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20TH INTERNATIONAL CONGRESS OF ENDOCRINOLOGY
18TH ASIA OCEANIA CONGRESS OF ENDOCRINOLOGY
21ST ASEAN FEDERATION OF ENDOCRINE SOCIETIES CONGRESS

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The publication of the abstracts for the 20th International Congress of Endocrinology, 18th Asia Oceania Congress of Endocrinology and 21st ASEAN Federation of Endocrine Societies Congress as a special edition of the Journal of the ASEAN Federation of Endocrine Societies is a service of the journal to its member societies. The statements and opinions expressed in this publication are those of the individual authors and do not necessarily reflect the views of the Journal of the ASEAN Federation of Endocrine Societies (JAFES). The abstracts included have been selected by the Congress' Scientific Committee and have not undergone the editorial deliberation and peer review of the JAFES. JAFES is not responsible or liable in any way for the currency of the information, for any errors, omissions or inaccuracies, or for any consequences arising therefrom. With respect to any drugs mentioned, the reader is advised to refer to the appropriate medical literature and the product information currently provided by the manufacturer to verify appropriate dosage, method and duration of administration, and other relevant information. In all instances, it is the responsibility of the treating physician or other healthcare professional, relying on independent experience and expertise, as well as knowledge of the patient, to determine the best treatment for the patient.

About ISE

Since its foundation in 1960, the International Society of Endocrinology (ISE) has pursued the worldwide advancement of education, science and patient care in endocrinology.

Today, the society forms the global network integrating all areas of endocrinology and metabolism. We unite the global endocrinology community to facilitate international cooperation between our member organisations and stakeholders.

We provide a platform to coordinate scientific exchange, education and partnerships between endocrinology organisations and healthcare professionals around the world.

We particularly focus on supporting early career endocrinologists around the world and championing endocrinology networks in developing countries and regions.

Our International Congress of Endocrinology – ICE – is organised every two years in a different region of the world, in collaboration with one of our members, and serves as the main outlet to disseminate the latest developments in the broad field of endocrinology.

For more information, please visit: https://www.isendo.org

About EMSS

Endocrinology and Metabolic Society of Singapore (EMSS) is the *de facto*, national-level, independent, and non-profit group representing and supporting the educators, clinical practitioners and scientists involved in Endocrinology and Metabolic Medicine

The Endocrine and Metabolic Society of Singapore was established in 1971. Since its inception, the Society has played a leading role in advocating and supporting the advancement of teaching, clinical practice and research in Endocrinology and Metabolism.

The society mainly aims to advance the knowledge and practice of medicine in the field of Endocrinology and Metabolism.

For more information, please visit: http://emss.org.sg

About AFES

The ASEAN Federation of Endocrine Societies (AFES) consists of endocrinologists from the nations of Southeast Asia. Its objective is to promote and coordinate activities among the component endocrine societies and to advance the knowledge and practice of medicine in the field of endocrinology and metabolism in the member countries. The first congress was inaugurated in 1981 to provide the platform to achieve this object. It was held in in Yogyakarta, Indonesia under the sacred shadow of the ancient temple of Borobudur. Since then, it has been held once in every 2 years in Southeast Asian countries and brings together endocrinologists in the region and beyond to promote endocrinological research and knowledge and to strengthen the ties of those who practice endocrinology in the region.

AFES publishes a journal named the **Journal of the ASEAN Federation of Endocrine Societies (JAFES)** twice a year. It is an OPEN ACCESS, internationally peer-reviewed, English language, medical and health science journal that serves the endocrine window between the ASEAN region and the world, featuring original papers and publishing key findings from specialists and experts of endocrinology.

For more information, please visit: https://asean-endocrinejournal.org/index.php/JAFES/about

About FESAO

The Federation of Endocrine Societies of Asia and Oceania (FESAO) was founded in 1990 in Jakarta, Indonesia. The federation members consist of Associations/Societies of Endocrinology and Metabolism of each country in the Asia Oceania Region, with the aim of strengthening the cooperation and understanding among clinicians and scientists in the region that FESAO covers.

FESAO promotes the sharing of knowledge and experience from all member countries to provide better medical care in the field of endocrinology, metabolism and diabetes, while establishing itself as a conduit for sharing knowledge, collaborating in research, and networking of clinicians/scientists who have an interest in these fields.

Message

We have successfully completed our 21st congress of the ASEAN Federation of Endocrine Societies (AFES) virtually in Singapore over 4 full days of sessions from the 25th to 28th of August 2022. This was the first time it was held in conjunction with the 20th International Congress of Endocrinology and the 18th Asia-Oceania Congress of Endocrinology. It was heartening to see the staunch support from the ASEAN and the global region. As with all previous AFES congresses, we have consolidated the abstracts that were sent in to the congress for publication in the Journal of the ASEAN Federation of Endocrine Societies – JAFES.

A warm congratulations to all authors whose abstracts have been accepted. These abstracts have been received from the region and globally and showcase advances in the field of endocrinology despite the challenges that are still plaquing the world by Covid. They serve as a not just a repository of part of the body of knowledge gleaned in the congress, but memories of the meeting itself and are testament to the resilience of the endocrine community at large.

As chairperson of the joint congress, it gives me great pleasure then to present these to you and to once again give thanks to all the contributors to the meeting and are integral to its success- the local organising committee, the programme organising committee and the various societies behind this congress – the International Society of Endocrinology, the Federation of Endocrine Societies of Asia-Oceania and the ASEAN Federation of Endocrine Societies.

As President of AFES, I want to thank all who have taken some time out to grace this joint meeting in virtual Singapore and allowed us to showcase ASEAN to you, no less of which are the faculty and the attendees. Special thanks must also go to the ASEAN nations strongly backing the congress that brings us all together every couple of years to renew our bonds of friendship.

I hope to meet you again soon physically in the near future.

Dr Vivien Lim
Chairperson
AFES2017 Local Organising Committee
President
ASEAN Federation of Endocrine Societies (AFES)

Message

Dear Delegates,

Greetings from Singapore. A very warm welcome to all the participants of our conference.

This special edition of the JAFES presents the abstracts of the 20th International Congress of Endocrinology, the 21st ASEAN Federation of Endocrine Societies Congress, and the 18th Asia Oceania Congress of Endocrinology.

The theme of our Congress is "Global Partnership in Facing the Current Challenges in Endocrinology." This theme was chosen because we believe all of us can work better together in building a stronger bond among the international endocrine community, especially in the face of the great challenges posed by the pandemic.

We would like to express our heartfelt appreciation for the abstracts submitted. We recognise your outstanding efforts as demonstrated by the high-quality research work presented in the abstracts.

We are most impressed by the enthusiasm and support we received despite the challenges faced by everyone in the midst of the pandemic and the conference being converted to a virtual format.

Many thanks to all our Program Committee members for the grading and assessment of all the abstract submitted.

We are looking forward to seeing all of you again in Singapore.

Dr Stanley Liew
President
Endocrine and Metabolic Society of Singapore (EMSS)
President
Federation of Endocrine Societies of Asia and Oceania (FESAO)

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ORAL PRESENTATIONS

OP-1-1

ASSOCIATION OF HIF1A rs142179458 WITH BODY ADIPOSITY IN MULTI-ETHNIC ASIANS WITH TYPE 2 DIABETES

https://doi.org/10.15605/jafes.037.AFES.01

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OBJECTIVES

Hypoxia is known to contribute to obesity and its related metabolic disorders. Our preliminary data derived from whole-exome sequencing suggested an association of the hypoxia-inducible factor 1 α (HIF1α) rs142179458 variant with type 2 diabetes (T2D). However, the impact of this HIF1α variant on adiposity remains unclear. The study sought to identify the relationship between the HIF1α rs142179458 and the obesity phenotype.

METHODOLOGY

The study involved participants from the Singapore study of macro-angiopathy and microvascular reactivity in type 2 diabetes (SMART2D) study (n = 2010; age = 57 ± 11; 51.3% males). The subjects were screened for the possibly damaging HIF1α rs142179458 (c.1045g>a [p. asp349asn]) variant [minor allele frequency: 0.00459 (all), 0.02719 (East Asians)] in genome-wide genotyping. The association of the HIF1α genotype with anthropometric variables was assessed using Chi-square test, Pearson's correlation, and regression analyses.

RESULTS

Among the subjects, 2.5% (n=50) carried the HIF1α variant (ag/aa) and displayed higher body mass index (BMI) than the wildtype genotype (29.8 ± 6.9 versus 27.6 ± 5.2 kg/m^2 p=0.004). Hip circumference and percentage body fat were also markedly higher in the former group. A positive correlation was observed between the HIF1α variant and the anthropometric parameters analyzed (all p<0.05). HIF1α variant was associated with BMI using the Asian BMI cut-off of 23.5 kg/m^2 even after adjusting for age, gender, and ethnicity (odds ratio:1.21, 95% CI:0.99-1.47, p=0.020).

CONCLUSION

HIF1α rs142179458 variant is associated with increased adiposity in adults with T2DM. We postulate that alteration in HIF1α gene may cause dysregulation of the adaptive response to hypoxia, resulting in body mass index gain and potentially aggravating diabetes.

OP-1-2

GLUCOSE TOLERANCE STATUS AT 3 TO 18 MONTHS POSTPARTUM OF SRI LANKAN FEMALES WITH A HISTORY OF GESTATIONAL DIABETES MELLITUS

https://doi.org/10.15605/jafes.037.AFES.02

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OBJECTIVES

Gestational diabetes mellitus (GDM) refers to glucose intolerance, first recognised during pregnancy that usually resolves after birth. Females with previous GDM have an increased risk of developing type 2 diabetes mellitus (T2DM) later in life. Hence, we aimed to investigate the distribution of and risk factors for dysglycaemia in females with previous GDM.

METHODOLOGY

Females (n=992) from five hospitals in Sri Lanka with GDM as per IADPSG criteria were identified. Of those, 515 (51.92%) followed up at 3 to 18 months postpartum. Sociodemographic, medical and anthropometric data were collected, and 75-g OGTT and HbA1C testing were carried out.

RESULTS

Within 18 months (median 6 months) of the pregnancy in which they were diagnosed with GDM, 250 (48.54%) females were dysglycaemic, including 50 (9.69%) and 200 (38.76%) with T2DM and prediabetes, respectively as per the ADA criteria. Mean postpartum HbA1C was 5.37 (±0.35)%, 5.70 (±0.45)% and 7.85 (±2.19)% for those with normoglycemia, prediabetes and T2DM, respectively. Females with a higher postpartum BMI [or 1.08 per 1 kg/m^2 greater BMI (95% CI 1.03-1.12)], waist circumference [or 1.04 per 1-cm greater waist circumference (95% CI 1.03-1.06)], postpartum screening interval [or 1.13 per 1-month greater screening interval (95% CI 1.03-1.24)], use of insulin during pregnancy [or 5.44, 95% CI (2.35-12.56)] and history of GDM [or 3.64, 95% CI (1.80-7.35)] had a higher likelihood of developing dysglycaemia.

CONCLUSION

The high post-pregnancy conversion rates of GDM to T2DM reported in this study reinforce the need for mandatory postpartum screening and identification of predictors which could improve accurate risk stratification of patients during pregnancy.

