for CI and outcome after CI were analyzed.

Results: Twenty-eight of 244 patients (11%) presented with CI based on reference assessment of MRI. One CI occurred before initial surgery and one case of CI after release of intracystic pressure by a cyst catheter. 26 of 28 CI were detected after surgical tumor resection at a median postoperative interval of one day (range: 0.5-53 days). Vascular lesions during surgical procedures were documented in 7 cases with CI. There was a trend ($p=0.060$) towards higher initial presurgical tumor volume in CI patients compared with non-CI patients. Differences with regard to surgical approach did not reach statistical significance. In all 12 irradiated patients, CI occurred before irradiation. Multivariate analyses showed that hydrocephalus and gross-total resection (GTR) at the time of primary diagnosis/surgery were independent risk factors for CI. PFS was lower after CI (0.316 ± 0.094) when compared with the subgroup of patients without CI (0.571 ± 0.039). After CI, quality of life (PEDQOL) and functional capacity (FMH) were impaired.

Conclusion: CI occurs in 11% of CP cases. Tumor size, degree of resection and increased intracranial pressure are risk factors, which should be considered in the planning of surgical procedures for prevention of CI.

Disclosure of Interest: None Declared

ICE2021-1421

DO WE NEED A PITUITARY DISEASES REGISTRY IN LATVIA?

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Introduction: Pituitary diseases result in clinical consequences and increased mortality due to tumors mass effects or due to pituitary hypersecretion/insufficiency. Pituitary diseases/tumors registry enables identification of diagnostic and prognostic highlighters and evaluation of long-term clinical outcomes. The registry improves guidelines and cost-effective pituitary diseases management and care.

Objectives: Our work provides the registry study, which is designed to create a database of pituitary diseases patients in Latvia for the first time.

Methods: We collected 3 yrs data from pts medical records with pituitary diseases mainly from Clin. Univers. Hosp. Outpatient Clin. and from 4 Outpatients Clin. which were the workplaces of the authors. Prospective cohort analysis was performed based on demographic, MRI, lab data, data on medications, doses, and regimens, information on co-morbidities and concomitant medications. We collect 355 pts with pituitary diseases: prolactinomas, CNFA, acromegalies, empty sella syndrome, Cushing's disease (CD), Rathke's pocket cysts, meningiomas, craniopharyngioma, pituitary aplasia and hypoplasia, TSH-omas, germinoma, glioma, chondrosarcoma, pericytoma.

Results: 355 pts (71.7% women) with pituitary diseases were registered from July 2016 to July 2019. The mean age in the cohort was 43.4 yrs (range 18–83 yrs). Prolactinomas were the most common adenomas (40.8%), followed by CNFA (28.5%), acromegaly (16.1%) and than empty sella syndrome (5.1%), CD (2.3%), Rathke pocket cysts (2.3%), meningiomas (1.4%), craniopharyngiomas (1.1%), pituitary aplasia and hypoplasia (0.8%), TSH-omas (0.6%), germinoma (0.3%), glioma (0.3%), chondrosarcoma (0.3%), pericytoma (0.3%). Pts in this cohort most often received drug therapy with any medication alone (octreotide LAR, lanreotide, bromocriptine, cabergoline, pegvisomant) in 50.5% of cases; various types of combination therapy in 13% of cases (octreotide LAR/lanreotide with bromocriptine or cabergoline or pegvisomant). The majority of 94.7% of pts (n = 336) had 1 or more co-morbidities. The majority of pts (81.7%) were treated with 1 or more concomitant medication.

Conclusion: Based on the study of the pituitary disease registry in Latvia, a unified database of pituitary diseases pts has been created. A state founded registry may be set up in the future.

Disclosure of Interest: None Declared

ICE2021-1430

EVALUATION OF MAGNETIC RESONANCE IMAGING OF PITUITARY GLAND, SPHENOID SINUS AND SURROUNDING STRUCTURES IN PATIENTS WITH NON-FUNCTIONING PITUITARY ADENOMA

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Introduction: Anatomic associations between pituitary gland and sphenoid sinus (SS) are important in the management and follow-up of the patients with nonfunctioning pituitary adenoma (NFPA).

Objectives: We aimed to evaluate magnetic resonance imaging (MRI) findings of SS, pituitary gland and related structures in patients with NFPA and compare to a control group.

Methods: This study was conducted in a tertiary referral hospital between January 2018 and July 2020. Sixty-five patients diagnosed with NFPA and age and gender matched controls (n=40) were included.

Results: The mean age was 37.46±11.2 in NFPA group and 41.97±14.88 in control group, and they were similar (p=0.103). SS mucosal thickness greater than 1 mm was determined in a higher proportion of NFPA group (67.7%) than in control group (12.5%) (p<0.001). A mucosal thickness greater than 3 mm was present only in NFPA group (43.1%). The distance between optic nerves was longer in NFPA group compared to controls (p<0.001). Adenoma volume was correlated with distance between the two optic nerves (r=0.728, p<0.001), with petrous intercarotid distance (ICD) (r=0.561, p<0.001), and with cavernous ICD (r=0.408, p<0.001).

Conclusion: SS mucosal thickening and longer distance between optic nerves were associated with NFPA. A possible pituitary adenoma should be sought, if mucosal thickening is detected on MRI in patients without any signs of rhinosinusitis. Patients with NFPA and SS mucosal thickening may be referred to a specialist of otorhinolaryngology to exclude a possible sinus disease.

Disclosure of Interest: None Declared

ICE2021-1441

BODY COMPOSITION AND NUCHAL SKINFOLD THICKNESS IN PEDIATRIC BRAIN TUMOR PATIENTS

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Introduction: Obesity, cardiovascular disease, and relapse/progression have major impact on prognosis in pediatric brain tumor patients. Cranial MRI is part of routine follow-up.

Objectives: In a cross-sectional study, we analyzed nuchal skinfold thickness (NST) on MRI performed for brain tumor follow-up monitoring as a novel parameter for body composition and cardiovascular disease in 177 brain tumor patients (40 WHO grade 1–2 brain tumors; 31 grade 3–4 brain tumors; 106 craniopharyngioma), and 53 healthy controls.

Methods: NST was quantified on T1-weighted cranial MRI images of the midline performed on 1.5 Tesla MRI scanners according to a standardized procedure. First, a line was drawn crossing the two anatomically defined points: basion (anterior margin of the foramen magnum) and opisthion (posterior margin of the foramen magnum). The diameter of subcutaneous nuchal fat was measured over this line to the nearest 0.01 cm using OsiriX® (Pixmeo SARL, Switzerland). Arithmetic mean of NST as measured in triplicate by three independent persons was analyzed. The interrater reliability of the used arithmetic mean of NST was 0.982.

Results: Associations of NST with body mass index (BMI), waist-to-height ratio, caliper-measured skinfold thickness, and blood pressure were analysed in brain tumor patients and healthy controls. Craniopharyngioma patients showed higher BMI, waist-to-height ratio, NST and caliper-measured skinfold thickness when compared with brain tumor patients and healthy controls, whereas these differences were not detectable between brain tumor patients and healthy controls. However, WHO grade 1–2 brain tumor patients were observed with higher BMI, waist circumference and caliper-measured triceps skinfold thickness when compared to WHO grade 3–4 brain tumor patients. NST showed high correlations with BMI, waist-to-height ratio, and caliper-measured skinfold thickness. NST, BMI and waist-to-height ratio had predictive value for cardiovascular disease in terms of increased blood pressure, and in multivariate analysis, only BMI was selected for the final model resulting in an odds ratio of 1.25 (1.14–1.379). In craniopharyngioma patients with hypothalamic involvement/lesion or gross-total resection, rate and degree of obesity were increased.

Conclusion: As monitoring of MRI and body composition play an important role in follow-up after brain tumor, we conclude that NST could serve as a novel useful parameter for assessment of body composition and cardiovascular disease risk in brain tumor patients.

Disclosure of Interest: None Declared

ICE2021-1473

THE MYSTERIOUS CASE OF PITUITARY APOPLEXY

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Introduction: A 25 year old lady presented to her GP with 2 months history of frontal headaches and fatigue. She had no other significant past medical history and had a 2 year old daughter. Routine TFT in primary care showed secondary hypothyroidism which prompted check of pituitary profile. (TSH 0.16, FT4 5.2, Prolactin 976, Cortisol 25). Patient was called for short synacthen test but patient did not attend it. An urgent endocrine referral was made.

Case Description: Due to ongoing fatigue, patient presented in ED where a pituitary hormonal profile showed similar picture as initial bloods. Patient was given emergency hydrocortisone.

During her endocrine consultation in clinic she was so lethargic that she was administered emergency hydrocortisone. She also reported other symptoms like weight loss, polyuria, polydipsia and non-expressive galactorrhoea. Pre-clinic bloods showed panhypopituitarism:(TSH 0.01, FT4 11.1, FSH 4.4, LH<0.2, oestradiol <73, prolactin 1127, IGF1 21, urine osmolality 287, s.osmolality 287, urine sodium 22, s.Sodium 145). She was prescribed oral hydrocortisone and desmopressin.

An urgent MRI Pituitary showed 2cm macroadenoma with suprasellar extension abutting optic chiasm. Formal visual fields check revealed mild superior bitemporal hemianopia. The impression was non-functioning pituitary macroadenoma causing stalk prolactinemia, with panhypopituitarism and chiasm compression. She was started on cabergoline 0.25 mg weekly and urgent neurosurgical advice was sought.

She was planned for urgent trans-sphenoidal pituitary surgery, but pre-op MRI pituitary could not identify any macroadenoma. All findings from initial MRI pituitary scan were completely resolved. Headaches and galactorrhoea were settled. The case was discussed in MDT and a working diagnosis of lymphocytic hypophysitis causing partial anterior and posterior hypopituitarism was made. Cabergoline was stopped but she continued hydrocortisone and desmopressin.

Her pituitary hormonal profile showed progressive improvement with time:

07/01/2019 TSH< 0.01, FT4 10.2, FSH 4.2, LH 0.5, oestradiol 111, Prolactin 198, s.osmolality 294.

23/09/2019 TSH 2.84, FT4 12.5, FSH 7.4, LH1.9, oestradiol 173, prolactin 558, S.osmolality 289.

Clinical discussion: This case indicates the recovery of anterior pituitary hormonal profile with lymphocytic hypophysitis despite initial panhypopituitarism. Her gonadotrophin axis and posterior pituitary has still not recovered.

Disclosure of Interest: None Declared

ICE2021-1489

PITUITARY MACROADENOMA PRESENTING AS A SYNCHRONOUS OCCURRENCE OF ACROMEGALY AND CUSHING'S DISEASE

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Introduction: A functional pituitary adenoma can produce various anterior pituitary hormones of similar lineage simultaneously. Prevalence of Acromegaly ranges from 38 to 80 cases per million making it an infrequent disease. Rise in Prolactin frequently comes with Growth Hormone elevations. Hypogonadism, secondary thyroid or adrenal failure may also accompany as effects of pituitary compression by tumor mass. Its concurrent presentation with Cushing's Disease wherein Adrenocorticotrophic Hormone (ACTH) of different development lineage is even a rarer circumstance. This is the first reported case in the Philippines.

Case Description: A case of a 23-year-old female presented with an unusually taller stature, coarsened facial features typical of acromegaly, acral changes, sonorous voice, acanthosis nigricans on neck and seborrhea during physical examination. History revealed 5 years of intermittent headaches associated with blurring of vision. Visual field examination showed bitemporal hemianopsia. Patient also reported gradual increase in shoe and ring sizes. Biochemical work up revealed an exceedingly unsuppressed Growth Hormone level of 110 ng/ml after a 75-grams glucose load (*NV*: <1ng/mL). An unsuppressed 8am Serum Cortisol after a 1mg-Dexamthasone Suppression Test were also noted in 2 occasions, 9.66mcg/dL and 39.1mcg/dL (*NV*: <1.8mcg/dL) associated with elevated morning Plasma ACTH of 23.40pmol/L (*NV*: 9-11pmol/L). Prolactin, TSH, FSH, LH, DHEA-S and electrolytes were within normal. Prediabetes was noted with elevated fasting blood glucose (125 mg/dL) and Hba1c (6.1). Magnetic Resonance Imaging of brain with pituitary showed a large (2.4 x 4.1 x 4.3cm) lobulated enhancing sellar mass lesion with prominent left suprasellar component displacing infundibulum and compressing optic chiasm and left parasellar components with sphenoid sinus extension, consistent with pituitary macroadenoma. Abdominal and chest imaging were unremarkable. Patient advised for pituitary surgery and further immunohistochemistry staining of pituitary mass postoperatively.

Clinical discussion: Synchronous elevations of Growth Hormone (GH) and Adrenocorticotrophic Hormone (ACTH) causing Acromegaly and Cushing's Disease respectively is a rare occurrence that warrants this report. More studies, cases and investigations on this manifestation could be done to better understand this incident in the clinical setting.

Disclosure of Interest: None Declared

ICE2021-1566

PITUITARY METASTASES – MANAGEMENT AND OUTCOME OF THREE CASES FROM A TERTIARY CARE CENTRE

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Introduction: Pituitary metastasis is a rare complication of malignancy, seen predominantly in elderly patients. Breast and lung malignancies are the most common aetiology, and diabetes insipidus (DI) is the most frequent presenting symptom. We describe a series of three patients with pituitary metastases managed at our centre.

Case Description: Case 1: A 70 years old man presented with headache for two weeks and right eye ptosis, followed a week later by ptosis of the left eye. On examination he had bilateral 3,4 and 6th cranial nerve palsy. Evaluation revealed panhypopituitarism. MRI brain with gadolinium contrast showed an enhancing sellar mass with bilateral cavernous sinus invasion. He also had a swelling over the right shoulder; patient had ignored his shoulder pain for 6 months. MRI imaging and biopsy of the right scapular lesion confirmed chondrosarcoma. A ¹⁸F-DG PET scan showed multiple thoracic vertebral metastases. He was initially treated with dexamethasone in view of severe headache, and later changed to prednisolone, along with thyroxine. Within a week, he developed paraplegia secondary to multiple vertebral metastases, and succumbed after 3 weeks.

Case 2: A 55 years old man diagnosed to have carcinoma caecum and operated elsewhere a year back presented with nodal, liver and lung metastasis. He was found to have central DI and imaging showed infundibular metastasis, he was treated with desmopressin. Six months later he developed panhypopituitarism. Due to extensive disease, he received palliative chemoradiotherapy, but succumbed within a year after presentation.

Case 3: A 42 years old man presented with multiple cranial nerve palsies, vomiting and polyuria. He was diagnosed to have central DI and hypopituitarism. MRI scan of the brain revealed a contrast enhancing thickened pituitary stalk, pituitary gland and anterior hypothalamus. Biopsy of the pituitary mass was consistent with a poorly differentiated malignant neoplasm- the primary source could not be ascertained. He underwent extensive evaluation including whole body ¹⁸F-DG PET scan and bone marrow biopsy which were non-contributory. He succumbed to gram negative septicaemia within 3 weeks.

Clinical discussion: Although the treatment of hormonal deficits due to pituitary metastases is not difficult, the prognosis remains poor due to the aggressiveness of the primary malignancy. Most of them underwent palliative treatment due to extensive disease, and all patients succumbed in less than a year.

Disclosure of Interest: None Declared

ICE2021-1581

INFLUENCE OF THE CIRCADIAN CLOCK ON DAILY PATTERN OF ANTERIOR PITUITARY HORMONE LEVELS: CONSEQUENCES OF A DESYNCHRONIZED MODERN LIFESTYLE

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Introduction: The circadian rhythmicity is generated by a cell autonomous circadian clock, which modulates the daily expression pattern of many responsive genes within tissues, including the anterior pituitary gland. The serum levels of anterior pituitary hormones exhibit a circadian pattern and regulate functions related to growth, reproduction, metabolism and stress response. However, the molecular mechanism responsible for the generation of these oscillations is unknown. Moreover, changes in the population's lifestyle are associated with biological rhythms disturbances in sleep-wake and feeding-fasting cycles, reproduction and hormonal balance.

Objectives: Thus, considering the circadian rhythmicity importance for synchronized internal responses to environmental changes and the crucial role of anterior pituitary hormones in the maintenance of homeostasis, we aimed to evaluate the consequences of circadian clock disruption on the daily pattern of synthesis and secretion of anterior pituitary hormones.

Methods: *In silico* analysis of promoter and regulatory regions of *Tshb*, *Pomc*, *Gh*, *Fshb*, *Lhb* and *Prl* genes were performed in order to localize consensus-binding sites for the clock and/or controlled-clock components. The synthesis and secretion of anterior pituitary hormones were evaluated in wild-type and *Cry1^{-/-}Cry2^{-/-}* double knockout mice (KO) submitted to light-dark (L:D) and dark-dark (D:D) conditions for 7 and 12 days, respectively. GH, PRL and corticosterone blood concentrations were measured by ELISA using tail-tip blood samples collected every 10 min during 6 h for GH (ZT0-6) or 4 h (ZT0-4) for PRL and, every 6 h over 24 h under the L:D and D:D conditions for corticosterone. The total RNA was extracted from anterior pituitaries collected at ZT0 and 12 and the transcript contents were evaluated by RT-qPCR.

Results: Our results showed that all pituitary hormone genes exhibit putative clock and/or clock-controlled components binding-sites in their promoter or regulatory regions. The absence of a functional clock in the KO model was confirmed by the desynchronization of locomotor-activity pattern in D:D conditions. Both mRNA content of anterior pituitary hormones and GH, PRL and corticosterone blood levels were altered in the absence of a functional clock (*Cry1^{-/-}Cry2^{-/-}* animals).

Conclusion: Thus, our results suggest a direct regulation of circadian clock in pituitary hormone biosynthesis, which might comprise the molecular basis of the endocrine disorders, frequently observed in the modern lifestyle.

Disclosure of Interest: None Declared

ICE2021-1582

TRIIODOTHYRONINE INCREASES THE CIRCADIAN CLOCK EXPRESSION IN RAT ANTERIOR PITUITARY BY TRANSCRIPTIONAL MECHANISMS

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Introduction: Pituitary hormone secretion fluctuates over 24h, reflecting a possible role for of the intrinsic circadian clock in these oscillations. Both Hypo and Hyperthyroidism alter the pituitary hormone synthesis/secretion, however, the interaction between thyroid hormones and circadian clock in pituitary is unknown.

Objectives: The goal of this study was to characterize whether T3 modulates the circadian clock expression in anterior pituitary cells.

Methods: Male rats were divided in euthyroid, hypothyroid and hyperthyroid and euthanized every 3h, across 24h; afterwards, the pituitaries were excised and total RNA was extracted and evaluated for gene expression. One and Two-way ANOVA and cosinor analysis were applied to evaluate the time-of-day-dependent differential expression for each gene/group and their interactions. In addition, the T3 transcriptional regulation of clock genes promoters was evaluated in GH3 cells transfected with mouse *Bmal1* or *Nr1d1* promoters by Luciferase assay.

Results: The hyperthyroidism increased the expression of all core clock components and the mesors of *Bmal1* and *Nr1d1* were increased compared to euthyroid animals. In hypothyroid rats, the circadian pattern of *Bmal1* and *Per2* expression was lost, while the mesor of *Nr1d1* was reduced. *In silico* analysis pointed out the putative existence of thyroid hormone responsive elements in promoter or regulatory regions of *Bmal1* and *Nr1d1* genes. The *in vitro* analysis showed that T3 rapidly increases the activity of both *Bmal1* and *Nr1d1* promoters.

Conclusion: Our data indicate a role of T3 in the modulation of clock gene expression in pituitary cells, which could be related to the altered pituitary hormone secretion observed in hypo and hyperthyroid conditions.

Disclosure of Interest: None Declared

ICE2021-1620

PREVALENCE OF THROMBOEMBOLIC EVENTS IN PATIENTS WITH ENDOGENOUS CUSHING SYNDROME AND ITS RELATIONSHIP WITH HYPERCORTISOLISM

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Introduction: Venous thrombosis has frequently been reported in patients with endogenous Cushing's.

Objectives: The aim of this study was to evaluate the prevalence of thromboembolic event (TEE) in patients with endogenous Cushing syndrome (CS) of benign origin in the population studied in Hospital Italiano de Buenos Aires (HIBA) during the last eleven years.

Methods: The electronic medical records of all patients with a diagnosis of endogenous CS of benign origin from January 2008 to June 2019 were collected. Regarding thromboembolic events, data were obtained from the information available in the Institutional Registry of Venous Thromboembolic Disease (RIET). Data collection was done with an excel form and the protocol was approved by the Institution's Ethics Committee.

Results: There were 122 CS patients that met inclusion criteria. Average age was 43 years and 82.8% female. Fourteen patients with TEE were registered in this series, which constitutes a prevalence of 11.5% CI 95% (6.4-18.5). Regarding the type of TEE, 7 (50.0%) patients had deep venous thrombosis (DVT) and 8 (57.1%) developed pulmonary embolism (PE). One of the patients developed DVT and PE. Of all the risk factors for TEE evaluated, only one patient had major surgery coinciding with TEE.

Conclusion: Venous thromboembolic disease is a health problem worldwide, with an incidence adjusted for age and sex based on more than 1 case per 1000 patients per year. The mean age of the patients included in this study was 43 years, which corresponds to an incidence in the general population of 0.3 per 1000 person years. This would suggest that patients with CS have more than a 10-fold increased risk of developing TEE.

Randomized controlled clinical trials are needed to determine the choice, intensity, and duration of thromboprophylaxis in patients with CS. In CS, where diagnosis and treatment are often a challenge, a multidisciplinary approach is needed to determine risk factors for TEE and initiate thromboprophylaxis in the initial evaluation of patients.

Disclosure of Interest: None Declared

ICE2021-1640

CARDIAC EVALUATION OF PATIENTS WITH ACROMEGALY IN BUENOS AIRES

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Introduction: Cardiovascular complications are usual in patients with acromegaly and represent one of the main causes of death, however, information about their prevalence and prognosis is scarce in our setting.

Objectives: Describe findings on cardiovascular evaluation in a cohort of patients with acromegaly in a tertiary care center in the city of Buenos Aires.

Methods: Between 2019 and 2020, cardiovascular studies were performed in patients with a confirmed diagnosis of acromegaly, with a period of illness between 10 years and 6 months prior to the cardiovascular evaluation. Physical examination, electrocardiogram, echocardiogram, 24-hour ambulatory blood pressure monitoring, and stress tests were evaluated.

Results: Out of 21 evaluated patients, 5 did not perform cardiac studies, remaining 16 subjects for the analysis. 13 cases (81.25%) were females, and the mean age at diagnosis was 40 (± 11). Median time from symptoms onset to final evaluation was 6 years (IQR 4-10). acromegaly status, treatments, and cardiovascular findings are described in table 1.

| variable | results |
|-----------------------------|-------------|
| GH baseline | 21.2 (16) |
| GH final | 2.22 (1.6) |
| IGF-1 baseline | 3.53 (1.42) |
| IGF-1 final | 0.3 (0.5) |
| macroadenoma | 87.5% |
| somatostatin analogues | 87.5% |
| dopamin agonists | 60% |
| pegvisomant | 12.5% |
| radiotherapy | 25% |
| surgery | 75% |
| controlled disease | 68.7% |
| years to controlled disease | 4.1 (4.4) |
| systolic blood pressure | 122 (16) |
| diastolic blood pressure | 74 (8) |
| heart rate | 77 (9) |
| BMI | 30.8 (7) |
| confirmed hypertension | 28.6% |
| symptomatic heart failure | 6.25% |
| sinus rhythm | 100% |
| QRS (mm) | 112 (52) |
| QT (Bazzet) | 412 (34) |
| Sokolow (mm) | 9.4 (1.6) |
| LVDD | 46 (5) |
| LVEF | 65% (10) |
| IVS (mm) | 11 (1.1) |
| METS | 7.1 (1.8) |
| non dipper | 40% |
| beta blocker | 25% |
| ACE-i / ARBs | 50% |
| thiazides | 12.5% |
| calcium antagonists | 12.5% |
| furosemide | 6.25% |

Conclusion: Cardiac complications of acromegaly are frequent, however prompt treatment seems to have mitigated these complications in this series. Cohorts with more patients are needed to confirm these findings.

Disclosure of Interest: None Declared



ICE2020-1101

MALIGNANT TRANSFORMATION OF A BENIGN GLUCAGONOMA AFTER A PROLONGED PERIOD WHILE THE PATIENT REMAINS ASYMPTOMATIC.

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Introduction: Glucagonoma are rare neuroendocrine tumors arising solely in the pancreas and approximately 25 % of glucagonoma cases start in a benign form. We hereby report a 76 -year-old male who was initially diagnosed with asymptomatic benign glucagonoma. Follow-up surveillance 13 years later shows that the tumor has undergone differentiation into a malignant form.

Case Description: 63-year-old man was referred for evaluation of an enhancing lesion (2.7 cm) at the pancreatic tail. He was completely asymptomatic with normal physical exam. Initial labs: normal except for elevated serum glucagon level (206 pg/mL, ref 0-60). A 2-hour oral GTT confirmed the autonomy of glucagon secretion by the tumor. Somatostatin and other tumor markers were normal. PET scan showed abnormal uptake at the distal pancreatic tail, correlating with the CT scan findings. The patient underwent laparoscopic distal pancreatectomy, with removal of a 2.8cm mass which predominantly expressed glucagon. Plasma glucagon level in the peripheral venous blood and intraoperative splenic vein dropped to <50 pg/mL immediately after the surgical resection. Following surgery patient remained completely asymptomatic for the next 13 years. Abdominal MRI and PET scan revealed a 4-cm pancreatic mass with hepatic metastases. Biopsy of the hepatic lesion confirmed glucagonoma. Patient was treated with Lanreotide which has normalized the serum glucagon levels and the tumor size remained stable for the 12 months of follow up.

Clinical discussion: The complete remission without any treatment lasting for more than 13 years confirmed the benign nature of the tumor. It is also reported that gluconomas less than 2 cm in size has less potential for metastasis. The usual recommendation is to monitor these patients post-resection to a maximum of 10 years although in our patient the malignant nature of the tumor was expressed 13 years after initial resection. The reason for malignant transformation after this prolonged period remains unknown.

This case highlights the importance of continuous monitoring neuroendocrine tumors even beyond 10 years after surgery.

Disclosure of Interest: None Declared

Oncology NE tumors

ICE2020-1126

GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS: A 20-YEARS EXPERIENCE OF A PRIVATE THIRD-LEVEL HOSPITAL IN THE INTERIOR OF ARGENTINA

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Introduction: There have been few publications of epidemiological studies about neuroendocrine tumors in Argentina

Objectives: We aimed to describe the experience of a reference center in Mar del Plata

Methods: We conducted a retrospective study of patients with gastroenteropancreatic neuroendocrine tumors (GEP-NET) diagnosed and treated at the private hospital in Argentina, between January 2000 and December 2019.

Results: We registered 127 cases of NETs 60,4% GEP-NET, 39,4% TNE no-GEP (bronchial/pulmonary, medullary thyroid carcinoma, thymic, ovary and pheochromocytoma/paraganglioma). The study included 77 patients (female 54%) and mean age was 61 ys. GEP-NET included: small intestine (25%), pancreas (21%), appendicular (17%), colorectal (14.5%), gastric (12%), unknown primary (6.5%), Meckel's diverticulum (2.6%), and duodenal (1.3%)
The most frequent initial symptoms were in 86% abdominal pain, weight loss, abdominal discomfort, gastrointestinal bleeding, diarrhea, intestinal obstruction, flushing and in 14% patients diagnosis was incidental. 74% were non-functional and 97% sporadic.

The tumors were classified as per the 2017 World Health Organization classification: NET grade 1: 60%, grade 2: 37%, grade 3 (NEC): 3% and one patient with mixed neuroendocrine and non-neuroendocrine neoplasm. Distant metastases were reported in 64% patients (NET grade 1: 60%; NET grade 2: 73%, NET grade 3 (NEC): 100%.

76% of the patients underwent surgery, somatostatin analogues were administered in 29% and chemotherapy, radioterapy and target therapy in 4%.

The 5-year overall survival (5yOS) by grade was 97% and 86% for G1 and G2 respectively and less than 12 months for the NEC. According to the stage, (5-year S) in patients without metastases or with locoregional metastases was 100% and it reduces to 68% when the metastases are distant. The overall survival at 5 years was 89%.

Conclusion: In our study population, more than 50% of NETs are GEP. Sporadic, non-functioning, well-differentiated, low-grade NETs predominate, but with a high percentage of metastasis at diagnosis. 26% had hormonal hypersecretion and in only 3% was associated with a genetic disease. The highest 5yOS was associated with low Grade and absence of metastases, but the presence of locoregional metastases did not modify the 5-year OS.

Disclosure of Interest: None Declared

ICE2021-1412

LEYDIG CELL TUMORS AND CURCUMIN: FIRST APPROACHES TO A PROMISING BOND

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Introduction: Leydig cells (LC) comprise the interstitial androgen-secreting population of the testis. Dysregulation of LC proliferation may give rise to Leydig cell tumors (LCT): the most common non-germ cell testicular tumors, associated with endocrine dysfunctions. LCT incidence is currently increasing, and patients respond poorly to chemo and radiotherapy, with an average survival time of two years; orchiectomy or tumorectomy are the main treatment options. Curcumin (CUR) is present in the rhizome of the plant turmeric. It is widely used as a culinary spice and as a dietary supplement due to its beneficial health effects. Since the first pieces of evidence on curcumin anticancer potential were collected, a myriad of therapeutic effects have been described.

Objectives: To determine whether curcumin has any effect on LCT growth.

Methods: *In vitro* assays: proliferation assessment by [³H]-thymidine incorporation, cell cycle analysis by flow cytometry, and apoptosis assessment by TUNEL in the MA-10 murine tumor LC line. *In vivo* assays: chorioallantoic membrane assay (CAM) for angiogenesis determination and evaluation of LCT growth in a syngeneic mouse model of LCT, generated by inoculation of MA-10 cells in CB6F1 mice (n=6 per group). Once the tumor was established, the mice were treated every other day for 15 days with CUR 20 mg/kg or vehicle (10% DMSO in corn oil). One-way ANOVA and the Tukey test were used. Tumor growth curves were analyzed using a two-way ANOVA, the Holm-Sidak test and non-linear regression.

Results: Curcumin inhibited LC proliferation *in vitro* (Control: 31555±2672 vs CUR 40 µM: 15700±1372 cpm p<0.0001), arresting cell cycle progression in G2/M (Control: 12.3±1.5 vs CUR 80 µM: 24.3±1.2% p<0.05) and inducing apoptosis. The *in vivo* CAM assay showed that curcumin increases MA-10 cells' pro-angiogenic potential (Control: 13.3±2.3 vs CUR 40 µM: 28.8±3.4 branch points p<0.01). Analysis of LCT growth curves indicated that curcumin decreases tumor growth (Vehicle: 13.8±1.6 vs CUR: 8±1.1 mm³ p<0.0001) and final tumor weight (Vehicle: 0.9±0.05 vs CUR: 0.6±0.03 g p<0.05). Curcumin did not affect the general health conditions of the mice.

Conclusion: Though further research is needed concerning its pro-angiogenic effect, curcumin has shown a strong antitumor effect that poses it as a natural agent that could be used for the reduction of LCT volume before surgery or the potentiation of other treatment strategies.

Disclosure of Interest: None Declared

ICE2021-1423

PATIENT-DERIVED MODELS OF PRIMARY AND METASTATIC PROSTATE CANCER SHOW ANDROGEN RECEPTOR ENHANCER AMPLIFICATIONS CONFER TREATMENT RESISTANCE

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Introduction: The androgen receptor (AR) is the main therapeutic target for advanced prostate cancer. Yet, amplifications of the AR occur in up to 80% of men with castration-resistant prostate cancer (CRPC). Recent studies have uncovered that these amplifications not only include the *AR* gene, but often encompass a distal enhancer. This represents a long-overlooked, non-coding mechanism of resistance to AR-directed therapies, including enzalutamide.

Objectives: Our goal was to study the progression of prostate cancer before and after amplification of the *AR*. To do this, we used tumour samples from a castrate-sensitive primary tumour and castrate-resistant metastasis of the same patient. We also established serially transplantable patient-derived xenografts (PDX) for functional and genomic studies.

Methods: Serially transplantable PDXs were established in testosterone-supplemented, immunocompromised male mice by the Melbourne Urological Research Alliance (MURAL). Tumours were profiled using whole genome sequencing and RNA sequencing. To determine the responses of PDXs to therapy, host mice were castrated or treated with AR-directed inhibitors (enzalutamide, apalutamide), chemotherapy (docetaxel, cabazitaxel), or a BET inhibitor (ZEN-3694).

Results: Based on whole genome sequencing of the matched patient-derived models, alterations associated with poor prognosis, such as *TP53* and *PTEN* loss, existed prior to androgen deprivation therapy, followed by co-amplification of the *AR* gene and enhancer after the development of metastatic CRPC. The PDX of the primary tumour, without the *AR* amplification, was sensitive to AR-directed treatments including castration, enzalutamide, and apalutamide. The PDX of the metastasis, with the *AR* amplification, had higher AR and AR-V7 expression in castrate conditions, and was resistant to castration, apalutamide, and enzalutamide *in vivo*. It remained sensitive to docetaxel. Treatment with a BET inhibitor outperformed the AR-directed therapies for the metastasis, as measured by tumour regression of some, but not all, grafts.

Conclusion: This study highlights the importance of *AR* enhancer amplifications in the development of CRPC. It also provides novel matched PDXs to test potential treatments that target the over-abundance of AR in tumours with *AR* enhancer amplifications.

Disclosure of Interest: M. Lawrence Conflict with: Zenith Epigenetics, Pfizer, L. Porter: None Declared, A. Bakshi: None Declared, A. Clark: None Declared, D. Goode: None Declared, G. Risbridger Conflict with: Zenith Epigenetics, Pfizer, R. Taylor Conflict with: Zenith Epigenetics, Pfizer

Oncology NE tumors

ICE2021-1442

A CASE OF REFRACTORY HYPOGLYCEMIA RELATED WITH A PLEURAL SARCOMA. DOEGE-POTTER SYNDROME, A FORGOTTEN ENTITY

Gustavo Lopez , Diego Salamanca*

Introduction: Doege-Potter syndrome is a rare clinical entity with low incidence and a difficult diagnosis. Described in 1930 by Doedje and Potter, this is a condition which consists of an intrathoracic tumor associated with symptomatic hypoglycemia.

Case Description: The purpose of this report is to expose a case of symptomatic hypoglycemia in a 64 year old male patient with medical history of Vitiligo, who presented to the emergency room for hypoglycemia of 23 mg/dL associated with tachycardia, diaphoresis and an altered state of consciousness, requiring an intravenous load of 10% Dextrose without improvement, thus being necessary to start continuous infusion with 50% dextrose and glucagon. Vital signs were stable with blood pressure 142/74 mmHg, heart rate 83 bpm, respiratory rate 17 rpm, BMI 25.9 kg/m². Physical exam was as follows with hypoventilated breath sounds in the left lower lung base and the laboratory reports highlighted the following results: IGF-I: 47 ng/mL (122- 400 ng/ml), peptide C: 0.08 ng/mL (0.5- 2.0 ng/ml), hydroxybutyrate: 0.01 mmol/L. The CT Thorax shows a left intrathoracic mass that extends to the parietal pleura and deviates to the left the cardiomedial line. He was then sent for a left lower pulmonary lobectomy and left parietal pleurectomy with immediate improvement in blood glucose values. The biopsy shows a tumor size: 24x10x19 cm, spindle-cells with vesicular nuclei and frequent mitoses 7/10 xc compatible with a sarcomatous solitary fibrous tumor.

Clinical discussion: This type of tumor represents 8% of the total benign neoplasias in the thorax and 10% of pleural tumors. Hypoglycemia is rare in this tumor, occurring only in 5% of the cases related to the abnormal production of Insulin growth factor type 2 (IGF-II) which is capable of stimulating the insulin receptor and inhibiting hepatic gluconeogenesis and stimulating peripheral glucose uptake leading to refractory hypoglycemia as presented in this patient. With improvement of his hypoglycemia following his tumor resection it was very suggestive of Doege-Potter Syndrome. Based on the rarity of this case, we deem it important to give it relevance due to its difficult diagnosis and low incidence of presentation.

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Disclosure of Interest: None Declared

Oncology NE tumors

ICE2021-1542

A CASE OF REFRACTORY HYPOGLYCEMIA RELATED WITH A MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 WITH AN UNUSUAL PRESENTATION

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Introduction: Multiple Endocrine Neoplasia Type 1 (MEN 1) syndrome is known to classically result in parathyroid, pituitary, and pancreatic islet cell tumors, with a prevalence of 1 / 30,000 habitants. being parathyroid adenomas more frequent (100%), prolactinomas (75% -100%) and gastrinomas (80% -100%).

Case Description: A 54-year-old male patient with a clinical history of arterial hypertension, hyperparathyroidism secondary to a resected parathyroid adenoma and hyperprolactinemia due to a pituitary adenoma, in treatment with Cabergoline who presented to the emergency room and for the last 10 months, has persistent long episodes of dizziness, palpitations, amnesia and disorientation that improve with food intake. During his time in the emergency room, an episode of hypoglycemia of 35 mg/dL was documented requiring an intravenous load of 10% dextrose. Vital signs were stable with blood pressure 135/70 mmHg, heart rate 92 bpm, respiratory rate 16 rpm without abnormal findings in the physical exam. A fasting test was done with laboratory reports and highlighted the following results: Insulin fasting test: > 4 Uu / mL (<3 Uu / mL), Peptide C: >0.2 nmol / L (<0.2 nmol / L), Proinsulin: >6 pmol / L (<5 pmol / L), Beta-hydroxybutyrate: <2.7 mmol / L, with positive result for endogenous hyperinsulinism. The CT abdomen shows a 2.7 cm mass in the tail of the pancreas. He was then sent for surgical resection of the pancreatic lesion. The biopsy shows: neuroendocrine tumor compatible with insulinoma. The patient continues to have hypoglycemic symptoms, Octreoscan was performed, showing an intense focus mass with overexpression somatostatin receptors in close contact with the right renal hilum. He was sent for a second surgery intervention of this mass with a biopsy result: Paraganglioma. However, the patient continues with episodes of symptomatic hypoglycemia, suspecting possible metastasis, a PET/CT is requested, that shows a left retroperitoneal mass, related to a high-grade tumor. A third intervention was done by a laparotomy with resection of the entire mass, with resolution of the hypoglycemia. The pathology shows an Hibernoma.

Clinical discussion: Based on the rarity of this case, we deem it important to give it relevance due to its difficult diagnosis and low incidence of presentation.

Disclosure of Interest: None Declared

Pediatrics

ICE2020-1176

VITAMIN D STATUS AMONG EMIRATI CHILDREN AND ADOLESCENTS: RELATIONSHIP TO OBESITY, DIABETES AND METABOLIC PARAMETERS

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Introduction: Prevalence of diabetes and obesity in adults, and also children and adolescents, is high in the Middle East. Severe vitamin D deficiency has been linked to increased risk of diabetes. Reports on vitamin D status and its relationship to metabolic parameters in children and adolescents in the UAE are limited.

Objectives: This research seeks to determine the prevalence of vitamin D deficiency and its predictors in children and adolescents. It aims to explore relation of fat mass, fat percentage, muscle mass and muscle free mass with vitamin D levels.

Methods: This cross-sectional study was conducted in 736 children and adolescents with obesity and diabetes attending an outpatient diabetes speciality clinic, Abu Dhabi. Anthropometric measures, blood glucose and other metabolic parameters were collected. Body composition was assessed by bioelectrical impedance analysis (Tanita, Tokyo, Japan) and provided measures on fat mass, fat percentage, fat free mass, muscle mass and total body water. Vitamin D deficiency was defined by US Endocrine Society guidelines; as sufficient ($>72.5\text{nmol/L}$), Insufficient ($50\text{-}72.5\text{nmol/L}$) and deficient ($\leq 50\text{nmol/L}$).

Results: The prevalence of vitamin D deficiency, insufficiency, and sufficiency was 73.9%, 18.7% and 7.3% respectively. An inverse correlation was observed between age ($r=-0.416$, $p<0.0001$) and vitamin D levels. Females had more than double the likelihood of vitamin D deficiency compared to males [Odds Ratio (OR): 2.60 (95% confidence interval (CI): 1.85, 3.67)]. A significant positive association was observed between the high density lipoprotein (HDL) cholesterol and vitamin D levels ($r=0.16$, $p=0.008$). No significant correlation was observed between low density lipoprotein (LDL), triglycerides (TG), and total cholesterol (TC). There was no significant association between fasting blood glucose with vitamin D levels or across vitamin D groups. Adiposity measures including fat mass, fat mass percentage, body mass index (BMI) correlated negatively with vitamin D levels ($p<0.0001$). Muscle mass and fat free mass also showed an inverse association with vitamin D levels ($p<0.0001$).

Conclusion: Vitamin D deficiency is highly prevalent in children and adolescents with diabetes and obesity in UAE. Our findings highlight imperative associations between vitamin D levels and metabolic parameters in children and adolescents with obesity and diabetes. Vitamin D replacement initiatives are being implemented at public health level and need further emphasis.

Disclosure of Interest: None Declared

Pediatrics

ICE2020-1179

RAMADAN FASTING AMONG OLDER CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES: A REAL WORLD STUDY FROM THE UAE

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Introduction: Ramadan fasting (RF) is a religious obligation for all healthy adult Muslims. The sick including patients with type 1 diabetes (T1D) and pre-pubertal children are exempt, but many choose to fast for cultural and other reasons.

Objectives: In this “real world” study, we have investigated glycaemic control (HbA1c, and continuous glucose monitoring-CGM, or flash glucose monitoring-FGM) in the context of RF in children and adolescents with T1D and compared outcomes in patients on multiple daily injections (MDI) and those on continuous subcutaneous insulin infusion (CSII) among the patients.

Methods: Children and adolescents with T1D, and their families seen at ICLDC, who were insisting on fasting in the ensuing Ramadan were educated about diabetes management during RF. Insulin dose was adjusted and remote medical support was made available as necessary. Data on reported number of fasting days, hypoglycaemia episodes, and diabetic ketoacidosis (DKA) were obtained through patient and family interviews. Information on weight, HbA1c, and blood glucose levels from CGM/FGM before (within one month prior), during, and after (within one month afterwards) Ramadan were retrieved retrospectively from the electronic database. Data are presented as mean \pm SD.

Results: 47 patients, all with T1D (age 13.40 ± 2.42 years; diabetes duration 4.6 ± 3.1 years; 29 (61.7%) males (age 13.69 ± 2.54 years); 18 (38.3%) females (age 12.94 ± 2.21 years) ; 26 (55%) on MDI and 21 (45%) on CSII were included in the study. 42 (89%) were able to fast for 22.3 ± 8.7 days during Ramadan. No statistically significant differences were seen in CGM/FGM generated mean blood glucose level before, during, and after Ramadan [one-way ANOVA ($F(2,80)=1.600$, $p=0.21$ -Table 1)], and in mean HbA1c (9.0 ± 1.7 v $8.7 \pm 1.3\%$) and weight (53.3 ± 18.0 v 54.9 ± 19.3 v kg) between pre and post-Ramadan periods ($p=0.10$ and $p=0.60$, respectively). Between MDI and CSII, there was no significant difference in fasting days ($p=0.49$), frequency of hypoglycaemia episodes ($p=0.98$), DKA frequency ($p=0.37$), HbA1c level ($p=0.24$), and weight ($p=0.11$) after Ramadan.

Image:

| Mean blood glucose | mg/dL | p-Value (one-way ANOVA) |
|-----------------------|------------------|-------------------------------|
| Pre-Ramadan (n=32) | 226.5 ± 54.6 | 0.21 |
| During Ramadan (n=19) | 251.6 ± 46.2 | |
| Post-Ramadan (n=32) | 225.7 ± 58.8 | |

Table 1. CGM/FGM calculated mean blood glucose level before, during, and after Ramadan.

Conclusion: Although RF for children and adolescents with T1D particularly those with poor glycaemic control involve high risks, patients do undertake RF due to religious or other reasons. Our data show no significant deterioration in indicators of overall glycaemic control which remained inadequate. RF should be discouraged in children with poorly controlled T1D.

Disclosure of Interest: None Declared

Pediatrics

ICE2020-1181

MODY DIAGNOSIS AND OPPORTUNITY TO AVERT INSULIN THERAPY - A CASE SERIES

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Introduction: Prevalence of MODY is 1.2% in pediatric diabetes population. Patients can be misdiagnosed as T1DM or T2DM by as much as 36% and 51%. GCK (MODY 2) and HNF1A/HNF4A (MODY3) are the most common forms. Despite improvement in cost and testing strategy (panel testing instead of step-wise approach), it remains underutilized. These conditions do not require insulin therapy. We present 2 cases of each, and lessons learned.

Case Description: MODY 2 Case 1. 4 yo M referred for hyperglycemia in the 300's during surgery. A1c 6.4%. MGM and MGM's siblings have diabetes. Diabetes autoantibodies (DAA) negative. C-peptide 5.4 (NL 0.78 - 5.19 ng/ml). MODY panel (GeneDx) showed heterozygous mutation in GCK gene (c.70 C>T). Patient remains off insulin. Family advised to undergo genetic testing.

MODY 2 Case 2. 8yo M diagnosed at local ED with "new onset T1DM" when he presented with polyuria, polydipsia, and random BG 237. A1c 6.7%, C-peptide 1.9, started on basal-bolus insulin but low insulin requirement, DAA negative. MODY panel showed pathogenic variant in GCK gene. Pt weaned from insulin, A1c unchanged (6.3-7%). Mother found to have same mutation.

MODY 3 Case 1. 16 yo F, referred by PCP who started her on insulin a year prior after an incidental finding of hyperglycemia. A1c 7.5% at diagnosis. Mom, MGM have diabetes, unknown type (MGM thin by report). DAA neg, C-Peptide 1.74. MODY Panel showed HNF1A gene mutation for R131Q. She was switched to Glyburide, blood glucose in the 90's range.

MODY 3 Case 2. 10 yo M referred from the ED for "new onset T1DM", A1c 7.6%, started on basal-bolus insulin, but lost to follow up for a yr. Brother has MODY 3. DAA neg, C-Peptide 3.1. Targeted gene sequencing showed HNF1A gene mutation. He was switched to Glyburide, A1c improved to 6.7% but increased to 9.3% for noncompliance.

Clinical discussion: A high index of suspicion for MODY should be maintained in nonobese, DAA-negative patients diagnosed before 25yo. DAA and genetic testing can be costly but diagnosis can dramatically alter diabetes management and overall cost of management may be lower. Patients with MODY 2 do not develop vascular complications associated with diabetes, nor require pharmacotherapy. MODY 3 patients may be safely switched to sulfonylurea monotherapy. Relatives previously misdiagnosed with T1DM/T2DM will also need testing. More education for health care providers is warranted for appropriate management of this condition.

Disclosure of Interest: None Declared

Pediatrics

ICE2021-1271

EARLY RECOGNITION OF CONSUMPTIVE HYPOTHYROIDISM WITH INFANTILE HEPATIC HAEMANGIOMA

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Introduction: Infantile hepatic haemangiomas (IHH) are the most common hepatic vascular tumours in children. Consumptive hypothyroidism can arise as a result of these benign tumours. We report on a neonate diagnosed with IHH, where abnormal thyroid function tests were noted and improved without thyroxine replacement. We believe this was due to treatment of the haemangiomas with propranolol, highlighting the importance of prompt diagnosis and recognition of complications that can arise from IHH.

Case Description: A four week old female was admitted with increased work of breathing. She had recently been an inpatient with a similar presenting complaint and was treated for pulmonary hypertension and cardiac failure. There had been no antenatal concerns and she was born at term via normal vaginal delivery weighing 3.99kg. A birthmark on the right lower back had been noted post-delivery. Newborn screening for congenital hypothyroidism was negative. There was no relevant family or social history. Her regular medications were spironolactone, furosemide and sildenafil. On examination, she was tachypnoeic with subcostal recessions and normal oxygen saturations. A 5cm palpable liver edge was noted, along with a further haemangioma on her left loin. Alpha-fetoprotein and gamma-glutamyl transferase levels were raised. Ultrasound of her abdomen showed hepatomegaly with a diffuse abnormal heterogeneous echotexture and focal lesions. She was found to have increased thyroid stimulating hormone (TSH) and free thyroxine (T4) levels of 17.70mU/L and 29.7pmol/L respectively. A further abdominal ultrasound at a tertiary hepatology centre confirmed multiple hepatic haemangiomas, hence propranolol was commenced at 44 days old. Significant improvement of thyroid function tests were consistently noted thereafter, with no other changes to her medications. At 99 days of age, TSH and T4 levels were both normal at 1.73 mU/l and 21.5 pmol/L respectively.

Clinical discussion: Hepatic haemangiomas have been reported to produce an excess of type 3 iodothyronine deiodinase, leading to rapid degradation of thyroxine and T3 into inactive metabolites. This consumptive hypothyroidism occurs particularly in multifocal and diffuse types of IHH, requiring higher thyroxine doses than in congenital hypothyroidism. We postulate that diagnosing and treating IHH early can improve thyroid function by reducing the type 3 iodothyronine deiodinase produced and potentially negate the need for very high doses of thyroxine replacement or treatment at all.

Disclosure of Interest: None Declared

Pediatrics

ICE2021-1318

DENSITOMETRIC PARAMETERS DURING THE TRANSITION STAGE IN PATIENTS WITH GH DEFICIENCY (GHD) ON RGH: FIRST EXPERIENCE IN ARGENTINA

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Introduction: Many studies have shown that adult patients with a history of childhood-onset GHD have lower bone mineral density (BMD) because of reductions in cortical thickness, cortical cross-sectional area, and overall cortical content, as compared with healthy controls, resulting in a potential risk for fractures. GH therapy in patients with GHD may evidence benefits on bone 9 to 10 months after the initiation of therapy.

Objectives: To evaluate the efficacy of GH therapy in patients during the transition from childhood to adulthood on BMD.

Methods: Forty-five GHD patients in the transition stage (15-24.9 yr) were evaluated prospectively and after 1 to 2 years of follow-up. Persistence of GHD was confirmed in all cases. Seven patients were lost to follow-up; the remaining 38 patients were divided into two groups: treated group (TG), 20 patients (12 females) resumed GH therapy, and non-treated group (NTG), 18 patients (7 females) did not resume therapy. Multiple pituitary deficiencies were present in 90% of patients in the TG and in 88.9 % of patients in the NTG, and in all cases adequate replacement of pituitary deficiencies was confirmed. The TG received GH therapy for 1 to 2 yr, starting with 0.1 mg/day, and gradually up-titrating the dose to normalize serum IGF-1 levels. The following parameters were evaluated in all cases: BMD of the left femoral neck (FN) and lumbar spine L1-L4 (LS) by densitometry (DEXA, LUNAR®) at baseline (TG_B/NTG_B) and after follow-up (TG_{post}/NTG_{post}).

Baseline vs post results were compared in each group (Wilcoxon matched-pairs rank test).

Results:

| Md and Range | TG _B | TG _{post} | NTG _B | NTG _{post} |
|--------------|---------------------------|------------------------|------------------------|------------------------|
| IGF1(SDS) | -4.2* (-7.9 to -1.5) | -0.6 (-1.4 to 1.5) | -2.0 (-3.6 to 2.0) | -2.6 (-4.7 to 2.7) |
| FN(z score) | -1.35** (-2.9 to 0.7) | -0.85 (-2.5 to 0.3) | -1.4 (-3.9 to -0.2) | -1.4 (-4.4 to -1.2) |
| LS(z score) | -1.8*** (-3.7 to -0.4) | -1.5 (-2.4 to 0.9) | -1.6 (-5.0 to -0.5) | -1.9 (-3.7 to -0.9) |

* p< 0.0001 vs TG_{post}, ** p=0.078 vs TG_{post}, *** p=0.0034 vs TG_{post}

Conclusion: Our results showed that GH therapy in GHD patients in the transition stage significantly improved BMD in the LS, and a tendency towards significance was observed in the FN.

Our findings appear to support the fact that maintenance of GH therapy in GHD patients in the transition stage would contribute to improve peak bone mass acquisition, especially as regards the trabecular bone (LS). This might contribute to decrease the risk of osteopenia, osteoporosis and pathological fractures during adulthood.

Disclosure of Interest: None Declared

Pediatrics

ICE2021-1364

RECURRENT HYPOGLICEMIAS IN 18P DELETION SYNDROME – WHEN SUSPECT HORMONAL DEFICIENCY?

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Introduction: 18p Deletion Syndrome is a rare defect caused by a deletion of all or part of the short arm of the chromosome 18. The incidence could be estimated at about 1:40.000 live-born infants. Hypopituitarism has been associated in this syndrome in 13% of the cases. Neonatal hypoglycemia is an ordinary symptom in children with hypopituitarism. If the correct diagnosis is delayed this symptom will persist and the neurodevelopment can be compromised.

Case Description: A 6,8 years old girl was referred to the paediatric endocrinologist for recurrent hypoglycemias. She was a second daughter of a non consanguineous couple, without any prenatal risk factors, delivered by term caesarean section, weight 3020g and length 47cm. The craniofacial abnormalities were diagnosed at birth. In the second day of life she had her first hypoglycemic episode and convulsive crises. She had also hepatosplenomegaly and cholestasis. Until the present data she had 4 others hospitalizations for hypoglycemic convulsive crises and in none of them the hypoglycemia was investigated. She had also an important short stature, a poor weight gain specially after the first year of life (Figure 1 and 2) and a compromised neurodevelopment. The parents neglected the Genetics doctor's appointments and the 18p Deletion Syndrome diagnosis was postponed until 6 years and 5 months – karyotype 46,XX Del (18)(p). The paediatric endocrinologist performed the properly investigation evidencing GH, ACTH and Thyroid Stimulating Hormone (TSH) deficiencies.

Clinical discussion: The case presents a girl with recurrent hypoglycemia since the second day of life associated to important short stature, craniofacial abnormalities without the properly investigation. The 18q Deletion Syndrome dysmorphic features are not specific and can be found in other genetic syndromes but the association with recurrent hypoglycaemia and a short stature leads to a GH deficiency suspicion. The GH and ACTH deficiencies are responsible for this clinical condition - hypoglycemia and short stature.

18p Deletion Syndrome is a rare condition but can be easily diagnosed by a G banded Karyotype. The hormonal deficiencies are rare but in children with hypoglycemia must be investigated. The hypopituitarism mechanism is nuclear but GH, ACTH and TSH deficiencies have already been described.

The neonatologists must be aware of serious hypoglycemias in dysmorphic children and the emergency rooms paediatricians also should be more careful in hypoglycemias with short stature and dysmorphias.

Image:

Figure 1. Weight/age growth chart WHO 2007

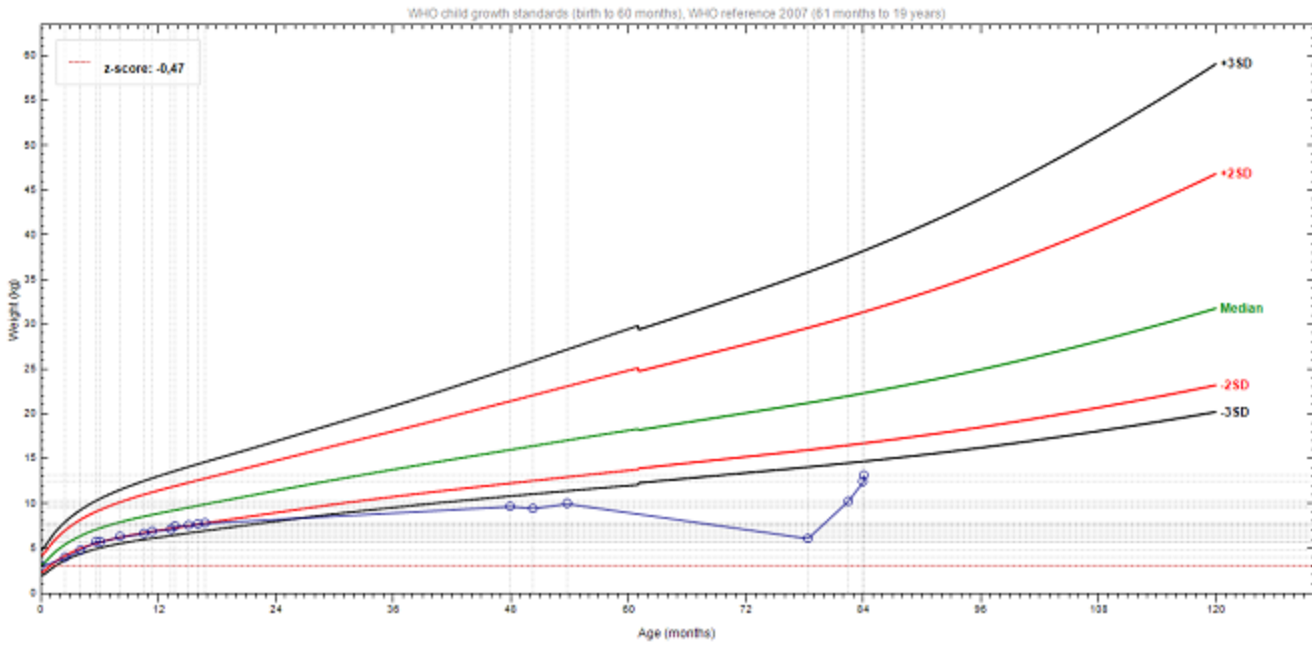
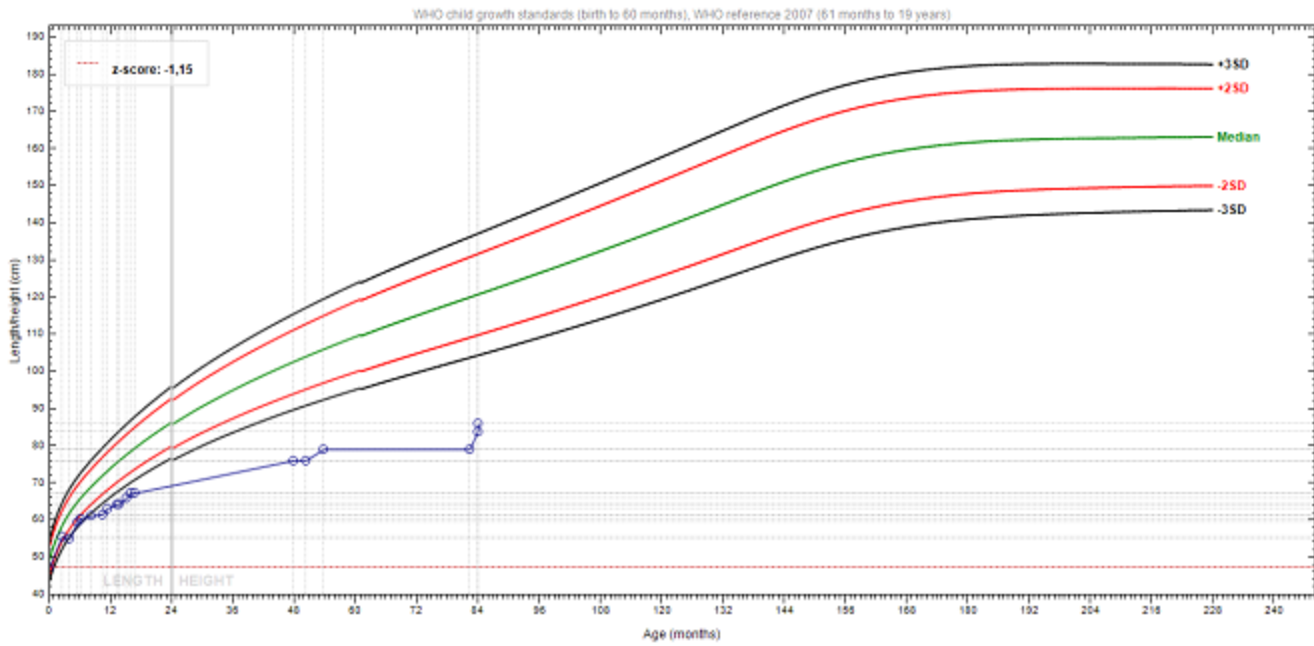


Figure 2. Length/age growth chart WHO 2007



Disclosure of Interest: None Declared

ICE2021-1368

IMPACT OF POST-DOSE SAMPLING TIME ON IGF-1 SDS WITH LONG-ACTING SOMATROGON (HUMAN GROWTH HORMONE - HGH-CTP) THERAPY

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Introduction: IGF-1 is a biomarker used to evaluate the efficacy and safety of hGH replacement therapy. Sustained values of IGF-1 SDS > +2 may require hGH dose reduction. For daily hGH therapy, IGF-1 assessment is typically made without concern for time after dose. For weekly-administered long-acting treatments, interpretation of IGF-1 SDS requires knowing the time of IGF-1 assessment with respect to dose administration. Previous studies of once-weekly somatrogen showed IGF-1 peaked ~48 hours (hrs) post-dose and values at ~96 hrs post-dose best reflected mean IGF-1 over the weekly dosing interval [1].

Objectives: Data from a global phase 3 non-inferiority study (NCT02968004) comparing somatrogen with Genotropin confirmed the IGF-1 SDS monitoring paradigm for weekly products.

Methods: Enrolled subjects were randomized to receive either somatrogen once weekly (0.66 mg/kg; N=109) or Genotropin once daily (0.034 mg/kg; N=115). IGF-1 was sampled ~5 times during the 52 weeks of the study, resulting in 535 samples obtained after the first dose of somatrogen that were suitable for inclusion in the analysis.

Results: The previously developed model, with adjustments to 2 parameters (baseline IGF-1, EC₅₀) and adapted to fit IGF-1 values without somatrogen concentration data, fit the IGF-1 data with minimal bias. IGF-1 SDS values were calculated using Bidlingmaier's equations [2]. IGF-1 SDS values were then simulated at 6-hr timepoints throughout the dosing interval, and mean IGF-1 was calculated over the dosing interval regardless of the sampling time post dose. Of the 151 samples measured 48–72 hrs post-dose (representing peak IGF-1), 26 (~17%) had IGF-1 SDS > +2. The mean of modeled values at 96 hrs was close to the calculated mean IGF-1 SDS values. At 96 hrs post-dose, 11/535 (~2%) of modeled IGF-1 SDS values were > +2; this compares to 10/535 values (< 2%) of mean IGF-1 SDS values.

Conclusion: In conclusion, IGF-1 SDS values need to be interpreted in the context of timing of the IGF-1 sample relative to the most recent somatrogen dose. Samples obtained 96 hrs post-dose best represent mean IGF-1 levels over the dosing interval while values obtained between 48–72 hrs post-dose represent values closer to peak IGF-1 levels. Of the samples collected from 109 patients during the 12-month somatrogen treatment period, 10/535 (< 2%) of the estimated weekly mean IGF-1 values over the dosing interval were > +2 SDS.

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2. Bidlingmaier M, *et al.* J Clin Endocrinol Metab 2014;99:1712

Disclosure of Interest: D. Fisher Conflict with: P Less Than, A. Pastrak Conflict with: Opko Health, J. Choe Conflict with: Opko Health, J. Korth-Bradley Conflict with: Pfizer, Conflict with: Pfizer, M. Wajnrajch Conflict with: Pfizer, Conflict with: Pfizer, J. Cara Conflict with: Pfizer, Conflict with: Pfizer

Pediatrics

ICE2021-1377

SOMATROGON GROWTH HORMONE IN THE TREATMENT OF PEDIATRIC GROWTH HORMONE DEFICIENCY: RESULTS OF THE PIVOTAL PEDIATRIC PHASE 3 CLINICAL TRIAL.

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Introduction: Somatrogen (hGH-CTP) is a long acting re-combinant human growth hormone (rhGH; somatropin) in development for once-weekly treatment of pediatric patients with growth hormone deficiency (pGHD). A 12-month phase 2 trial of somatrogen administered once weekly vs Genotropin administered once daily in patients with pGHD showed that somatrogen (0.66 mg/kg/wk) had a similar safety and efficacy profile to Genotropin (0.24 mg/kg/wk). This report summarizes top-line results from a global phase 3 pediatric trial (NCT02968004).

Objectives: The trial's objective was to test non-inferiority of somatrogen administered once weekly compared to Genotropin administered once daily in hGH-naïve, prepubertal children with pGHD.

Methods: 224 subjects were enrolled and randomized 1:1 to receive either once-weekly somatrogen (0.66 mg/kg/wk) or once-daily Genotropin (0.24 mg/kg/wk) for 12 months. Randomization was stratified by geographic region, peak GH level and age. The primary endpoint was annualized height velocity (HV) at month 12; secondary endpoints included HV at month 6, change in height SDS at months 6 and 12, IGF-1 and IGF-I SDS, immunogenicity, and safety.

Results: At baseline, mean (SD) age and height SDS of the somatrogen (N=109, 75.2% male) and Genotropin (N=115, 68.7% male) groups were 7.83 (2.66) and -2.94 (1.29), and 7.61 (2.37) and -2.78 (1.27), respectively. One subject in each group discontinued the study, and 95% of completers continued into an open-label extension study. At month 12, HV was 10.10 cm/yr in the somatrogen group and 9.78 cm/yr in the Genotropin group; the treatment difference of 0.33 cm/year favored somatrogen and the lower bound of the two-sided 95% confidence interval of the treatment difference (-0.24) was higher than the pre-established non-inferiority margin, demonstrating non-inferiority of once-weekly somatrogen vs daily Genotropin. HV at month 6 (10.59 cm/yr vs 10.04 cm/yr), and change in height SDS at months 6 (0.54 vs 0.48) and 12 (0.92 vs 0.87) were numerically higher in the somatrogen vs Genotropin-treated groups, respectively. The majority of adverse events were mild to moderate in severity (somatrogen: 78.9%, Genotropin: 79.1%) and, overall, weekly somatrogen was generally well-tolerated and comparable to daily Genotropin.

Conclusion: This pivotal phase 3 trial demonstrates that somatrogen once weekly is non-inferior to Genotropin once daily and that once-weekly somatrogen has a safety profile similar to daily Genotropin treatment.

Disclosure of Interest: C. Deal Conflict with: OPKO, Pfizer Inc, A. Pastrak Conflict with: OPKO Health, L. Silverman Conflict with: Novo Nordisk, Conflict with: OPKO, Pfizer Inc, S. R. Valluri Conflict with: Pfizer Inc, Conflict with: Pfizer Inc, M. Wajnrajch Conflict with: Pfizer Inc, Conflict with: Pfizer Inc, J. Cara Conflict with: Pfizer Inc, Conflict with: Pfizer Inc

Pediatrics

ICE2021-1462

SECONDARY HYPERPARATHYROIDISM IN ADOLESCENT OBESITY IS RELATED TO WEIGHT STATUS

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Introduction: Elevated serum PTH concentrations are common in obesity, but the pathogenesis of obesity-associated hyperparathyroidism is not well understood. Hypovitaminosis D, low-grade inflammation as well as insulin resistance have been associated with secondary hyperparathyroidism in adult as well as childhood obesity.