OP-1-3

THE EFFECT OF TIRZEPATIDE IN PEOPLE WITH TYPE 2 DIABETES: AN UPDATED META-ANALYSIS OF SURPASS TRIAL

https://doi.org/10.15605/jafes.037.AFES.03

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OBJECTIVES
Tirzepatide acts as a dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist. Up to now, no subgroup meta-analysis has compared the efficacy and safety of tirzepatide in type 2 diabetes compared to each class of diabetic treatment. This meta-analysis aimed to investigate this knowledge gap.

METHODOLOGY
Studies were searched using the keywords: [(type 2 diabetes mellitus) or (diabetes mellitus) or (diabetic)] and (tirzepatide) in several databases of Cochrane Central Register of Controlled Trials (CENTRAL), Pubmed, ScienceDirect, Ovid. All references were reviewed using critical appraisal center for evidence-based medicine checklist. The descriptions of the extracted data are guided by Preferred Reporting Items for Systematic Reviews (PRISMA) statement with grade approach. This study is registered in prospero: id crd42022328793. Two hundred sixty-five papers were initially collected, and seven studies pooled and entered review synthesis.

RESULTS
Seven RCTs involving 3562 patients were analysed. Over 12–52 weeks, individuals receiving tirzepatide had significantly greater lowering of HbA1C [mean difference (MD) = -1.4% (95% confidence interval (CI): -1.71 to -1.1); $p<0.01$; $i^2 = 96.8\%$], fasting glucose [MD = -29.1 mg/dl (95% CI: -36.37 to– -21.93); $p<0.01$; $i^2 = 99.1\%$], 7-point SMBG [MD = -19.94 mmol/l (95% CI: -36.37 to -21.93); $p<0.01$; $i^2 = 100\%$]. Weight loss was also greater than 5%. [RR = 22.07 (95% CI: 6.3 to 77.3); $p<0.01$; $i^2 = 98.2\%$].

CONCLUSION
Tirzepatide led to a higher decrease in glycaemic HbA1C than placebo and insulin. FPG was significantly lower in the tirzepatide arm compared to the GLP-1 RA group.

OP-1-4

USING A CACO-2 AND THP-1 CO-CULTURE MODEL TO EVALUATE INTESTINAL BARRIER PROTECTIVE PROPERTIES — EFFECTS OF DEXAMETHASONE

https://doi.org/10.15605/jafes.037.AFES.04

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OBJECTIVES

Increased intestinal permeability or so-called "leaky gut," is considered an early event in the development of obesity and diabetes. It is likely driven by the translocation of bacteria-derived products such as lipopolysaccharide (LPS) from the intestinal lumen into the blood stream leading to low-grade inflammation. A co-culture model of intestinal barrier dysfunction was used to characterize the mechanisms of barrier protection induced by an anti-inflammatory drug.

METHODOLOGY

In co-cultured CACO-2 and THP-1 cells representing the intestinal epithelium and immune cells, respectively, barrier dysfunction was induced using LPS and quantified by measuring trans-epithelial electrical resistance (TEER). Dexamethasone was tested for its barrier-protective properties by application to the apical side. Dexamethasone concentration was quantified on apical and basolateral sides after 24-hour treatment using liquid chromatography/mass spectrometry. Cytokine release was determined using a multiplex chemiluminescence assay (mesoscale discovery). Expression of selected tight junction (TJ) proteins was assessed using immunocytochemical staining and confocal imaging.

RESULTS

Dexamethasone significantly ($p=0.009$) improved TEER by 30%, while 74% of the dexamethasone remained on the apical side and 24% was detected basolaterally. Dexamethasone significantly decreased interleukin (IL)-6 ($p<0.0001$), tumour necrosis factor α ($p<0.0001$) and IL-1β ($p=0.051$) release by THP-1 cells. However, confocal imaging revealed that dexamethasone did not improve the localization of occludin, claudin-2 or zonula occludens-1 when compared to LPS-induced cells.

CONCLUSION

Dexamethasone improved barrier function likely due to its anti-inflammatory effect. However, it could not prevent localization of the pore-forming claudin-2, which may explain the presence of residual barrier dysfunction in this model.

OP-1-5

ATHEROGENIC INDEX OF PLASMA, MEDIATED BY PIGMENT EPITHELIUM-DERIVED FACTOR IS ASSOCIATED WITH CHRONIC KIDNEY DISEASE PROGRESSION IN TYPE 2 DIABETES

https://doi.org/10.15605/jafes.037.AFES.05

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OBJECTIVES
Atherogenic index of plasma (AIP) is a novel marker of atherosclerosis and cardiovascular disease. Its role in chronic kidney disease (CKD) progression is unknown. Pigment epithelium-derived factor (PEDF) has anti-oxidant, anti-angiogenic and anti-inflammatory properties, and its circulating level may be elevated in CKD. We investigated the association between AIP and CKD progression, with possible mediation by PEDF, in type 2 diabetes (T2D).

METHODOLOGY
We conducted a prospective study on 1496 patients (mean age 57.6 ± 10.1 years) from SMART2D cohort. AIP was calculated as the logarithmically transformed ratio of triglyceride to high-density lipoprotein. CKD progression was defined as deterioration across KDIGO estimated glomerular filtration rate categories with ≥25% decrease from baseline. Enzyme-linked immunosorbent assay was used to quantitate PEDF. We examined the association between AIP in quartiles and CKD progression using cox proportional regression, adjusting for demographics, clinical characteristics and medications. This research was approved by an ethics committee.

RESULTS
Over follow-up of up to 11.0 years, 49.8% of the participants had CKD progression. Compared to quartile(q)1, q2, 3 and 4 AIP were positively associated with CKD progression with unadjusted hazard ratio(HR) of 1.27 (95%confidence interval (CI) 1.02-1.57; p=0.033), 1.44 (95% CI 1.17-1.79; p=0.001) and 1.81 (95% CI 1.47-2.23; p<0.001) respectively. Quartile 4 AIP remained positively associated with CKD progression in the fully adjusted model [HR 1.32 (95% CI 1.06-1.64; p=0.013)]. Binary mediation analysis revealed that PEDF accounted for 27.3% of the association between AIP and CKD progression (p=0.008).

CONCLUSION
Higher AIP, mediated by PEDF, is an independent predictor of CKD progression in T2DM. AIP is a simple and inexpensive index for predicting CKD progression for potential use in routine clinical practice.

OP-2-1

ASSOCIATIONS OF NON-INVASIVE PARAMETERS OF LIVER STEATOSIS AND FIBROSIS WITH RENAL IMPAIRMENT IN TYPE 2 DIABETES: A 6-YEAR LONGITUDINAL ANALYSIS

https://doi.org/10.15605/jafes.037.AFES.06

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OBJECTIVES

We examined the associations of non-invasive parameters of liver steatosis and fibrosis with renal impairment, and the mediatory role of the pro-angiogenic factor leucine-rich α-2 glycoprotein 1 (LRG).

METHODOLOGY

Adults with type 2 diabetes (T2D; n = 2,057) were recruited by the Singapore study of macroangiopathy and microvascular reactivity in type 2 diabetes (SMART2D) study and followed up for 6 years. Baseline liver steatosis [(hepatic steatosis index (HSI) and Zhejiang university index (ZJU)] and liver fibrosis [aspartate transaminase/alanine transaminase ratio (AAR) and bard] scores were calculated. Plasma LRG1 levels were quantified using immunoassay. Study outcomes were estimated glomerular filtration rate (eGFR) decline of ≥40% and albuminuria progression. In an independent T2D group (n = 47), cross-sectional correlations between transient elastography readings and renal markers were explored.

RESULTS

In the cross-sectional study, liver steatosis and fibrosis parameters derived from either composite scoring systems or elastography were associated with increased albuminuria and reduced renal function, respectively. Among individuals with follow-up data, 32.4% (n = 481/1484) developed eGFR decline, while 38.3% (n = 503/1312) had albuminuria progression. Multivariable cox regression analyses revealed that AAR (hazard ratio:1.56; 95% CI:1.15–2.11, p=0.004) and bard (hazard ratio:1.16, 95% CI:1.04–1.28, p=0.005) predicted eGFR decline. Binary mediation showed that LRG1 accounted for 34.2% and 28.1% of the effects of AAR and bard scores on the risk of eGFR decline, respectively. In contrast, liver steatosis but not liver fibrosis indices (HSI, ZJU) independently predicted albuminuria progression.

CONCLUSION

Liver steatosis is associated with worsening of albuminuria. Similarly, liver fibrosis is associated with renal function decline, potentially driven by increased inflammation and angiogenesis.

OP-2-2

HIGH NEUTROPHIL/LYMPHOCYTE RATIO PREDICTS RENAL FUNCTION DECLINE IN MULTI-ETHNIC ASIANS WITH TYPE 2 DIABETES – A LONGITUDINAL COHORT STUDY

https://doi.org/10.15605/jafes.037.AFES.07

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OBJECTIVES
We evaluated the utility of baseline neutrophil/lymphocyte ratio (NLR) as a predictor of renal function decline in a multi-ethnic Asian cohort with type 2 diabetes (T2D), and the mediatory effect of extracellular water/total body water (ECW/TBW) ratio.

METHODOLOGY
Adults with T2D (n = 1,224) were recruited by the DKD-onset and progression risk factors (DORIS) study, and prospective clinical data were extracted from the electronic health record. Cox regression analyses examined the associations between NLR and renal function decline defined as estimated glomerular filtration rate decline of ≥40%. Improvements in risk discrimination were assessed by Harrell's c-statistics. The mediatory role of ECW/TBW ratio estimated by bioimpedance method was assessed using binary mediation.

RESULTS
Compared with those with stable renal function, elevated NLR levels were observed in individuals who experienced renal function decline over a 1.8-year follow-up period. NLR was associated with the renal outcome in the unadjusted cox model (hazard ratio:1.39, 95% CI:1.23–1.57, p<0.001), and the association persisted after covariate adjustment (hazard ratio:1.38, 95% CI:1.19–1.59, p<0.001). Addition of NLR to a multivariable model consisting of demographics, T2D duration, metabolic and renal parameters, and use of antihypertensive medications significantly improved risk discrimination (p=0.030). The ECW/TBW ratio mediated 19.9% of the indirect effect of NLR on renal function decline.

CONCLUSION
Systemic inflammation as reflected by increased NLR is associated with renal function decline in multi-ethnic Asian adults with T2D, mediated by the presence of excess extracellular fluid. Hence, treatment strategies to ameliorate chronic inflammation and fluid overload may potentially attenuate renal function deterioration in T2D.

OP-2-3

ASSOCIATION OF TRAJECTORY OF BODY SHAPE INDEX WITH ALL-CAUSE AND CAUSE-SPECIFIC MORTALITY: RESULTS FROM TEHRAN LIPID AND GLUCOSE STUDY (TLGS)

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OBJECTIVES
The aim of the current study was to examine how the trajectory of body shape, assessed through a body shape index (ABSI), could predict mortality in a prospective cohort of the Tehran Lipid and Glucose Study (TLGS) over a 20-year period.