Objectives: We investigated the prevalence of increased serum PTH values in overweight and obese adolescents and explored a correlation with vitamin D deficiency, insulin resistance, hyperleptinemia and low-grade inflammation.

Methods: Fasting serum concentrations of glucose, insulin, calcium, phosphorus, magnesium, creatinine, fibrinogen, PTH, 25-OH vitamin D (25OHD) and leptin were measured in 92 overweight (BMI > 1.3 SDS) or obese (BMI > 2.3 SDS) adolescents, aged between 10.6 and 19 years. In addition, pubertal staging, standard anthropometrics and body composition analysis by DXA were performed. Pearson correlation analysis and Student T testing were performed. PTH and 25OHD were measured by the Cobas 8000 e601 platform.

Results: Median (range) serum PTH was 42.7 (18.5 – 85.9) ng/L. Elevated (for gender and age) PTH concentrations were found in 64 (28 male) adolescents. No significant difference in mean PTH concentration was found between male (n = 35) and female patients, between patients with overweight (n = 10) and obesity, between patients with (n = 52) and without vitamin D deficiency and with (n = 45) and without elevated fasting insulin concentration. Serum PTH correlated negatively with age (r: -0.26; p < 0.05), serum calcium (r: -0.26; p < 0.05) and plasma fibrinogen (r: -0.27; p < 0.01) and positively with body weight SDS (r: 0.25; p < 0.05) and body height SDS (r: 0.23; p < 0.05). Correlations of serum PTH with weight SDS, plasma fibrinogen and serum calcium remained significant after adjusting for age and height SDS. No significant correlations between serum PTH and BMI SDS, body fat percentage and serum concentrations of phosphorus, magnesium, leptin or 25OHD were found.

Conclusion: In conclusion, secondary hyperparathyroidism is observed in two thirds of overweight and obese adolescents and correlates with the weight status. Hyperparathyroidism in obese adolescents does not indicate vitamin D deficiency, low-grade inflammation or insulin resistance.

Disclosure of Interest: None Declared

Pediatrics

ICE2021-1598

A PARAOVARIAN STEROID CELL TUMOUR: A RARE CASE OF VIRILIZATION

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Introduction: Steroid cell tumour is a rare subtype of virilizing ovarian sex cord-stromal tumour. Presence of this tumour in broad ligament and pre-pubertal age group is even rarer. Here, we report the case of an extraovarian steroid cell tumour in pre-pubertal girl.

Case Description: A 10-year-old girl presented with progressive virilisation for last one year in form of hirsutism, deepening of voice and acne. She was born to a 3rd degree consanguineous marriage with no contributory past, family and medical history. On examination, she had normal vitals, muscular built, hirsutism with Modified Ferriman Galwey score of 36 (out of 48), acne and SMR A2 P4 B1 with clitoromegaly measuring 2*1.5 cm.

Her laboratory findings were suggestive of normal renal, hepatic and thyroid profile. LH and FSH were suppressed (<0.1 and 0.19 mIU/ml respectively) with raised DHEAS (378 mcg/dl), 17 OHP (12.3 nmol/L) and Androstenedione (>10ng/ml). Tumor markers (a fetoprotein, bHCG and CA 125) were negative.

Ultrasonography of abdomen revealed a cystic lesion with internal echoes and septations measuring 5.1*3.7 cm in left adnexa with no separate visualisation of left ovary. These findings were corroborated by contrast enhanced CT of the abdomen.

Diagnosis of androgen secreting tumour was made. She underwent laparotomy and both ovaries were visualised separately and were intact. A vascular solid mass was seen arising in left broad ligament from left lateral wall of uterus extending from fundus to cervix. This mass was excised after ligating the vascular and thin connective tissue between mass and uterine wall. Histopathological report was suggestive of sex-cord stromal cell tumour with subsequent immunohistochemistry confirming the diagnosis of Steroid cell tumour (inhibin and calretinin positive).

Clinical discussion: Steroid cell tumour is a rare entity. The age of presentation and it's paraovarian location makes our case a unique entity.

Disclosure of Interest: None Declared

Pediatrics

ICE2021-1629

PRECOCIOUS PUBERTY AND FAMILIAL NEUROFIBROMATOSIS

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Introduction: Neurofibromatosis, caused by defects in the NF1 tumor suppressor gene located at chromosome 17q11.2, is a chronic progressive disease that can affect several body segments. Optic nerve gliomas occur in 12–15% of these patients, usually within the first decade of life. Several series have shown an association with endocrine disorders including puberty changes in affected patients. We report a case of early central precocious puberty in a seven-years-old boy associated with familial neurofibromatosis.

Case Description: The schoolboy presents a 14 months history of accelerated growth, voice changes, pubic hair appearance, and increased genital volume. Physical examination revealed: Weight 52 Kg, Height 1.66m, normal thyroid, asymmetric face with left nodule, Acne, Café au lait spots on trunk, pubarca was at stage P3 and testis G3. He presented lumps on all his body since he was 3 years old, similar to nodules presented by his father. In the exams, bone age 12 years Basal serum LH was 23 IU/dl FSH was 52.5 IU/dl, testosterone was 643 ng/dl. Nasal wing biopsy showed neurofibroma with myxoid degeneration. Magnetic resonance imaging showed multiple lesions affecting the thalamus, nucleocapsular regions, hypothalamus, brainstem and cerebellar white matter, Optic gliomas with chiasmatic and prechiasmatic involvement on the left. There was also plexiform neurofibroma inferior to the left orbital cavity, in addition to neurofibromas in the paravertebral regions, in the carotid, parotid and masticatory spaces. Abdominal tomography showed multiple paravertebral neurofibromas in the lumbosacral, thoracoabdominal, and pelvis segments. Therapy with a GnRH agonist (Leuprolide 3.75) at 28-day intervals was instituted. After one-year therapy, growth continued at a normal rate, LH and testosterone levels reduced and the signs of virilization did not progress further. The lesions on MRI were stable and no significant vision impairment was present during the follow-up.

Clinical discussion: Abnormal pubertal timing can adversely affect a child's physical and psychosocial well-being and may be caused by a range of generally benign or pathologic etiologies, although the risk for organic CPP is higher in boys and in younger patients. The indicated treatment must be preceded by systematic investigation. This case illustrates the variability of expression in the association between precocious puberty and neurofibromatosis, including sign evolution, even within the same family.

Disclosure of Interest: None Declared

Reproduction Female

ICE2020-1069

SECONDARY AMENORRHEA AND INFERTILITY AS A PRESENTATION OF MOSAICISM 45X/46XX.

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Introduction: There is a close relationship between the karyotype and phenotype of patients with gonadal dysgenesis, which has its highest phenotypic expression in monosomy 45X or Turner syndrome (TS). In mosaicisms 45X/46XX, somatic and visceral changes are attenuated. Spontaneous puberty occurs in 16% of TS patients and in 40% of those with mosaicism 45X/46XX; however in an unpredictable time some patients may develop gonadal failure and infertility.

Case Description: 34 year old patient, consults to the Endocrinology department for TSH adjustment due gestational desire. She refers to being diagnosed Hypothyroidism due Hashimoto's thyroiditis and Diabetes mellitus type 2. Present normal sexual development, menarche at 13 years, with regular cycles. At the age of 22, she started began oligoamenorrhea that was treated with oral contraceptive which she abandoned due to gestational desire 1 year ago, and then amenorrhea is started. She have 1.43 m of height and 53 kg, normal development of secondary sexual characteristics and absence of particular somatic disorders (without the Turner phenotype) except for short stature. The pelvic ultrasound showed a small uterus and non-visualized ovaries. Blood chemistry with total cholesterol 325 triglycerides 210, glucose 109 HBA1C 5.2%, antiGAD negative. The hormonal study revealed a serum FSH concentration of 38 mUI/mL and LH of 16 mUI/mL with oral conceptives (2016), which is repeated in amenorrhea FSH 33 mUI/mL and LH of 26; estradiol less than 5 pg/mL, TSH, prolactin and cortisol values normal. Antimulleriana hormone 0.01. The diagnosis of HYPERERGONOTOTROPIC AMENORRHEA and early ovarian failure is made. We request KARYOTYPE and return 45X(15)/46Xx(14) 1 ring of the long arm of the X chromosome. Progesterone test: negative. She presented regular menses induced with combined treatment with estradiol valerate and norgestrel. After 6 months of treatment, she presented normal uterine and annexes size. She is in egg donation plan for she gestacional desire.

Clinical discussion: The present case illustrates the broad clinical spectrum of 45X/46XX mosaicism in a patient with different degrees of her ovarian function, which started with a normal menarche, followed by ovarian failure with hypergonadotropic secondary amenorrhea. This case demonstrates the importance of the exhaustive study of patients with secondary amenorrhea since the early detection of these cases would lead to the preservation of their fertility as early as adolescence and ensure their fertility.

Disclosure of Interest: None Declared

Reproduction Female

ICE2020-1102

BILATERAL LEYDIG CELL TUMORS IN A POSTMENOPAUSAL WOMAN

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Introduction: Severe hyperandrogenism in post-menopausal women is rare. It may be caused by either benign or malignant neoplasms of the adrenal or ovary. We report a rare case of a post-menopausal woman with hirsutism associated with virilization due to Leydig cell tumors (LCT) of both ovaries.

Case Description: 61 yo female presented for evaluation of hirsutism. She had also been experiencing increased facial hair growth, deepening of voice, clitoromegaly, alopecia, and acne. Physical examination: normal vital signs. Patient had signs of virilization, including coarse hair along her upper lip, chin, lower abdomen and inner thigh with Ferriman–Gallwey score of 8, acne, and clitoromegaly. She had no signs of acanthosis nigricans or Cushing syndrome.

Base line labs: Hemoglobin 16.2 gm/dL (ref 12.0 to 15.5), total testosterone 803 ng/dL (ref 3-41), free testosterone 20.2 pg/mL (ref 0.0-4.2), estradiol 77 pg/mL (<6.0–54.7), estrone 148 pg/mL (ref 7-40), FSH 11.5 mIU/mL (ref 25.8 - 134.8), LH 6.90 mIU/mL (ref 7.7 - 58.5), androstenedione 28 ng/dL (ref 17-99), DHEAS 99.9 mcg/dL (ref 19-205), dehydroepiandrosterone 512 ng/dL (ref 31-701), inhibin A 2.3 pg/mL (ref <5), inhibin B <7.0 pg/mL (ref 00-16.9), 17-alpha hydroxyprogesterone 187 ng/dl (ref <51). Similarly a transvaginal US did not show any ovarian pathology, however MRI of the pelvis showed homogeneous ovarian enhancement bilaterally and based on this information a diagnosis of ovarian hyperthecosis was considered and patient underwent laparoscopic bilateral oophorectomy. Pathology confirmed: LCT in both ovaries.

Clinical discussion: Hyperandrogenism, especially serum testosterone in the male range with rapidly progressive hirsutism or virilization signs in a female indicates tumor etiology. Androgen-secreting ovarian tumors are usually small and often embedded in the ovary. Transvaginal US is useful in the diagnosis of ovarian tumors. Although 5 cases of bilateral LCT are reported in the literature, LCT is unilateral 95% of the time, the pathogenesis of Leydig cell proliferation and LCT is unclear. In conclusion, androgen secreting tumors should be considered in women (especially in post-menopausal state) with hyperandrogenism and hirsutism. In fact, diffuse stromal Leydig cell hyperplasia and small Leydig cell tumors may be missed on imaging and in some cases only pathology can confirm the result.

Disclosure of Interest: None Declared

Reproduction Female

ICE2020-1135

BASIC CLINICAL AND HORMONAL CHARACTERISTICS OF A COHORT OF CHILEAN TRANSEXUAL MEN

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Introduction: Trans Men,(TMS) are biological women with male identity, genetic, epigenetic, perinatal and hormonal theories have been raised but, even one is not sure what the origin of this condition is. In TMS, a higher frequency of oligomenorrhea, hirsutism and Pcos syndrome has been reported, as well as normal hormone levels. The baseline characteristics of hormone levels have been described in very few studies, and in not study that considers the South American population

Objectives:

This study describe the hormonal values and clinical characteristics of a group of trans Chilean men before starting their treatment with reverse hormone therapy (RHT)

Methods:

100 HTS that consulted in Endocrinology at the Hospital San Borja Arriaran and private consultations, for the onset of RHT, with a psychiatric evaluation that rule out mental illness mistaken for transsexuality and without a history of Hypogonadism, sexual differentiation disorders or chronic diseases, and contraceptive use , were evaluated. They were evaluated for weight, BMI, Testosterone, Shbg, Estradiol, LH, and E/T Ratio($10^*E/T$) with RAI method, in follicular phase (in those not in Amenorrhea), and ultrasound looking for Rotterdam criteria of Pcos

Results:

| | |
|--------------------------|-----------|
| n | 100 |
| Age of perception | 4,7±2 |
| Menarchia | 12±3 |
| Pubarchia | 9±3 |
| Telarchia | 10 ±1 |
| Menstrual irregularity % | 45 |
| Pcos % | 28 |
| Age consulting | 22,2±9,1 |
| Weigth kg | 80±12 |
| BMI | 26,5±2 |
| Waist cc | 85±12 |
| Endometrium thickness mm | 3±2,1 |
| Lefth Ovar vol | 15±3,2 |
| Right ovar vol | 11±5,3 |
| Pcos (Rotterdam) % | 32 |
| Lh lu/dl | 3,4±2,8 |
| Testosterone ng/dl | 73,7±11,5 |
| Estradiol pg/dl | 68.6±108 |
| Shbg nmol/lt | 49±23 |
| E/T RATIO | 17,2 |

Conclusion:

We find that the prepuberal characteristics and the perception of being TMS are consistent with the general population and what is described. Our population resulted with a high % of menstrual irregularities and history of Pcos, according to overweight and a high waist , suggesting increase in visceral fat. The ovaries and endometrium were normal, but ultrasoundly 32% Pcos criteria were found. Hormonal values resulted within normal ranges, however the E/T Ratio

stands out, which was on average higher than that described in premenopausal populations (approx 14)but this not result significant The E/T Ratio has been negatively correlated with cardiovascular risk in postmenopausal women, it is possible that the increase in testosterone may decrease this ratio, and these data force us to observe in the future the cardiovascular and metabolic risk of the population of Trans Men described

Disclosure of Interest: None Declared

Reproduction Female

ICE2020-1206

LIPID AND ANTHROPOMETRIC PROFILE OF OVERWEIGHT FEMALE VOLUNTEERS ON ETONOGESTREL (ENG) IMPLANON® IMPLANT.

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Introduction: The etonogestrel-releasing subdermal implant is a long-term contraceptive method with high efficiency. The metabolic effects resulting from the implant were extensively studied in women with normal weight but not with overweight and obese women. A previous study has shown that the implant did not directly increase the risk of cardiovascular diseases in eutrophic women because it was observed a significant increase in lipid profile. This study approaches preliminary results of the first data collected (baseline), drawn from a larger study aiming at analyzing the effects of diabetogenic e lipogenic in women on Implanon® for one year.

Objectives: To assess lipid and anthropometric profile in overweight or obese female volunteers who agreed on using the Implanon® implant as their only contraceptive method.

Methods: Descriptive study of transversal cut involving 91 female volunteers aged 18 to 40 years receiving family planning assistance from CAISM at UNICAMP. In the beginning of the study, the assessment took into consideration the following factors: BMI, waist circumference, waist-hip-ratio (WHR), total cholesterol, LDL, HDL, Triglycerides (TG), and AST/ALT. The data collected were analyzed by descriptive measures. The study is sponsored by FAPESP (2018/17375-0).

Results: The population that was studied, was composed of 24% of overweight women with older age 34.1 ± 6.0 years and had more children 1.8 ± 1.0 compared to obese women. The female volunteers presented waist-circumference above the standard defined cut-off point as stated by World Health Organization (WHO) defining ≥ 80 cm as a risk factor of cardiovascular diseases. They also presented waist-hip-ratio above the recommendation by WHO, which states $>0,85$ and indicates the risk of metabolic complications. The lipid profile was within normal limits considering the LDL, HDL, TG, AST/ALT.

Conclusion: The female volunteers showed, at the beginning of the study, risk factors for cardiovascular diseases assessed by anthropometric indicators. Nevertheless, the lipid profile was within normal range. The hypothesis is that after a year using Implanon® no significant changes will be observed in BMI, waist circumference, WHR. However, it is expected an increase in the parameters of cholesterol, HDL, LDL, and TG. If it is found that the use of Implanon® contributes to the increase in disorders of the lipid metabolism of overweight users, the results may present the need for medical and nutritional monitoring during the use of the method.

Disclosure of Interest: None Declared

Reproduction Female

ICE2021-1319

PREVALENCE AND ASSOCIATED FACTORS OF FEMALE SEXUAL DYSFUNCTION IN WOMEN WITH TYPE 2 DIABETES MELLITUS IN INDONESIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Female sexual dysfunction (FSD) is a neglected major complication of diabetes. However, there is scarcity of data in Indonesia, which is currently ranked as the 7th in the world for the number of people with diabetes mellitus.

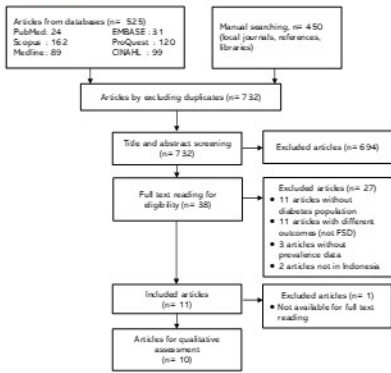
Objectives: Our study aims to analyze the prevalence and factors of FSD among females with type 2 diabetes mellitus (T2DM) in Indonesia.

Methods: This systematic review was conducted using the PRISMA standard. Literature searching was performed in PubMed/Medline[®], CINAHL[®], EMBASE[®], Proquest[®], Scopus[®], Indonesian local journals/ databases, and libraries, considering human clinical studies. All observational and experimental studies in searching keywords “sexual”, “diabetes”, and “Indonesia” with MeSH terms (English and Bahasa) were included, without time of study or language restriction. Risk of bias was rated using Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence study. Pooled prevalence and odds ratio of associated factors of FSD were analyzed using STATA.

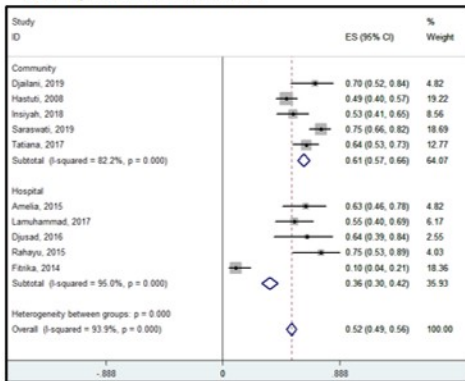
Results: Ten studies with cross-sectional designs included 572 females with T2DM in both community and hospital settings. Five studies had low risk of bias. The prevalence of FSD ranged 9.8 – 78.2% and with random-effect model, it showed pooled prevalence 0,52 (95% CI 0,49-0,56; I-squared 93,9%, p = 0.000) and 0,62 (95% CI 0,58-0,66; I-squared 68,7%, p = 0.001) if one study was excluded from the analysis due to unstandardized FSFI value. Desire and arousal dysfunction were the most prevalent FSD domains in females with T2DM. Age more than 45 years old, menopause, the use of antihypertensives, and HbA1c level were associated with FSD. GRADE recommendations on outcomes were very low to moderate quality.

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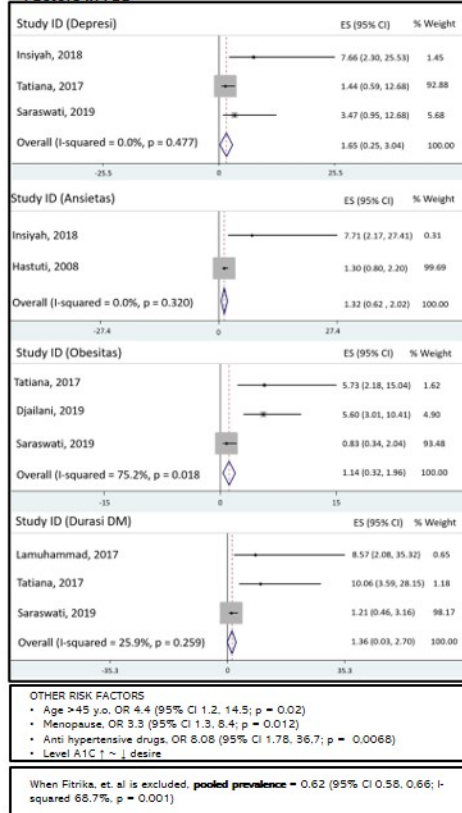
PRISMA



Pooled prevalence of 10 studies



Factors in FSD



Conclusion: FSD was prevalent among T2DM females in Indonesia and was associated with aging and metabolic factors. Association towards psychological factors need to be further scrutinized.

Disclosure of Interest: None Declared

ICE2021-1448

**A YOUNG FEMALE WITH SECONDARY AMENORRHEA AND HIRSUTISM-STEROID CELL TUMOR OF OVARY
–A RARE CASE REPORT**

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Introduction: Scully described the term “steroid cell tumor of the ovary” in 1979.[1] These tumors are divided into three subtypes according to their cells of origin: stromal luteoma, leydig cell tumor and steroid cell tumor, not otherwise specified (NOS). Out of these, the steroid cell tumors, NOS account for about 56% of steroid cell tumors. The incidence of steroid cell tumors, NOS is more common in women of child bearing age group, especially the third and fourth decades [2]. A majority of steroid cell tumor NOS are unilateral and well circumscribed and their size varies from 1.2 to 45 cm [2]. NOS, sometimes produce hormones other than testosterone, for example, estradiol secretion has been reported in 6–23% of patients. These tumors have been associated with Cushing's syndrome in 6–10% of cases [3, 1,4].

Preoperative evaluation for women with virilization includes a bimanual examination, serum testosterone, DHEA-S, and computerized tomography (CT) of the adrenals and ovaries. [5]. Ultimate diagnosis is made by histology. Microscopically, the neoplastic cells have abundant clear vacuolated cytoplasm with rich vascularity, and absence of atypia or necrosis.

Objectives: We report a case of young female with secondary amenorrhea and hirsutism for 5 years diagnosed as steroid cell tumor.

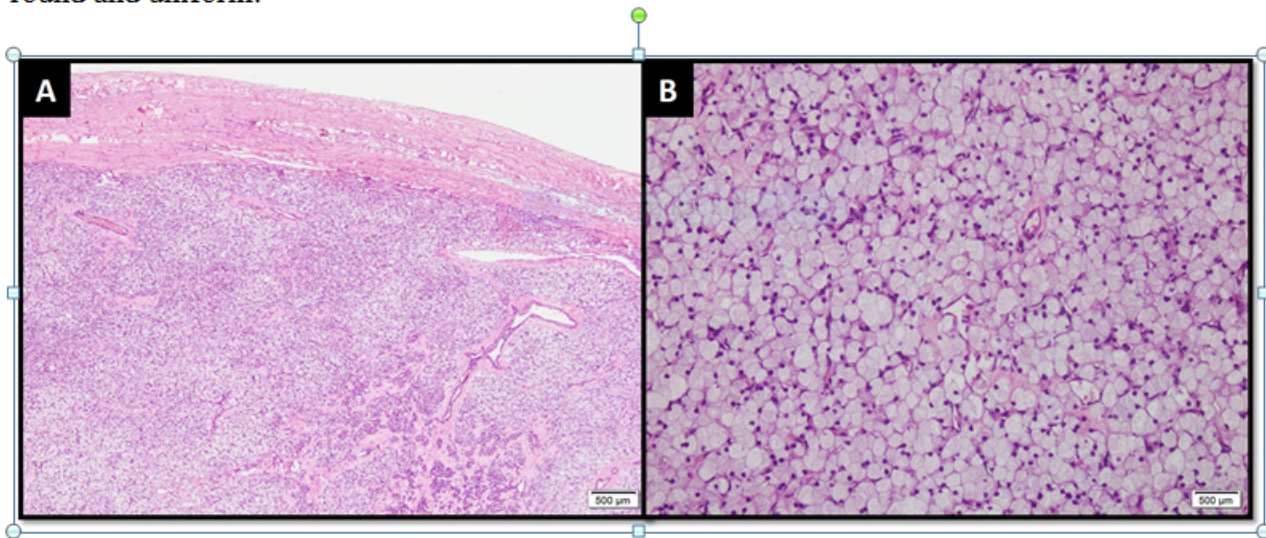
Methods: Clinical, laboratory, radiological and pathological data of the case is presented.

Results: 25 years old female presented with secondary amenorrhea, hirsutism for 5 years, raised blood pressure for 2 years and weight gain. Before 2015 she had regular cycles. On examination Ferimann Gallwey score was 25, no proximal myopathy and no striae were seen. Workup revealed low LH (0.14mIU/ml), low FSH (0.76mIU/ml), high testosterone (527ng/dl), Normal Thyroid functions, Normal DHEA level (147 ug/dl), high 17-OH Progesterone level (10.9ng/ml), normal ODST(0.70). CT scan pelvis revealed left ovarian mass adherent to the sigmoid colon abutting the fundus of uterus and right ovary. She underwent laparotomy, left salpingo-oophorectomy and total omenectomy. Histopathology of left ovarian mass revealed **steroid cell tumor**. Postoperatively testosterone level and 17 -OH Progesterone level were normal.

Image:

Figure legends:

Figure [A] Low power view of tumor showing cells arranged in sheets. [B] The neoplastic cells are polygonal with distinct cell borders and abundant clear cytoplasm. The nuclei are small, round and uniform.



Conclusion: Any patient who presents with virilism would be investigated to determine if the high testosterone levels are of an adrenal or ovarian origin. Steroid cell tumors of ovary should be considered a cause of virilisation .

Disclosure of Interest: None Declared

ICE2021-1464

WAIST TO HEIGHT RATIO: CORRELATION WITH INSULIN RESISTANCE INDEX AND CARDIOVASCULAR RISK FACTORS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME.

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Introduction: Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disturbances in women of reproductive age. It is characterized by hyperandrogenism (H), oligoanovulation (O), and/or polycystic ovaries (P). Besides its well-known effects on reproductive health, it is also linked to increased cardiovascular risk. Due to the difficulties in directly measuring adiposity, simple anthropometric measurements play a crucial role in clinical practice.

Objectives: To investigate the correlation between the waist-to-hip ratio (WHR), insulin resistance index, and cardiovascular risk factors in women with PCOS.

Methods: Design: Case-control study.

Setting: Academic Department of Endocrinology and Diabetes.

Patient(s): Two hundred and thirty-eight women with PCOS and 94 healthy subjects, aged 18-35 years, were evaluated as cases and controls, respectively. The PCOS patients were separated into four phenotypes according to the Rotterdam criteria: A (H+O+P n=132), B (H+O n=43), C (H+P n= 40), and D (O+P n= 23).

Intervention (s): Different anthropometric and biochemical parameters were analyzed: body mass index (BMI), waist circumference, waist/hip ratio (W/H), waist/height ratio (WHR), free androgen index (FAI), insulinemia (Ins), lipid profile and indices of insulin resistance and sensitivity (HOMA-IR, Triglycerides / HDL-c, QUIKI, Lipid Accumulation Product (LAP)). Metabolic syndrome (MS) was defined by the ATP III consensus.

Results: The WHR was positively correlated with: weight, W/H, Ins, HOMA, LAP ($r > 0.6$, $P < 0.0001$); systolic blood pressure, diastolic blood pressure, FAI, Triglycerides, Triglycerides / HDL-c ($r: 0.4$ to 0.6 , $P < 0.0001$) and negatively with: QUIKI, HDL-c ($r < -0.4$ $P < 0.0001$). The ROC curve determined a cut-off value of the WHR ≥ 0.48 to detect MS; OR 0.12 (0.03-0.5); $P < 0.0001$. The sensitivity (IC 95%) and negative predictive value (IC 95%) to detect or rule out, respectively, MS were: 97,73 % (94,05 – 100) and 96,15 % (89,97- 100). PCOS phenotype A had higher BMI, WHR, Insulin, FAI and MS compared to the rest of phenotypes and control group ($P < 0.01$).

Conclusion: In our studied population, the WHR showed to be an inexpensive indicator of MS in PCOS patients. Its high sensitivity and simplicity make it an appropriate method in clinical practice to identify the phenotypes of women with PCOS who are likely to have cardiovascular risk factors.

Disclosure of Interest: None Declared

Reproduction Female

ICE2021-1545

THE FOETAL PROGRAMMING EFFECTS OF A MILD GESTATIONAL FOOD RESTRICTION PROTOCOL IN MICE: ARE THE RESULTS COMPARABLE WITH THOSE OF INTRAGESTATIONAL GHRELIN ADMINISTRATION?

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Introduction: Severe food restriction during pregnancy and/or lactation (50% food restriction or more) induces fetal programming. It is not clear nevertheless, if these effects are the consequence of maternal increased levels of ghrelin (Ghrl), a food scarcity signal. Furthermore, it has not been investigated if mild food restriction is also able to exert fetal programming.

Objectives: The objectives of this study were to explore 1) if a 15% food restriction protocol during pregnancy in mice, programs the postnatal development of the offspring, with emphasis on reproductive function, and 2) to assess if the administration of Ghrl to mice dams, exerts effects that mimic those obtained by mild caloric restriction.

Methods: Adult female mice were 15% food restricted or injected with 4 nmol/animal/day of Ghrl during pregnancy. Control animals were injected with the vehicle. After birth, pups did not receive further treatment. Parameters evaluated in pups were birth weight, body weight evolution, physical and neurobiological maturation, puberty onset and reproductive function at adulthood.

Results: Pups from food restricted dams were thinner at birth (vs Ghrl) but caught up. Pups from Ghrl dams were heavier at birth and gained more weight. This effect was not associated with differences in plasma IGF-1 levels. Dams food restriction delayed the physical maturation of the offspring (pinna detachment and eyes opening), while Ghrl advanced it. Intra gestational food restricted pups showed also an impaired response to the surface righting reflex. Dams food restriction and Ghrl administration advances vaginal opening in the offspring and, at adulthood, pups from food restricted mice showed a significant decrease in viable litter size, plasma progesterone and an increase in the percentage of females with embryo loss. Ghrelin male pups delayed testis descent. Changes in puberty onset were not associated with Kiss1 expression in hypothalamic nuclei (arcuate and anteroventral periventricular). At adulthood, male pups from food restricted dams showed a decrease in epididymal sperm motility and viability.

Conclusion: In mice, a mild food restriction protocol during gestation exerts long lasting effects on physical, neurobiological and sexual maturation of the offspring, affecting also reproductive function at adulthood. These effects are not comparable with those of intra gestational Ghrl administration.

Disclosure of Interest: None Declared

ICE2021-1618

SERUM LEVELS OF ENDOCANNABINOIDS IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME AND COMPARISON WITH HEALTHY CONTROLS

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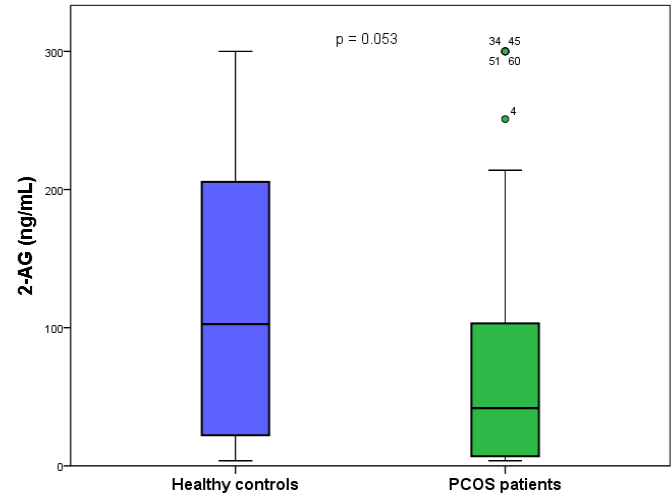
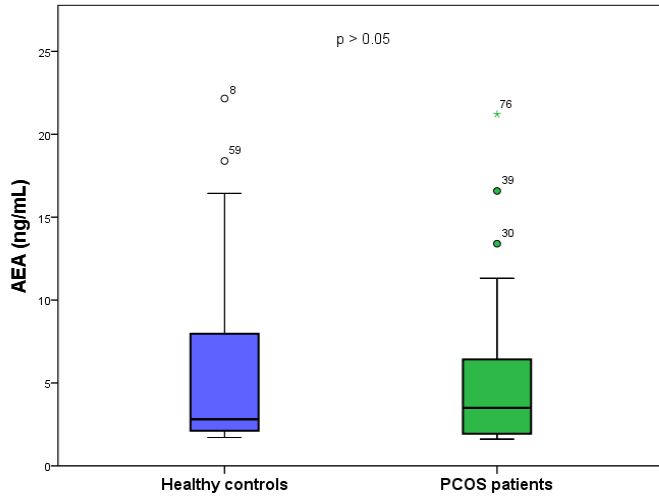
Introduction: Two of the most studied members of the endocannabinoid system (ECS) are arachidonoyl ethanolamide (anandamide, AEA) and 2-arachidonoyl glycerol (2-AG). The ECS has been confirmed to have effects on metabolism, energy and appetite control, ovarian function, and woman reproduction. Its role in polycystic ovary syndrome (PCOS) pathogenesis has already been suggested [1].

Objectives: The aim of the study is to determine serum levels of AEA and 2-AG in PCOS patients and compare them with healthy controls.

Methods: The study consisted of 54 patients with PCOS (25.9 ± 5.3 years) fulfilling the Rotterdam criteria [2] and 26 healthy participants (27.8 ± 5.1 years) without any known reproductive and metabolic conditions. Patients and controls were matched by age and BMI. Detailed anthropometric measurements, hormonal tests, and pelvic ultrasound were obtained in line with predefined rules between the 3rd and 5th day of a menstrual cycle [3]. AEA and 2-AG serum levels were determined by ELISA kits. Normally distributed data were presented as mean \pm SD, while skewed – median (IQR).

Results: Women with PCOS and healthy controls showed similar anthropometric and metabolic parameters. Both groups did not differ in BMI (27.6 ± 7.3 vs 28.5 ± 7.3 [$p > 0.05$], respectively). The PCOS group had increased total testosterone, DHEAS, androstenedione, and 17-OH-progesterone levels (all $p < 0.001$), free androgen index ($p = 0.002$), modified Ferriman-Gallwey score ($p = 0.001$), and elevated LH/FSH ratio ($p = 0.035$). Patients with PCOS and controls did not differ in the serum levels of AEA (3.5 [4.5] vs 2.8 [6.3], $p = 0.704$). Although the difference did not reach "statistical significance", a trend was observed toward lower levels of 2-AG in PCOS women compared to controls (80.3 [96.3] vs 102.6 [184.9], $p = 0.053$) (Figure 1).

Image:



Conclusion: PCOS patients have similar levels of AEA and 2-AG compared to healthy controls.

Disclosure of Interest: None Declared

Reproduction Male

ICE2020-1187

EARLY GONADOTROPIN SUPPRESSION PREDICTS LIKELIHOOD OF SPERM SUPPRESSION IN MALE HORMONAL CONTRACEPTIVE GEL CLINICAL TRIAL PARTICIPANTS

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Introduction: The only available reversible male contraceptive methods are condoms and withdrawal. Reversible male methods are under development. A Phase IIb multicenter, open label study is underway to determine one-year contraceptive efficacy of a topical gel containing testosterone and the progestin, Nestorone® (Nes/Tes).

Objectives: Our goal is to develop a male hormonal contraceptive that is effective, safe, reversible, acceptable and user-controlled. The current objective is to determine whether early gonadotropin suppression or lack thereof can predict likelihood of achieving sperm suppression.

Methods: The study plans to enroll 420 couples. Following enrollment, male subjects enter a suppression phase in which they apply study gel daily. Gonadotropins (FSH and LH) and sperm levels are followed every four weeks. Two sperm counts < 1 million/mL are required to enter efficacy. To date, 115 couples have enrolled at nine US and international sites and completed at least 8 weeks of treatment. We compared LH levels at week 4 of treatment between subjects who achieved full sperm suppression (< 1 million/mL), partial suppression to oligospermia (1-5 million/mL), or did not suppress (> 5 million/mL) to assess whether gonadotropin suppression (LH < or \geq 0.5 IU/L) at week 4 is predictive of either achieving or failing to achieve later sperm suppression.

Results: Full suppression was achieved by 78% of men, 8% partially suppressed and 14% did not suppress. Of subjects who fully suppressed to < 1 million/mL, 14% achieved this level by week 4, 57% by week 8, and 85% by week 12. LH values of < 0.5 IU/L at week 4 were significantly associated with likelihood to fully suppress if treatment continued ($p < 0.001$). The group that failed to suppress had a significantly higher percentage of subjects with LH levels \geq 0.5 IU/L at week 4 compared to the group that fully suppressed (75% vs 16%, $p < 0.001$). Differences between the full and partial suppression groups did not reach significance for the LH \geq 0.5 IU/L threshold (16% vs 45%, $p = 0.055$); although, only 9 subjects had partial suppression. LH levels \geq 0.5 IU/L at week 4 of treatment were 64% sensitive for predicting failure to achieve sperm suppression to < 1 million/mL by 12 weeks or longer of treatment.

Conclusion: Early suppression of LH is associated with, but does not ensure, achieving sperm suppression for men using daily Nes/Tes gel. Lack of LH suppression at week 4 may predict non-responsiveness and may be useful to guide counseling early in the suppression process.

Disclosure of Interest: J. Long Conflict with: US government, C. Wang: None Declared, S. Page: None Declared, C. Dart: None Declared, R. Sitruk-Ware: None Declared, D. Blithe Conflict with: US government

Reproduction Male

ICE2020-1226

EFFECT OF LETROZOLE IN MEN WITH HYPOGONADOTROPIC HYPOGONADISM WITHOUT OBESITY COMPARED TO NON-HYPOGONADIC CONTROLS

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Introduction: Aromatase inhibitors such as Letrozole(L) have been used in men with reversible Hypogonadotrope Hypogonadism(IHH), associated with obesity at weekly doses. There are no described experiences of its use in non-obese patients, so its use in HH patients is evaluated, without obesity and compare its effect in non-hypogonadic patients

Objectives: Determine the effectiveness and security of Letrozole one week ,in non-obese IHH patients

Methods: In andrological consultation, men who consulted for possible Hypogonadism (H) were evaluated. they were measured BMI,Lh,Testosterone (T),Estradiol(E2),Shbg, Tsh,prolactin (RIA). They were ruled out:H hypergonadotrope, Hypothyroidism, hyperprolactinemia,DM , morbid obesity, and chronic decomposed diseases. They were divided into 25 H Hypogonadotrope(IHH):testosterone(T) less than 300ng/dl plus low or normal LH and 30 controls :T greater than 300 ng/dl). Prior consent,receiving Letrozole 1.5mgr, weekly, for 3 months, comparing baseline results and post-treatment, plus delta(∇) between post-treatment values. libido was self-assessed by perception of decrease plus 50% pretreatment.

Results:

| | IHH | Controls | P |
|--|----------------|-----------------|------|
| N | 25 | 30 | |
| Age years | 42 \pm 14 | 40 \pm 16 | ns |
| BMI | 33 \pm 6,4 | 27 \pm 4,4 | 0,06 |
| BMI Post | 33 \pm 5,22 | 29 \pm 5,4 | ns |
| T ng/dl | 239,5 \pm 46 | 437 \pm 97 | 0.05 |
| E2 pg/dl | 26 \pm 25,6 | 40,1 \pm 32 | ns |
| LH lu/li | 3,1 \pm 1,67 | 3,5 \pm 1.32 | ns |
| Shbg nmol/lt | 19,2 \pm 9,9 | 32.2 \pm 23 | 0,01 |
| Shbg Post | 18 \pm 9 | 30,2 \pm 21 | 0,04 |
| T Post L | 597 \pm 58 | 853 \pm 45 | 0,02 |
| ∇ Shbg Post (%) | -14 \pm 24 | -12 \pm 26 | ns |
| T Post (%) | 58.4 \pm 14 | 45,1 \pm 19 | 0,05 |
| E2 Post | 21,3 \pm 21 | 28,1 \pm 25 | ns |
| ∇E2 Post (%) | 18,7 \pm 12 | 25,2 \pm 16 | ns |
| LH Post | 12 \pm 7,5 | 12 \pm 9,2 | ns |
| ∇LH Post (%) | 62,8 \pm 20 | 59,6 \pm 25 | ns |
| FCT pg/ml | 6,8 \pm 2,5 | 9,4 \pm 3,2 | 0,04 |
| FCT Post | 18,2 \pm 5,9 | 21,7 \pm 13,1 | ns |
| ∇FCT Post (%) | 2,3 \pm 1,2 | 2,4 \pm 1,3 | ns |
| Libido (%) | 7 \pm 2 | 8 \pm 3 | ns |

Conclusion: L for 3 months was effective in increase T levels. Those studied was relatively young and overweight, however, post-therapy BMI did not change. E2 levels did not decrease significantly and neither LH levels increase and Shbg decrease.Libido decreased no significantly.

The increase in T was significantly higher in IHH, indicating that in this population the L had an inhibitory effect of aromatization at the periphery level, testicular,fat?, which adds to the hypothalamic central effect, which is the main

mechanism described in the obese population to increase T. The dose of 1,5mgr per week ,turned out to be safe and effective in controls and IHH , independent of patients IBM

Disclosure of Interest: None Declared



ICE2021-1418

THE IMPACT OF GU INFECTIONS ON SPERM DNA FRAGMENTATION, OXIDATIVE STRESS AND WHO SEMEN PARAMETERS IN INFERTILE MEN.

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Introduction: Sperm DNA fragmentation has emerged as a potential biomarker of male infertility. Multiple factors may contribute towards sperm DNA damage, most notably oxidative stress. Infection is associated with oxidative stress thus, genitourinary infections (GU) may play a significant role in male infertility. There is limited evidence to suggest that bacteria impair spermatogenic function. Consequently, cultures are not routinely incorporated into clinical diagnostic protocols for male infertility.

Objectives: To determine the prevalence of genitourinary infections in infertile men and their effects on sperm.

Methods: A retrospective analysis of men attending for diagnostic semen analysis between 1st January 2015 and 31st December 2019. GU infections were identified by polymerase chain reactions and cultures of urine and semen. DNA fragmentation was measured by sperm chromatin structure assay or Comet. Levels of reactive oxygen species (ROS) were determined by chemiluminescence, and standard semen analyses were performed according to World Health Organization guidelines (2010). The data was non-parametric, therefore median values were given.

Results: This study included 770 infertile men, in which 43.0% (n=331) had a GU infection. Semen parameters were compared to the 57.0% (n=439) men who were non-infected. Of the 331 patients with GU infections, a semen or urine infection was identified in 45.0% (n=149) and 42.3% (n=140) respectively. The remaining 12.7% (n=42) had both semen and urine infections. Patients with semen or urine infections had significantly higher levels of ROS than non-infected patients (14.70 vs 12.95 vs 2.85 relative light units/second/10⁶ sperm respectively; p<0.001). Furthermore, both DNA fragmentation assays demonstrated that patients with genitourinary infections had greater DNA fragmentation than non-infected patients (p<0.001). Sperm concentration, motility and morphology were similar between the patient cohorts (p>0.05).

Conclusion: Genitourinary infections are common in infertile men and may impair sperm quality by increasing oxidative stress and DNA fragmentation. Consideration should be given to the value of assessing urine and semen for infection in cases of unexplained infertility.

Disclosure of Interest: C. Ho: None Declared, D. Vaughan-Constable: None Declared, J. Ramsay: None Declared, C. Jayasena Conflict with: NIHR Post-Doctoral Fellowship, T. Tharakan: None Declared, T. Yap: None Declared, S. Minhas: None Declared, S. Homa: None Declared

Reproduction Male

ICE2021-1468

PREVALENCE OF ANDROLOGICAL AND CLINICAL HISTORY IN PATIENTS WITH MALE BREAST CANCER

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Introduction: Breast carcinoma in men is a rare disease, it represents less than 0.5% of cancer diagnoses in men. There is no prevalence data in Argentina. The analyzed evidence proposes that the imbalance of the ratio between androgens and estrogens may lead to the proliferation of ductal breast cancer cells. Several studies have shown a relationship between male breast cancer (MBC) and antecedents such as Klinefelter syndrome, delayed puberty, infertility and cryptorchidism, testicular trauma or orchitis, conditions often associated with gynecomastia.

Objectives: We intended to estimate the prevalence of andrological backgrounds associated with male breast cancer, as well as the anthropometric and clinical characteristics of the studied population.

Methods: Observational, Descriptive, Cross-Sectional, Retrospective Study.

Patients who consulted at the Hospital Italiano of Buenos Aires between 01/01/2010 and 01/12/2018, were included men according to their original biological sex, all were older than 18 years and presented a history of breast cancer.

Results: We included 57 men with breast cancer. The average age was 71 years, interquartile range 30.5. 53.1% presented obesity and 61.90% diabetes (Table 1). Regarding the andrological history, 6.25% had infertility, 23.4% gynecomastia, and 94.44% had sexual dysfunction. 45.45% presented biochemical hypergonadotrophic hypogonadism. No patient had a history of Klinefelter Syndrome (Table 2).

Image:

Table 1: Anthropometric and clinical history in patients with male breast cancer.

| CLINICAL HISTORY | n | % |
|-------------------|------------|------|
| Age (RIQ) | 71 (59-78) | |
| Obesity | 26/49 | 53,1 |
| Diabetes | 13/21 | 61,9 |
| Osteoporosis | 7/21 | 33,3 |
| Hyperthyroidism | 1/21 | 4,76 |
| Liver disease | 2/21 | 9,52 |
| Family background | 12/23 | 52,2 |

Table 2: Andrological history in patients with male breast cancer.

| ANDROLOGICAL HISTORY | n | % |
|------------------------------------|-------|------|
| Infertility | 2/49 | 6,3 |
| Gynecomastia | 11/32 | 23,4 |
| Sexual dysfunction | 17/18 | 94,4 |
| Orchitis | 2/4 | 50 |
| Testicular trauma | 5/8 | 62,5 |
| Androgen Therapy | 3/52 | 5,8 |
| Klinefelter syndrome | 0 | |
| Hypogonadism Hypergonadotrophic | 5/11 | 45,5 |

Conclusion: We identify similarities with the literature about the prevalence of obesity, diabetes and infertility in patients with MBC. Many of these factors support the need to explore the role of endogenous hormones. More research is required in this field to improve physician's daily practice and give accurate advice to patients with increased risk for this disease.

Reproduction Male

ICE2021-1483

EVALUATION OF ENZYME ACTIVITY OF HUMAN HSD17B3 USING ANDROGEN RECEPTOR-MEDIATED TRANSACTIVATION

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Introduction: 17 β -Hydroxysteroid dehydrogenases (17 β -HSDs, HSD17B) catalyze the reduction of 17-ketosteroids and the oxidation of 17 β -hydroxysteroids to regulate the production of sex steroids. Among HSD17B family, 17 β -HSD type 3 (HSD17B3) is expressed in testicular Leydig cells and contributes to development of male sexual characteristics by converting androstenedione (A4) to testosterone (T). Mutations of HSD17B3 genes cause a 46,XY disorder of sexual development (46,XY DSD) as a result of low T production. Therefore, the evaluation of HSD17B3 enzymatic activity is important for understanding and diagnosing this disorder.

Objectives: The evaluation of HSD17B3 enzymatic activity is important for understanding and diagnosing this disorder. Although various amino acid substitutions of HSD17B3 have been reported in previous studies, the enzymatic activities of these proteins were often not defined. This is probably due to the difficulties that such enzymatic activities have been evaluated by quantifying the conversion of A4 into T using radioactive isotopes and liquid chromatography-mass spectrometry-mass spectrometry (LC-MS/MS).

Methods: We adapted a method that easily evaluates enzymatic activity of HSD17B3 proteins by quantifying the conversion from A4 to T using androgen receptor (AR)-mediated transactivation. HEK293 cells were transfected to express human HSD17B3, and incubated medium containing A4.

Results: HEK293 cells were transfected to express human HSD17B3, and incubated medium containing A4. Depending on the incubation time with HSD17B3-expressing cells, the culture media progressively increased luciferase activities in CV-1 cells, transfected with the AR expression vector and androgen-responsive reporter. These luciferase activities reflected T concentrations in culture media defined by LC-MS/MS. Establishment of HEK293 cells expressing various missense mutations in the HSD17B3 gene revealed that mutations with the manifestation of 46,XY DSD show the marked reduction of enzymatic activities, whereas mutants without the manifestation of 46,XY DSD show similar activities as the wild-type protein.

Conclusion: This system can provide a valuable tool to evaluate the enzymatic activities of mutant HSD17B3 proteins.

Disclosure of Interest: None Declared

Reproduction Male

ICE2021-1548

DO AGING, DRINKING AND HAVING AN UNHEALTHY WEIGHT HAVE A SYNERGIC IMPACT ON SEMEN QUALITY?

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Introduction: Several factors, both intrinsic and extrinsic, are known to exert detrimental effects on sperm quality. Among them, age, alcohol consumption and body mass index (BMI) are known to impact on male reproductive health. However, studies evaluate these factors separately, and currently there are no reports about their possible combined effects.

Objectives: To examine the combined effects of age, alcohol consumption and body mass index on seminal parameters.

Methods: Design: Retrospective study of a sample of 12695 patients attending an andrology laboratory in Cordoba-Argentine (from 2011 to 2017). Data on patients age and daily alcohol intake were voluntarily provided by patients. Patients weight and height were recorded in the andrology laboratory, to calculate BMI. Seminal parameters evaluated were: Semen volume, sperm concentration, total sperm count, motility, morphology, nuclear maturity, viability and membrane functional integrity. The primary outcome was the possible synergic interaction between these three factors on seminal quality and the order in which these factors affect each seminal parameter.

Results: Almost all the seminal parameters evaluated in this study were affected by at least, two synergic interactions, except for nuclear maturity that records only one synergy (Age x Alcohol), and sperm morphology, which records the three synergic interactions. Age x BMI showed more synergic effects than other combinations, suggesting that these two factors may have a higher detrimental effect than alcohol consumption. In the logistic regression analysis, age was the more powerful factor, since it impacted first in six from the nine seminal parameters evaluated; BMI was the second. Like in a previous study, we found a J-shape association between BMI and semen quality, with not only obesity but also underweight affecting seminal quality. Alcohol consumption was the parameter that impacted last in the logistic regression analysis, except for nuclear maturity that seems to be especially affected by alcohol.

Conclusion: All the factors considered in this study showed a synergic impact on semen parameters, and each combination included at least one extrinsic factor (BMI or alcohol consumption). It is possible to assume that reducing the exposure to lifestyle risk factors is a promising alternative for improving sperm quality in infertility patients.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1009

THYROID AUTOREGULATION: 2-iodohexadecanal INHIBITS THYROGLOBULIN GENE EXPRESSION THROUGH THE ACTIVATION OF PPARGAMMA

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Introduction: Iodine plays an important role in thyroid physiology and proliferation (Thyroid Autoregulation). The biosynthesis of iodolipids has been observed in the thyroid gland and their participation in thyroid autoregulation has been suggested. 2-iodohexadecanal (2-IHDA) was isolated as the major iodolipid formed in the thyroid and we have shown that this iodolipid can inhibit several thyroid parameters. A possible mechanism of 2-IHDA action would involve the Peroxisome Proliferative Activated Receptors (PPARs).

Objectives: To study the potential role of PPARs in the mechanism of action of 2-IHDA

Methods: In silico analysis of consensus sequences for PPAR binding in the promoter region of relevant genes for thyroid physiology was performed using the PROMO 3.0 application. We decided to study the effect of PPARs on Tg gene expression. FRTL-5 cells were cultured and treated for 24 h with increasing doses of 2-IHDA. Tg mRNA levels were assessed by RT-qPCR. The transcriptional activity of the Tg gene was determined by reporter gene assays using the pTg -688 and the pTg -688 PPAR mutated construct coupled to luciferase. The binding of PPAR γ to the Tg promoter was performed by chromatin immunoprecipitation (ChIP) studies. Since the Tg promoter region has only one site for PPAR gamma, assays were performed applying rosiglitazone maleate agonist, siRNAs and inhibitors (GW9662) to this isoform.

Results: Reporter gene assays revealed that 2-IHDA promoted the transcriptional activity of PPAR γ . The PPAR γ agonist mimicked the repressor effect of 2-IHDA on Tg mRNA levels. GW9662 and the PPAR γ siRNA reversed the effect of 2-IHDA. ChIP analysis revealed that 2-IHDA promoted an increase in PPAR γ interaction with the Tg promoter. Transfection studies showed an inhibition on Tg gene expression caused by 2-IHDA while transfection with the pTg-688 PPAR mutated construct showed no effect.

Conclusion: 2-IHDA modulates Tg gene expression by inducing PPAR γ repressor activity.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1021

PAPILLARY AND MEDULLARY CARCINOMA OF THE THYROID GLAND AS A COLLISION TUMOR: REPORT OF A CASE

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Introduction: Thyroid carcinomas are classified mainly into two groups according to their cell of origin: papillary and follicular tumors, arising from the follicular epithelium, and medullary neoplasms, in which the origin are parafollicular C-cells. Very few cases of truly collision tumors of follicular and medullary origin have been described around the world.

Case Description: 58-years-old woman, presents with a 1 cm thyroid nodule. She had normal thyroid function, no specific autoimmunity, and physical examination showed no pathological findings. Fine needle aspiration was performed. The cytologic characteristics were suspicious of papillary carcinoma (Bethesda V category). Serum calcitonin levels were in the normal range. A total thyroidectomy was performed.

Gross findings. On cut section of the right lobe, a tumoral mass of 0.8 cm was noted.

Microscopic pathologic findings. The tumoral nodule was a papillary proliferation, consisting of an atypical epithelial proliferation with follicular and trabecular structures, cells with moderate atypia, ground glass nuclei and intranuclear cytoplasmic inclusions. Inside this papillary proliferation, it was noted a solid area consisting of isles of smaller cells with granular chromatin nuclei. Immunohistochemistry of this area was positive for calcitonin. No C-cell hyperplasia was observed.

The patient was treated with 30 mCi I-131 to ablate the remnant tissue. The whole body scan showed uptake only in the thyroid bed. Calcitonin and CEA levels remained in the normal range. Protooncogen RET mutation is being studied at the moment.

Clinical discussion: According to the review published in 2010 by Sadow PM and Hunt JL, there are three scenarios in which it is possible to find a medullary carcinoma accompanied by a second tumor derived of the follicular epithelium: Concurrent but anatomically distinct medullary and follicular carcinomas. This situation is not uncommon, since the high rate of papillary thyroid cancer in the population.

The two tumors merging into one another, which is known as true collision tumor.

Medullary and follicular derived carcinomas that are intimately intermixed, these are known as true mixed medullary-follicular carcinomas.

We classified our patient's tumor as a true collision papillary and medullary carcinoma. Prognostic factors are unclear, since there are very few cases reported in the literature. In the case of our patient, we believe it will be probably linked to the papillary component.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1053

DIAGNOSIS OF MYXEDEMA COMA IN A PATIENT PRESENTING WITH UNEXPLAINED RHABDOMYOLYSIS

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Introduction: Rhabdomyolysis is a syndrome that causes the breakdown and release of skeletal muscle cell contents into the systemic blood circulation, resulting in muscle pain, weakness, and swelling. Can be associated with several diseases including metabolic disorders that are often overseen.

Case Description: A 20 years-old healthy man presented with dark urine and myalgias for two days. Laboratory workup was significant for isolated transaminitis with normal bilirubin levels. Creatinine kinase (CK) was elevated at 40,603 and diagnosed with rhabdomyolysis. Patient was on training for the National Guard with exstenuos physical activity five days prior. He was given aggressive fluid resuscitation with intravenous fluids. On second day of hospitalization he was noticed confused and lethargic. A multinodular goiter was palpable on neck examination. Thyroid stimulating hormone was elevated at 58.35 mIU/mL with free T4 0.050 ng/mL. Other causes of rhabdomyolysis and transaminitis were excluded and with high suspicion for Hashimoto's thyroiditis thyroperoxidase antibodies were obtained and found elevated at 1000 IU/mL. Neck ultrasound demonstrated diffusely enlarged, heterogeneous, hypervascular thyroid with two discrete nodules. Clinical presentation was consistent with myxedema coma and treated with stress doses of steroids and IV levothyroxine. Improvement was assessed with daily TSH and CK levels.

Clinical discussion: Myxedema coma is an extreme complication of hypothyroidism in which patients exhibit multiple organ abnormalities and progressive mental deterioration. It occurs when the body's compensatory responses to hypothyroidism are overwhelmed. Mild to moderate elevation in CK levels is a common finding in hypothyroidism, but only in a very small proportion of these patients muscular involvement will progress to hypothyroidism-induced rhabdomyolysis. There is no clear explanation for the relationship between hypothyroidism and rhabdomyolysis; it is thought to be related with inhibition of mitochondrial activity in muscle cells as well as dysregulation of many metabolic pathways such as Krebs cycle, fatty acid catabolism and glycolytic energy production. In conclusion, this case presentation reminds us the need for high clinical suspicion of metabolic disorders such as hypothyroidism/myxedema coma, in patient's presenting rhabdomyolysis of unclear cause. Prompt diagnosis of myxedema coma with early intervention could prevent fatalities.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1090

UTILITY OF SHEAR WAVE ELASTOGRAPHY IN COMBINATION WITH TI-RADS AND ATA CLASSIFICATIONS FOR DIFFERENTIATING MALIGNANT FROM BENIGN THYROID NODULES

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Introduction: Ultrasonography (US) is the first choice for the examination of thyroid nodules (TN). Sonographic patterns proposed by ATA guidelines and TIRADS classifications can be used to establish the risk of malignancy of TN and guide the indication of fine-needle aspiration cytology (FNA-C). Shear Wave Elastography (SWE) is a new, promising technique for the study of TN. To date, it is uncertain the diagnostic value that SWE could add to ATA and TIRADS classifications

Objectives: To evaluate the diagnostic performances of SWE alone and in combination with TI-RADS and ATA classifications in differentiating benign and malignant TN

Methods: From January 2019 to January 2020 all adult patients with TN were examined using US and SWE before US-guided FNA-C and were included into a retrospective database. SWE and US were performed using an Aplio 300 (Canon Medical Systems) scanner by the same operator. TIRADS (ACR 2017) and ATA risk of malignancy (2015 ATA guidelines) were assessed. ROC curve was analyzed to calculate the best cut-off value of SWE mean elasticity index (E_{mean}). TIRADS 5 and ATA high risk suspicious patterns were considered “positive” test results. Sensitivity(Se), specificity (Sp), positive and negative predictive value (PPV and NPV) were determined

Results: Clinical records from 145 patients (median age 58 yo (17-76), women 84%) and 183 TN (mean size 20.8 ± 11.8 mm) were analyzed. Ten TN with Bethesda III (n=5) and IV (n=5) cytology were excluded from the analysis due to lack of histological data. In 9 patients (n= 3, Bethesda V; n=6, Bethesda VI) the pathology report was diagnostic for papillary thyroid carcinoma. None of the patients with Bethesda II cytology underwent surgery and these TN were considered benign. The best SWE E_{mean} cut-off value for differentiation of benign from malignant TN was 29.5 Kpa (Se 89%, Sp 95%, PPV 48%, NPV 99%). The area under the curve was 0.91 (95%CI 0.79-1, p=<0.001) which represents an excellent accuracy. Se, Sp, PPV and NPV for each test are detailed in Table 1

Table 1. Diagnostic performances different tests

| | Se | Sp | PPV | NPV | AUC |
|------------------------------|-----|------|------|-----|------|
| TIRADS 5 | 89% | 98% | 70% | 99% | 0.94 |
| ATA high risk | 77% | 98% | 67% | 99% | 0.88 |
| SWE ≥29.5 Kpa | 89% | 95% | 48% | 99% | 0.91 |
| TIRADS 5 + SWE ≥29.5 Kpa | 78% | 100% | 100% | 99% | 0.89 |
| ATA high risk + SWE 29.5 Kpa | 67% | 100% | 100% | 98% | 0.83 |

Conclusion: Using a 29.5 Kpa threshold, SWE alone showed a poor risk of malignancy (PPV 48%) although it could be useful in avoiding unnecessary FNA-C (NPV 99%). The combination of SWE and TI-RADS or ATA risk classifications offers the best risk of malignancy (PPV 100%)

Disclosure of Interest: None Declared

Thyroid

ICE2020-1116

TSH STABILITY IN HYPOTHYROID PATIENTS TREATED WITH LIQUID L-THYROXINE

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Introduction:

Patients with hypothyroidism are usually treated with levothyroxine (L-T4) and monitored once a year to evaluate their thyroid-stimulating hormone (TSH) levels.

Objectives:

Since not extensive studies were conducted about the stability of TSH levels in hypothyroid patients (not reporting any malabsorption issues) treated with liquid L-T4, with respect to those treated with tablet L-T4, we aimed to deepen this topic.

Methods:

We enrolled patients having normal TSH serum levels at the basal evaluation, without any malabsorption or drug interference issues, who were in treatment with liquid or tablet L-T4.

Six-hundred-and-two hypothyroid patients in treatment with liquid L-T4 were compared to three-hundred-and-one hypothyroid subjects in treatment with tablet L-T4; both groups were matched by age and gender. All the enrolled patients were followed for two years, and TSH, FT3, FT4 serum values were assessed after one and two years.

Results:

The parameters taken into account at the first abnormal TSH value were gender, age, body mass index, history of chronic autoimmune thyroiditis, initial TSH level, and levothyroxine dose. These parameters, at the time of initial normal TSH, were not associated significantly with time to abnormal TSH values.

Normal TSH values were recorded: 1) after 1 year, in 89% of the patients who received L-T4 liquid formulation, while only in 82% of patients who received tablet L-T4; 2) after 2 years, in 86% of patients administered with L-T4 liquid formulation, whereas only in 74% of patients with tablet L-T4 ($p < 0.05$).

Conclusion:

In conclusion, we suggest the better efficacy of the liquid L-T4 formulation, with respect to the tablet L-T4 one, for the treatment of hypothyroid patients in the long term follow-up.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1127

RATIONAL USE OF LABORATORY TESTS REQUESTS IN BIOCHEMICAL ASSESSMENT OF THYROID FUNCTION.

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Introduction: TSH, FT4, T3 and T4 represent the major tests requests for assessing thyroid function in the endocrine laboratory. Although these tests are not expensive, their huge demand, not only restricted to endocrine specialists, represents an important expense for the health care system.

Objectives: To evaluate number of requests for thyroid function tests and assess patterns of requisition in different centers to check their adequation to international recommendations.

Methods: Thyroid tests requests were surveyed in a 5 years period. Here we present data from twelve laboratories from Buenos Aires city for year 2018 as representative of the period. 3 out of 12 labs (L1 to L3) were able to classify requests according to origin: endocrine physician (E) vs other physicians (NE). Parameters evaluated were:

- Number of requests for TSH, T3, T4, FT4 and anti thyroperoxidase antibodies (ATPO) related to the total number of patients per year.

Indexes per year calculated were:

- Test Selection Index (TSI): $T3/TSH$, $FT4/TSH$, $T4/TSH$, $ATPO/TSH$. It reflects the request relative to TSH requests, expected values <1 .

- Request Adequation Index (RAI): $FT4/T4$. It reflects better adequacy of requests, expected value >1 .

Results: Only in 1 out of 12 labs (L12, pediatric institution) the indexes showed that TSH requests are usually made together with thyroid hormones. FT4 was the major request after TSH in 10 out of 12, whereas T4 was the major one in L7. $T4/TSH$ and $T3/TSH$ TSI indexes showed great variability between labs, reflecting different modes in test requisition in our area. However, except in L7, these indexes turned to be similar in the same institution, showing the common request of T3 and T4 along with TSH. (Table 1). The great variability of FT4/T4 Index (11.6, calculated as Max/Min), points out that FT4 request was not always prioritized over T4. In L1 to L3 laboratories, higher numbers of requests were observed for FT4 in E over NE, showing a higher RAI.

Image:

| | TSI | | | | RAI |
|-----|--------|---------|--------|----------|--------|
| | T3/TSH | FT4/TSH | T4/TSH | ATPO/TSH | FT4/T4 |
| L1 | 0.38 | 0.70 | 0.34 | 0.24 | 2.07 |
| E | 0.32 | 0.94 | 0.11 | 0.43 | 8.54 |
| NE | 0.38 | 0.67 | 0.36 | 0.23 | 0.71 |
| L2 | 0.25 | 0.52 | 0.38 | 0.22 | 1.39 |
| E | 0.18 | 0.53 | 0.44 | 0.18 | 1.2 |
| NE | 0.3 | 0.52 | 0.32 | 0.29 | 0.56 |
| L3 | 0.12 | 0.37 | 0.11 | 0.13 | 3.42 |
| E | 0.15 | 0.79 | 0.17 | 0.17 | 3.57 |
| NE | 0.13 | 0.3 | 0.1 | 0.1 | 1.47 |
| L4 | 0.11 | 0.69 | 0.10 | 0.45 | 6.36 |
| L5 | 0.45 | 0.81 | 0.52 | 0.25 | 1.56 |
| L6 | 0.40 | 0.63 | 0.37 | 0.14 | 1.71 |
| L7 | 0.17 | 0.37 | 0.67 | 0.20 | 0.54 |
| L8 | 0.46 | 0.80 | 0.41 | 0.35 | 1.97 |
| L9 | 0.26 | 0.45 | 0.29 | 0.14 | 1.56 |
| L10 | 0.33 | 0.65 | 0.20 | 0.12 | 3.20 |
| L11 | 0.14 | 0.37 | 0.18 | 0.06 | 2 |
| L12 | 0.99 | 0.99 | 0.99 | 0.33 | 1.0 |

Conclusion: As different patterns of request for thyroid function tests were observed through the calculated indexes, an opportunity arises to reach a consensus for these requests. Our results showed better use of resources when requisitions are made from endocrine professionals. This is also shown in different publications, where all efforts are directed to adequacy of demand for laboratory tests in order to achieve a rational use of thyroid function tests.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1155

IN PROPERLY SELECTED PATIENTS WITH DIFFERENTIATED THYROID CANCER, LOBECTOMY IS AN ADEQUATE OPTION FOR INITIAL MANAGEMENT: EXPERIENCE OF A LATIN AMERICAN COUNTRY

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Introduction: Management of differentiated thyroid carcinoma (DTC) has shifted towards an individualized approach, including the extent of surgery. The latest ATA guidelines endorsed lobectomy for selected intrathyroidal tumors up to 4cm. There is scarce data regarding lobectomy outside first-world reference centers.

Objectives: The aim of this study is to report a cohort of patients with DTC treated with lobectomy in a developing Latin-American country.

Methods: We included patients with intrathyroidal DTC up to 4 cm, without suspicious contralateral findings and no lymph node metastases in the preoperative ultrasound, treated with lobectomy. Patients were classified according to ATA guidelines recurrence risk category and 8th edition of AJCC/UICC staging system. In patients followed for at least 6 months, response to treatment was classified according to ATA. TSH was maintained <2.0 uUI/mL.