METHODOLOGY
The study included 5587 participants greater than 35 years old from the TLGS who were free of cardiovascular disease and cancer at baseline and completed the initial assessment and at least one additional follow-up examination. ABSI trajectories were developed in 6 phases over 18 years of follow-up from 2000 to 2018 using GMM. The primary outcomes were overall and cause-specific mortality, including death from cardiovascular disease (CVD), non-CVD causes, and non-cancer causes. Cardiovascular events were also considered secondary outcomes.

RESULTS
During a mean follow-up of 15.8 years, 566 (20.68 %), and 178 (6.56 %) deaths from all-cause and CVD mortality were identified, respectively. The small ABSI - marked increase (TR2) (adjusted HR, 1.36; 95%CI, 1.04-1.79) and large ABSI - marked increase trajectory (TR3) (adjusted HR, 1.41; 95% CI, 1.04-1.91) were associated with higher subsequent risks of all - cause mortality and non-CVD mortality (adjusted HR for TR2, 1.38; 95% CI, 1.00-1.91; adjusted HR for TR3, 1.43; 95% CI, 1.00-2.05) as well as an increased risk for CVD (adjusted HR for TR2, 1.40; 95% CI, 1.14-1.71; adjusted HR for TR3, 1.42; 95% CI, 1.13-1.78) and CHD (adjusted HR for TR2, 1.53; 95% CI, 1.19-1.97; adjusted HR for TR3, 1.48; 95% CI, 1.12-1.96).

CONCLUSION
ABSI trajectories may be associated with subsequent risk of mortality and CVD events.

OP-3-1

IMPROVEMENTS IN HYPERTENSION AND DIABETES MELLITUS WITH OSILODROSTAT IN PATIENTS WITH CUSHING'S DISEASE: EXPLORATORY ANALYSES FROM THE PHASE III LINC 3 STUDY

https://doi.org/10.15605/jafes.037.AFES.09

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OBJECTIVES
This study aimed to explore blood pressure (BP) and glucose homeostasis changes with osilodrostat therapy in patients with Cushing's disease (CD) with baseline hypertension and diabetes mellitus (DM) during LINC 3 (nct02180217).

METHODOLOGY
Adult patients with CD with mean urinary free cortisol (MUFC) >1.5x ULN received osilodrostat for 48 weeks (w). Baseline hypertension was defined as a prior diagnosis of hypertension, use of antihypertensive medication, and/or SBP/DBP >130/>90 mm Hg. Baseline DM was defined as a prior diagnosis of T2DM, use of antidiabetic medication, HbA1C ≥6.5%, and/or FPG ≥126 mg/dl.

RESULTS
At baseline, 119/137 patients (87%) had hypertension. Mean SBP/DBP decreased with osilodrostat therapy. Baseline SBP >130 mm Hg (n=79) decreased to ≤130 mm Hg at w12, w24 and w48 in 58%, 51% and 49% of patients respectively. Baseline DBP >90 mm Hg (n = 50) decreased to ≤90 mm Hg at w12, w24 and w48 in 72%, 62% and 66% of patients respectively. Blood pressure did not increase in patients without baseline hypertension. An equal number (n = 34[40%]) stopped or reduced the dose of the medication and increased the dose/number of antihypertensives during the study among the 85 patients taking antihypertensives prior to recruitment. At baseline, 61/137 patients (45%) had DM. FPG decreased from ≥100 mg/dl at baseline (n = 36) to <100 mg/dl by w12, w24 and w48 in 58%, 64% and 44%, respectively. More patients taking antihyperglycemics at baseline stopped/reduced the dose (n = 21/43[49%]) compared to those who increased the dose/number of antihyperglycemics during the study (n = 10/43[23%]). Neither change in BP nor blood glucose parameters correlated with changes in UFC from baseline.

CONCLUSIONS
Consistent improvements in comorbid hypertension or DM occurred in many patients with CD receiving osilodrostat for 48 weeks. Concomitant adjustments in medications for hypertension and DM were required in some patients, including for those with improvements in the status of these comorbid conditions.

OP-3-2

USING OBJECTIVE MEASURES AND PATIENT-REPORTED OUTCOMES TO ASSESS DISEASE ACTIVITY FOR PATIENTS WITH ACROMEGALY: BASELINE DATA FROM THE ACRODAT® STUDY

https://doi.org/10.15605/jafes.037.AFES.10

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OBJECTIVES
We report an interim analysis of data captured from 258 subjects from the post-marketing surveillance study to evaluate the clinical utility of ACRODAT®.

METHODOLOGY
This is an international and randomized study (clinicaltrials.gov nct 04349839). Patients were randomly assigned to the ACRODAT® group or the standard practice group and followed-up over a 2-year period. Primary endpoint was the change from baseline in local IGF-I values after 24 months of management. Patients were recruited from medical centres in Denmark (142), France (56), Belgium (34), Spain (21) and Sweden (5). Participating countries also included Italy, Germany, Austria and Switzerland.

RESULTS
One hundred twenty-eight patients were enrolled in the ACRODAT® group and 130 patients in the standard practice group. Patients had a mean (SD) age of 56 ± 13 years, a median time since diagnosis of acromegaly of 114 [5-576] months, and 44 % of the patients were male. Eighty three percent had previously undergone pituitary surgery. Likewise, 83 % were receiving one or more medications for acromegaly at baseline. Investigators used the change in IGF-1 from baseline to determine the disease to be controlled in 182 (71 %) and not controlled in 76 (29 %). Average follow-up period was 11 [0-21] months.

CONCLUSION
This study provided valuable insights on the benefit of ACRODAT® on the normalization or maintenance of normalized IGF-I levels and improvement of disease activity status after a 2 year follow-up period.

OP-3-3

SUCCESS RATE OF GONADOTROPIN-RELEASING HORMONE AGONIST VERSUS GONADOTROPIN-RELEASING HORMONE ANTAGONIST IN POOR RESPONDERS UNDERGOING IN VITRO FERTILIZATION: A SYSTEMATIC REVIEW

https://doi.org/10.15605/jafes.037.AFES.11

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OBJECTIVES
To determine the optimal protocol for poor IVF responders, this systematic review aimed to evaluate their outcomes when subjected to protocols using gonadotropin-releasing hormone (GnRH) agonist compared to protocols using antagonist.

METHODOLOGY
Studies were searched using keywords: [(gonadotropin-releasing hormone agonist) or (gonadotropin-releasing hormone antagonist) or (GnRH)] and [(in vitro fertilization) or (IVF)] in Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, and ScienceDirect published between the years 2012-2022. All references were reviewed using critical appraisal centre for evidence-based medicine checklist. The descriptions of the extracted data are guided by preferred reporting items for systematic reviews (PRISMA) statement. Six studies pooled and entered review synthesis.

RESULTS
Five RCTs were identified enrolling 1279 participants with ages between 35 to 42 years old with 2 to 10 weeks of follow up. Two studies revealed that GnRH agonist showed significantly higher pregnancy rates and implantation rates compared to GnRH antagonist (29.3% vs 14.1% respectively, p=0.0291 and 19.40% vs. 10.30%, respectively p=0.022). None of the studies showed that GnRH antagonist resulted to significantly higher pregnancy rates compared to GnRH agonist. Furthermore, one study showed that GnRH antagonist resulted in significantly higher cancellation rates compared to GnRH agonist.

CONCLUSION
Protocols using GnRH agonist result in better outcomes with higher pregnancy and implantation rates, and lower cancellation rates compared to those using GnRH antagonist in patients with poor IVF response.

OP-3-4

GENETIC CHARACTERIZATION OF A FAMILIAL PATHOGENIC VARIANT OF MAX GENE ASSOCIATED WITH PHEOCHROMOCYTOMA, PARAGANGLIOMA AND DUODENAL/ PANCREATIC NEUROENDOCRINE TUMOURS

https://doi.org/10.15605/jafes.037.AFES.12

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OBJECTIVES

A 30-year-old male was diagnosed with pheochromocytoma based on hypertension, imaging and biochemistry. He underwent a 14-susceptibility gene panel for PPGLs (Invitae, USA) that revealed a germline pathogenic nonsense heterozygous MYC-associated factor X (MAX) variant (c.223c>t p.arg75*). The patient's father (61 years old) was found to carry the same germline mutation which led to the diagnosis of a functional abdominal paraganglioma and two neuroendocrine tumors (NETs) in his pancreas and his duodenum that were operated on.

Our objective was to determine the causal role of the familial germline MAX pathogenic variant in the development of PPGLs and NETs.

METHODOLOGY

Leucocyte DNA was extracted from blood cells and tumoral DNA was extracted from FFPE tissues. All 5 exons of the MAX gene (nm_002382.4) were studied by Sanger sequencing. The amplicons were directly sequenced using the applied biosystems 3730xl DNA analyzer (Mcgill University, Genome Quebec, Qc, Canada).

RESULTS

The germline MAX mutation (c.223c>t p.arg75*) was confirmed in both leucocyte DNA and all tumoral DNA (son: PHEO, father: PGL and NETs). The wild-type max allele was lost in the tumoral DNA of the father's PGL. A second somatic pathogenic variant of MAX c.263t>c (p.leu88pro) was identified in the duodenal NET and was predicted to be likely deleterious (CADD score 31).

CONCLUSION

We report the rare association of a familial germline MAX mutation presenting with PPGLs and NETs. A second hit in the MAX gene in the duodenal NET supports the hypothesis that MAX mutations might be associated with multiple endocrine tumors.

OP-3-5

ASSOCIATION BETWEEN GLUCOCORTICOID DOSE WITH BMI AND GLUCOCORTICOID-RELATED COMORBIDITIES: DATA FROM TILDACERFONT PHASE 2A TRIALS IN CLASSIC CONGENITAL ADRENAL HYPERPLASIA

https://doi.org/10.15605/jafes.037.AFES.13

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OBJECTIVES
Classic CAH treatment requires cortisol replacement to prevent life-threatening adrenal crises. However, the absence of cortisol feedback loop leads to persistent HPA activation and overproduction of adrenal androgens. Current treatment requires lifelong exposure to supraphysiologic glucocorticoid (GC) doses to suppress adrenal androgens.

Tildacerfont, an oral once-daily CRFR1 antagonist, decreased ACTH and androgens in patients with CAH in clinical trials, raising the possibility of improving disease control while decreasing the risks associated with lifelong GC exposure. This study describes GC-associated risks in the trial populations.

METHODOLOGY
This post-hoc, cross-sectional analysis characterizes the comorbidity profiles of subjects in two phase 2 studies stratified by GC dose.

RESULTS
Twenty-six adult participants, 58% female with an average age of 37 years [range 18-66], had a mean GC dose of 30.6 mg HCe/d [range 10-60 mg]. Evaluation by baseline GC dose [<30 mg (n = 9), ≥30 mg (n = 17)] showed trends toward higher BMI in the higher dose group, 32 vs. 29 kg/m^2, with more subjects meeting the criteria for obese II/III designation in the high dose group, 22% vs. 29%.