Results: Sixty-four patients were included, age 38±11.1 years, 50 (78%) women and 20 (31%) had positive anti-thyroglobulin antibodies (TgAb). Forty-four (69%) patients had papillary thyroid cancer (PTC), 7 (11%) follicular thyroid cancer (FTC) and 13 (20%) noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). All patients were AJCC/UICC stage I. Risk of recurrence was low in 51 (80%) and intermediate in 13 (20%). Six (9.4%) patients required completion thyroidectomy and radioiodine: 4 for angioinvasion and 2 for solid-variant PTC; all cases are currently free of disease. Thirty-nine patients had follow-up of at least 6 months, i) there were no cases of structural incomplete response, ii) fourteen (36%) had positive TgAb, which decreased their concentration a median of 44% (-6.5% to -89.4%), and increased in none of them. No cases had hypocalcemia and 6 (9.4%) had transient dysphonia.

Conclusion: Our study shows that in appropriately selected patients, lobectomy, as suggested by ATA guidelines, is an adequate treatment option for DTC in a Latin-American developing country.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1166

PRE ABLATION STIMULATED THYROGLOBULIN AND ITS VALUE AS A PREDICTOR OF EVOLUTION IN DIFFERENTIATED THYROID CANCER

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Introduction: During last years, follow-up of patients with differentiated thyroid cancer (DTC) has changed, prioritizing treatment's individualization based on initial recurrence risk and response to therapy classifications. Pre ablation stimulated Tg (psTg) has been proposed in different studies as a prognostic marker of persistent/recurrent disease.

Objectives: -Correlate psTg with response to therapy system in patients treated in our institution

-Determine a cut-off value of psTg to establish which patients have more risk of persistent/recurrent disease

Methods: In this retrospective study, patients ≥ 18 years old followed for at least one year were included. All of them received radioactive iodine therapy (RIT) after total thyroidectomy. psTg was measured prior to RIT under thyroid hormone withdrawal. Risk of recurrence (ATA 2015) and mortality (TNM AJCC 8th edition) classifications were used at initial evaluation. Response to therapy (ATA 2015) was determined at last visit and psTg was compared between excellent response to therapy (ER), structural incomplete (SIR), biochemical incomplete (BIR) and indeterminate response (IR). Tg and anti-Tg antibodies (TgAb) analyses were performed at the same laboratory using electrochemiluminescence immunoassay (Cobas, Roche). Patients with positive TgAb, without total thyroidectomy or subsequent RIT and who had not surgery in our institution were excluded.

Results: 70 patients were included (49 females, 21 males); mean age at diagnosis was 49.10 years. The median follow-up was 76.5 months; 97.4% had papillary thyroid cancer. Median psTg was 16.65 ng/ml (range 0.1 to 7573). Most patients were classified as TNM stage I (88.57%). According to ATA 2015 classification, 50, 15 and 5 patients had low, intermediate and high risk of recurrence, respectively. At last visit, 54 patients had ER to therapy, 4 SIR, 7 BIR and 5 IR. There was a significant difference in psTg between ER and SIR to therapy ($p=0.003$), with no difference between ER and either IR or BIR (Table 1). ROC curve analysis demonstrated that a cut-off value of psTg <10 ng/ml had a high accuracy to predict excellent response (sensitivity 54.41%, specificity 90.9%, AUC: 0.74).

Image:

Table 1. Response to therapy and characteristics of the patients

| | ER (n=54) | SIR (n=4) | BIR (n=7) | IR (n=5) | p value |
|---------------------------|------------------------------------|------------------------------------|-------------------------------------|-------------------------------------|---------|
| Age years (mean \pm SD) | 50.66 \pm 13.40 | 45.25 \pm 6.02 | 40.86 \pm 14.10 | 43.80 \pm 12.44 | 0.2127 |
| psTg (ng/ml) | Median 9.50* Range (0.10 – 766) | Median 157* Range (78.73 – 813) | Median 37.40 Range (9.29 – 2270) | Median 47.14 Range (7.98 – 7573) | 0.0030* |
| TNM stage | | | | | |
| I n (%) | 49 (71%) | 3 (4%) | 6 (9%) | 4 (6%) | 0.6385 |
| II n (%) | 5 (7%) | 1 (1%) | 1 (1%) | 1 (1%) | |
| ATA recurrence risk | | | | | 0.002 |
| low n (%) | 44 (62.86%) | 0 (0%) | 5 (7.14%) | 1 (1.43%) | |
| intermediate n (%) | 10 (14.28) | 2 (2.86%) | 0 (0%) | 3 (4.28%) | |
| high n(%) | 0 (0%) | 2 (2.86%) | 2 (2.86%) | 1 (1.43%) | |

*p=0.003 between ER and SIR

Conclusion: In this study, psTg evidenced an adequate correlation with response to therapy system, showing that a higher value of psTg had a greater likelihood of SIR to therapy. A psTg cut-off value <10 ng/ml was found as a good predictor of disease-free status in our DTC patients.

FROM HYPOTHYROIDISM TO HYPERTHYROIDISM, UNUSUAL FORM OF INITIAL PRESENTATION OF GRAVE'S DISEASE. ABOUT TWO CASES

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Introduction: Graves' disease (GD) and Hashimoto's Thyroiditis (HT) are autoimmune thyroid diseases with different pathological characteristics. *Graves' triad* includes signs in the thyroid (goiter), ophthalmopathy and thyroid dermopathy; they can occur in isolation or together and generally have no diagnostic doubt.

The conversion of hypothyroidism to hyperthyroidism is a rare event and only few case reports have been described in the literature.

The proposed mechanism to describe this phenomenon is a variation in the concentration balance of TSH antireceptor antibodies in the thyroid that can be stimulating (TSAb) with manifestation of hyperthyroidism or blocking (TBAb) showing a pattern of hypothyroidism.

Case Description: Case 1: 56-year-old female known hypothyroid in treatment with levothyroxine (T4) 7 years ago.

Consultation for palpitations, tremor and weight loss, eye pain and retraction. Laboratory TSH ≤ 0.005 uU/ml and FT4 4.57 U/ml.: AntiTPO ≥ 1000 (vn: 35UI/ml); TRAb ≥ 40 (VN: 1.75U/l). T4 is suspended and antithyroid is started. She presented Active Graves' Ophthalmopathy (GO) with corticosteroid requirement and improvement after treatment.

Case 2: Hypertensive female, 54 years old, comes for cervical discomfort, denies other symptoms; with laboratory TSH 81.2 uU/ml and FT4 0.18 ng/dl; ANTI TPO 37 U/ml (≤ 5.1 U / ml). Start treatment with T4. Nine months later, she presented palpitations with TSH 0.008 uU/ml, TRAB 3.95 (≤ 1.75 U/l). Doppler thyroid ultrasound: Characteristics of the autoimmune process. T4 is suspended. Suppressed TSH persists with clinical thyroid hyperfunction, antithyroid was started, leading to euthyroidism.

Clinical discussion: The conversion of autoimmune hypothyroidism to EG is a rare clinical situation. This phenomenon has been shown to occur due to an alteration in the balance of concentrations between TSAbs and TBAbs and its effects on thyroid tissue. Physicians should be alert to the phenomenon of spontaneous conversion from hypothyroidism to hyperthyroidism, or vice versa, in a subset of patients with autoimmune thyroid disease.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1209

EXTRACELLULAR VESICLES RELEASED BY TRIODOTHYRONINE-STIMULATED DENDRITIC CELLS INDUCE A PRO-INFLAMMATORY PROFILE OF ALLOGENIC MURINE SPLENOCYTES

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Introduction: The relationship between the neuroendocrine and immune systems is essential for homeostatic maintenance. We reported that physiological levels of triiodothyronine (T3) activate mice dendritic cells (DCs) through thyroid hormone receptors (TR β), inducing Th1 and Th17 proinflammatory responses and restraining tolerogenic signals. These results were exploited with success in an antitumor DC-based vaccination protocol *in vivo*. Besides, we described that *in vitro*, nano-sized extracellular vesicles (EVs) released by T3-stimulated DCs (T3-DCs) activate syngeneic DCs, contributing to paracrine DC communication. However, the immune modulatory role of T3-DCs derived EVs on T cells is still unknown.

Objectives: To evaluate the immune response induced by T3-DC released EVs in allogenic splenocytes.

Methods: Bone marrow DCs obtained from C57BL/6 WT mice were stimulated (or not, control: C) with T3 (10nM) for 18h. DC-secreted EVs (DCs-EVs) were isolated by differential ultracentrifugation of the supernatant (2,000g: 2K; 10,000g: 10K; and 100,000g: 100K). Allogenic splenocytes were obtained from BALB/c mice and stimulated with DC-EVs for 6 days. Proliferation, intracellular and secreted cytokine production were analyzed by flow cytometry and ELISA assays, respectively. Statistical analysis: Sidak's multiple comparisons test. P<0.05 was considered statistically significant.

Results: We demonstrated that all DC-EVs fractions (T3 and C) evaluated trigger splenocyte proliferation. Both, T3-100K and T3-2K EVs increase CD8 splenocyte subpopulation (vs C-100K and C-2K, respectively). Moreover, the secretion of IFN- γ (p<0.001) and IL-17 (p<0.01) were augmented in the splenocytes after T3-2K stimulus (vs C-2K). Similarly, T3-10K upregulated IL17 secretion (p<0.01; vs C-10K).

Conclusion: Results showed that DC-EVs induce splenocyte proliferation *in vitro*. T3-DC released EVs can activate naïve splenocytes, with fraction dependence. After T3-100K and T3-2K EVs exposure, CD8 subpopulation increase. Besides, the pro-inflammatory cytokines IFN- γ and IL17 secretion augment after T3-2K or T3-10K stimulus. Thus, EVs are involved in the extracellular mechanism triggered by T3-DCs to spread their pro-inflammatory adaptive immune signature. These results reinforce previous findings reporting that T3-DCs are driving cytotoxic and pro-inflammatory responses, with Th1 and Th17 polarization. Further ongoing studies will enlighten this issue, providing valuable tools to manipulate the immunogenic potential of T3-DCs and their released EVs.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1217

CASE REPORT: PAPILLARY THYROID CARCINOMA IN TWO SISTERS WITH ATAXIA TELANGIECTASIA SYNDROME

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Introduction: Ataxia telangiectasia(AT)is an autosomal recessive disorder primarily characterized by cerebellar degeneration, telangiectasia, immunodeficiency, radiation sensitivity and increased cancer incidence (25% lifetime risk) due to genome instability and defective DNA repair. Hematopoietic system malignancies predominate. Thyroid cancer is not frequent (<1%).

Aim: to report 2 pediatric patients with A-T and papillary thyroid carcinoma (PTC)

Case Description: Patient 1:16 years-old female diagnosed with AT at 9 years with a history of recurrent pneumonia,progressive cerebellar ataxia and oculo-cutaneous telangiectasia referred to Endocrinology for a palpable fast-growing thyroid nodule. Ultrasound (US) showed a 20mm mixed isoechoic nodule with microcalcifications on the right lobe and a similar subcentimeter nodule on the left lobe. FNAB result was suspicious for PTC (Bethesda V). Total thyroidectomy and central neck compartment dissection confirmed an intermediate risk PTC (T3N1aM0). Thyroglobulin (TG) after surgery was 20ng/ml with negative ATG antibodies. Considering the increased sensitivity to radiations we did not indicate ablative radioiodine treatment. Two years later she has a suppressed TG of 1.3ng/ml and negative cervical US. Patient 2: 14 years-old sister with AT diagnosed at 4 years. After the sisters' PTC diagnosis, cervical US was performed showing a micronodular thyroid gland. 6 months later a subcentimeter mixed nodule was found. With a Bethesda IV FNAB result (suspicious for follicular neoplasm), total thyroidectomy and central neck compartment dissection were indicated. Histology confirmed a classic PTC (T1N0M0) with postsurgery of TG:13.2ng/ml. At 1 year of follow-up she remains free of disease.

Clinical discussion: Although PTC is not frequent in AT, it occurred in both sisters at 16 and 14 years of age. According to recommendations we decided not to administer 131I in patient 1/both patients due to the increased sensitivity to ionizing radiation and increased cancer risk. Nonetheless, both had an excellent response to initial therapy being disease free at 2 and 1 years of follow-up Based on the literature evidence the youngest reported AT patient with PTC was 9 years old, so it would be advisable to search for thyroid nodules in AT patients by palpation or US from this age onwards. The screening of the younger sister allowed the finding of PTC at an earlier stage. Thyroid gland palpation and US should not be missed in the follow-up of AT patients.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1235

THE IMPACT OF THE FREQUENCY OF CLINIC VISITS ON THYROTOXICOSIS TREATMENT OUTCOMES

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Introduction: Thyrotoxicosis is common endocrine disorder in UK with prevalence of around 2% in women and 0.2% in men.

Most common causes are Grave's disease, Multinodular goitre and Toxic nodules.

The choice of treatment modality rely on Doctor -Patient preferences.

Early and appropriate treatment is important in preventing cardiovascular and metabolic complications such as Osteoporosis and Throid storm.

Treatment options include anti-thyroid medications ,RAI,and Thyroidectomy ,with anti thyroid drugs are usually first line treatment.

Objectives: Effect of frequency of visits in patients diagnosed with thyrotoxicosis started on anti-thyroid medications on the outcome of treatment.

Methods: Reterospective studies of data collected from outpatient endocrinology clinic with patient treated for thyrotoxicosis between 2016-2019.

Inclusion criteria was patient who completed the course of anti-thyroid treatment.

Study conducted on 85 cases out of which 63 met the criteria.

Results: 63 patients includes in study ,who fulfill the criteria and complete treatment in the period of study.

51% of patients visited endocrine clinic less than 6 times ,out of which 66% have less than 4 visits during the course of treatment.

46% patients had relapse out of which 72% visited more than 6 times while 28% had less than 6 visits.

The most frequent visits noticed in patients with relapse.

Only 41% patients with relapse received definitive treatment either surgery or Radioactive iodine Therapy.

Conclusion: On the basis of studies ,all the patients diagnosed with thyrotoxicosis does not essentially require frequent visits.

The number of visits ideally should be in between 4-6 times since after diagnosis and start of treatment till the completion of treatment .

More frequent visits does not impact or change the management plan of Hyperthyroidism.

Our additional recommendation is to emphasize more on compliance of patients to treatment and follow the advice of Endocrinologist.

Disclosure of Interest: None Declared

Thyroid

ICE2020-1237

LEVELS OF THYROGLOBULIN MESSENGER RNA IN THE FOLLOW -UP OF DIFFERENTIATED THYROID CANCER PATIENTS

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Introduction: The postoperative follow up of patients with differentiated thyroid cancer is based on the levels of serum thyroglobulin measured by immunoassay and imaging studies, mainly neck ultrasound. However, antithyroglobulin antibodies interfere with this measurement and produce falsely low thyroglobulin levels that can be misleading in up to 30% of patients. Thus, the search for alternative methods to assess the presence of circulating thyroglobulin is warranted.

Objectives: Assess the sensitivity, specificity, and predictive values of messenger RNA of thyroglobulin (Tg-mRNA) levels measured by quantitative RT-PCR in the blood of patients followed for differentiated thyroid cancer. Exploratory analyses of Tg-mRNA levels in patients followed for differentiated thyroid cancer without Radioactive Iodine (RAI) ablation.

Methods: This is a prospective study of Tg-mRNA levels measured with quantitative RT-PCR in patients followed for differentiated thyroid cancer without evidence of disease (69), and persistence of structural disease (23), as well as 28 patients without evidence of disease who had not received RAI ablation. The primers used had been previously published by Boldarine et al. (J Clin Endocrinol Metab. 2010;95(4):1726-33. <https://doi.org/10.1210/jc.2009-135>) and encompassed a region free of alternative splicing. Quantification was performed using a standard curve generated by the amplification of Tg mRNA of a surgical specimen of thyroid tissue. Results were analyzed using the Unity Real-Time program and expressed as fg/μg ARN. We constructed a ROC curve to identify the best cutoff level to distinguish between patients with structural disease persistence and without evidence of disease.

Results: We recruited 120 patients who had undergone total thyroidectomy for thyroid cancer, and 92 had received RAI ablation. Tg mRNA levels were not significantly different between patients with structural persistence [0.133 fg/μg ARN (0.07-0.33)] and those with no evidence of disease [0.10 fg/μg ARN (0.08-0.17)] (P<0.06). Patients who had not received RAI ablation showed Tg mRNA levels similar to those who had [0.11 fg/μg ARN (0.05-0.27)]. Test sensitivity was 69.6%, specificity was 59.4%, negative predictive value was 85.4% positive predictive value 36.4%

Conclusion: Our experience shows that Tg-mRNA could be useful as a rule-out test in selected cases, but its low sensitivity and specificity precludes its usefulness as a first-line test.

Disclosure of Interest: None Declared

Thyroid

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TYPHOID THYROIDITIS: DOES THIS TERM EXISTS?

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Introduction: Typhoid thyroiditis: Does this term exists?

Case Description: A 36-year old lady presented with fever and neck pain and tenderness for more than 2 months.

She first presented to another hospital with a fever of 38-39 C and severe neck pain and tenderness on the thyroid radiating to left ear. She had thyroid tests done and it showed high Ft3 and Ft4 and suppressed TSH. She had an ultrasound of thyroid and showed a thyroid nodule which was hypoechoic TIRADS 4. Fine needle aspiration cytology showed multinucleated giant cells with few follicular cells and epithelioid granuloma. A diagnosis of Dequervain's thyroiditis was made and analgesia given. She did not improve after 2 weeks and she was given steroids. She felt better, her neck pain and tenderness were improving but then after tapering the dose of steroids she started getting severe pain and tenderness again and fever of 39 C.

At this point she came to our hospital. She had a fever of 38.5 C and joint pains. She was admitted for a possible fever of unknown origin. Chest X ray was unremarkable as well as blood, urine and stool cultures. Brucella test negative. Widal test showed Salmonella typhi O and H >1/640 and paratyphi negative. Her CRP was 18.1 (N up to 0.5) and she had a raised FT4 2.56 ng/dl (N up to 1.7) and FT3 10.3 pmol/L (N up to 6.8) and TSH 0.008. WCC was 13.1 (neutrophils 79%), Hb 11.7 and Platelets 370. She was given IV ceftriaxone for 14 days. She improved and her neck tenderness and pain settled. Her fever gradually came down to 36.5 -37.5 C. Her anti thyroid peroxidase and anti-thyroglobulin and TSH receptor antibodies were negative. She was discharged and after 4 weeks her thyroid tests normalised and Widal test improved with S typhi (O) 1:80 and (H) 1: 160.

Clinical discussion: This is probably typhoid thyroiditis evidenced by improvement in thyroid tests only after treating typhoid. To my knowledge this was not reported before. Although Dequervain's thyroiditis is usually secondary to a viral illness, in this case it was probably triggered by typhoid fever. Widal test is not the gold standard but because of the long duration of the typhoid fever, the blood and stool culture do not show the Salmonella typhi. The only other option would have been a bone marrow culture but it was deemed too invasive and the results would have taken too long to wait for. In case of a fever lasting for a long time, it is prudent to start thinking laterally and thyroiditis in this case was a red herring, a secondary rather a primary cause of fever.

Disclosure of Interest: None Declared

Thyroid

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IMPROVEMENT OF TREATMENT RESISTANT DEPRESSION IN A PATIENT WITH PRIMARY HYPOTHYROIDISM AND THR92ALA5' TYPE 2 DEIODINASE GENE POLYMORPHISM WITH MULTIPLE DAILY DOSES OF TRIIODOTHYRONINE

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Introduction: The augmentation pharmacologic therapy used in patients with treatment-resistant depression (TRD) includes drugs such as lithium, buspirone, triiodothyronine (LT3) and other drugs. We report a patient with TRD and primary hypothyroidism who responded to a combination of LT3, given in divided doses, and levothyroxine (LT4), rather than LT4 alone, even though the serum TSH levels were in the normal range with these treatments. Interestingly, the patient had a Thr92Ala5' type 2 deiodinase polymorphism.

Case Description: A 54-year old male presented to our emergency room with suicidal ideation 8 years ago. The patient had severe depression and developed uncontrollable urges to surf the internet, generally prohibited sites, approximately 3 months prior to his visit to the emergency room. He had noted a 12-lbs weight gain, cold intolerance, dry skin, and excessive sleepiness for 3 months. Patient was admitted to the psychiatry ward and laboratory testing showed a serum TSH 180 μ IU/mL, FT4 0.48 ng/dL, total T3 46 ng/mL, and TPO antibody 278 IU/mL. A thyroid ultrasound was consistent with Hashimoto's thyroiditis.

A diagnosis of major depressive disorder and primary hypothyroidism was made. He was started on citalopram (20 mg/day) and levothyroxine (175 mcg/day). The Beck Depression Scores (BDS) during the initial weeks was 37.5 ± 5.1 (Mean \pm SD) (normal 0-9) with corresponding TSH 164 ± 133 μ IU/mL, FT4 0.70 ± 0.25 ng/dL, and total T3 61 ± 7.9 ng/mL. Two weeks later the dose of citalopram was increased to 40 mg/day and then buspirone 10 mg/day was added. At the end of 11 months the BDS was 27.81 ± 2.1 with a corresponding TSH 1.5 ± 0.1 μ IU/mL. After 4 months, 7.5 mg of aripiprazole was added. After 11 months of treatment, he was treated with a combination of LT4 + LT3 (5 mcg once daily) and TSH became 0.76 ± 0.1 μ IU/mL with a corresponding BDS of 18.0 ± 1.9 . When he was on LT4 + LT3 TID he was able to discontinue all antidepressants and he had no urge to surf on internet. His depression was controlled by over-the-counter drugs (S-adenosylmethionine and rhodiola). A genetic test confirmed Thr92Ala5' deiodinase 2 polymorphism.

Clinical discussion: In our patient, there was a good correlation between the BDS improvement and the serum T3 levels ($r: -0.7$ p-value: 0.01). Thus, in patients with Thr92Ala5' deiodinase 2 polymorphism TID T3 dosing may significantly improve depression. Additional studies are needed.

Disclosure of Interest: None Declared

Thyroid

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RAPIDLY PROGRESSIVE COGNITIVE DECLINE AND VARICELLA ZOSTER BLISTERS ASSOCIATED WITH TEPROTUMUMAB IN 2 PATIENTS WITH GRAVES' ORBITOPATHY

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Introduction: Teprotumumab, an IGF-1R antagonist, was approved for treatment of Graves' orbitopathy (GO) in 2020. Common side effects include nausea, diarrhea, muscle spasms, hearing impairment, dysgeusia, headache, dry skin, infusion reactions, and hyperglycemia. We report here 2 cases of unexpected adverse effects.

Case Description: **Patient #1** is a 76-year-old man with Graves' disease diagnosed in 2018, treated with methimazole 2.5mg every other day. His GO manifestations included diplopia, proptosis, and exposure keratopathy. He lived independently. After the 4th dose of Teprotumumab, his family noted 6-weeks of rapidly progressive cognitive decline characterized by behavioral changes, confabulation, memory deficit, delirium/delusions/mania. He was admitted to neurology service and subsequent doses held. Lumbar puncture was unremarkable. TFT was normal with elevated TSI but normal TRAb and TPO/TgAb. Encephalopathy-autoimmune panel was unremarkable. EEG showed no epileptiform activity. Head MRI/MRA showed cerebral amyloid angiopathy without stenosis or aneurysms in the intracranial arterial vasculature. Symptoms progressed with IV glucocorticoids and IV Ig therapy. He subsequently underwent plasmapheresis with resolution of symptoms.

Patient #2 is a 48-year-old man with Graves' disease and GO diagnosed in 2018, initially treated with methimazole and subsequently underwent total thyroidectomy in 2019. Patient is euthyroid on levothyroxine. Ophthalmic signs and symptoms included significant proptosis and retrobulbar pain. He was started on teprotumumab infusions. After his 4th dose, he noted painful vesicles in a dermatomal distribution on his right posterior thigh. DFA stain was positive for varicella zoster, and rashes resolved with valacyclovir therapy.

Clinical discussion: Paraneoplastic/autoimmune encephalitis syndromes can be associated with antibodies to neuronal cell surfaces/synaptic proteins and may occur in the presence or absence of cancer. The incidence of varicella-zoster infection is associated with the immune status of the patient, disease-related immunocompromised, or iatrogenic immunosuppression, with age being the major risk factor. This could be incidental, or related to other disorders, or perhaps teprotumumab may have activated auto-immunity. The exact mechanisms for rapidly progressive cognitive decline and shingles remains unclear.

Disclosure of Interest: None Declared

Thyroid

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LOW-DOSE PREDNISONE THERAPY IS EFFICACIOUS IN TREATING PAINFUL SUBACUTE THYROIDITIS

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Introduction: Subacute thyroiditis (SAT) usually presents with neck pain, radiating to ears and is often associated with hyperthyroidism. Currently the available treatment involves administration of NSAID or in more symptomatic patients prednisone 40mg daily tapered over 6 weeks or longer. We report successful treatment of 3 patients (Pts) with SAT with low-dose prednisone therapy (20mg/day) (LDP20) initially and tapered over 4 weeks.

Case Description: Patient 1: A 32-year-old female presented with severe neck pain radiating to both ears and low-grade fever of 2-weeks duration. Two weeks prior, patient had cold-like symptoms. Physical examination: HR 110bpm, hand tremors, tender anterior neck, thyroid 30-gms in size. Labs: ESR 92 mm/hr, CRP 3.2 mg/dL, TSH <0.005 uIU/mL, free T4 2.71 ng/dL, total T3 168 ng/mL. Thyroid scan and uptake showed a 24-hrs uptake <1%, thyroid gland not visualized, consistent with SAT. Patient was treated with atenolol and LDP20 tapered over 4 weeks with resolution of symptoms and normalized TFT.

Patient 2: A 19-year-old female presented with left-ear pain, anterior neck pain, fever, and extreme fatigue. PE: HR 111bpm, heat shield present, tender thyroid, brisk DTR. Lab: CBC normal, ESR 98 mm/hr, CRP 9.9 mg/dL, TSH <0.01 uIU/mL, free T4 3.8 ng/dL, total T3 210 ng/mL. Thyroid scan and uptake: uptake <1%, no thyroid gland visualized and SAT was diagnosed. Patient was started on LDP20 and atenolol with resolution of symptoms and normalization of TFT at week 7.

Patient 3: A 38-year-old man presented with fever, fatigue, severe neck pain, palpitation and a weight loss of 8 pounds. PE: HR 120 bpm, tender thyroid, brisk DTR. Lab: normal CBC, ESR 128 mm/hr, CRP 11.9 mg/dL, TSH <0.001 uIU/mL, free T4 4.2 ng/dL, total T3 201 ng/mL. Thyroid scan: thyroid gland not visualized and uptake was < 1%. SAT was diagnosed and patient was treated with propranolol and LDP20 with resolution of symptoms and normalized TFT at week 8.

Clinical discussion: SAT is a painful disabling thyroid disorder apparently caused by a viral infection; and NSAID or high-dose steroid treatment remains the standard of care. We have treated 3 Pts with relatively lower doses of prednisone than previously recommended and attained remission successfully. Thus side effects can be avoided with lower prednisone dose.

Disclosure of Interest: None Declared

Thyroid

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DESICCATED THYROID EXTRACT VS. SYNTHETIC T3/T4 COMBINATION VS. LT4 MONOTHERAPY IN THE TREATMENT OF PRIMARY HYPOTHYROIDISM WITH SPECIAL ATTENTION TO THE GENE POLYMORPHISM.

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Introduction: Before the availability of levothyroxine (LT4), patients were treated with desiccated thyroid extract (DTE). When switching from DTE to LT4, despite adequate dosing based on serum TSH levels, some patients still feel unwell with fatigue, mental fogging, weight gain etc. A recent randomized, crossed over study between DTE vs. LT4 showed that once-daily DTE caused modest weight loss and possible improvement in mental health scores without appreciable adverse effects; also, nearly half of the study patients preferred DTE over LT4. A few studies showed that LT4/T3 combination had beneficial effects in improving quality of life relative to LT4 alone. Furthermore, patients with CC genotype in the deiodinase 2 polymorphism responded more favorably with LT4/T3 combination than T4 monotherapy.

Objectives: This study investigated the efficacy and effectiveness of DTE vs. LT4/T3 combination vs. LT4 monotherapy in hypothyroid patients based on genotypic differences of deiodinase 2.

Methods: This was a prospective, randomized, crossover study. 75 subjects completed the study. There were 3 arms: DTE, LT4+T3 combination, and LT4 alone. Each subject was randomly allocated to one of these 3 arms for 12 weeks. The primary endpoint was post-treatment score on the 36-point thyroid symptom questionnaire. Secondary endpoints were weight, general health questionnaire, the Beck depression inventory, Wechsler Memory testing, lipid panels and thyroid function tests.

Results: There was no significant difference between the 3 arms on the thyroid symptom questionnaire ($p=.32$), and the secondary outcomes showed no between group differences. Auditory memory index ($p=.008$), and visual working memory index ($p=.02$) were higher in the Hashimoto's than non-Hashimoto's group. There was no significant primary or secondary outcome difference among various genotypes of deiodinase 2. There was no relationship between Hashimoto's vs. non-Hashimoto's based on genotypes or likelihood of carrying Thr92AlaD2 polymorphism. Though there was no statistically significant preference for any treatment, numerically more patients with Hashimoto's preferred DTE and LT4/T3 combination than LT4-monotherapy.

Conclusion: There was no significant difference between hypothyroid patients taking DTE vs. LT4/T3 combination vs. LT4 monotherapy. Numerically, Hashimoto's patients tended to prefer DTE and LT4/T3 combination. Also, there was no observed relationship between Hashimoto's and polymorphism. Further studies with more patients may be needed.

Disclosure of Interest: None Declared

Thyroid

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TREATMENT OF GRAVES' DISEASE WITH A COMBINATION OF LOW IODINE DIET AND POTASSIUM IODIDE PLUS RADIOACTIVE IODINE TREATMENT.

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Introduction: Graves' disease (GD) is usually treated with radioactive iodine I¹³¹ (RAI), thionamides or surgery. Of these, RAI remains the safest and most efficacious treatment. We report 3 patients with GD who were treated with low iodine diet (LID), followed by RAI and subsequent potassium iodide (SSKI) administration.

Case Description: Patient 1- A 50-year-old male was diagnosed with GD and treated with methimazole. Three weeks later CBC showed an absolute neutrophil count 820. After discontinuing methimazole, he was placed on prednisone 40mg daily and LID. Two weeks later (24-hours urine iodine <50 mcg) and patient received 15mCi I¹³¹. 72 hours later he was administered SSKI one drop BID for 3 days. Two months later, he required levothyroxine for hypothyroidism.

Patient 2 - A 23-year-old female presented with new onset GD. Patient was started on methimazole and atenolol. Four weeks later she developed severe generalized erythematous rash. After treating with prednisone for one week she was placed on LID and treated with 15 mCi I¹³¹. Four months later she required levothyroxine for hypothyroidism.

Patient 3 - A 40-year-old man presented with new onset GD. He refused to take methimazole due to fear of adverse effects. After placing him on prednisone along with LID for 2weeks, he was treated with I¹³¹ 15 mCi. 72 hours later he received SSKI one drop BID for 3 days. Prednisone was discontinued 2 weeks later. Patient remained euthyroid for the next 12 months of follow up.

Clinical discussion: LID given before RAI therapy has a potential of depleting total iodine pool which can increase the I¹³¹ uptake and facilitate b-radiation in thyroid gland. SSKI following RAI can improve retention of I¹³¹ in thyroid gland and reduce the recycling of radioactivity. In summary, a LID prior to RAI and SSKI following RAI treatment be beneficial in certain patients with GD.

Disclosure of Interest: None Declared

Thyroid

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DUAL BRAF AND PKCA INHIBITION DIMINISHES CELL VIABILITY IN THYROID CANCER CELLS

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Introduction: Thyroid carcinoma (TC) is the most common endocrine neoplasia. Its incidence has increased in the last 40 years worldwide. About half of TC are driven by an acquired activating mutation in the BRAF oncogene. While targeted therapies have improved outcomes in melanoma patients, most TC patients become resistant or recur suggesting that new or additive non-cross-reactive therapies are needed. We have previously shown that PKC α mediates TSH and thyroid hormones proliferative effects in TC. Recent evidence indicates that PKC α overexpression and BRAF mutation should contribute together to tumorigenesis and resistance to anticancer therapies.

Objectives: To analyze whether PKC α expression together with the presence of BRAF^{V600E} confer an advantage over tumor growth.

Methods: 8505C anaplastic and WRO follicular TC cell viability was evaluated by Cell Titter Blue (CTB) assay. Protein modulation was measured by Western blot. RNAi transfection was used to knock down PKC α and BRAF expression. Vemurafenib (PLX) and GF109203X (GF) were used to inhibit BRAFV600E and PKC α , respectively. *In silico* analysis on Papillary Thyroid Carcinoma (TCGA, Cell 2014) was performed using CBioPortal.

Results: We found that by inhibiting BRAF expression in TC cells with BRAF mutation, PKC α expression also decreases, suggesting that the latter is downstream of BRAF. Furthermore, a decrease in the expression of the proliferation marker PCNA was observed in BRAF-depleted cells. To begin to study the combined inhibition of PKC and BRAF, CTB assays were performed with increasing doses of PLX in presence or absence of the PKC inhibitor GF at a selective concentration in TC cells carrying BRAF mutation. We found a decrease in cell viability in a dose-dependent manner with PLX ($p < 0.0001$) even higher with the combined treatment ($p < 0.5$). Finally, we performed bioinformatic analysis on a TC patient's cohort with BRAF^{V600E} and divided it in low and high PKC α protein expression subsettings. Protein expression analysis showed an upregulation in proliferation mediators and BRAF signaling pathway effectors in the second group, enhancing the potential benefit on targeting both proteins in TC patients.