Trends were apparent in the baseline comorbidities reported in medical history: psychiatric disorders, including depression, anxiety, ADHD, and insomnia, occurred in 2/9 (22%) vs 8/17 (47%), obesity occurred in 3/9 (33%) vs. 8/17 (47%). Cushingoid features were reported in 0/9 vs 2/17 (12%). Both patients with Cushingoid features were on dexamethasone. Osteopenia/osteoporosis was reported in 1/9 (11%) vs 5/17 (29%). No meaningful differences were noted in baseline medications used.

CONCLUSIONS
In these studies, subjects with a higher GC dose exhibited a higher BMI and reported more GC-related comorbidities.

OP-4-1

INCIDENCE AND ASSOCIATED CLINICAL FACTORS OF THYROID DYSFUNCTION DURING TYROSINE KINASE INHIBITOR THERAPY AMONG NONTHYROIDAL CANCER PATIENTS: A RETROSPECTIVE STUDY

https://doi.org/10.15605/jafes.037.AFES.14

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OBJECTIVES
Tyrosine kinase inhibitors (TKIS) have been demonstrated to induce thyroid dysfunction—most commonly, hypothyroidism. Newer TKIS have been increasingly used, hence, this study aimed to determine the incidence and clinical profile of TKI-induced thyroid dysfunction in the University of Santo Tomas Hospital (USTH), Philippines.

METHODOLOGY
A retrospective observational study of TKI-treated non-thyroidal cancer patients >18 years old with available TSH determination from 2013 to 2020 at USTH was done.

RESULTS
From 127 TKI-treated patients, 61 had TSH determination. Incident thyroid dysfunction was 41%. Thirty-one percent had hypothyroidism (i.e., 24% overt [mean TSH 16.64 uIU/ml]; 7% subclinical [mean TSH 7.10 uIU/ml]). Hypothyroidism observed classified according to TKIS were as follows: pazopanib (81%, 9/11), gefitinib (33%, 4/12), imatinib (9%, 2/22), osimertinib (100%, 2/2) and afatinib (100%, 2/2) [p<0.001]. The median time at risk was 8 and 26 months for overt and subclinical hypothyroidism, respectively. Fifty seven percent were given levothyroxine (50-100 mcg/day). Seventy-one percent had persistent hypothyroidism (higher median TSH 16.8 uIU/ml, p=0.009). Average time to recovery of transient hypothyroidism was 40 months. Ten percent had hyperthyroidism (highest rate in bosutinib). Median number of months to occurrence of hyperthyroidism was 1.5. Non-small cell lung cancer patients were 73.85% less likely to maintain euthyroidism (p=0.021). No other clinical risk factors were associated with the development of thyroid dysfunction.

CONCLUSIONS
Surveillance for thyroid dysfunction is important during TKI therapy due to an incidence of 41% (31% hypothyroidism, 10% hyperthyroidism). Median time to occurrence of overt hypothyroidism and hyperthyroidism was 8 and 1.5 months, respectively. Except for solid cancer diagnosis, no other demographic profiles were associated with thyroid dysfunction.

OP-4-2

NUCLEAR YAP INDUCES AGGRESSIVE THYROID TUMORS AND CONFERS PRIMARY RESISTANCE TO VEMURAFENIB

https://doi.org/10.15605/jafes.037.AFES.15

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OBJECTIVES

YAP overexpression or activation promotes tumorigenesis in many human cancers. However, mutations in the YAP-Hippo pathway are rare. Despite this, nuclear YAP correlates with poor prognosis in various cancers and its aberrant activation induces EMT, proliferation, a pro-tumoral microenvironment and metastasis. YAP is implicated in resistance to targeted therapies; the mechanisms are unknown. We investigated YAP localization, pathway dependency, and its role in response to BRAF-inhibitors in thyroid cancer.

METHODOLOGY

We screened 52 thyroid cancer cell lines and 62 tumor samples for illegitimate nuclear YAP. We engineered doxycycline-inducible thyroid-specific mouse model expressing YAPS127A, alone or in combination with endogenous expression of BRAFv600E. We generated cell lines expressing dox-inducible shmiR-E-YAP and/or YAPS127A and used cell viability, invasion assays, immunofluorescence, western-blotting, qRT-PCRS, flow cytometry, RNA-seq and in vivo tumorigenesis.

RESULTS

We found that 27/52 thyroid cancer cell lines had constitutively aberrant nuclear YAP, which rendered them dependent on YAP for viability, invasiveness and sensitivity to a YAP inhibitor. Nuclear YAP was found frequently in human thyroid cancers, especially in those harboring BRAF/RAS-driver mutations. Constitutively nuclear YAP was sufficient to induce thyroid tumor formation in vivo and in cooperation with BRAFv600E induced a more aggressive phenotype. Presence of nuclear YAP in BRAF-mutant thyroid cells conferred resistance to vemurafenib through transcriptional activation of nrg1/her2/her3; which was abrogated by silencing YAP and relieved by pan-HER kinase inhibitors.

CONCLUSIONS

YAP activation generates a dependency on this transcription factor. Nuclear YAP governs intrinsic resistance to RAF kinase inhibitors and induces a gene expression program in BRAFv600E-mutant cells encompassing effectors in the NRG1 pathway.

OP-4-3

COMPARISON OF PREGNANCY OUTCOMES IN SUBCLINICAL HYPOTHYROIDISM WITH EUTHYROIDISM: A PROSPECTIVE COHORT STUDY

https://doi.org/10.15605/jafes.037.AFES.16

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OBJECTIVES
This study aimed to compare the pregnancy outcome between euthyroid and women with subclinical hypothyroidism (SCH) (TSH: 2.5 – 4 mIU/L) with and without thyroid peroxidase antibodies (TPOAB).

METHODOLOGY
A total of 178 pregnant females were recruited in the first trimester and those with TSH between 0.1 - 2.4 mIU/L were considered as euthyroid and 2.5 – 4 mIU/L were labelled as SCH. Females with SCH underwent testing for TPOAB. All females were followed until delivery. The maternal complications, mode of delivery and perinatal outcomes were assessed.

RESULTS
Among those with SCH there was a significantly higher proportion of overweight, obese females (46% vs 69%,p=0.031). The GDM rate was significantly higher (23% vs 16%; p=0.006) in females with SCH when compared to euthyroid females. TPOAB were present in 15 % of women with SCH. Rates of GDM (71% vs 29%; p=0.023), still births (75% vs 25%; p=0.001) were higher and IUGR / SGA (26% vs 72%; p = 0.027), VLBW / LBW (24% vs 81%, p=0.021), need for resuscitation such as suction /oxygen by mask (7% vs 93%, p=0.005) were significantly lower in females with TPOAB versus those without antibodies amongst females with SCH.

CONCLUSIONS
There appears to be no difference in pregnancy outcomes between females with SCH and euthyroid females except for GDM which was probably due to the presence of higher BMI. Future prospective studies with larger sample size are required to understand better the pregnancy outcomes in SCH in those with and without TPOAB.

OP-4-4

IDENTIFYING COMBINATION THERAPIES FOR ANDROGEN RECEPTOR POSITIVE AND NEGATIVE PROSTATE CANCER

https://doi.org/10.15605/jafes.037.AFES.17

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OBJECTIVE

Advanced prostate cancer develops varying mechanisms of resistance to androgen receptor (AR)-directed treatments. This includes heterogeneous alterations in the AR pathway and transformation into AR-negative phenotypes. To improve patient outcomes, it is necessary to identify new treatment strategies for diverse forms of advanced prostate cancer. This study aimed to identify effective combination treatments from novel patient-derived models representing the spectrum of prostate cancer.

METHODOLOGY

We obtained samples of castrate-sensitive and castrate-resistant prostate cancer to establish patient-derived xenografts and characterised their features using histopathology, RNA and DNA sequencing. We conducted an *in vivo* screen of candidate therapies (n=1/treatment), and validated them in expansion cohorts (n = 6-8/treatment).

RESULTS

We established the Melbourne Urological Research Alliance (MURAL) cohort of 59 xenografts from 30 patients. The histopathological and genomic features of the xenografts represent diverse subtypes of prostate cancer. This includes tumors with mutations, amplifications and structural rearrangements of the AR gene and AR-negative neuroendocrine pathology. The histopathology of the xenografts recapitulated the original specimens. An *in vivo* screen of eight combination therapies across eight xenografts showed promising activity of talazoparib, a poly(ADP-ribose) polymerase (PARP) inhibitor, combined with carboplatin. In expansion cohorts, this combination treatment significantly decreased tumour growth in 4 out of 5 xenografts with AR-positive and AR-negative prostate cancer.

CONCLUSIONS

Our patient-derived models expand the capacity for preclinical testing of prostate cancer with diverse forms of resistance to AR-directed treatments. In addition, the combination of a PARP inhibitor and carboplatin is effective for both AR-positive and AR-null prostate cancer.

OP-4-5

LACTATE RESPONSIVE PROTEIN LRPGC1 REGULATES LIVER LACTATE METABOLISM THROUGH ERRγ-MEDIATED TRANSCRIPTION OF TFAM GENE

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OBJECTIVES

The metabolism of lactic acid (LA) in the liver is essential to prevent lactic acidosis, which is frequently seen in metabolic disorders and severe infection. However, the molecular mechanism through which LA regulates its own metabolism is largely unknown. In this report, we describe an LA-responsive form of metabolic regulator PGC1α, named LRPGC1, which mediates and activates liver LA metabolism.

METHODOLOGY

Subcellular dynamics of LRPGC1 was monitored by living-cell imaging. LA consumption, gene expression levels and mitochondrial activities were analyzed using the PGC1 gene knockout cells. Survival rates were measured in a mouse model of lactic acidosis which received liver-targeted siRNA or selective agonist.

RESULTS

Following LA stimulation, LRPGC1 translocates from the cytoplasm to the nucleus through deactivation of nuclear export signals, and thereby interacts with the nuclear receptor ERRγ (Estrogen-related receptor gamma) and upregulates TFAM, which ensures mitochondrial biogenesis. Knockout of PGC1 gene in HEPG2 hepatocarcinoma cells decreased LA consumption and TFAM expression, which were rescued by LRPGC1 expression. These LRPGC1-induced effects were mediated by ERRγ and mitochondrial activation. The response element for LRPGC1/ ERRγ signalling pathway was identified in a TFAM promoter. Notably, liver-targeted silencing of LRPGC1 reduced the survival of a mouse model of lactic acidosis, whereas pharmacological activation of ERRγ significantly ameliorated the survival of the mouse model.

CONCLUSIONS

Present findings demonstrate LA-responsive transactivation via LRPGC1 that highlights an intrinsic molecular mechanism for LA homeostasis. This novel therapeutic avenue may reverse life-threatening lactic acidosis via activation of LRPGC1/ ERRγ signalling pathway.

POSTER PRESENTATIONS

ADRENAL

PP-A-01

FEMINIZING ADRENOCORTICAL CARCINOMA WITH SUBCLINICAL CUSHING'S SYNDROME IN A YOUNG ADULT MALE

https://doi.org/10.15605/jafes.037.AFES.19

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BACKGROUND
Adrenocortical carcinoma is a rare endocrine neoplasm which are hormonally active in almost 50% of cases. Feminizing adrenal tumors are only seen in 1-2% of ACC.

CASE
A 39-year-old Filipino male presented with a seven-month history of bilateral gynecomastia, intermittent epigastric pain and unintentional weight loss. Initial work-up revealed a large, heterogeneously-enhancing adrenal mass (24.9 x 12.6 x 18.2 cm) on abdominal computed tomography. Hormonal assessment showed elevated DHEAS (43.75, NV: 3-14.2 umol/L), estradiol (3212.4, NV: 11.65-82.13 pg/ml) and suppressed FSH (<0.08, NV: 1.0-10.5 mIU/ml) and LH (< 0.05, NV: 1.9-9.4 mIU/ml).

Serum cortisol remains unsuppressed after 1 mg dexamethasone test (18.71 ug/dL). The clinical findings of bilateral gynecomastia with no signs of hypercortisolism associated with elevated estradiol and unsuppressed cortisol pointed to a diagnosis of adrenal tumor with mixed hormonal secretion. The patient underwent left adrenalectomy, nephrectomy, pancreatectomy with splenectomy. Histopathology revealed diffuse staining with synaptophysin and weak to moderate staining with MELAN-A and inhibin with 40% Ki-67 index consistent with adrenocortical carcinoma. Five days postoperatively, repeat hormonal workup showed a decrease in estradiol (2326.1 pg/ml) and normalization of FSH (1.48 mIU/ml).

CONCLUSION
Functional ACC is more likely to present with metastatic disease than non-functional ACC, and portends shorter survival. Feminizing ACC has been associated with worse prognosis that is inversely related with estradiol levels. Estrogen excess results from an increase in substrate and presence of aromatase activity within the tumor. This case underscores the importance of hormonal profiling of ACC patients and its associated prognostic implications.

PP-A-02

EPIDEMIOLOGIC PROFILE AND CLINICAL OUTCOMES OF PATIENTS WITH PHEOCHROMOCYTOMA AT THE PHILIPPINE GENERAL HOSPITAL

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OBJECTIVES
Pheochromocytomas are rare catecholamine-secreting neuroendocrine tumors. They exhibit great variability in terms of clinical behavior which makes it challenging to diagnose. This study aims to describe the epidemiologic profile and to determine the clinical outcomes of patients with pheochromocytoma at the Philippine General Hospital.

METHODOLOGY
We reviewed the medical records of 30 adult patients with clinical, biochemical and histopathologic-proven diagnosis of pheochromocytoma from January 2010 to December 2021. Demographic, clinical characteristics and clinical outcomes were collected. Outcome measures included clinical and/or biochemical remission, recurrence and metastasis.

RESULTS
The median age at diagnosis of pheochromocytoma was 37.5 years (IQR 28-55).The most common metabolic comorbidities detected were glucose intolerance (60%) and hypertriglyceridemia (23.3%). Majority of the patients were hypertensive (90%) on diagnosis. Two-thirds of patients presented with classic features of pheochromocytoma while the remaining third presented with adrenal incidentalomas. Recurrence was found in 17% of subjects, where in those with younger age of presentation (25 years vs 46.5 years, p=0.0229) and bilateral pheochromocytoma (0 vs 75%, p=0.002) had higher likelihood of recurrence. Metastatic pheochromocytoma was found in 10% of the subjects in our institution.

CONCLUSION

Although majority of the patients presented with symptoms related with catecholamine excess, almost one third of the patients had incidental discovery. Incidence of pheochromocytoma recurrence and metastasis in our setting has been shown to be comparable with current available studies. This study has demonstrated a low rate of genetic testing likely due to limited access to the test in our setting.

PP-A-03

HYPOKALAEMIA AND COMORBIDITIES ARE COMMON AT INITIAL PRESENTATION IN PATIENTS WITH PRIMARY HYPERALDOSTERONISM

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OBJECTIVES

Primary hyperaldosteronism (PH) is the most common endocrine cause of hypertension (HTN) and is associated with end organ damage. About 30% of cases present with hypokalemia. Studies on the presentation of PH among the Indian population is lacking. This study evaluated the presenting characteristics of patients with PH from Eastern India.

METHODOLOGY

This is a retrospective study that included Saline Suppression Test (SST) confirmed PH patients.

RESULTS

The study involved seventy-eight confirmed PH patients with mean age of 55 ± 13 years and male-to-female ratio of 1.5:1. Mean duration of HTN was 13.3 ± 7.6 years and 62% had HTN more than 10 years. Mean SBP and DBP was 165.1 ± 13.5 mm Hg and 96.2±14.4 mm Hg, respectively. The mean number of anti-hypertensive medications was 3 ± 0.7. Majority presented with hypertension and hypokalemia (78%), 52% of which were spontaneous while 26% were diuretic-induced. About 14% presented with resistant HTN and 8% with adrenal incidentaloma. Overall, 64% of subjects had resistant HTN. Approximately 16.7% of patients experienced hypokalemic periodic paralysis. Mean serum sodium and potassium levels were 139.4 ± 2.3 mmol/l and 3.08 ± 0.6 mmol/l, respectively. Mean eGFR was 71.8 ± 20.8 ml/min/1.73 m^2, with 39.7% having Stage 3 CKD. Majority (95%) had comorbidities from end organ damages, with 43% having multiple comorbidities.

CONCLUSION

Our study revealed a high proportion of hypokalemia and resistant hypertension at detection of PH suggesting delayed diagnosis. A significant number of patients had comorbid illnesses due to end organ damage at presentation, highlighting the need for awareness, early screening and appropriate management of PH.

PP-A-04

IDENTIFICATION OF ALDOSTERONE E-DRIVER SOMATIC MUTATIONS IN CELL-FREE DNA FROM ADRENAL VEIN SAMPLES OF PRIMARY ALDOSTERONISM PATIENTS

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OBJECTIVES

Cell-free DNA fragments (cf-DNA) of tumour cells are often found in the blood downstream to the tumour due to the high apoptosis/necrosis rate of the cells. Primary aldosteronism (PA), a curable cause of secondary hypertension, is commonly due to an autonomous aldosterone-producing adenoma (APA) that harbours a somatic mutation in an aldosterone-driver gene. We aimed to determine the utility of cf-DNA genotyping from adrenal vein samples (AVS) for aldosterone-driver gene mutations as a biomarker for APA.

METHODOLOGY

Genotyping of cf-DNA from AVS of PA patients was performed using the Agena MassARRAY platform. In this study, six samples of cf-DNA from three PA patients were interrogated.

RESULTS

Of the three PA patients, two had unilateral APA and one had bilateral APA. Of the six cf-DNA samples, two samples from the same patient (right adrenal and left adrenal) were found to have a mutation in an aldosterone-driver gene. Genotyping of the cf-DNA of the right AVS yielded a CTNNB1 S45P mutation whereas the cf-DNA of the left AVS had a KCNJ5 G151R mutation.

CONCLUSION

These results suggest that the genotyping of cf-DNA of APA from AVS samples is promising to detect the somatic mutations present in the APA. However, as AVS is an invasive procedure, genotyping of cf-DNA from peripheral blood may be investigated as an alternative. Therefore, further work is needed to ensure this strategy can be non-invasive as then it can be used as a screening method before AVS.

PP-A-05

ELUCIDATING THE EFFECTS OF MUTATIONS IN Q209 OF GNA11 ON CELL APOPTOSIS IN HUMAN ADRENOCORTICAL CELLS

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OBJECTIVES

Gain-of-function mutations, Q209H, Q209P and Q209L, of GNA11 were recently found to occur in CTNNB1 mutant aldosterone-producing adenomas (APAs). These mutations were also found to be present in the hyperplastic zona glomerulosa adjacent to the double-mutant APAs. This study aims to investigate the effects of GNA11 Q209 mutations on tumorigenesis through measurement of cell apoptosis in the human adrenocortical cell line, HAC15.

METHODOLOGY

HAC15 was transfected with GFP-tagged GNA11 Q209H, Q209L, Q209P or wild-type (WT) plasmids. To note, HAC15, a subclone of H295R cells, inherently has the CTNNB1 S45P mutation. 48 hours post-transfection, cell apoptosis was assessed using the Pacific Blue™ Annexin V/SYTOX™ AADvanced™ apoptosis assay (BD Biosciences, USA). The supernatants and cells were harvested for aldosterone and cortisol determination, and RNA isolation.

RESULTS

HAC15 cells transfected with GNA11 mutants, Q209H, Q209L and Q209P, had elevated aldosterone production compared to WT at 62.4% (p=0.001), 71.2% (p=0.001) and 59.5% (p=0.001), respectively. Cortisol production was only slightly elevated in HAC15 cells transfected with Q209H (19.7%, p=0.01) and Q209L (24.6%, p=0.01), compared to WT. CYP11B2 mRNA expression was also upregulated compared to WT by 3.5 folds (p=0.001) for Q209H, and around 8 folds (p=0.001) for Q209L and Q209P. Analysis of flow cytometric apoptosis assay showed GNA11 mutants did not affect cell apoptosis.

CONCLUSION

The findings suggests that GNA11 Q209 mutation increases aldosterone secretion of adrenocortical cells with no or little effect on apoptosis rate. Further experiments on cell proliferation are needed to rule out whether GNA11 Q209 mutations affects tumorigenesis.

PP-A-06

UTILITY OF ADRENAL VENOUS SAMPLING IN ACTH-INDEPENDENT CUSHING'S SYNDROME PRESENTING WITH BILATERAL ADRENAL ADENOMA

https://doi.org/10.15605/jafes.037.AFES.24

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BACKGROUND

Adrenocorticotropic Hormone (ACTH)-independent Cushing's syndrome in a patient with bilateral adenoma poses a management challenge to clinicians. Utilization of adrenal venous sampling (AVS), as in this case, is instrumental in the precise localization of the functioning adenoma which will ensure the best management for these patients.

CASE

We report the case of a 67-year-old Filipino who presented with gradual weight gain for 3 months described as rounding of the face and increasing abdominal girth. The diagnosis of ACTH-independent Cushing's syndrome was based on undetectable ACTH and an unsuppressed cortisol level by dexamethasone suppression test. CT scan revealed bilateral adrenal adenomas measuring 1.1 x 0.9 cm (APxT) in the right and 1.1 x 1.3 cm (APxT) in the left. AVS was done using cortisol levels adjusted by plasma aldosterone. This successfully lateralized the hypersecretion of cortisol to the left adrenal gland, hence a unilateral laparoscopic left adrenalectomy was done.

Treatment was successful with post-operative laboratory confirmation of adrenal insufficiency. The patient was subsequently placed on glucocorticoid replacement until HPA axis recovery.

CONCLUSION

AVS adjusted by plasma aldosterone is a useful technique in localizing ACTH-independent CS in patients with bilateral adenoma to lateralize the lesion before planned surgery where unilateral adrenalectomy may be performed. Successful lateralization of the lesion may potentially spare the patient from lifetime or continuous corticosteroid replacement. In the unavailability of catecholamine or epinephrine, aldosterone ratio can be used to confirm success of adrenal vein cannulation.