Conclusion: Our results establish that the effective dual PKC α and BRAF blockade can significantly drive tumor proliferation inhibition. The results obtained could provide new therapeutic targets and alternatives to the treatments currently used for this disease.

Disclosure of Interest: None Declared

Thyroid

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MYXEDEMA COMA: ABOUT A CASE

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Introduction: Myxedematous coma is a rare endocrinological emergency associated with organ dysfunction and with a mortality up to 50%. Its diagnosis and treatment presents a challenge in older adults due to its latent symptoms and the presence of comorbidities that may limit the initiation of aggressive therapy.

Case Description: It is reported a case of a self reliant 85 year old woman with a history of arterial hypertension and type 2 diabetes mellitus, who is taken by her son to the emergency service after presenting 20 days of progressive drowsiness, food rejection and loss of strength in the extremities.

The physical examination revealed normotension, bradycardia (56 bpm), normothermia (36°C) and adequate O₂ saturation (98%). She showed a puffy and pale face, palpebral and limb edema and a cold, dry and scaly skin. Thyroid was not palpable. Neurologically, she was somnolent, disoriented, inattentive, bradypsychic, overcoming gravity in 4 extremities and without neurological focality.

Analytics revealed severe hyponatremia (100 meq/l) and moderate hyperkalemia (2.6 meq/l). Electrocardiogram without abnormalities. She is admitted to the intensive care unit for monitored correction of electrolyte disorder. 36 hours later, the patient progresses with greater consciousness compromise until stupor and temperature of 35.5°C, with persistent bradycardia. The study was completed with thyrotropin (45.7 mu/ml), free thyroxine (0.06 ng/dl) and triiodothyronine (<0.195 ng/dl). Echocardiogram and Brain MRI without alterations. Chest X-Ray showed mild pleural effusion. Myxedematous Coma Score is calculated, obtaining a total of 65 points.

The family was re-interrogated, obtaining the antecedent of hypothyroidism with hormonal treatment suspension 1 year ago. Thyroid ultrasound compatible with chronic thyroiditis.

In absence of intravenous thyroid hormones, treatment with oral levothyroxine by nasogastric tube and intravenous hydrocortisone was started. This last was suspended after ruling out adrenal insufficiency. The patient had a favorable progress.

Clinical discussion: Myxedema coma is the most serious complication of hypothyroidism, occurring more frequently in older adults, women and in patients with previous diagnosis of hypothyroidism who had suspended therapy, as in the case resented. Although it is a very rare entity, it should always be suspected in cases of conscience compromise, to manage it opportunely and avoid the mortality rates that it entails.

Disclosure of Interest: None Declared

Thyroid

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A DEMOGRAPHIC PROFILE OF ACS ASSOCIATED WITH THYROID DYSFUNCTION IN A NORTH INDIAN POPULATION

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Introduction: Thyroid dysfunction has an important bearing on the cardiovascular system leading to hypertension, dyslipidemia, heart rhythm disorders, obesity etc.

Objectives: The primary objective is to determine the prevalence of thyroid dysfunction in patients with Acute Coronary Syndrome, including STEMI, NSTEMI and Unstable Angina groups. The secondary objective is to see if there is an association between the thyroid dysfunction groups and the euthyroid group with the various risk factors for CAD.

Methods: The study was conducted in the cardiology department of BHMRC, New Delhi. Patients with ACS above the age of 18 years, presenting within 24 hours of their symptom to the coronary care unit were enrolled in the study.

Results: A total of 171 ACS patients were analyzed. Out of 171, 94 (72%) were males with a mean age of 59 years. There was a statistical difference in the prevalence of thyroid dysfunction vs Euthyroid status in all age categories. According to gender, the prevalence of thyroid dysfunction was 19 (47%) in males vs 21 (53%) in females, the difference being statistically different ($p=0.04$). Regarding the correlation with serum lipid levels, there is a statistically significant difference in the thyroid status and decreased HDL C, Increased total cholesterol, triglyceride and increased VLDL C. However, differences were not different for LDL C. There is a statistically significant difference in the association between thyroid dysfunction and Euthyroid group in terms of Creatinine. There is a significant correlation between eGFR and various categories of thyroid dysfunction.

Conclusion: Our prospective study conducted on patients admitted with ACS in a tertiary care hospital had 23 % of patients having abnormalities of thyroid function. Subclinical hypothyroidism was the commonest abnormality (23%), followed by overt hypothyroidism (9%). Sub-clinical hyperthyroidism was uncommon (1.5%). Euthyroid sick syndrome was seen only in 4% of patients. STEMI followed by NSTEMI were the diagnosis in patients with thyroid dysfunction. There was a predilection for elderly females with a high prevalence of dyslipidemias as compared to the euthyroid group. Patients with hypothyroidism had a predilection for renal dysfunction. The LVEF in the group with hypothyroidism had a trend to be lower. Hypothyroidism seems to be an important risk factor in patients with ACS especially STEMI.

Disclosure of Interest: None Declared

Thyroid

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RECURRENCE OF FOLLICULAR THYROID CARCINOMA AS SUBCUTANEOUS METASTASIS AFTER 10 YEARS OF TOTAL THYROIDECTOMY

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Introduction: Follicular thyroid carcinoma (FTC) is the second most common cancer of the thyroid and occurs more commonly in women over 50 years of age. Follicular carcinoma patients with extensive vascular invasion exhibit a poorer prognosis, and distant metastases are occasionally present. Hematogenous metastasis is most commonly observed. We present the case of a patient who sustained a subcutaneous lesion diagnosed as metastasis of a follicular thyroid carcinoma operated 10 years earlier.

Case Description: A 78-year-old woman with a personal history of hypertension, diabetes mellitus and total thyroidectomy in 2008 due to extensively invasive follicular thyroid carcinoma (pT3N0M0) was seen in our department. He completed ablative treatment with ¹³¹I and initial TSH suppression over two years. In the periodic follow-up (every 6 months) serum levels of thyroglobuline (Tg) and anti-thyroglobuline antibodies (Anti-Tg antibodies) were made Ten years after the first surgery (2019) a subcutaneous nodule was referred near the scar of cervicotomy

After studying this mass (ultrasound, fine needle aspirate and CT), it was diagnosed as a cervical recurrence of the follicular carcinoma

An exploratory cervicotomy was performed, where subcutaneous lesions were found, both in the prethyroid musculature and in the right central compartment, extending to the mediastinum. It was also found a local invasión of the right internal jugular vein. Thus, a partial resection of the recurrence was performed.

The definitive anatomopathological study showed a poorly differentiated carcinoma in all samples submitted

Radioactive iodine therapy and external radiotherapy treatment were indicated.

Currently serum levels of Tg and Anti-Tg antibodies are undetectable

Clinical discussion: - Although differentiated thyroid carcinoma has a good prognosis and 10-year survival greater than 95%, late recurrence may occur, as in the case that we present, even 10 years after initial surgical treatment.

- Once again, insist on the importance of the value of Tg and Ac antiTg in the follow-up as evidence of recurrence. The elevation of these values is due, generally, to cervical recurrence.

- Surgical treatment is always indicated to decrease tumor mass and when complete resection is not possible. Adjuvant treatments (¹³¹I and external radiotherapy) are fundamental for both local and distant control of the disease.

- Long-life follow up is recommended in thyroid cancer patients.

Disclosure of Interest: None Declared

Thyroid

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THORACIC DUCT FISTULA AFTER THYROID SURGERY

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Introduction: Thoracic duct injury and chyle fistula is a rare complication (incidence of 1-5.7%) after thyroid surgery with a significant negative impact on the patient if not managed properly.

The thoracic duct is particularly susceptible to inadvertent injury during dissection in the low neck during lymphadenectomy.

We present two patients, whom underwent surgery for thyroid cancer, that developed a thoracic duct fistula in the postoperative period. Conservative treatment with nutritional measures and somatostatin or octeotride, was administered. Prompt identification and treatment of a chyle fistula are essential for optimal surgical outcome.

Case Description: Case 1: it involves a smoker and toxic drinker 65 year old man diagnosed as papillary carcinoma with left lateral lymphatic involvement (cT3N1M0). A total thyroidectomy, with central bilateral and functional lateral lymphadenectomy were performed. Intraoperatively a thoracic duct injury was suspected, and repaired. Nevertheless on the second post-op day the patient developed a chylous fistula. Treatment was initiated with parenteral nutrition and somatostatin administration. After 1 week of conservative treatment, somatostatin was replaced by octeotride every 12 hours, achieving closure of the fistula within 72 hours.

Case 2: it involves a 49-year-old woman with a history of hyperthyroidism treated with oral antithyroid drugs. In the course of the studies carried out, a suspicious lesion of malignancy was found. FNAB was performed and revealed the diagnosis of papillary carcinoma (Bethesda V) with left lateral lymphatic involvement (cT1N1M0). Total thyroidectomy, bilateral central lymphatic and left functional lymphadenectomy were performed. On her second post-op day there was an outflow of milky liquid in the drainage. Chylous fistula was diagnosed. The oral route was discontinued, parenteral nutrition was administered, with supplements. Treatment was prescribed with octeotide and at 48 hours the chylous fistula disappeared

Clinical discussion: Although chylous fistula after thoracic duct injury is infrequent in thyroid surgery, it should be kept in mind as a complication after lateral cervical lymphadenectomy, especially on the left side.

The cornerstones of the treatment of chylous fistula are physical rest, dietary changes, Parenteral nutrition with nutritional supplements (medium chain triglycerides) and adequate drainage.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1335

THE COMBINATION OF HYPERTROPHIC CARDIOMYOPATHY AND HYPERTHYROIDISM

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Introduction: The combination of hypertrophic cardiomyopathy and hyperthyroidism gives rise to a complex clinical picture as some of the symptoms and signs may be common to both conditions.

Case Description: We report a case of 39 years old patient admitted for evaluation of a suspected hypertrophic cardiomyopathy. Anamnesis showed a sudden death event in the brother. The patient suffered dyspnea for 4 months without syncope. Clinical examination found blood pressure at 100/60 mmHg and heart rate at 75 bpm. Cardiovascular examination revealed a 3/6 systolic murmur in the mitral focus and a 3/6 systolic murmur in the aortic focus. The ECG showed a regular sinus rhythm at 75 bpm, an electric left ventricular hypertrophy and a Q wave of pseudo necrosis in septo apico-lateral territory. Echocardiography showed an aspect of asymmetric left ventricular hypertrophy predominantly septal, with the presence of a SAM and acceleration of the flow with a gradient of obstruction at rest at 53mmHg. Ventricular function was 60%. Cardiac MRI confirmed a diffuse hypertrophy involving the septum up to 17mm of maximum thickness with an obstruction to the ejection of the left ventricle as well as the presence of a focus of intramyocardial fibrosis at the level of the septum and the LV junction. The blood samples showed a collapsed TSHus at 0mIU/l and an elevated level of T3 at 5.5ng/l. The patient was placed on beta-blocker and synthetic antithyroid drugs with indication for monitoring his heart disease without surgical indication.

Clinical discussion: The clinical diagnosis of hypertrophic cardiomyopathy in the presence of hyperthyroidism is difficult to make since many of the physical signs are common to both diseases, viz, rapid upstroke pulse, mild hypertension, left ventricular type of cardiac impulse, and a systolic murmur at the left sternal edge. Dysrhythmias commonly occur in both conditions, multiple ventricular ectopic beats and atrial fibrillation, and although pre-excitation has been recorded in thyrotoxicosis, it is not possible to state if either hypertrophic cardiomyopathy or thyrotoxicosis is the cause of this abnormality. Hopefully, our patient didn't experience any dysrhythmias. Thyrotoxicosis has been known to cause cardiac hypertrophy as shown by necropsy studies, but no contemporary data exist to compare these changes with the features of hypertrophic disease. Thyrotoxicosis should be treated rapidly to prevent dysrhythmias in such patients which could be extremely lethal especially in patients with a high gradient of obstruction.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1337

VALPROIC ACID INCREASES RADIATION SENSITIVITY OF ANAPLASTIC THYROID CARCINOMA CELLS

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Introduction: Histone deacetylase (HDAC) inhibitors have emerged recently as promising anticancer agents. The antitumor activity of HDAC inhibitors has been linked to their ability to induce gene expression through acetylation of histone and nonhistone proteins. Anaplastic thyroid cancer (ATC) is a rare and aggressive malignancy. Radiotherapy (RT) is one of the main modalities of treatment for ATC. In most patients, surgical resection is not possible. Therefore, RT either as altered fractionation or in combination with chemotherapy has an important role in achieving local control.

Objectives: The objective was to study the effect of valproic acid in the radiation response at different doses in an ATC cell line.

Methods: Cells (8505c) were incubated with 1 mM VA and irradiated with gamma rays at different doses (2 and 5 Gy). Radiation response was analyzed by clonogenic assay. Cell cycle and cell death were measured 24 and 48 h after irradiation. DNA damage and Ku80 expression were evaluated 30 min and 24 h after irradiation. MicroRNA (miR) expression was analyzed by microarray analyses at 2 Gy.

Results: A reduction of survival fraction at 2 Gy was observed in the treated cells ($p < 0.05$). VA treatment increased apoptotic cell death 24 and 48 h after irradiation at 5 Gy ($p < 0.001$ and $p < 0.05$, respectively). Average γ H2AX foci number was increased at 30 min with VA ($p < 0.01$). Average foci size and the frequency of foci larger than $1.0 \mu\text{m}^2$ were enhanced at 24 h in the 2 Gy+VA cells ($p < 0.01$). Ku80 expression was reduced in the 2+AV (30 min) compared to 2 Gy. We found 36 significantly up- (25) or downregulated (9) miRs in the 2 Gy+VA cells compared to irradiated only cells. A pathway enrichment analysis for differentially expressed (DE) miRs was performed using the online Database for Annotation, Visualization and Integrated Discovery (DAVID). In the top 20 DE miRs, miR-27a-3p (fold change:-3.95, $p < 0.0082$), miR-26a-5p (fold change:-2.12, $p < 0.0065$) and miR-486-5p (fold change:3.14, $p < 5.24 \times 10^{-5}$) presented as targets, genes functionally enriched in signal pathways related to DNA damage response, cell cycle, apoptosis and the Wnt/ β -catenin signaling pathway.

Conclusion: These results suggest that VA pretreatment could have an important role in enhancing the effect of radiation in ATC cells. Particularly, the radiosensitizing effect could be mediated by a reduction in the DNA damage repair capacity at low doses (2 Gy).

Disclosure of Interest: None Declared

Thyroid

ICE2021-1338

THE IMPACT OF COEXISTENT CHRONIC LYMPHOCYTIC THYROIDITIS ON PROGNOSIS IN PAPILLARY THYROID MICROCARCINOMA

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Introduction: The coexistence of papillary thyroid carcinoma (PTC) and chronic lymphocytic thyroiditis (CLT) has been reported to range from 0,5 to 38 %(1). The impact of coexistent CLT on prognosis in papillary thyroid micro carcinoma (PTMC) remains controversial. The aim of this study was to determine whether CLT was associated with favorable prognosis in PTMC.

Case Description: It was a retrospective study which included the patients with PTMC, treated at our Department from January 2005 to December 2017.

There were a total of 56 patients. The mean age of these patients was 45,2 years. Three patients underwent a lobectomy and 53 underwent a total thyroidectomy. A central lymph node dissection was performed for 31 patients, associated to a modified lateral lymph node dissection in 9 patients. There were 9 patients with CLT in our study population. There were no significant differences in terms of age and sex between the PTMC and PTMC+CLT groups ($p= 0,08$ and $0,58$ respectively). The PTMC was unifocal in 39 patients and multifocal in 17. There was no significant association between CLT and the type unifocal or multifocal of the PTMC. Extra thyroidal extension was observed in one patient. CLT was not associated with extra thyroidal extension ($p= 1$). According to the extent of nodal metastasis, seven patients presented as N1a and four presented as N1b. There were no significant differences between the PTMC and PTMC+CLT groups ($p= 0,07$). The mean follow-up duration was 36 months. Recurrence occurred in two patients. CLT was not a risk or protector factor for recurrence in PTMC patients ($p=0,06$).

Clinical discussion: It was reported that the coexistent CLT was associated with a lower frequency of extra thyroidal extension and had insignificant protective effect on nodal metastases and prognosis in PTMC(1,2). In our study, we did not find any significant association between these factors. A large prospective study could provide more powerful evidence for the correlation of CLT and PTMC.

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Disclosure of Interest: None Declared

Thyroid

ICE2021-1342

FOLLICULAR THYROID MICRO CARCINOMA: DIAGNOSIS AND TREATMENT

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Introduction: Although papillary micro carcinoma is largely studied, very few reports and studies are present in literature about follicular thyroid microcarcinoma (mFTC), mainly for its low incidence(1). No data is available for mFTC and little is known about its incidence, biological behaviour, prognosis and treatment (2).

The aim of this study was to investigate the diagnostic and therapeutic characteristics of mFTC.

Case Description: A retrospective study about mFTC patients, treated at our Department from January 2005 to December 2017. We collected 5 cases with mFTC among the 61 patients with thyroid micro carcinoma (8%). They were one man and four women (mean age 54 (range 28 - 70) years). None had undergone previous neck irradiation. Primary indication for surgery was a suspected malignancy for one case and a goitre in 4 cases. All patients had total thyroidectomy, associated to a central neck dissection in one case. The mFTC was unifocal in all cases. Tumour size was 8,4 (range 5–10) mm. Vascular infiltration was found in two tumours and penetration of the capsule in four. None had extra thyroidal extension. One patient had nodal metastases. According to the 2015 ATA risk classification, 4 patients were at low risk and one patient was at intermediate risk. Following surgery, long-term thyroid hormone was administered. It was a replacement therapy in four cases and a suppressive treatment (suggested target TSH value <0,1mUI/L) for one patient. Two patients underwent postoperative ¹³¹I therapy. After a mean follow-up period of 3 years, all patients remained disease-free.

Clinical discussion: There are no specific regulations in the guidelines for the surgical treatment of mFTC(1). According to some authors, there is evidence that mFTCs without vascular invasion have an excellent prognosis even with limited thyroidectomy. However, in the other cases total thyroidectomy should be performed(3).

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Disclosure of Interest: None Declared

Thyroid

ICE2021-1348

HYPERTHYROIDISM IN OUTPATIENTS DURING THE COVID 19 PANDEMIC. EXPERIENCE OF A REFERRAL CENTER IN THE CITY OF BUENOS AIRES

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Introduction: Different changes in thyroid function have been described in Covid 19 + patients, including subacute post-infection thyroiditis and reactivation of autoimmune hyperthyroidism.

Although attention has been focused on the viral infection, the stressful situation arising from the pandemic and especially quarantine, should be considered as another determinant of thyroid changes. This should also affect non-Covid population.

OBJECTIVES 1) To evaluate new cases of hyperthyroidism diagnosed in non-Covid outpatient from an endocrinology referral center in the City of Buenos Aires during the pandemic 2) Determine its etiology, severity. 3) To compare it with cases diagnosed in the same period of the previous year.

Case Description: MATERIAL and METHODS There were 435 Total T3 determinations reviewed, between the start of Covid quarantine in Argentina 03/20/2020 and 11/20/2020. The results above the upper reference limit (175 ng/dl) were analyzed. It was possible to establish the number of patients with clinical hyperthyroidism diagnosis who made their first consultation during this period. Thyroid status was confirmed with Total T4 and TSH determinations. The number of cases was established in the same period of the previous year, using the same system. Aetiology was established with clinic, evolution and TSI/TRAb

Total T3, total T4, TSH and TSI, were measured by the IMMULITE 2000 XPi enzyme-linked chemoluminescence assay, Siemens. TRAb was measured by Cobas e411 electrochemiluminescent assay, Roche

Statistics Student T Test- Fischer Test

Clinical discussion: Results

| | March-November 2020 n=15 | March-November 2019 n=30 | |
|--|-----------------------------|--------------------------|---------|
| TT3 Determinations | 435 | 1132 | |
| Hyperthyroid Patients | 33 | 57 | |
| 1st Consultation | 15/33 | 30/57 | |
| | | | p |
| TT3 ng/dl | 417.79±160.69 | 278.03±111.47 | p<0.001 |
| TT4 ug/dl | 19.53±4.83 | 18.56±4.02 | NS |
| TSH uUI/L | <0.001 | <0.001 | NS |
| TSI >0.55 UI/L | 14/15 | 26/30 | NS |
| TRAb >1.75 UI/L + Autoimmune Etiology | 14/15 | 26/30 | NS |
| Not -autoimmune | 1/15 | 4/30 | NS |
| Lesional | 0 | 0 | |

Conclusions

1) During the pandemic, 15 new cases of hyperthyroidism were diagnosed. Such figure represents half the number of cases in comparison with the previous year.

- 2) Autoimmune etiology prevalence was similar.
- 3) No lesional thyroiditis was detected in those outpatients, clinically non-Covid evaluated from elevated T3.
- 4) Total T3 was significantly higher in 2020, reflecting that only the most severe hyperthyroidism cases attended consultation

Disclosure of Interest: None Declared

Thyroid

ICE2021-1357

NOX-4 AND SELENIUM INFLUENCES IN THYROID PI3K SIGNALING IN THYROID CELLS.

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Introduction: Na/I symporter (NIS) mediates iodide (I) uptake in the thyroid gland, the first and rate-limiting step in the biosynthesis of thyroid hormones. Thyrotrophin (TSH) and insulin/IGF-I regulates the expression and function of NIS. While TSH has stimulatory effects, insulin/IGF-I exerts its inhibitory effects through the PI3K/akt pathway. Iodine excess inhibits NIS expression through PI3K/akt pathway activation which involves ROS production. Other factors like TGFB1 and the 2-iodohexadecanal (2-IHDA), have inhibitory effects on NIS expression while Selenium stimulates it. We reported that NADPH oxidase NOX4 knockdown prevents the increase of intracellular ROS and reverts the inhibitory effect on NIS induced by iodide excess.

Objectives: The aim of this work was to analyze the role of NOX4, Iodoheptadecanal (2-IHDA) and Selenium on PI3K/akt pathway activation and NIS expression in thyroid cells.

Methods: FRTL-5 cells were pretreated with and without Selenium (0.1 μ M) and after 48 h cells were incubated with TSH, TSH +KI (10 and 100 μ M) or 2-IHDA (10 and 30 μ M) in the presence or absence of Selenium. ROS was evaluated by the DCFH-DA-derived fluorescence. GPx, NIS and TGFB was evaluated by Real Time PCR. For siRNA target knockdown of NOX-4 FRTL-5 cells were transfected with siRNA NOX4 (50 nM) or Scrambled and cultured in the presence or absence of KI (100 μ M) for 1 h. Akt/p-akt was analyzed by immunocytochemistry and western blot.

Results: Selenium pretreatment reverted the effect of iodine excess on ROS levels ($p < 0.01$) and GPx expression ($p < 0.01$), akt phosphorylation ($p < 0.05$) and NIS expression ($p < 0.05$). Besides Selenium increased GPX-1 (1.5 fold, $p < 0.05$), NIS (1.8 fold, $p < 0.05$) and decreased TGFB1 ($p < 0.05$) mRNA. 2-IHDA induced akt phosphorylation (1.8 fold, $p < 0.05$), the PI3K inhibitor (LY294002) and Selenium reverted the inhibitory effect of 2-IHDA on NIS and GPx mRNA gene transcription. Even though 2-IHDA induced TGFB1 (2 fold, $p < 0.05$) and treatment with TGFB inhibitor (SB431542) did not reverse the inhibitory effect of 2-IHDA or iodine excess on NIS expression. KI treatment induced Akt phosphorylation in scrambled siRNA-transfected cells but not in NOX4 siRNA transfected cells ($p < 0.05$).

Conclusion: These results suggest that NOX4 and Selenium plays a critical role in Akt phosphorylation in FRTL-5 cells that influence NIS expression.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1359

THYROID CANCER MULTICENTER STUDY IN ADULT POPULATION OF CORDOBA (ARGENTINA): A RETROSPECTIVE (1999-2019) 20 – YEARS STUDY

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Introduction: The incidence of thyroid cancer (DTC): true or due to diagnostic improvement is on the rise. STUDY DESIGN: Retrospective analysis.

Objectives: To evaluate the prevalence and variables associated with response to treatment in Province of Cordoba (Argentina).

Methods: Data of contributing Centers in public and private settings. Outcomes of interest were sex prevalence, trend in rural areas with environmental toxics, and Hashimoto's thyroiditis (HT) as a risk factor.

Results: Total patients were 369 : 27% from Public and 73% from Private Centers, 58% from urban and 42% from rural areas. Female (F) / Male (M) ratio : 4.5. Mean±SD age at diagnosis (AD): 46 ± 13years. Predominant histological type: papillary (96.2%). The prevalence (P) was 10.45 and 34.5 cases per year between 1999 -2012 and between 2013 – 2019 respectively with an increase in microcarcinomas in the last years. A higher % of cases was observed in M, both in fumigated areas (FA) vs. no fumigated areas (NFA): (M 8% vs. F 6% and M 13% vs F 3% respectively), (p: 0.006). the same as a higher percentage of broad capsular invasion (M 23% vs. F11% and M 5% vs. F 3%) respectively. p: 0,040. Recurrence risk (RR) was higher in both Men and Women in FA vs. NFA (M 23% vs. 6% and F 11% vs. 5%) respectively. AD was different in FA vs. NFA: 35-39 vs 50 -54 years respectively (p: 0.0001). Diabetics showed a higher P compared to non-diabetics, (39% vs. 29%) p: 0.001) ,: The influence of autoimmunity (on tumor aggressiveness and response to treatment showed that positive TgAb patients (+TgAb) had more extensive lymphovascular invasion compared to negative TgAb pt (- TgAb). OR : 14.83 (95% CI: 3.21 - 68.41). Also, + TgAb had a higher RR (OR : 3.01 (95% CI: 1.10 - 8.23) and P (OR : 2.62 (95% CI: 1.36 - 5.04) compared to (-TgAb); + TPOAb patients had 70% of excellent response vs. 30% of -TPOAb p: 0.0008.

Conclusion: Data were established for DTC trend in Province of Cordoba (Argentina). There are an heterogeneous incidence across different areas, increased and at earlier age in rural areas with environmental toxics. Size and tumor aggressiveness were higher in males than in women. + TgAb should be regarded as a risk condition for an active search for R or P disease. Until the association HT and DTC is clarified, patients with HT should monitored periodically for underlying thyroid malignancy.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1372

HETEROGENEOUS PRESENTATION OF AUTOIMMUNE THYROID DISORDERS IN ONE FAMILY

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Introduction: Autoimmune thyroid disorders (AITDs) are common affecting around 5% of the general population mainly women less than 50 years of age (1). The etiology is multifactorial including genetic, environmental and endogenous factors (2). The most common types are Graves and Hashimoto thyroiditis, Progression from Graves' hyperthyroidism to chronic autoimmune thyroiditis and hypothyroidism is well recognized (3). We are reporting multiple members from one family diagnosed as AITDs presenting with thyrotoxic symptoms and had variable clinical courses, the diagnosis based on clinical and biochemical findings because of limitation of services.

Case Description: The first member is the father, he presented at 5th decade of age with goiter, palpitation, tremor and weight loss. Thyroid hormones were high for what he was started on antithyroid drugs (ATD), he was refusing radioactive iodine (RAI). Over 4 years of follow up his clinical condition was fluctuating between hypothyroidism euthyroidism and hyperthyroidism later he developed spontaneous remission for five years then hypothyroidism. The second patient is his son, he presented at 5th decade of age with goiter palpitation tremor and weight loss. Clinically he had a unilateral exophthalmos, the laboratory findings showed hyperthyroidism. He received 4 months of ATD then kept on remission for 5 years. Next member was his second son who presented in the 4th decade of age with palpitations tremor and weight loss, thyroid hormone was high with a granulocytosis, he was started on ATD, after 6 months he developed remission. The last member was the daughter, she was diagnosed to have hyperthyroidism in the second decade of age, when she presented with palpitation heat intolerance tremor weight loss with no extra-thyroid symptoms. She was started on ATD with fluctuating course for 9 years. Finally, she received RAI and maintained on thyroxine replacement, she was recently diagnosed with Rheumatoid Arthritis.

Clinical discussion: Although no serological tests were done to any of the patients, the autoimmunity of the illness was suggested by multiple findings in this family. Having a fluctuating response to treatment over years in some members, indicating the probability of existing stimulating and blocking anti TSH receptor antibodies, the extra thyroid manifestations like exophthalmos and a granulocytosis in different members are another clue in addition to the coexistence of another autoimmune disease like rheumatoid arthritis. AITDs can have a spectrum of presentations among one family

Disclosure of Interest: None Declared

Thyroid

ICE2021-1379

FAMILY PRIMARY HYPERPARATHYROIDISM IN THREE PATIENTS CARRIERS OF THE MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 MUTATION.

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Introduction: Multiple endocrine neoplasia type 1 (MEN1) is a rare heritable disorder classically characterized by a predisposition to tumors of the parathyroid glands, anterior pituitary, and pancreatic islet cells

The main problem is the management of those members of the family diagnosed with MEN1 because Multiple parathyroid tumors causing hyperparathyroidism are the most common manifestation.

It has also resulted in differences of opinion with respect to optimal surgical management of this disorder because patients with classical MEN1 are at high risk of recurrent hyperparathyroidism after apparently successful subtotal parathyroidectomy and need for another operation in the future

Case Description: We present three cases of MEN1 in the same family.

The index case was a 17-year-old girl who in a study for primary amenorrhea and headache, detected a pituitary lesion compatible with a macroprolactinoma associated with hypercalcemia and confirmed in subsequent blood test. The MEN1 mutation was confirmed with a genetic study

The second case is the mother of the previous patient, a 43-year-old patient with a history of renal colic, severe asthenia, and emotional lability associated with hypercalcemia, hypercalciuria, and osteopenia.

The third case is the 67-year-old grandmother with a history of significant bone pain without a history of nephrolithiasis associated with hypercalcemia, hypercalciuria and osteopenia.

In the three cases, before surgery, blood tests, cervical ultrasound with puncture of suspicious lesions and cervical scintigraphy were performed. These studies were only able to locate a limited number of adenomas, underdiagnosing pathological parathyroid glands.

Subtotal parathyroidectomy associated with thymectomy was performed, with a good evolution of the patients during the postoperative period, being discharged with oral calcium and vitamin D. Only one of the patients reported symptoms that could be related to hypocalcemia, although currently the calcium levels of the three patients are normal.

Clinical discussion: A high suspicion and early genetic diagnosis is important for the correct treatment of these patients, this could avoid the appearance of symptoms related to prolonged hypercalcemia.

The low value of imaging tests to locate parathyroid adenomas makes it essential that this surgery be performed by experts surgeon in thyroid surgery, and it could also reduce the comorbidity of surgery and the risk of persistent or recurrent hyperparathyroidism in the future.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1389

TBBPA CAUSES NRF2-DEPENDENT EXPRESSION OF THYROID HORMONOGENIC GENES

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Introduction: Tetrabromo-bisphenol A (TBBPA) is a widely used flame retardant heavily polluting the environment. On the thyroid axis, TBBPA is capable to interfere with the T4-binding transthyretin or the nuclear T3-receptor. Less explored are its damaging effects to end-organs through generation of reactive oxygen species. Recently, thyroglobulin (*TG*) was described as a transcriptional target of Nrf2, the master regulator of oxidative stress in cells.

Objectives: To determine whether TBBPA could alter the expression of relevant thyroid genes through Nrf2 activation.

Methods: Human thyroid (Nthy-ori) cells were exposed to increasing concentrations of TBBPA (7.5, 15, 30 and 60 mg/ml) for 16 hours. Adult C57BL/6 mice were administered subcutaneous TBBPA at 500 mg/kg BW/day for 10 days. After sacrifice, plasma TSH and T4 were quantified by RIA and LC/MS-MS, respectively. RNA extraction, cDNA synthesis and qPCR were performed from cells and thyroid tissues to investigate gene expression changes in *NFE2L2* (Nrf2)-*KEAP1* functional pair, *HO-1*, *NQO1* and *TXNRD1* as antioxidant-responsive genes and *TG*, *TSHR* and *DEHAL1* involved in thyroid hormonogenesis. Significance was considered at $p < 0.05$ (*), $p < 0.01$ (**) or $p < 0.001$ (***)

Results: TBBPA-treated mice showed increased TSH (1.36* vs 1 mU/L) and decreased T4 (14.4** vs 23.5 ng/ml) compared to untreated animals. Gene expression variations are shown in the Table as folds from non-treated conditions. *In vitro*, *NFE2L2-KEAP1* increased their expression in a TBBPA dose-dependent manner. Antioxidant and thyroid-specific genes followed the same pattern. Gene responses were replicated in the *in vivo* mouse model.