PP-A-07

A CASE OF ECTOPIC CUSHING'S SYNDROME FROM AN OCCULT SOURCE IN A PATIENT WITH DIABETES, HYPERTENSION AND ACUTE PSYCHOSIS: THE DILEMMA IN PLANNING A CURE

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BACKGROUND

A 40-year-old patient with diabetes and hypertension, prior alcohol use and psychotic episodes, presented with accelerated hypertension associated with agitation and erratic behavior. Biochemical assessment revealed normal renal and hepatic function, elevated hepatic enzymes, spontaneous hypokalemia, poor glycemic control and central hypothyroidism.

In view of the patient's facial plethora, obesity, subtle striae and subtle pigmentation of periungual areas, Cushing's syndrome was considered. The baseline cortisol was significantly elevated while the adrenocorticotropic hormone (ACTH) was in the low-normal range. A two-day high-dose dexamethasone suppression test (HDDST) showed around 50% suppression. Imaging studies revealed a normal pituitary structure on MRI and bilaterally enlarged adrenal glands on adrenal CT. Inferior Petrosal Sinus Sampling (IPSS) revealed no gradient. The chest imaging did not reveal any suspicious nodules. Hence, we considered the patient to have an Ectopic Cushing's syndrome with an occult source. Medical therapy using ketoconazole was deferred in view of the elevated hepatic enzymes and psychological status. Following an educated decision with the family, bilateral adrenalectomy was done. The patient had an uneventful post-operative status with improvement of hyperglycemia, hypertension and behavior. Routine adrenal hormone replacement, anti-hyperglycemic and anti-hypertension therapies were continued with no untoward consequences.

CONCLUSION

In cases of clinically symptomatic ectopic Cushing's syndrome where the source remains occult despite expeditious work-up, aggressive management through bilateral adrenalectomy is a beneficial therapeutic option to selected patients such as in this case.

PP-A-08

REMISSION OF SURGICAL HYPOPARATHYROIDISM POST ADRENALECTOMY FOR CUSHING'S SYNDROME

https://doi.org/10.15605/jafes.037.AFES.26

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BACKGROUND
Adrenal insufficiency (AI) is a well-recognized cause of hypercalcemia. In patients with hypoparathyroidism, the effect of coexisting AI on calcium level has not been well-described.

CASE
We report a case of a patient with hypoparathyroidism who was able to discontinue her long-term calcium and calcitriol replacement after adrenalectomy for Cushing's syndrome.

A 63-year-old female with post-operative hypoparathyroidism after total thyroidectomy for papillary thyroid carcinoma (in 2005) was maintained on a stable dose of calcium carbonate 1 g BID and calcitriol 0.5 mcg BID. In 2015, she developed ACTH-independent Cushing's syndrome and underwent right adrenalectomy for a 3.6 cm right adrenal adenoma. Post-operatively, she was diagnosed with AI [serum cortisol 1.04 μg/dl (NV: 5.27–22.45)] and was symptomatic of glucocorticoid withdrawal syndrome despite up-titration of hydrocortisone replacement to 35 mg daily. Interestingly, she was found to have hypercalcemia (highest corrected calcium level 2.97 mmol/L), necessitating down-titration and eventual total discontinuation of her calcium carbonate and calcitriol replacement. She remained normocalcemic despite being off calcium and calcitriol for 4 months. As her symptoms improved, oral calcium and calcitriol were slowly resumed at lower doses (calcium carbonate 500 mg BID and calcitriol 0.25 mcg OD) to maintain her calcium level. On follow-up, she still has AI [8 am serum cortisol 25.4nmol/L (NV: 133 – 537)] and requires 15 mg daily hydrocortisone replacement.

CONCLUSION
The pathophysiology of hypercalcemia in AI is incompletely understood. Our case supported a parathyroid-independent mechanism. In rare cases of AI with concurrent hypoparathyroidism, close monitoring of calcium levels is needed for medication dose adjustments to achieve normocalcemia.

PP-A-09

RARE CASE OF EXCLUSIVELY DOPAMINE-SECRETING PARAGANGLIOMA IN MULTIPLE ENDOCRINE NEOPLASIA TYPE 2A (MEN 2A)

https://doi.org/10.15605/jafes.037.AFES.27

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BACKGROUND
Pheochromocytomas in MEN2A are usually intra-adrenal. Rarely, they may manifest as paragangliomas. Predominantly or exclusively dopamine-secreting pheochromocytomas and paragangliomas (PPGL) are rare with only 33 cases reported in the literature.

CASE
We report a case of exclusively dopamine paraganglioma in the context of MEN 2A.

A 72-year-old male was diagnosed with MEN2A following family screening in 1996. Genetic analysis revealed a mutation in codon 634 of the RET proto-oncogene (C634Y). He underwent total thyroidectomy for medullary thyroid carcinoma in 1996 and total parathyroidectomy for primary hyperparathyroidism in 1997. His yearly 24-hour urinary catecholamines had been within the normal ranges. However, in August 2019, his urinary dopamine was raised at 1033 μg/day (normal range: 64.0-400). Urinary adrenaline and noradrenaline were not elevated. Repeated 24-hour urinary metanephrines in August 2020 yielded an elevated 3-methoxytyramine level of 21.8 μmol/day (normal range: 0.10-1.79). Urinary metanephrines and normetanephrines remained within normal ranges. He has hypertension which is well-controlled on two agents. He is otherwise asymptomatic with no paroxysmal attacks of catecholamine excess. Iodine-131 meta-iodobenzylguanidine (I-131 MIBG) imaging revealed an avid lesion in the mediastinum with no tracer uptake at the adrenal glands. The patient declined further interventions.

CONCLUSION
Our case highlights the importance of measuring urinary or plasma dopamine even in MEN2A. Dopamine-secreting PPGL typically lacks the classical presentation of paroxysmal attacks and are often extra-adrenal. Exclusively dopamine-secreting PPGL is rare. To our knowledge, this represents the first case in a patient with MEN2A.

PP-A-10

RARE AND AGGRESSIVE METASTATIC PHEOCHROMOCYTOMA RECURRENCE IN A YOUNG ADULT MALE WITH MEN 2A SYNDROME

https://doi.org/10.15605/jafes.037.AFES.28

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BACKGROUND
Multiple Endocrine Neoplasia 2A (MEN 2A) is characterized by 70-100% risk of medullary thyroid cancer, 50% risk of pheochromocytoma, and 20-30% risk of primary hyperparathyroidism mainly caused by RET mutation. Pheochromocytoma in MEN 2A is almost always benign and often follows an indolent course.

CASE
We demonstrate the clinical course and challenges in the management of a case of metastatic pheochromocytoma recurrence in a patient with MEN 2A.

We present a 31-year-old male with histopathologically-confirmed bilateral pheochromocytoma occurring metachronously. He was subjected to left adrenalectomy and right adrenalectomy in 2014 and 2020, respectively. The patient was also diagnosed with primary hyperparathyroidism and medullary thyroid carcinoma presenting with mild hypercalcemia and multiple thyroid nodules. He underwent total thyroidectomy with neck dissection and left inferior parathyroidectomy. Genetic testing revealed the presence of a RET mutation. One year post-surgery, the patient had persistent elevation of 24-hour urine metanephrines [13.977 mg (NV: 0-1)]. Adrenal CT demonstrated a 2.1 cm ovoid focus in the right suprarenal region and I-131 MIBG scan showed avid uptake on the right frontal bone. Patient underwent excision of right adrenal bed and right frontal bone tumor which were confirmed to be metastatic pheochromocytoma on histopathologic report. He achieved normalization of 24-hour urine metanephrines 0.8 mg (0-1 mg) one month postoperatively.

CONCLUSION
Metastatic pheochromocytoma is only seen in less than 4% of MEN 2A. Metastatic PHEO recurrence has been reported only in few case reports and optimal management of these cases requires a multi-specialty approach.

PP-A-11

PHAEOCHROMOCYTOMA IN A PATIENT WITH SUSPECTED BIRT-HOGG-DUBÉ SYNDROME: AN INCIDENTAL OR COMPOSITE RELATIONSHIP?

https://doi.org/10.15605/jafes.037.AFES.29

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BACKGROUND
A rare case of phaeochromocytoma in a 57-year-old female patient with a provisional clinical diagnosis of Birt-Hogg-Dubé (BHD) syndrome is presented. Whether this is an incidental finding or whether a causative or composite relationship between these two entities remains to be fully described. As much as we are aware, our case would be the second of such association to be described in literature.

CASE
The patient's hospital record was reviewed after consent was obtained.

Bilateral renal cysts and a right adrenal lesion were first identified in the patient at age 48 from abdominal CT studies done for her recurrent bilateral flank pain. To date, two percutaneous drainages of cysts on the right kidney were done to relieve pain. Following assessment of patient at a tertiary hospital's genetics clinic at age 52, a provisional diagnosis of Birt-Hogg-Dube (BHD) syndrome was made for her bilateral renal cysts and notable skin lesions. Her CT chest study did not reveal lung cysts. Genetic mutation studies for FLHN, FH, MET, SDHB and VHL genes were negative. The patient's right adrenal lesion was under surveillance and eventually required right adrenalectomy for newly developed recurrent episodic hypertension at age 54. Histology showed paraganglioma-like appearance, a 2% Ki-67 index and a negative SDHB staining. The patient's daughter was also diagnosed with bilateral renal cysts and recurrent spontaneous pneumothoraces and a provisional diagnosis of DHB syndrome variant was also made for her.

CONCLUSION
Further research work into the above rarely-described clinical association needs to be done.

PP-A-12

INCREASED RISKS OF ATHEROSCLEROTIC HEART DISEASE, MALIGNANCY AND SLEEP APNEA WITH PRIMARY ALDOSTERONISM

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BACKGROUND
Primary aldosteronism (PA) is associated with increased risks of atherosclerosis, malignancy, and sleep apnea. We report a case of untreated PA complicated by coronary artery disease (CAD), renal cell carcinoma (RCC) and sleep apnea during the course of the illness.

CASE
Laboratory and radiological studies were performed at our hospital.

A 51-year-old male had a 12-year history hypertension and hypokalemia. His laboratory tests then showed plasma renin activity (PRA) 0.06 ng/mL/hr, aldosterone 6 ng/dL, normal plasma metanephrines and dexamethasone suppression test. Despite using several anti-hypertensive medications, his hypertension and hypokalemia remained poorly controlled. He was also diagnosed with sleep apnea and was placed on CPAP. At the age of 47 years, a diagnosis of Liddle syndrome was considered, and he was placed on amiloride. The following year, he was diagnosed with coronary artery disease. Repeat laboratory showed PRA <0.167 ng/ml/hr and plasma aldosterone 111.4 ng/dL. An abdominal CT revealed a left adrenal adenoma and a 1.8 cm left renal lesion suggestive of RCC. Adrenal venous sampling localized the left adrenal adenoma as the cause of PA. The patient underwent left adrenalectomy and left partial nephrectomy. Histopathology confirmed the diagnosis of adrenal adenoma and RCC. One week later, plasma aldosterone was 1.9 ng/dL and his hypertension improved with fewer medications without requiring potassium supplementation.

CONCLUSION
Our case illustrates that delayed diagnosis of PA may be associated with an increased risk of CAD, malignancy and sleep apnea. Early diagnosis and surgical intervention are recommended for aldosterone-producing adenoma.

PP-A-13

A NOVEL MUTATION ASSOCIATED WITH NON-CLASSICAL CONGENITAL ADRENAL HYPERPLASIA IN AN EMIRATI FEMALE

https://doi.org/10.15605/jafes.037.AFES.31

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BACKGROUND
Deficiency of the steroid 21-hydroxylase, encoded by CYP21A2 gene, accounts for 95-99% of all congenital adrenal hyperplasia (CAH) cases. We report a case of non-classical CAH (NCAH) due to a novel CYP21A2 mutation with unusual biochemical features.

CASE
A 24-year-old Emirati female with a BMI of 25.72 kg/m^2 presented with a history of repeated pregnancy losses (RPL) of spontaneous and in-vitro fertilization (IVF) pregnancies, hair fall and irregular menstrual cycles. She had acne, hirsutism, autoimmune thyroiditis and a thyroid nodule which were duly addressed. Biochemical tests showed very high levels of 17-OH progesterone (1071 ng/dL); however, testosterone, DHEAS and androstenedione levels were normal. Ovarian ultrasound showed no abnormalities.

In view of her known thyroid immunity and history of fatigue, screening of adrenal insufficiency using short synacthen test showed normal baseline, 30- and 60-minute values (239 nmol/L, 717 nmol/L and 850 nmol/L, respectively); unfortunately, paired 17-OH progesterone was not checked at the time. Genetic testing identified a novel heterozygous mutation c.337T>C p.(Tyr113His) in the CYP21A2 gene. This mutation is in a highly conserved region. Bioinformatic analysis suggests that it is highly likely to be pathogenic as a deletion of 8 codons (c332-339), including codon 337, is pathogenic.

CONCLUSION
We report an Emirati female patient with uncommon features of NCAH, including absence of classical hyperandrogenism due to a novel heterozygous variant. Genetic tests amongst relatives and additional molecular and clinical studies are planned to understand the role of this variant in CAH pathology.

POSTER PRESENTATIONS

BONE

PP-B-01

PRIMARY HYPERPARATHYROIDISM PRESENTING AS ACUTE PANCREATITIS: AN INSTITUTIONAL EXPERIENCE

https://doi.org/10.15605/jafes.037.AFES.32

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OBJECTIVES
To determine the clinical, biochemical and radiological profile of patients with primary hyperparathyroidism (PHPT) presenting as acute pancreatitis (AP).

METHODOLOGY
This is a retrospective observational study that has been approved by the institute's ethical committee. This study included 51 patients diagnosed with PHPT admitted at a tertiary care hospital in Puducherry, India between January 2010 and October 2021, who initially presented as AP. The diagnosis of AP was confirmed if two of the three following features were present: abdominal pain, levels of serum amylase or lipase greater than three times the normal and characteristic features on abdominal imaging.

RESULTS
Of the 51 patients with PHPT, twelve (23.52%) had pancreatitis- five (9.80%) were acute while seven (13.72%) were chronic. Compared to those without pancreatitis (PHPT-NP), most of those with AP were male, younger (35.20 + 16.11 vs 49.23 + 14.80 years, P=0.05) and had lower intact parathyroid hormone levels (125 vs 519.80, P=0.01). The mean serum calcium levels were similar in both PHPT-AP and PHPT-NP groups (11.66 mg/dL vs 12.46mg/dL, P=0.32). Patients with PHPT-AP presented more frequently with gastrointestinal symptoms like abdominal pain, nausea and vomiting than skeletal and renal manifestations.

CONCLUSION
This study has shown that AP may be the only presenting feature of PHPT. Acute pancreatitis on the background of elevated serum calcium levels should alert physicians to investigate on endocrine causes of hypercalcemia such as PHPT.

PP-B-02

SPONTANEOUS RESOLUTION OF PRIMARY HYPERPARATHYROIDISM AFTER BIOPSY-RELATED NECK HEMATOMA

https://doi.org/10.15605/jafes.037.AFES.33

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BACKGROUND
Surgical excision of the abnormal parathyroid gland remains the mainstay of treatment for primary hyperparathyroidism. We report a case of spontaneous resolution of primary hyperparathyroidism following a neck hematoma that developed post-biopsy of a thyroid nodule.

CASE
A 75-year-old male initially consulted with a urologist due to hematuria secondary to a left ureteric calculus. He was then found to have parathyroid-related hypercalcemia with a serum calcium of 3.10 mmol/L (2.18-2.60 mmol/L) and intact parathyroid hormone (iPTH) of 6.25 pmol/L (1.58-6.03 pmol/L). Serum total 25-hydroxyvitamin D was 67.19 nmol/L (76-250 nmol/L) for which cholecalciferol was initiated. Urinary calcium/creatinine ratio of 0.02 excluded familial hypocalciuric hypercalcemia. Imaging studies including neck ultrasound, computed tomography scan of the neck and thorax and Sestamibi parathyroid scan failed to localize the culprit lesion. He was then referred to a surgeon for exploratory parathyroidectomy. Before surgery, fine needle aspiration cytology (FNAC) of a cold thyroid nodule on the right was done which resulted in formation of a large neck hematoma. To our surprise, his calcium level started to normalise along with the resolution of the hematoma one month after the procedure. Follow-up laboratory data revealed normal calcium and PTH levels at 2.28 mmol/L and 3.87 pmol/L, respectively.

Parathyroid apoplexy leading to spontaneous resolution of hyperparathyroidism is rare but has been reported. This may explain spontaneous remission of primary hyperparathyroidism in the patient probably secondary to the hematoma postbiopsy. However, because adenoma recurrence is common, he is being closely monitored.

CONCLUSION
Large neck hematomas leading to parathyroid apoplexy may cause spontaneous resolution of hyperparathyroidism.

PP-B-03

ADVANTAGE OF EARLY LOCALIZATION IMAGING STUDIES IN PATIENTS WITH NORMOCALCEMIC HYPERPARATHYROIDISM

https://doi.org/10.15605/jafes.037.AFES.34

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OBJECTIVES
Currently, there is no clear evidence regarding the benefits of surgery for patients with normocalcemic hyperparathyroidism (NC-HPT). The goal of this study was to determine the usefulness of imaging to guide surgical treatment in patients with NC-PHPT.

METHODOLOGY
This is a retrospective study that included 221 patients with hyperparathyroidism seen during 2004-2020. Laboratory and imaging studies were performed at our hospital.

RESULTS
Of the 221 patients, only eight (3.6%) patients met the criteria for NC-HPT. The majority were female, aged between 42 to 82 years, with PTH levels ranging from 78 to 380 pg/mL. All patients were normocalcemic (9.8 to 10.3 mg/dL). Two patients had a history of nephrolithiasis. Only one patient had nonspecific fatigue as a symptom, while the rest were asymptomatic. DXA scan done showed that three patients had osteoporosis and three had osteopenia. On neck ultrasound, only two patients had parathyroid findings. However, on Sestamibi parathyroid scan, four patients had tracer localization. Three patients underwent parathyroidectomy with histopathological confirmation of adenomas ranging from 120 to 261 mg in weight (normal 20-40 mg).

CONCLUSION
In patients with NC-HPT, medical therapy such as cinacalcet is not indicated. Although it has been suggested that NC-HPT may represent an early stage of PHPT, complications like osteoporosis and nephrolithiasis may still occur. Prompt and timely imaging studies in this subset of patients may facilitate early surgical treatment if warranted. Subsequently, the occurrence of hyperparathyroidism-related complications may be prevented.

PP-B-04

COMPARISON OF CARDIOVASCULAR EVENTS AMONG USERS OF DIFFERENT CLASSES OF ANTI-OSTEOPOROSIS MEDICATIONS

https://doi.org/10.15605/jafes.037.AFES.35

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OBJECTIVES
Anti-osteoporosis medications have been associated with the occurrence of cardiovascular events. Therefore, we aimed to investigate the cardiovascular safety of hormone replacement therapy (HRT), bisphosphonates, anti-RANKL, parathyroid hormone (PTH) analogues and romosozumab in patients with osteoporosis.

METHODOLOGY
We evaluated 77 trials including 106,982 patients comparing five classes of anti-osteoporosis drugs and a placebo. We initially performed a standard, random-effect, pairwise meta-analysis for cardiovascular disease (CVD) risk to gather the available direct evidence of each drug class. For every possible pairwise comparison, the association between treatment and outcomes was obtained using odds ratios (ORs). Statistical heterogeneity was assessed along with its 95% confidence intervals. Network meta-analysis was then used to compare different available treatment strategies within a single analytical framework in a Bayesian setting.

RESULTS
Patients on hormone therapy, bisphosphonates, romosozumab and PTH had no increased cardiovascular risk compared to placebo. Anti-RANKL use revealed a significantly higher risk of CVD than placebo with a risk ratio of 1.25 [95% CI 1.07-1.45]. The SUCRA ranking confirmed that the use of anti-RANKL conferred the highest risk for CVD in patients with osteoporosis. Specifically, there was a significantly higher risk of coronary artery disease, cerebrovascular disease, angina and transient ischemic accident (RR 1.26 [95% CI 1.01-1.58]).On the other hand, HRT demonstrated a higher risk of venous thromboembolic events (VTE) (RR 1.96 [95% CI 1.53-2.51]).

CONCLUSION
From our network meta-analysis, the use of anti-RANKL such as denosumab increased the risk of composite cardiovascular outcomes, while HRT increased the risk of VTE.

PP-B-05

HYPOKALEMIA AS A NEGLECTED CAUSE OF METABOLIC BONE DISEASE: TWO CASE REPORTS

https://doi.org/10.15605/jafes.037.AFES.36

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BACKGROUND
Hypokalemia occurs secondary to several possible causes that ultimately lead to excessive potassium loss in the body. Long-standing hypokalemia via renal losses could lead to metabolic bone disease (MBD).

CASES
We report two cases of young patients who came in due to fractures. Both patients had a history of lower extremity paralysis. Biochemical analysis showed chronic hypokalemia and metabolic acidosis with normal anion gap, suggestive of renal tubular acidosis (RTA). Patient 1 had impaired renal function with a normal vitamin D level, while patient 2 had normal renal function but had low vitamin D. Genetic testing for RTA could not be performed due to resource constraints. Their MBD was confirmed by radiological assessment. Treatment of both patients involved correction of the acidosis and physical rehabilitation without the need for orthopedic intervention.

RTA is the most common cause of hypokalemia. It is characterized by a normal anion gap metabolic acidosis and renal potassium wasting. Chronic uncorrected acidosis could increase RANKL expression that will promote the differentiation of osteoclasts, leading to increased bone resorption. The most common skeletal manifestations of uncorrected RTA are rickets or osteomalacia, fracture, pseudofracture, secondary osteoporosis and sclerotic bone disease. Since our two patients came in with severe MBD, it would be difficult to reverse these changes and revert to optimal skeletal function.

CONCLUSION
In a patient with chronic hypokalemia and metabolic bone disease, RTA must always be considered as a cause. Increasing awareness regarding the causes of hypokalemia and its long-term impact on the body may facilitate early diagnosis and treatment, thereby preventing permanent sequelae such as MBD.