Image:

| TBBPA dose | Nthy-Ori 7.5 mg/ml | Nthy-Ori 15 mg/ml | Nthy-Ori 30 mg/ml | Nthy-Ori 60 mg/ml | Mice 500 mg/kg BW |
|-------------------------------|-----------------------|----------------------|----------------------|----------------------|----------------------|
| <i>NFE2L2</i> (<i>Nrf2</i>) | 1.1±0.1 | 1.4±0.3 | 2.1±0.3*** | 3.6±.3*** | 2.1±0.3** |
| <i>KEAP1</i> | 1.2±0.1* | 1.3±0.1** | 1.4±0.2* | 1.8±0.2** | 3.3±0.6* |
| <i>HO-1</i> | 1.3±0.2* | 1.2±0.1 | 2±0.3*** | 21±4*** | 2.9±0.7* |
| <i>NQO1</i> | 1.5±0.1*** | 1.6±0.2** | 1.9±0.1*** | 3.5±0.4*** | 3.2±0.4*** |
| <i>TXNRD1</i> | 1.4±0.2* | 1.9±0.3** | 2.3±0.2*** | 7±0.4*** | 9.9±1.6** |
| <i>TG</i> | 0.9±0.1 | 1.4±0.2 | 1.4±0.1** | 2.7±0.4** | 4.4±0.6** |
| <i>TSHR</i> | 1±0.1 | 0.9±0.2 | 0.9 | 1.3±0.1* | 3.9±0.7* |
| <i>DEHAL1</i> | 1.6±0.2** | 1.4±0*** | 2.3±0.3*** | 3.9±0.9*** | 2.5±0.3** |

Conclusion: TBBPA exposure causes hypothyroidism in mice, and induces transcriptional stimulation of both hormonogenic and antioxidant genes. The identification of ARE (Nrf2-responsive) elements in promoters of thyroid hormone synthesis genes (*TG*, *DEHAL1*) suggests a novel Nrf2-mediated mechanism of thyroid dysfunction by TBBPA involving oxidative stress within the thyroid gland.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1388

ASSESSMENT OF CHANGES IN QUALITY OF LIFE AFTER THYROID SURGERY IN OLDER ADULTS

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Introduction: Referral of an older adult with thyroid nodular disease to surgery remains a challenge. Potential improvement of the quality of life after surgery might help guiding this decision.

Objectives: To prospectively measure the impact of thyroid surgery on thyroid-related quality of life in older adults with thyroid nodular disease.

Methods: The Spanish version of the short-form Thyroid-Related Quality of Life (QoL) Patient-Reported Outcome (ThyPRO-39) expanded with the full 85-item ThyPRO scales on physical thyroid symptoms, was completed by all patients undergoing thyroid surgery during 2018-2019, for thyroid nodular disease at our Institution. The questionnaire was completed at admission and 6 months after surgery.

The instrument consists of four physical symptoms ThyPRO scales (Goiter, Hyperthyroid, Hypothyroid and Eye Symptoms), five mental well-being and function ThyPRO-39 scales (Tiredness, Cognitive Problems, Depressivity, Anxiety and Emotional Susceptibility), three QoL Impairment scales (Impaired Social life, Daily Life and Cosmetic Complaints) and one overall QoL impact single-item. The mental well-being and function scales, the QoL impairment scales (except Cosmetic Complaints) and the overall QoL-item is further summarized in the ThyPRO-39 Composite scale. Histological reports were classified as benign or malignant. Wilcoxon tests corrected for multiple testing and linear mixed models were used in statistical analyses.

Results: Out of 31 patients (74% female, age 71±7 years), 11 had malignant and 20 benign nodules.

After surgery, patients showed a significant improvement of the four physical symptoms, one of the mental well-being scales (Anxiety), two of the QoL Impairment scales (Impaired Social life and Cosmetic Complaints). Improvements in the following scores: Composite QoL scale, Goiter, Impaired Daily Life and Impaired overall QoL were observed mainly in the benign group (p for interaction <0.05) (Table1).

Image:

Table 1: ThyPRO Scores at Baseline and at Follow-up 6 Months After Treatment

| | Baseline (median Q1–Q3) | 6month (median Q1–Q3) | Unadjusted* | FDR– pvalue | BvsM interaction** |
|---|-------------------------------|-----------------------------|-------------|----------------|-----------------------|
| Goitre ¹ | 16 (2–25) | 2 (0–9) | 0.004 | 0.014 | 0.027 |
| Hyperthyroidism Symptoms ¹ | 19 (9–38) | 6 (0–19) | 0.000 | 0.001 | 0.393 |
| Hypothyroidism Symptoms ¹ | 25 (6–31) | 6 (0–25) | 0.005 | 0.014 | 0.229 |
| Eye Symptoms ¹ | 13 (6–31) | 3 (0–13) | 0.001 | 0.004 | 0.074 |
| Tiredness ² | 42 (25–67) | 33 (17–58) | 0.404 | 0.404 | 0.378 |
| Cognition ² | 14 (7–37) | 1 (1–21) | 0.246 | 0.344 | 0.514 |
| Anxiety ² | 34 (1–56) | 1 (1–26) | 0.010 | 0.020 | 0.304 |
| Depressiveness ² | 22 (7–37) | 29 (29–37) | 0.304 | 0.354 | 0.456 |
| Susceptibility ² | 36 (21–52) | 28 (28–36) | 0.165 | 0.256 | 0.426 |
| Impaired Social Life ³ | 8 (0–25) | 0 | 0.001 | 0.044 | 0.326 |
| Impaired Daily Life ³ | 7 (0–15) | 0 (0–7) | 0.285 | 0.354 | 0.027 |
| Cosmetic Complaints ³ | 12 (1–21) | 1(1–1) | 0.010 | 0.020 | 0.962 |
| Overall quality of life impact ⁴ | 0 (0–50) | 0 | 0.369 | 0.397 | 0.025 |
| Composite QoL score | 24 (16–41) | 19 (12–33) | 0.079 | 0.138 | 0.030 |

*Wilcoxon test. FDR, false discovery rate using Benjamini-Hochberg correction for multiple testing. **Interaction term modeled in linear mixed models adjusted for time and type of histology with subject-specific random effects. ThyPRO-39 scales: ¹physical symptoms, ²mental well-being and function, ³QoL Impairment and the ⁴overall QoL impact item. Histological reports were classified as benign (B) or malignant (M).

Conclusion: In older adults with nodular disease, surgery might resolve thyroid symptoms, anxiety, impaired social life and cosmetic complaints. Furthermore, in benign disease, improvement in goiter symptoms, impaired daily life and overall QoL were demonstrated. Further prospective studies of larger patient groups are needed to assess if ThyPRO may assist in the decision to refer older people with thyroid nodular disease for surgery.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1396

DECREASE IN THE VALUE OF INTRAOPERATIVE PARATHYROID HORMONE AS A PREDICTOR OF HYPOPARATHYROIDISM IN TOTAL THYROIDECTOMY

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Introduction: Hypoparathyroidism is the most common complication after total thyroidectomy, although in most cases it is transient.

Objectives: To predict this hypoparathyroidism to avoid indiscriminate treatment as well as the need for analytical studies in the immediate post-operative period. We present our experience with the determination of the percentage decrease of intraoperative PTH (PTH io) in the prediction of hypoparathyroidism after total thyroidectomy.

Methods: A prospective study is presented of 77 patients who underwent consecutive total thyroidectomies and were determined to have PTH io at anaesthetic induction and 10 minutes after total thyroidectomy. In addition, analytical studies were performed with the determination of calcium, albumin and corrected calcium 8 hours after surgery, and calcium, albumin, corrected calcium and PTH 24 hours after surgery. The presence of symptomatic or biochemical hypoparathyroidism (defined as corrected calcemia < 8 mg/dl and/or a PTH at 24 hours < 20 pg/ml) was assessed. An analysis of the ROC curve was developed to determine predictive cut-off values for hypocalcemia.

Results: 76.6% of patients were women with an average age of 53.3 years [23-79].

Thirty-eight patients presented with biochemical hypoparathyroidism within 24 hours of surgery and of these, 20 required calcium and vitamin D supplements in the immediate postoperative period.

Only 7 patients (9%) presented symptomatic hypocalcemia and required intravenous calcium treatment.

A decrease in PTH io > 72,1 % showed the greatest sensitivity and specificity in predicting post-thyroidectomy hypoparathyroidism.

Conclusion: The determination of the percentage drop in PTH io, in our experience, is a good predictor of post-operative hypoparathyroidism and can be used to indicate treatment in the immediate post-operative period, avoiding unnecessary analytical studies and treatments

Disclosure of Interest: None Declared

Thyroid

ICE2021-1422

LEVOTHYROXINE ABSORPTION TEST FOLLOWED BY DIRECTLY OBSERVED TREATMENT ON OUTPATIENT BASIS TO ADDRESS LONG TERM HIGH TSH LEVELS IN A HYPOTHYROID PATIENT.

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Introduction: Normally levothyroxine (LT₄) absorption occurs primarily in the small intestine within the first three hours of ingestion. In clinical practice, it is not infrequently seen that at least biochemical hypothyroidism persists even after adequately prescribed doses of LT₄. The most common explanation for elevated TSH is noncompliance, despite repeated counselling. In these cases, the LT₄ absorption test is a noninvasive and safe method for potentially distinguishing LT₄ malabsorption from pseudomalabsorption.

Case Description: A 45 year lady known case of primary hypothyroidism for 25 years was referred for persistent elevated TSH despite high dose Levothyroxine [(50 mcg) 6 tablets per day]. On examination, she is vitally stable, thyroid gland is not palpable, and her weight is 49kgs. On investigations, her TSH was >100.0 mIU/L, celiac serology was negative. Patient was asked to come in fasting state (at least 8 hours). (Table 1). She remain seated in outpatient department room for 1 hour, and then allowed to eat. Then she was allowed to leave and come back after 4 hours. Second sample was sent at 1.26 pm. The percentage LT₄ absorption was calculated using the following formula: % Absorbed = [Increment TT₄ mcg/dL x 10/total administered LT₄ mcg] x Vd (L) x 100. Where, increment in TT₄= peak TT₄- baseline TT₄. Volume of distribution= 0.442 x BMI. Normal absorption was considered to be >60%. Less than 60 % absorption means true malabsorption. Applying patient related values in the above formula, as increment TT₄: peak [TT₄] - baseline [TT₄] (13.9- 8.0= 5.9). Total administered dose = 1000 mcg. Volume of distribution (0.442 x 21.7= 9.59 L), so our result was 56.58%. She was planned to come every week for DOTS (Directly Observed Treatment Strategy) until further 5 weeks. TSH was checked after 6 weeks to see the response.

| COURSE OF LEVOTHYROXINE DOTS | | | | |
|------------------------------|--|---------|------------------------------------|------------------|
| | 24-8-2020 | | 01-10-2020 | 21-11-2020 |
| TSH | | | 0.173 | 2.86 |
| | 9.45 AM | 1.26 PM | Repeated one week after last DOTS. | |
| FT4 | 1.15 | 2.05 | 1.50 | 2.43 |
| T4 | 8.0 | 13.9 | 9.4 | 21.60 |
| On Thyroxine 50mcg | Tab Thyroxine 50 mcg 20 tabs given orally as DOTS. | | On 20 tabs/week, for 6 weeks. | On 20 tabs/week. |

Clinical discussion: There is no gold-standard method for the LT₄ absorption test, with various protocols advocated in the literature. However, it can provide valuable information for distinguishing malabsorption from pseudo-malabsorption. Strategies for enhancing compliance can include direct observation of medication administration, either through family or clinical support.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1428

EVALUATION OF ADHERENCE TO LEVOTHYROXINE AND OUT-OF-RANGE THYROID STIMULATING HORMONE LEVELS IN PREGNANT WOMEN WITH HYPOTHYROIDISM

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Introduction: Adherence to levothyroxine (LT4) and success to achieve thyroid stimulating hormone (TSH) goal in pregnancy has not been well-defined yet.

Objectives: We aimed to investigate adherence to LT4, success to reach TSH goal, and association between them in pregnant women with hypothyroidism.

Methods: Pregnant women with chronic autoimmune thyroiditis, surgical hypothyroidism and subclinical hypothyroidism whom LT4 was given at least 3 months were included. Those with secondary or tertiary hypothyroidism, isolated hypothyroxinemia of pregnancy, chronic illness, or thyroid cancer were excluded. According to Eight-item Morisky Medication Adherence Scale(MMAS-8) and TSH measurements in 3rd trimester, the patients were grouped as low adherence(MMAS-8 score<6) or medium/high adherence(MMAS-8 score≥6),and TSH in-range(0.3-2.5mIU/L) or out-of-range(≥2.5mIU/L).

Results: Of total(n=85), 57.64%(n=49) had medium/high adherence to LT4, and 41.17% (n=35) out-of-range TSH, but no association was found among them(p=0.937). LT4 initiation in pregestational period, surgical hypothyroidism, high LT4 dose in 2nd/3rd trimester, alternate-day dosing were positive predictors for medium/high adherence. Age, number of visits and dose adjustments, and less time between ingestion of LT4 and breakfast were associated with medium/high adherence. LT4 dose in 2nd trimester, dose increment at the beginning of pregnancy, vitamin D supplementation and negative anti-TPO were positively associated with in-range TSH.

Conclusion: Nonadherence and treatment failure were frequent, and no causal relationship was defined among them. Follow-up may improve adherence rather than TSH level. Our study is the first to reveal treatment success, adherence using MMAS-8, benefit of vitamin D supplementation on TSH, and effect of duration of LT4 use on adherence in hypothyroid pregnancy.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1484

INVASIVE FOLLICULAR THYROID CARCINOMA PRESENTING AS LARGE SARCOMA-LIKE SCAPULAR MASS WITH ROTATOR CUFF MUSCLES INVOLVEMENT

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Introduction: Follicular carcinomas occur frequently in women beyond the 5th decade of life as a slow-growing thyroid nodule. They are known to invade locally and metastasize distantly. Common sites for distant metastases are lungs and bones. The bones often involved are vertebrae, long bones and flat bones particularly the pelvis, sternum, and skull. Metastasis to scapula is an infrequent presentation and skeletal muscle metastasis is extremely rare.

Case Description: We present a case of metastatic follicular thyroid carcinoma that manifested as a large scapular mass on the right shoulder of a 65-year-old female patient. MRI of the right shoulder showed a big lobulated mass with central necrosis and non-delineation of the 4 rotator cuff muscles. Biopsy of the scapular mass revealed an invasive metastatic follicular carcinoma. A thyroid ultrasound showed a significant right thyroid nodule. The patient underwent total thyroidectomy and subsequent right total scapulectomy with biceps tendon transplantation attached to the clavicle. Histopathologic reports from both operations are consistent with invasive follicular carcinoma. The patient underwent radioiodine therapy. Follow-up showed no evidence of any functioning metastasis.

Clinical discussion: Distant metastasis at the time of presentation confers poor prognosis for patients with thyroid malignancies, thus yielding an increased understanding of follicular carcinoma is an essential matter of investigation including its rare presentations. Soft tissue metastasis is an uncommon initial presentation of follicular thyroid carcinoma. Synchronous metastasis to the bone and soft tissue particularly on the right scapula and surrounding skeletal muscles is a rare occurrence that warrants this report. Differential diagnosis of follicular thyroid carcinoma must be kept in mind whenever a sarcoma-like tumor is evaluated.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1490

ENDOTHELIAL DYSFUNCTION IN SUB CLINICAL HYPERTHYROIDISM

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Introduction: Subclinical hyperthyroidism (SH) is characterised by low serum concentration of thyrotropin (TSH) in the presence of normal serum thyroid hormones. SH is associated with increased prevalence of atrial fibrillation and few but not all studies have shown association of SH with cardiovascular disease (CVD) and increased mortality.

Lower number of circulating endothelial progenitor cells (CEPC) have been associated with endothelial dysfunction, whereas higher levels of circulating endothelial cells (CEC, marker of endothelial damage/injury) have been found in CVD. Increased levels of Asymmetric dimethylarginine (ADMA, an analogue of L-arginine, inhibit NO synthesis and impair endothelial function) have been reported and shown to be a predictor for CVD and all-cause mortality.

Objectives: We hypothesised that SH was associated with abnormal number of CEPC, CEC or ADMA contributing to endothelial dysfunction/injury, contributing to vascular risk. The primary aim of this study was to evaluate the effect of anti-thyroid drug carbimazole (compared to placebo) on levels of CEPC and CEC by flow cytometry and ADMA in peripheral blood of SH subjects.

Methods: CEPC/CEC counts by flow cytometry and ADMA in peripheral blood were measured in 30 SH subjects at baseline and after 6 months of treatment with either carbimazole or placebo in a randomised placebo-controlled design. All study subjects had milder form of SH with detectable serum TSH due to nodular goitre. Due to difficulty in recruitment, we included patients with vascular risk factors such as Diabetes but there is no significant difference between two groups in relation to those risk factors.

Results: There was no significant difference between two groups at baseline in relation to age, sex, BMI, blood pressure, TSH, FT4, and the presence of HT, hyperlipidaemia, Diabetes, atrial fibrillation and Ischaemic heart disease and the levels of CEPC/CEC and ADMA.

There was no significant difference in CEPC, CEC, and ADMA between Carbimazole and placebo group at 6 months. There was also no statistical difference in the above parameters if we compared the change or difference between two visits (visit 2 and visit 0 levels) in both groups.

Conclusion: There is no evidence of endothelial dysfunction or endothelial injury in our cohort of SH subjects. Due to small number of SH subjects studied, our finding needs to be confirmed in future studies with larger number of SH subjects.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1491

INFLAMMATORY MARKERS IN SUB CLINICAL HYPERTHYROIDISM

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Introduction: Subclinical hyperthyroidism (SH) is characterised by low serum concentration of thyrotropin (TSH) in the presence of normal serum thyroid hormones (both free thyroxine, FT4 and triiodothyronine FT3). SH is associated with increased prevalence of atrial fibrillation and few but not all studies have shown association of SH with cardiovascular disease and increased mortality.

Inflammation has been shown to play significant role in the pathogenesis of cardiovascular disease. Increased levels of C-reactive protein (CRP), Lipoprotein associated phospholipase A2 (Lp-PLA 2, an inflammatory marker plays a critical role in atherosclerosis), Neutrophil lymphocyte ratio (NLR) and Monocyte lymphocyte ratio (MLR) have been reported in conditions with increased cardiovascular risk.

Objectives: We hypothesised that SH was associated with abnormal levels of CRP, Lp-PLA2, Neutrophil lymphocyte ratio and Monocyte lymphocyte ratio contributing to atherosclerosis and or increased cardiovascular risk. The primary aim of this study was to evaluate the effect of anti-thyroid drug carbimazole (compared to placebo) on the inflammatory vascular markers such as CRP, Lp-PLA2, NLR, and MLR in peripheral blood of SH subjects.

Methods: CRP, Lp-PLA 2, NLR and MLR in peripheral blood were measured in 30 SH subjects at baseline and after 6 months of treatment with either carbimazole or placebo in a randomised placebo-controlled design. All study subjects had milder form of SH with detectable serum TSH due to multinodular goitre. Due to difficulty in recruitment, we included patients with cardiovascular risk factors such as Diabetes, but there is no significant difference between two groups in relation to those risk factors.

Results: There was no significant difference between the two groups at baseline in relation to age, sex, BMI, blood pressure, TSH, FT4, and the presence of vascular markers such as Hypertension, hyperlipidaemia, Diabetes, atrial fibrillation and Ischaemic heart disease.

We did not find any significant difference in the levels of CRP, Lp-PLA2, NLR and MLR between carbimazole and placebo groups. There was also no statistical difference in the above parameters if we compared the change or difference between two visits (visit 2 and visit 0 levels) in both groups.

Conclusion: There is no evidence of chronic inflammation in our small cohort of SH subjects. Our finding needs to be confirmed in future studies with larger number of SH subjects.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1505

CORRELATION BETWEEN SERUM THYROGLOBULIN LEVELS AND INVOLVED NECK COMPARTMENT IN PERSISTENT/RECURRENT NODE METASTASIS OF PAPILLARY THYROID CARCINOMA

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Introduction: Thyroglobulin (Tg), routinely used as a tumor marker for differentiated thyroid cancer (DTC) is a reliable marker in patients treated with total thyroidectomy and more definitive, for those treated with radioiodine. Considerably high Tg levels do suggest distant metastasis. Yet for the moderately increased levels, almost always indicating locoregional metastases-, the relationship between localization, tumor burden and serum Tg levels is not clear.

Objectives: We aimed to detect whether Tg level could predict the localization of the metastatic lymph node compartment in the neck, regardless of tumor burden, radioiodine treatment and TSH levels, in persistent/recurrent locoregional metastases.

Methods: 143 patients with persistent/recurrent locoregional papillary thyroid cancer (PTC) who underwent 172 neck dissections were included in this retrospective study. Three groups were formed regarding localization of lymph node metastasis (LNM): 1) central, 2) lateral, 3) both central and lateral LNM. We used mixed effects models to investigate the effect of LNM localization on Tg regardless of TSH level, tumor burden-defined with the number and the largest diameter of LNM- and receiving radioiodine therapy (RAI).

Results: Mean Tg levels were 1.43 µg/L for C LNM (n=47), 3.7 µg/L for L-LNM (n=99), and 8.60 µg/L for C+L LNM (n=26) groups. While the difference between Tg levels of L LNM and C+L LNM groups was not statistically significant (p=0.183), C LNM group exhibited significantly lower mean Tg level than the other groups (L LNM p=0.006 and C+L LNM p<0.001) (Table 1). Mixed effects models analysis showed C LNM caused significantly lower Tg values than L LNM and C+L LNM independent of TSH level, tumour burden and receiving RAI. The sample was divided into two groups according to the TSH value as <0.1 mU/l (suppressed, n:79) and > 0.1 mU/l (non-suppressed, n: 94). No difference was observed for Tg between C LNM and other groups in those who were followed with suppressed TSH. To discriminate C LNM from L LNM and C+L LNM, the optimal cutoff for Tg was 1.05 µg/L with an AUC of 0.714±0.058 (p<0.001, 95% CI=0.603-0.824). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were 74.7%, 70.4%, 87.7% and 50% for this cutoff, respectively.

Image:

TABLES

Table 1. Descriptive and clinical characteristics of the study sample (n=172)

| | C LNM n=47 | L LNM n=99 | C+L LNM n=26 | P |
|---|------------------------|-------------------------|------------------------|--------|
| Sex, n (%) | | | | 0.658 |
| -Female | 32 (68.1%) | 74 (74.7%) | 20 (76.9%) | |
| -Male | 15 (31.9%) | 25 (25.3%) | 6 (23.1%) | |
| Stage*, n (%) | | | | 0.834 |
| - I | 43 (91.5%) | 88 (88.9%) | 24 (92.3%) | |
| - II | 4 (8.5%) | 11 (11.1%) | 2 (7.7%) | |
| Age, Mean±SD | 48.0±11.3 | 47.9±13.2 | 42.4±14.5 | 0.247 |
| Age at diagnosis, Mean±SD | 39.4±11.3 | 38.5±12.6 | 34.2±14.1 | 0.989 |
| Disease duration at the time of neck dissection (years), Mean±SD | 3.91±3.45 | 3.87±4.32 | 2.91±3.89 | 0.582 |
| Diameter of primary tumor (mm), Mean±SD | 16.88±12.03 | 17.14±10.45 | 20.76±11.88 | 0.311 |
| Number of metastatic nodes, Mean±SD | 2.81±2.68 | 3.34±3.61 | 6.00±3.45 ^a | <0.001 |
| The largest diameter of LNM (mm), Mean±SD | 11.07±5.79 | 13.94±6.38 ^b | 13.51±7.21 | 0.046 |
| Thyroglobulin (Tg), µg/L, Mean±SD | 1.43±2.59 ^c | 3.70±5.78 | 8.60±15.94 | <0.001 |
| TSH (mU/l), Mean±SD | 1.53±2.91 | 2.30±8.06 | 0.74±1.23 | 0.201 |

LNM: Lymph Node Metastasis, C: Central, L: Lateral, C+L: Central + Lateral; a: Different from C and L (p<0.001); b: Different from C (p=0.043); c: Different from L and C+L (natural logarithm was applied, p=0.006 and p<0.001, respectively). *There were no patients with stage III or IV thyroid cancer.

Conclusion: C LNM seems to increase serum Tg level less than L LNM. Thus preoperative serum Tg level can assist to localize metastatic nodes in patients with persistent/recurrent disease.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1509

ASSOCIATION BETWEEN VITAMIN D AND THYROID AUTOIMMUNITY IN GEORGIAN ADULTS

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Introduction: There is contradicting evidence for the association between vitamin D deficiency and autoimmune thyroid diseases (AITD) with the balance tipping towards inverse correlation. To the best of our knowledge, this association has not been studied before in Georgia. Georgia is a South Caucasian country populated mainly with ethnic Georgians, thus diminishing the potential impact of ethnicity on this association.

Objectives: We investigated, for the first time, the association between vitamin D deficiency and thyroid autoimmunity in Georgian adults.

Methods: All people aged >18 years with measurements of both serum vitamin D levels and thyroid peroxidase antibody (TPOAb) levels in two medical centres in Georgia were included in the analysis. The study population was divided into cases (vitamin D deficient) and controls (vitamin D sufficient/insufficient). The strength of association was quantified by odds ratio. The strength and direction of association between vitamin D and TPOAb levels was measured with Spearman's rank-order correlation. Statistical significance was accepted at 95% confidence level ($p < 0.05$).

Results: 170 patients were included in the analysis, with a mean age of 43.9 ± 15.49 years (male: female- 1:4.28). 59.4% ($n=101/170$) were vitamin D deficient. 53.5% had positive TPOAb ($n=91/170$). In the case group, 60.4% ($n=61/101$) had positive TPOAb, compared to 43.5% ($n=30/69$) in controls. There was a significant difference in TPOAb positivity between the two groups ($p=0.0439$) with an odds ratio of 2.0 (OR>1, 95% CI: 1.1-3.7, $p=0.0308$). When adjusted for age, gender, and BMI, a percentage change of 14.8% was observed, increasing the odds ratio to 2.3 (OR>1, 95% CI: 1.2-4.5, $p=0.0169$). A significant inverse correlation was observed between vitamin D and TPOAb levels ($\rho=-0.16$, $p=0.0367$).

Conclusion: There is a significant and inverse association between vitamin D and thyroid autoimmunity. Further prospective study is needed to ascertain the relationship between vitamin D deficiency and autoimmune thyroid diseases in our region.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1512

EVALUATION OF THE CONTRIBUTION OF THE EU-TIRADS SYSTEM IN THE CHARACTERIZATION OF THYROID NODULES: RADIO-HISTOLOGICAL CORRELATION

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Introduction: Thyroid ultrasound (US) is a key examination for the management of thyroid nodules. Thyroid US is easily accessible, noninvasive and is a mandatory step in the workup of thyroid nodules. The EU-TIRADS aims to serve physicians in their clinical practice, to enhance the interobserver reproducibility of descriptions, and to simplify communication of the results.

Evaluation of the contribution of the EU-TIRADS system in the characterization of thyroid nodules by studying the correlation between ultrasound signs and anatomic-pathological findings

Objectives: Evaluation of the contribution of the EU-TIRADS system in the characterization of thyroid nodules by studying the correlation between ultrasound signs and anatomic-pathological findings

Methods: 5-year retrospective study of 350 thyroid nodules explored by cervical ultrasound in the imaging department medical at the Taher Sfar University Hospital in Mahdia and operated on in the ENT department.

Results: The cardinal signs on ultrasound are the major predictive signs of malignancy according to the EU-TIRADS system. Among these signs; the strongly hypoechoic appearance, the irregular contours and the presence of microcalcifications are predictive of malignancy according to our study. While the non-oval shape is not according to our results. In our study, the EU-TIRADS system has a sensitivity of 80% and specificity of 40%.

Conclusion: The ultrasound examination based on the EU-TIRADS classification is a key examination whose place in the management of nodules thyroid is no longer to be discussed. The perpetual evaluation of the system as well as its predilection criteria of malignancy would allow to improve it, in order to achieve maximum reliability.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1518

DIAGNOSTIC CHALLENGES OF THYROID CARCINOMA AND SARCOIDOSIS

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Introduction: Sarcoidosis (SA) is a chronic inflammatory disease characterized by non-caseating granulomas.

Lofgren's Syndrome (LS) is one of the most classic syndromes of the disease, which expresses acute SA. Associates erythema nodosum and bilateral hilar adenopathy and may coexist with polyarthritis and fever. Generally, has a limited course and resolves without treatment.

Case Description: A 44-year-old male patient was referred to our service for the treatment of papillary thyroid carcinoma (PTC) with multiple MTS in lymph nodes and lung.

He had a PET-CT scan with multiple hyper-uptake lymph nodes up to 3cm in the neck, chest, abdomen, and inguinal region. Multiple hyper-uptake bilateral lung nodules.

Biopsy of 2 mediastinal lymph nodes showed:

- 1- MTS of probable thyroid origin
- 2- Non-necrotizing granulomatous inflammation.

He refers antecedents of a prolonged febrile syndrome of 5 months of evolution associated with asthenia, joint pain, and erythematous nodular lesions in the extremities. Infectious causes were ruled out.

A thyroid ultrasound (US) revealed an hypoechoogenic, solid nodular image on the right lobe, with irregularly defined limits, measuring 14x13mm associated with suspicious bilateral lymph nodes

FNA: papillary carcinoma suspect, Bethesda V

A clinical diagnosis of LS was made, and it was decided not to initiate specific treatment for sarcoidosis due to the absence of target organ damage, so total thyroidectomy plus bilateral central dissection was performed. Histology: the right lobe tumor is a variant oncocyctic papillary carcinoma of 1.5cm in diameter, in contact with the thyroid capsule.

Recurrent lymph node dissection with MTS in 2 of 8 resected lymph nodes with disruption of the capsule

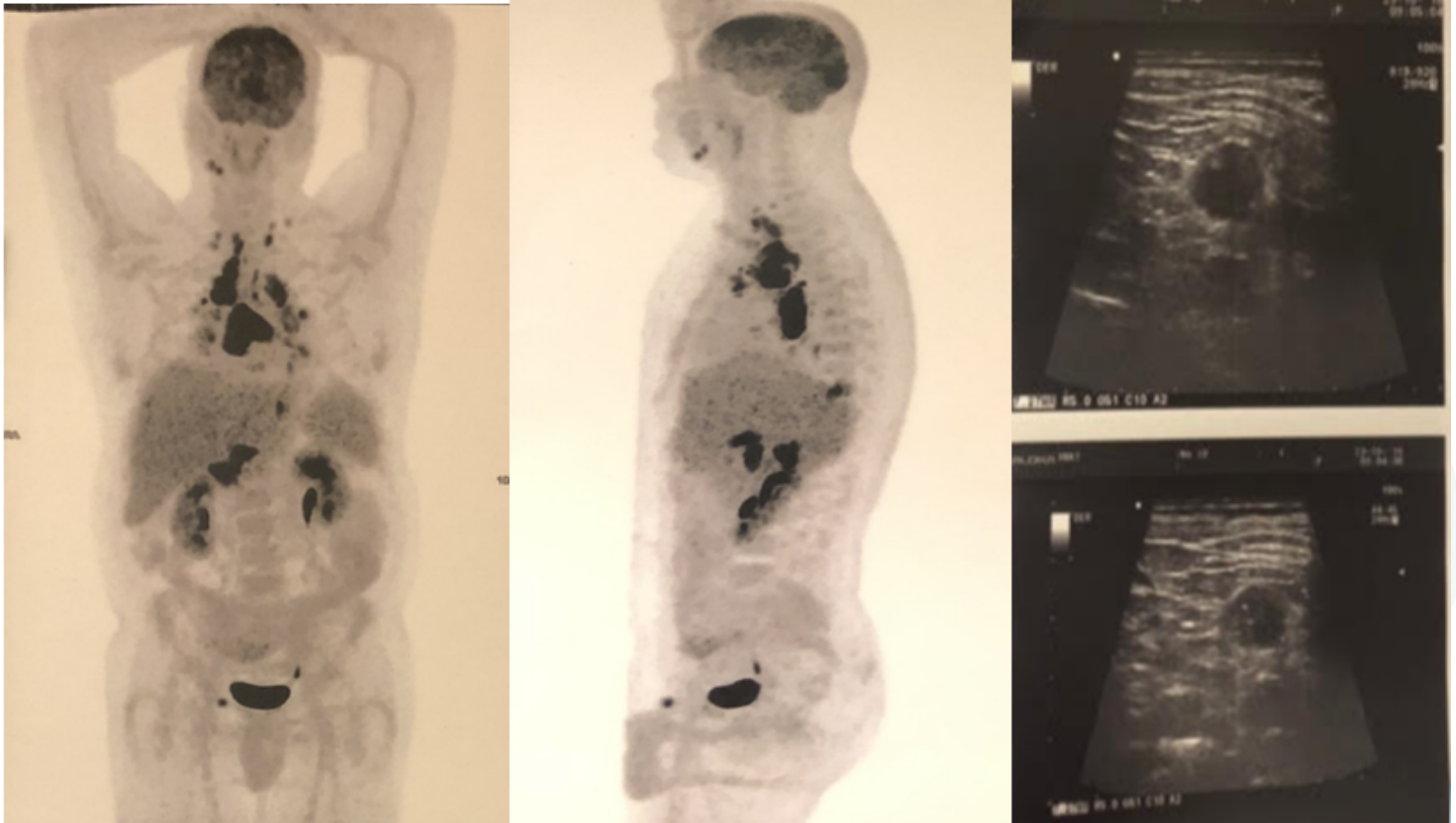
The tumor was staged as Stage I with an intermediate risk of recurrence, so an iodine 131 dose of 100mCi was indicated (TSH 34 uIU/ml, Thyroglobulin <0,1 ng/ml, TgAb <20 UI/ml). In RCT after, 3 foci of increased concentration of the radiotracer were evidenced in the thyroid bed.

Post-surgical studies:

- PET CT that reported a decrease in the size of the lymph node images at all levels.
- Neck US without evidence of pathological lymph nodes.
- Thyroglobulin <0.1 ng/ml and TgAb <20 IU/ml

Clinical discussion: SA and PTC can affect lymph nodes in the neck, so SA can mimic a metastatic PTC. The causal relationship between these entities is still unclear. PET-CT is an especially useful diagnostic tool to identify malignant lesions. Unfortunately, inflammatory diseases such as SA can also have high FDG uptake.

Image:



Disclosure of Interest: None Declared

Thyroid

ICE2021-1519

FINAL TIME EVOLUTION OF PATIENTS WITH DIFFERENTIATED THYROID CARCINOMA (DTC): COMPARATIVE ANALYSIS BETWEEN THE 7TH AND 8TH EDITION (ED) OF THE TNM.

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Introduction: The 8th Ed of TNM of the AJCC/UICC for DTC introduces changes in the categorization of patients (Ps) according age at diagnosis and criteria to define T3 category, allowing its better interpretation in order to optimize treatment and results obtained from follow-up (FU).

Objectives: To analyze the impact produced by the modifications of the 8th Ed of the TNM in Ps with DTC compared with the 7th Ed.

Methods: Retrospective study on 236 adult Ps with DTC treated with total thyroidectomy with/without radioablation and FU between 1-26 years (y). The following variables were recorded: age at diagnosis, sex, histological type, tumor size (≤ 1 , 1-4 and >4 cm), minimal extrathyroid extension (MEE) or gross extension (GE), lymph nodes, distant metastasis (MTS) and clinical outcome at the end of FU: excellent response (ER), biochemical incomplete response (BIR), structural incomplete response (SIR), indeterminate response (IR) and death. The TNM classification according to 7th and 8th was applied for comparative purposes. Statistical analysis: Pearson's Chi Square.

Results: The most frequent histological type was papillary in 212 (90%); 50 tumors < 1 cm (21%); 143 between 1-4 cm (61%) and 39 > 4 cm (16%); MEE in 81 (34%), GE in 18 (8%); lymph nodes MTS in 56 (24%) and 7(3%) with distant MTS. According to TNM 7th Ed: ≥ 45 y were 55% (n=129) and for 8th: ≥ 55 y were 22% (n=53). Comparing both Ed, the 8th showed a greater number of Ps in stages (S) I and II, with a 97% decrease in S III and 78% in S IV ($p < 0.0001$). 54 / 96 Ps from T3 by 7th changed category to T1a: 8 Ps, T1b: 17 Ps and T2: 29 Ps with 8th, remaining the rest in T3. 60% of the T4a according 7th changed to T3a and T3b by 8th ($p < 0.0001$). At the end of FU, we have data of 213 Ps, of which 137 (64%) had ER; 21(10%) BIR; 34 (16%) SIR and 34 (16%) IR. 9/213 died due CDT. The evolution at final time was similar in ER, BIR, SIR or IR for S I in both Ed. In S II, a lower percentage of Ps with ER was observed in 8th, with an increase in SIR, BIR and IR. One Ps of S III had BIR and 3 of S IV had SIR according to 8th.

Conclusion: In 8th Ed, a significant decrease in Ps T3/T4 and S III/IV changed to lower T and stages. The 8th Ed showed a tendency to relocate patients in stages of more favorable evolution at the end of the FU, which would allow optimizing the therapeutic approach and decision-making in clinical management. However 5/9 Ps who died from S III changed to S I and S II, requiring more experience when considering mortality risk using the 8th Ed.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1522

CORRELATION BETWEEN THYROID FUNCTION PARAMETERS AND LIPID LEVELS IN EUTHYROID PRE- AND POSTMENOPAUSAL WOMEN ON LEVOTHYROXINE REPLACEMENT THERAPY

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Introduction: Thyroid stimulating hormone (TSH) measurement is recommended as a follow-up marker in patients with autoimmune hypothyroidism and serves as the main indicator for dose adjustment. In patients on levothyroxine treatment however there has been controversial data regarding the correlation between TSH and free thyroxine (FT4) as well as the impact of the hormones on the lipid parameters especially in women of different age groups.

Objectives: To investigate the correlation between thyroid function parameters and lipid levels in euthyroid pre- and postmenopausal women on levothyroxine replacement therapy.

Methods: 130 women with autoimmune thyroiditis on levothyroxine replacement therapy were included in the study - 75 premenopausal women (mean age 34.9±7.6 years) and 55 postmenopausal women (mean age 58.3±7.6 years). Fasting morning levels of TSH, FT4, total cholesterol, HDL, triglycerides were measured, LDL was calculated using the Friedewald equation. All the women included had no significant medical conditions, incl. diabetes mellitus, were not taking metformin, lipid-lowering therapy or estrogen-containing drugs. All of the patients were euthyroid and had TSH and FT4 levels within the reference range (0.4-4.2 mIU/l and 7.86-14.40 pmol/l respectively).

Results: Postmenopausal women had considerably higher levels of total and LDL cholesterol and triglycerides than premenopausal women with no significant differences in thyroid function parameters and the mean levothyroxine dose. In premenopausal women there was a negative correlation between TSH and FT4 levels ($p=0.008$). TSH positively correlated with total cholesterol levels; FT4 showed negative correlation with total cholesterol ($p=0.001$), LDL cholesterol ($p=0.000$) and triglycerides ($p=0.034$). The total daily levothyroxine dose correlated with FT4 levels. In the group of postmenopausal women however there was no direct relation between TSH, FT4 and the levothyroxine dose. TSH and FT4 levels did not show any correlation with the investigated laboratory parameters.

Conclusion: Our results suggest that in young women with autoimmune hypothyroidism TSH in the lower half together with FT4 in the upper half of the reference range is associated with better lipid profile. In women after menopause the interaction between TSH and FT4 is not straightforward and there is no evidence to justify correction of levothyroxine dose when TSH is within the reference interval in order to affect lipid levels.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1523

THYROID NODULES IN CHILDREN

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Introduction: Pediatric thyroid nodules are rare: 0.2 – 1.4 % of child population. They are characterized by a high rate of thyroid cancer (22 – 26 %). **Objective:** To describe the epidemiological, clinical and therapeutic features of pediatric thyroid nodules.

Case Description: Methods

A retrospective study including 68 children (≤ 16 years), operated in our department (a period of 20 years).

Cervical ultrasonography and TSH (thyroid stimulating hormone) test were done in all cases. All of our patients were treated with thyroid surgery. The intraoperative examination was systematic.

Results

The mean age was 14,15 years [5 years – 16 years]. We noted a female predominance (70 %). The majority of patients (85 %) presented with an isolated anterior neck mass. TSH level was normal in 88 % of cases. Ultrasonography revealed a single nodule in 43% of cases.

Sixteen (24 %) patients had thyroid cancer. Papillary thyroid carcinoma was the most frequent histologic type (75 %). Histologic lymph node involvement was noted in 68 % of cases. Three patients had pulmonary metastasis. In the cases of malignant nodule, total thyroidectomy associated with central neck dissection were performed in all cases. Selective neck dissection (levels II, III and IV) was done in 80 % of cases. Radioactive iodine was indicated in 15 cases. Postoperative radiotherapy was indicated in one case (medullary thyroid carcinoma). Eleven patients had complete remission.

Clinical discussion: Thyroid nodules are less common in childhood than in adulthood. The risk of malignancy is more important in children. Pediatric thyroid cancers are more aggressive, with high risk of lymph involvement and distant metastasis. However, their prognosis is good.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1525

THYROID FUNCTION IN ADULTS WITH PRADER-WILLI SYNDROME

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Introduction: Prader-Willi syndrome (PWS) is a complex genetic syndrome in which hypothalamic dysfunction leads to hyperphagia and pituitary hormone deficiencies (PHD), among others. The majority of patients have intellectual disability (ID) and use of psychotropic drugs is frequent. Due to hypotonia and the low muscle mass associated with the syndrome, adults with PWS have a low basal metabolic rate (BMR) and a high risk of developing obesity. Therefore, exercise is extremely important. However, PHD like hypothyroidism can cause fatigue and exercise intolerance. If left untreated, hypothyroidism can lead to a further decrease in BMR, an increase in Body Mass Index (BMI) and increased cardiovascular risk. As mortality in PWS is high (3% yearly) and often related to cardiovascular problems and obesity, it is important to optimize thyroid function and other factors affecting BMR.

Objectives: To investigate the prevalence of hypothyroidism in adults with PWS and to provide practical screening recommendations.

Methods: In 122 adults with PWS (median age 29 y [IQR 21-39], median BMI 29 kg/m² [IQR 26-36]), we measured TSH, free T4 and T3 (the active form of thyroid hormone) and searched the medical history for use of medication and any pre-existing diagnosis of hypothyroidism. Moreover, we performed an extensive literature search and summarized the current literature on hypothyroidism, T3 and T4 levels in adults with PWS.

Results: Hypothyroidism was present in 17% and more prevalent in females (23%) than in males (10%), even though this was not statistically significant (P=0.06). Although within the reference range, serum T3 levels were relatively high compared to free T4 levels. T3 levels were significantly lower in patients that used psychotropic medication (n=45) than in patients that did not (median 1.7 [IQR 1.5-2.0] vs 2.1 [IQR 1.7-2.3], P=0.013).

Conclusion: We found a prevalence of hypothyroidism of 17% in adults with PWS (compared to 3% in the non-PWS population). T3 levels were relatively high, which might be explained by increased peripheral conversion of T4 to T3 by deiodinase type 2. Levels of the active thyroid hormone T3 were significantly lower in patients using psychotropic medication. Based on our findings, we recommend 1) yearly screening of thyroid hormone levels in adults with PWS to avoid negative effects of untreated hypothyroidism on BMR, BMI and cardiovascular risk and 2) extra monitoring of the active thyroid hormone T3 in patients using psychotropic drugs.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1552

THYROID AXIS AND COVID 19

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Introduction: Non-thyroidal illness syndrome (NTIS) is also known as low T3 syndrome. NTIS is characterized by low plasma T3, low or normal T4, or elevated reverse T3 (rT3), with normal or slightly decreased TSH. NTIS is a strong predictor of poor prognosis in critically ill hospitalized patients. Different thyroid hormone profiles were defined during critical illness. High fT4 with a low fT3 level in patients with coronary heart disease were significantly related to mortality. If NTIS is a physiologic response to a systemic inflammation or a maladaptation status is controversial. NTIS with low fT3 and a lower fT3/fT4 ratio was referred in patients with COVID-19. Furthermore, angiotensin-converting enzyme (ACE) 2, an receptor in the pathogenesis of COVID-19, was demonstrated to be expressed in the thyroid gland. SARS-CoV-2-related thyroiditis is recognized. The effects of COVID-19 on the thyroid axis remain uncertain.

Objectives: We aimed to study the characteristics of thyroid hormone levels in inpatients with COVID-19.

Methods: Prospective study: 57 covid-19 patients (29/57 ♂) with criteria for admission to a medical clinic from August to November 2020. Median age was 56 years (range(R) : 21-89). 3,6% was asymptomatic, 14,3% mild, 28,6% moderate and 53,6% severe. fT4, TT3, TSH, TgAb and TPOAb were analysed in addition to studies due to their underlying pathology. Data are expressed as median and R or mean \pm SD and %

Results: The median of TSH was 1.77 uIU/ml (R: 0.02-64.9), the X \pm SD of fT4 and TT3 was 1.22 \pm 0.3 ng/ml and 72.3 \pm 23.04 ng/dl respectively. Forty two/ 57 patients presented low T3. The profiles observed in this group are described in table 1. Two patients with positive TPOAb had high TSH, low T3 and normal fT4 and 3 only low T3.

Image:

Table 1: profiles observed in patients with low T3

| Low TT3 and High FT4 | | | Low TT3 and Low FT4 | | | Low T3 and Normal FT4 | | |
|------------------------|-------------------|---------------------|---------------------|-------------------------|---------------------|------------------------|-------------------------|----------------------|
| Low TSH (n=1) *1 | High TSH (n=1) | Normal TSH (n=9) | Low TSH (n=0) | High TSH (n=1) *2 | Normal TSH (n=4) | Low TSH (n=2) *3 | High TSH (n=4) *3 | Normal TSH (n=20) |

*¹ clinical hyperthyroidism (TSH <0.02, fT4 2,06 uUI/ml).

*² clinical hypothyroidism (TSH. 64.9 uUI/ml).

*³ high values of TSH: 5.22 - 9.61 uUI/ml and low TSH 0.21 y 0.34 uUI/ml.

Conclusion: 1-In this population of COVID-19 patients upon admission to hospitalization and excluding one clinical hypothyroid patient 73, 7% presented low T3.

2- In the patient with clinical hypothyroidism and negative antibodies as well as those with altered TSH, low TT3 and normal or high fT4 we cannot exclude destructive or autoimmune thyroiditis until the evolution is known.

3-Classic NTI with low T3, low or normal fT4 and normal TSH was observed in 42, 1% patients.

4- It should be noted the high prevalence of patients with low TT3, high fT4 and normal TSH.

We consider that is another face of NTI in COVID-19 as it was referred in patients with coronary disease. To our knowledge, this is the first descriptive report of different faces of NTI in COVID 19 patients.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1565

CORRELATION BETWEEN INFLAMMATORY PARAMETERS AND THYROID HORMONES IN PATIENTS WITH COVID-19

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Introduction: Non-thyroidal illness syndrome (NTI), (decreased T3 and/or T4 without increased TSH), has been reported in COVID-19 infection. In patients admitted with COVID-19 we found classic NTI presentation and a high prevalence of low T3, high freeT4 (FT4) and normal TSH, which could represent a different presentation of NTI. Low T3 and high FT4 have been associated with mortality¹.

Objectives: 1-To evaluate correlation of thyroid hormones with biochemical markers of inflammation and association with disease outcome in hospitalized patients with COVID-19. 2-To evaluate these parameters in the two profiles of NTI.

Methods: Prospective single-center study that included 55 consecutively patients with COVID-19 hospitalized from August to November 2020. 28/55 (50 %) were male, median age 56y (21-89). Clinical presentation: asymptomatic 3,6% (n=2), mild 14,3% (n=8), moderate 28,6% (n=16), severe 53,6% (n=30). 74,1% had pneumonia, 3,6% (n=2) died and 79,3% had favorable evolution. Thyroid hormones (T4, T3, FT4, FT3) and their ratios (T3/T4, FT3/FT4) were correlated with inflammatory parameters (albumin, ferritin, fibrinogen, erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], lactate dehydrogenase [LDH], D-dimer). Comparison between hormone levels, clinical presentation and outcome was performed. Statistical analysis: Spearman correlation, Mann Whitney test and Kruskal-Wallis test.

Results: We found correlation between thyroid hormones and their ratios with inflammatory parameters (Table). T3/T4 ratio was lower in severe vs mild/moderate disease [7.5 (4.5-15.5) vs 9.2 (5.8-18.1); p=0.04] and in patients who died vs those discharged [5 (4.53-5.6) vs 8.1 (4.7-18.1); p=0.03]. High FT4 NTI had lower albumin [3.4 (3-4) vs 3.7 (3-4); p=0.03], higher ferritin [1202 (930-7127) vs 435 (101-2232); p<0.05] and tendency to higher fibrinogen [681(583-798) vs 508 (307-807); p=0.06] than normal/low FT4 NTI. No patient with mild disease at onset had high FT4.

Image:

| | Correlations (p<0.05) | | | | | |
|------------|-----------------------|---------|---------|---------|---------|---------|
| | T4 | FT4 | T3 | FT3 | T3/T4 | FT3/FT4 |
| Albumin | | R -0.55 | R 0.61 | | R 0.64 | R 0.56 |
| Ferritin | | | | R -0.49 | R -0.5 | R -0.47 |
| Fibrinogen | | R 0.41 | R -0.56 | R -0.42 | R -0.69 | R -0.54 |
| ESR | R 0.33 | R 0.47 | | R -0.35 | R -0.49 | R -0.46 |
| CRP | | | | | R -0.35 | |
| LDH | | | | R -0.37 | | R -0.43 |
| D- Dimer | | | R -0.47 | R -0.42 | R -0.49 | R -0.4 |

Conclusion: In this cohort, both thyroid hormones correlated with inflammation parameters and worse clinical outcome. In NTI group with high FT4, inflammatory parameters were more marked and presentation of the disease more severe.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1588

TITLE: A YOUNG FEMALE WITH RIEDEL'S THYROIDITIS

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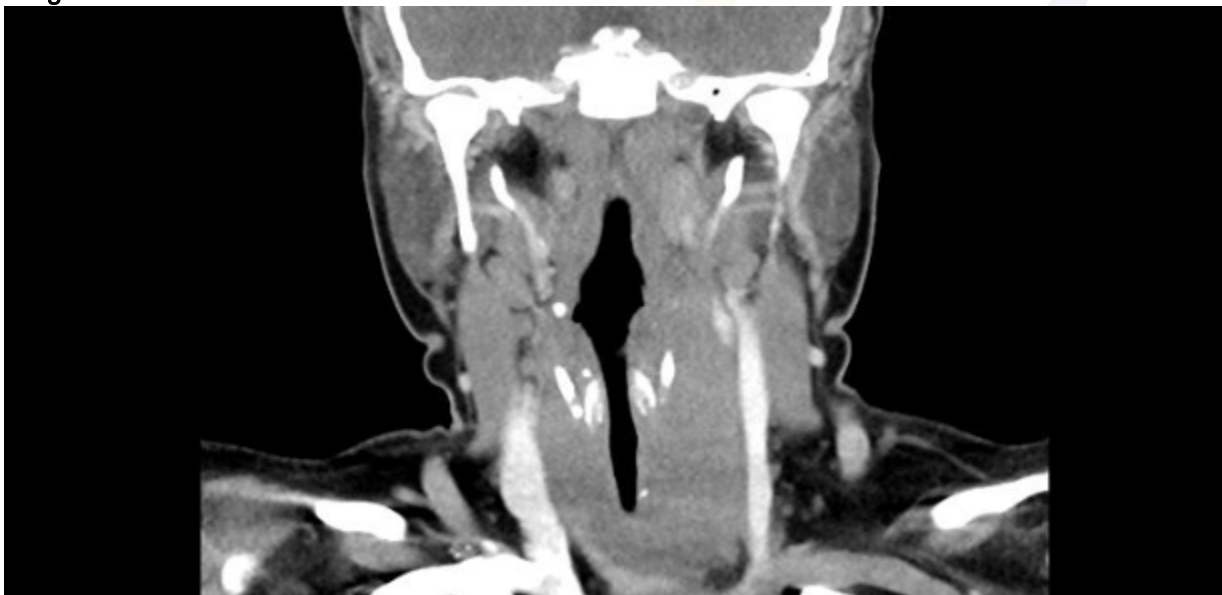
Introduction: We describe here a rare case of young female with Riedel's thyroiditis. It is a rare condition, with a prevalence of 1 per 100,000 inhabitants, which affects more frequently women between 30 and 50 years of age. Most patients have normal thyroid function, although it is reported that up to 30% have hypothyroidism. Diagnosis can be challenging due to unspecific symptoms that overlap with other disorders.

Objectives: We report a case of young female found to have Riedel's thyroiditis on workup.

Methods: Clinical, laboratory, radiological and pathological data of the case is presented.

Results: 36 years old female known case of hypothyroidism for 10 years presented with history of painful hard thyroid swelling for 7 months, compressive symptoms (dysphagia and shortness of breath), hoarseness of voice and sore throat. On examination there was stony hard swelling, fixed with underlying structures. There was no associated lymphadenopathy. Investigations showed TSH : 0.613 , ESR **55** .Ultrasound neck showed enlarged left lobe measuring 106 x 38mm containing multiple nodules. The **largest left sided nodule is hypoechoic, it is encasing the major vessels and the thyroid cartilage** .Coarse calcification also identified within this nodule. There no increased vascularity identified in this nodule. The right lobe is entirely replaced by ill-defined **hypoechoic nodule** which is measuring 72 x 51 mm. This is **also encasing the thyroid cartilage and containing coarse areas of calcification**. No significant lymphadenopathy noted. **Thyroid scan showed reduced radiotracer uptake in the region of the thyroid gland**. CT scan neck showed thyroid gland is enlarged especially the left lobe with retrosternal extension. It measures **77x59x45mm**. It is slightly displacing the trachea towards the right side and causing mild compression. No neck lymphadenopathy. **Trucut biopsy of thyroid gland showed predominantly sclerotic collagenous tissue with dense histiocytic and mild lymphoid infiltrate**. She was started on steroids (tab prednisolone 30 mg BID).She responded well to it within 4 weeks. Gradually her steroids were tapered over period of 8 months.Repeat ultrasound after 1 year showed significant reduction in the size of both lobes of thyroid.

Image:



Conclusion: Riedel's thyroiditis is a rare disease that is difficult to diagnose using preoperative diagnostic tools because it can mimic malignant neoplasm or the fibrous variant of Hashimoto thyroiditis during preoperative physical, radiologic and pathologic examination.

Disclosure of Interest: None Declared



Thyroid

ICE2021-1594

CORRELATION BETWEEN ULTRASONOGRAPHY AND THYROID ANTIBODIES IN ALBANIAN POPULATION COHORT

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Introduction: Hashimoto thyroiditis is frequently seen in clinical practice. Thyroid ultrasonography is commonly used for the diagnosis together with hormonal tests and thyroid antibodies.

Objectives: Aim of this study was to evaluate the role of ultrasonography of thyroid gland as a screening method in early detection of thyroid dysfunction in Hashimoto thyroiditis especially in the subclinical phase.

Methods: Testing included 456 patients examined for thyroid disorders during 2018-2020. All patients underwent ultrasound examination of thyroid gland and blood tests FT4, FT3, TSH, anti-TPO and anti-TG. The patients were divided into two groups. Group A with positive autoantibodies (at least one of them) and Group B with negative thyroid antibodies. We assessed correlation between antibody activity and ultrasonographic parameters such as heterogeneity, hypoechogenicity, micronodular pattern and blood flow.

Results: Hypoechogenicity, heterogeneity and micronodular pattern were associated with significantly higher TPO antibodies activity $p < .001$. Hypoechogenicity had 96% sensitivity and 89.3% specificity. Micronodularity was the most specific parameter with a specificity 99.4%. There were significant correlations for changes in blood flow $p < .001$ between the two groups.

Conclusion: The ultrasound screening of thyroid gland plays an important role in early detection of thyroid dysfunction. Decreased ultrasound echogenicity represents the most significant marker of altered thyroid gland function in Hashimoto thyroiditis, while micronodularity is the most specific parameter.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1595

NTRK GENE REARRANGEMENTS IN NIFTP: WHICH ROLE?

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Introduction:

NTRK rearrangements have been reported in a small subset of papillary thyroid carcinoma (PTC) with clinically aggressive behaviour as local invasion and distant metastases. We describe a case of NTRK1 rearrangement in well-circumscribed tumor with follicular pattern and low-grade features.

Case Description:

Case Report

A young woman underwent a total thyroidectomy for a AUS/FLUS lesion of 12 mm in size detected in the right lobe. The histology revealed a follicular patterned neoplasia with papillary-like nuclear features and overall well-circumscribed margins with focal irregular interface between tumor and surrounding parenchyma. The BRAFV600E immunohistochemical (IHC) evaluation was negative, while we detected NTRK1 rearrangement by FISH. Conversely IHC stain with anti-pan TRK antibody resulted negative. Although the tumor presented histological features reminiscent of NIFTP, the identification of NTRK1 rearrangement led us to made the diagnosis of follicular variant papillary thyroid carcinoma (FVPTC).

Material and Method

We performed NTRK1/2/3 rearrangements using a commercially available break-apart probes (Empire Genomics, New York) on formalin-fixed paraffin embedded tissue (FFPE). Case showing more than 20% of aberrant cells was defined as positive. To analyzed the sensitivity of anti-pan TRK antibody (clone EPR17341, Ventana platform) IHC stain was also carried out.

Clinical discussion:

To our knowledge, NTRK1/3 fusion have so far only been found in classical PTC and infiltrative FVPTC. We described for the first time a follicular patterned tumor with histological features reminiscent of NIFTP, but harbouring NTRK1 rearrangement and we open the question whether NTRK fusion may represent a very early genetic event in molecular pathogenesis of thyroid neoplasia and may occur in NIFTP. Further research is needed to elucidate the clinico-pathological landscape of NTRK-rearranged thyroid carcinoma (NTRC), the pathogenic role and clinical significance of NTRK fusions found in thyroid nodules and cancer.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1596

'MY THYROID GAVE ME STROKE': A CASE OF GRAVES DISEASE WITH MOYAMOYA SYNDROME

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Introduction: Graves disease is the most common cause of hyperthyroidism in childhood with a peak incidence during early adolescence. Acute ischaemic stroke is a rare complication of Graves disease and when associated with characteristic involvement of internal carotid arteries with extensive collateral development on MRI, it is termed as Moyamoya Syndrome. Here, we report a case of Graves disease complicated by acute cerebral event.

Case Description: A 16-year-old female presented with progressive fatigability, tremors and neck swelling for last 15 days. In retrospective history; fidgety behaviour, insomnia, hypersalivation, increased sweating and heat intolerance was elicited. There was no associated contributory medical and family history. She was afebrile, tachycardic and hypertensive with wide pulse pressure. Her physical examination showed exophthalmos, warm-moist peripheries, tremors and Stage III goitre.

Her thyroid function test showed serum TSH of <0.01 uIU/ml (0.7-6.4), TT3 of >8 ng/ml (0.7-2.0) and TT4 of >24 ug/dl (4.5-11.0). TRAB antibody were positive. A diagnosis of Graves disease was made and was started on anti-thyroid (carbimazole) and b-blocker (propranolol).

On treatment, her thyroid profile showed an improving trend. But after 15 days of treatment, she developed left-sided weakness and slurred speech. On neurological examination, dysarthria with left sided motor weakness was present. Her MRI angiogram showed acute non-haemorrhagic infarct in right frontal lobe, caudate nucleus, putamen and insular lobe cortex with thinning and irregularity of bilateral ICA and MCA with multiple tufts of collaterals in supra-sellar cisterns and thalamo-striatal branches consistent with diagnosis of Moyamoya syndrome.

Anti-thyroid drug and b-blocker were continued. Antiepileptics, anti-platelet, anti-hypertensives and anti-raised ICP measures were initiated. On treatment, she showed both clinical and biochemical improvement. Currently she is on physiotherapy for left hemiparesis and regular follow up for her thyroid status.

Clinical discussion: Acute cerebral ischaemic event due to underlying thyrotoxicosis is a rare association. Thus, all Graves patient should undergo careful evaluation of clinical sign and symptoms suggestive for any acute ischaemic events as well as screening MR angiogram in predisposed individuals to Moyamoya syndrome to prevent stroke and subsequent morbidity-mortality.

Disclosure of Interest: None Declared

Thyroid

ICE2021-1621

FETAL GOITER: OPPORTUNITY FOR ANTENATAL TREATMENT WITH INTRA-AMNIOTIC THYROXINE.

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Introduction: Fetal goiter is an extremely rare complication of pregnancy. It can be associated with fetal hyperthyroidism, hypothyroidism and rarely with euthyroid status. Pre-natal ultrasonography (US) presents an opportunity for *in-utero* treatment.

Case Description:

A routine ultrasound done in other center in a 32 year-old woman, gravida 2, detected a fetal neck mass that was diagnosed as fetal goiter and the patient was sent to our institution for further follow up. Her past medical history was relevant for Hashimoto's Thyroiditis that was diagnosed four years before the current pregnancy. At that time the patient had elevated TPO antibodies and euthyroid status. She began treatment with L-T4. Actually, the intake is 88 mcg/day.

At 2nd trimester fetal morphologic US scan done at 22 weeks of gestation, fetal goiter was detected. The trachea appeared to be narrowed by compression and doppler evaluation revealed an increased vascularisation. The neck was hyperextended and 5D rendering volume depicted a prominent bilobed gland (area 6.8 cc RR 0.08 + 0.05, Figure 1). No signs of polyhydramnios or fetal anomalies were detected. Maternal thyroid evaluation showed TSH 1.81uIU/mL and negative TRAbs. Hypothyroidism was confirmed by fetal blood sampling via cordocentesis (TSH 76 mIU/L (RR 3.9–9.7) and total T4 2.6 mcg/dL (RR 3.43–7.39)) and by amniotic hormone levels (free T4 0.5 ng/dL (RR 0.4–4.5) and TSH 1.69 mIU/L (RR 0.1–0.5)). *In-utero* treatment was initiated with 400 mcg per week of L-T4 injected into the amniotic sac, and later increased to 600 mcg. A total of eleven intra-amniotic injections were administered between 24 and 35 weeks gestation resulting in a progressive reduction in the goiter (area 1.60 cc), which relieved the pressure on the trachea, and normal flexion of the fetal neck was restored. At 31 weeks, amniotic hormone levels were normal.

Elective cesarean section was performed at 36.3 weeks of gestational age, and a female neonate was delivered with Apgar scores of 9/10, weighting 2950 g. A goiter was not clinically apparent at delivery and the serum level of thyroglobulin postnatal was <0.04 ng/mL. The infant was discharged home on the second day of life with L-T4 treatment. Currently, she is 7 months old with adequate growth and normal psychomotor development.

Clinical discussion: Advances in prenatal imaging techniques and in fetal hormonology now allow for identification of disorders of thyroid function in the fetus.

Image:



Figure 1. 5-D image showing fetal goiter

Disclosure of Interest: None Declared

Thyroid

ICE2021-1628

THE APPREHENSION CAUSED BY AN UNPLANNED USE OF LUGOL'S IODINE

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Introduction: Lugol's iodine is used for 10 days prior to thyroidectomy to improve hyperthyroidism, reduce vascularity, and blood loss. It is also used for severe thyrotoxicosis and thyroid storm. We present a case of hyperthyroidism where we focus on certain management issues.

Case Description: A 50-year-old lady presented on April 2020 with a relapse of Graves' disease. Her first episode was treated from August 2015 to April 2019 with propylthiouracil after having had adverse effects with carbimazole. In April 2020, freeT4 was 32.9 pmol/L (11-23) and TSH was <0.01 mU/L (0.27-4.5). TSH Receptor antibodies were 13 U/L (0-1.74). Propylthiouracil was re-initiated and the dose titrated. No symptomatic improvement was noted despite receiving maximal doses of propylthiouracil (400 mg/day in divided doses), though she claimed to be fully compliant with the treatment. Hence, amidst the Covid crisis, she was hospitalized with an intention to provide supervised propylthiouracil to exclude non-compliance, and once thyroid function improves, to arrange an inpatient thyroidectomy. Her blood picture on admission was freeT4 >100, FreeT3 34.9 pmol/L (3.1-6.8), and TSH <0.01 and her Burch-Wartofsky Point Scale (BWPS) score for thyroid storm was 25. With the provisional diagnosis of impending thyroid storm on a background of poor clinical response to propylthiouracil, lugol's iodine was initiated with an intention to arrange thyroidectomy in 10-14 days as the definitive treatment. However, the feasibility of having a surgery during the pandemic was not considered at the time of initiation. During her stay, her thyroid profile started to improve within 3 days of initiating lugol's iodine (Free T4 67.6, TSH <0.01) and within 10 days near normal thyroid function were achieved (freeT4-26.0, freeT3-7.03).

She was referred to the ENT team for consideration of an emergency surgery. After repeated desperate communications, we succeeded to convince the ENT team to accept for emergency thyroidectomy. Still due to unforeseen circumstances related to Covid and due to interdepartmental miscommunications, the surgery happened only 16 days after lugol's iodine initiation.

Clinical discussion: Lugol's iodine blocks the release of thyroid hormones. This Wolff-Chaikoff effect starts within 24-48 hours and last until 10-14 days, after which escape occurs which might worsen hyperthyroidism (after 21 days). In our case, lugol's iodine should have been started after assessing feasibility for thyroidectomy.

Disclosure of Interest: None Declared

Thyroid

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INTRAUTERINE EXPOSURE TO PHTHALATE DEHP DISRUPTS THE HYPOTHALAMIC-PITUITARY-THYROID AXIS OF OFFSPRING RATS DURING ADULT LIFE

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Introduction: Di (2-ethyl-hexyl) phthalate (DEHP) is a known disruptor of the thyroid function. However, there are few studies about its effects during the intrauterine period. This period is essential for adequate fetal development and gene programming of different tissues. These processes are related to the higher or lower susceptibility of individuals to develop several diseases during adulthood.

Objectives: To evaluate the impact of maternal DEHP exposure during pregnancy on the hypothalamus-pituitary-thyroid (HPT) axis function of their offspring rats during adulthood.

Methods: Pregnant *Wistar* rats were orally treated during the gestational period with corn oil (control) or corn oil supplemented with DEHP (0.48 and 4.8 mg/kg/day). Offspring male and female rats were euthanized on the 90th postnatal day. Hypothalamus, pituitary, thyroid, kidney and liver were collected, and gene and protein expression were analyzed using RT-qPCR and Western Blotting. Serum measurements were performed by ELISA.

Results: In the female rats, both treatment doses increased the TRH and TSHb gene/protein expression in the hypothalamus and pituitary, respectively. In the thyroid both doses of DEHP exposure reduced NIS, TSHR, TG, TPO, NKX2.1, PAX8, FOXE1 gene/protein expression. Consistent with these results, female rats presented reduced T4 serum levels. However, T3 serum levels were not significantly affected, possibly due to the greater expression of type 1 deiodase (DIO1) in the liver and kidney of these animals. Male offspring rats presented an increased mRNA/protein expression of TRH in the hypothalamus and of TSHb in the pituitary, especially at the lowest dose of treatment. In the thyroid, NIS, TSHR, FOXE1, PAX8 and TPO expression were decreased especially at the lowest dose of treatment. T4 and T3 serum concentration were not altered in these animals. The 0.48mg/kg dose has induced the expression of DIO1 in the liver of these animals.

Conclusion: The intrauterine exposure to DEHP, in lower doses than the NOAEL, disrupted the HPT axis of male and female offspring rats. Nevertheless, apparently, different mechanisms are involved in the regulation of the axis function in male and female rats. This study suggests that DEHP exposure increases the susceptibility to the development of thyroid dysfunction during adulthood.

Disclosure of Interest: None Declared