PP-B-06

ROLE OF BONE MINERAL DENSITY ADDED TO FRACTURE RISK ASSESSMENT TOOL IN THERAPEUTIC DECISION-MAKING FOR OSTEOPOROSIS IN A MALAYSIAN POPULATION

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OBJECTIVES
To examine the role of bone mineral density (BMD) added to Fracture Risk Assessment tool(FRAX) in therapeutic decision-making for osteoporosis in a Malaysian population.

METHODOLOGY
Data were collated from four centers in Malaysia. This study included individuals ages 40 to 90 years old who underwent routine BMD. Patients who had metabolic bone disease or were on anti-osteoporotic treatment were excluded. Ten-year probability of major osteoporotic fractures (MOF) and hip fractures (HF) was calculated using FRAX+BMD and FRAX-BMD. Treatment recommendations for FRAX+BMD and FRAX-BMD were compared and categorized as 'concordant' and 'discordant.'

RESULTS
A total of 1381 participants were included in the study, with the majority being female. There was strong correlation between FRAX+BMD and FRAX-BMD for both MOF (r = 0.889, p<0.001) and HF (r = 0.796, p<0.001). Concordance of 80.1% (p<0.001) was seen in treatment recommendation between FRAX+BMD and FRAX-BMD (treatment recommended n = 505; no treatment recommended, n= 601). Concordance was highest in the youngest and eldest age groups with 91.1% and 85.8%, respectively. Among the discordant, FRAX-BMD underestimated treatment recommendation in 147 (10.6%) and overestimated in 128 (9.2%) participants. Age was the sole important predictor of discordance in treatment recommendations comparing both groups. FRAX-BMD had the least underestimation of treatment among the 80 to 90-year-old group (0.9%) and least overestimation in the 40 to 69-year-old group (1.2%).

CONCLUSION
FRAX-BMD had a good correlation with FRAX+BMD in a Malaysian population and is an acceptable alternative for treatment decision-making in situations where BMD services are not readily available.

PP-B-07

DILEMMAS IN THE DIAGNOSIS AND MANAGEMENT OF OSTEOPOROSIS IN A PATIENT WITH ALKAPTONURIA: SUCCESSFUL TREATMENT WITH TERIPARATIDE

https://doi.org/10.15605/jafes.037.AFES.38

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BACKGROUND
Management of osteoporosis in patients with alkaptonuria can be challenging. We report a patient with alkaptonuria who was successfully treated with teriparatide.

CASE
Laboratory and DXA were completed at our hospital.

A 69-year-old female with a diagnosis of alkaptonuria came in for osteoporosis follow-up. Following the diagnosis of multiple joint arthritis, she underwent several joint replacement surgeries. She also sustained fragility fractures in the foot. Physical exam revealed bluish discoloration of the conjunctiva, normal S1, split S2 and IV/VI systolic murmur over the right parasternal border. She also had limited mobility of the thoracic and lumbar spines, wrists, ankles, knees and hip joints. Laboratory examination revealed the following results: serum PTH 33 pg/mL, 25-OH vitamin D 28 ng/mL, osteocalcin 12 mg/mL, C-telopeptide 318 pg/mL, tyrosine 79.1 umol/L, 24-hour urine homogentisic acid 4.2 gms. Genetic testing showed compound heterozygous mutation for the HGD C. 496T2T>C and HGD C.1102A < G (p.mev368Va) variants, consistent with a diagnosis of alkaptonuria. DXA scan done at the age of 56 years showed osteoporosis (T score of -2.7 over femoral neck, -2.5 over total hip). She was treated with alendronate for 5 years in addition to nitisinone. While on alendronate, she sustained fragility fractures of the right radius and left ankle. After 5 years of alendronate, the patient was transitioned to teriparatide 20 mcg subcutaneously daily for 2 years, followed by annual intravenous zoledronic acid. For the subsequent seven years, the patient led an active life with no fractures. Follow-up DXA showed improvement to osteopenia at the radius. The presence of degenerative arthritis made the other sites difficult to interpret.

CONCLUSION
In this subset of patients, bisphosphonates are not as effective in preventing fragility fractures. However, teriparatide has shown some promise as an alternative treatment.

PP-B-08

HYPERCALCEMIC HYPERPARATHYROIDISM WITH UNIDENTIFIABLE PARATHYROID ADENOMA: THE LIMITATIONS OF IMAGING MODALITIES

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BACKGROUND
Symptomatic hyperparathyroidism is often missed. After confirming autonomous hyperparathyroidism, identification of a single culprit gland is impeded by limitations in imaging modalities. Although the culprit gland has been identified as the adenoma, recurrence in the remaining glands is also worrisome.

CASE
We present a case of a female diagnosed with autoimmune hypothyroidism with proximal muscle weakness who self-medicated with NSAIDs and homeopathic tablets. Laboratory examinations revealed persistently elevated serum calcium with low phosphorus despite discontinuation of the above medications. Normalization of TSH with thyroxine has been achieved within 6 weeks. Hypercalcemia was attributed to autonomous hyperparathyroidism. Initial imaging did not reveal any nodule in the neck nor an uptake in nuclear imaging. Originally, a parathyroidectomy with autotransplantation of half a normal parathyroid into the sternocleidomastoid muscle was planned, however, the patient refused any surgical intervention. Instead, she was started on medical therapy with cinacalcet. Following a year of therapy, due to the cost of cinacalcet in India, the family opted for surgery.

A pre-operative computed tomography scan of the neck revealed a nodule in the right paratracheal region. Total parathyroidectomy with autotransplantation of half of the normal gland was done.

CONCLUSION
In India, fortifying food with vitamin D is not done. Nutritional deficiencies may contribute to the development of secondary hyperparathyroidism and tertiary hyperparathyroidism if untreated. In the management of these conditions, the role of total parathyroidectomy and autotransplantation cannot be discounted.

PP-B-09

EVALUATION OF FRACTURE RISK AMONG TYPE 2 DIABETES PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION RECEIVING DIFFERENT ORAL ANTICOAGULANTS

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OBJECTIVES
Patients with type 2 diabetes are at higher fracture risk owing to the attenuated bone turnover and impaired bone microarchitecture. The comparative effect of warfarin over non-vitamin K antagonist oral anticoagulants (NOACs) on incident fractures among patients with type 2 diabeteswith atrial fibrillation (AF) remains to be elucidated.

METHODOLOGY
This was a retrospective propensity-score weighted population-based cohort study of adults with type 2 diabetes and AF who were started on warfarin or NOAC between 2005 and 2019, identified from the electronic database of the Hong Kong Hospital Authority. The primary outcome was a composite of major osteoporotic fractures (hip, clinical vertebral, proximal humerus and wrist). Hazard ratios (HR) were calculated using Cox proportional hazard regression models.

RESULTS
This study included 15,770 patients with type 2 diabetes and AF (9,288 on NOAC and 6,482 on warfarin). During a median follow-up of 20 months, 551 patients (3.5%) sustained major osteoporotic fractures (201 in the NOAC group [2.2%]; 350 in the warfarin group [5.4%]). The adjusted cumulative incidence was lower among NOAC users than warfarin users (HR 0.80, 95% CI 0.64-0.99, p=0.044). Subgroup analyses showed consistent protective effects against major osteoporotic fractures among NOAC users across sex, age, HbA1c, duration of diabetes and history of severe hypoglycemia, compared with warfarin users.

CONCLUSION
Among patients with type 2 diabetes and AF, treatment with NOAC was associated with a lower risk of major osteoporotic fractures than warfarin. NOAC may be the preferred anticoagulant from the perspective of bone health.

POSTER PRESENTATIONS

DIABETES

PP-D-01

METABOLIC AND CIRCULATING microRNA PROFILING DURING MATERNAL DIABETES AND DIFFERENCES BY DIABETES TYPE

https://doi.org/10.15605/jafes.037.AFES.41

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OBJECTIVES

In pregnancies complicated by maternal diabetes, metabolic and epigenetic effects such as dysregulated microRNA (miRNA) expression, may influence pregnancy outcomes. This study aimed to assess the effect of maternal diabetes type on metabolic and circulating miRNA expression.

METHODOLOGY

C-peptide, total and high molecular weight (HMW) adiponectin, C-reactive protein (CRP) and triglyceride concentrations were quantified in serum (16 to 27 weeks gestation) from women with pregestational type 1 diabetes (T1D, n = 7), type 2 diabetes (T2D, n = 14), new T2D (n = 12), gestational diabetes mellitus (GDM, n = 17) and normoglycaemia (n = 24) using enzyme-linked immunosorbent assays (ELISA). MiRNAs were profiled in a subset of samples using the human serum/plasma miScript miRNA PCR array (n = 4 per group).

RESULTS

Lower C-peptide total and HMW adiponectin levels with higher CRP levels were observed in women with T2D and GDM compared to women with T1D and normoglycaemia. The expression of miR-19b-3p was lower in women with GDM (9.8-fold, p=0.033); miR-20a-5p was lower in women with T1D (4.5-fold, p=0.047) and miR-29a-3p was higher in women with T2D (1.8-fold, p=0.002). Several other miRNAs were differentially expressed between the diabetes groups but were not statistically significant. Bioinformatic analysis identified messenger RNA targets common and unique to the differentially expressed miRNAs.

CONCLUSION

Metabolic parameters and miRNA levels differed according to the type of maternal diabetes. MiRNA expression differences between T1D, T2D and GDM could be related to intrauterine hyperglycemia and epigenetic programming. These findings may be interesting areas for further studies.

PP-D-02

DIABETIC ENCEPHALOPATHY: A HISTOPATHOLOGICAL UPDATE

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OBJECTIVES

We aimed to examine small vessels in the brain for histological changes in patients with type 2 diabetes mellitus and diabetic encephalopathy.

METHODOLOGY

We studied the histopathological changes in the brain in 17 autopsy cases. The microscope slides were stained with Hematoxylin and Eosin, Nissl and Bielschowsky methods and PAS-reaction.

RESULTS

The high density of the capillary network, especially in the cortex of the frontal and temporal areas, together with segmental spasm and an expansion of the perivascular space of Robben-Virchow were observed. The early changes in the capillary wall were determined not only by the thickening of the basement membrane with the accumulation of PAS-positive substances but also by its cleavage with the proliferation of endothelial cells. Late manifestations of vessel changes include capillary fibrosis, characterized by the presence of argentophilic reticulin and collagen fibers and proliferation of pericytes in the capillary wall. Thin-walled microaneurysms, early morphological manifestations of diabetic encephalopathy, were also seen. Segmental fibrinoid necrosis with the formation of miliary dissecting aneurysms and parietal and obstructive thrombi were seen in areas of ischemic necrosis of brain tissue in the cortical cerebral arteries. Neurodystrophic changes

in neurons, loss of small-cell perivascular spongiosis and plaque formation were quite pronounced. The most obvious changes were in the upper layers of the cortex where focal atrophy was more prominent than laminar. A large number of corpora amylacea can be significant not only in the foci of necrosis but also in areas of chronic ischemia.

CONCLUSION

Cerebral microangiopathy is a morphological sign of diabetic encephalopathy.

PP-D-03

MORPHOLOGICAL CHANGES OF THE BRAIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND COVID-19

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OBJECTIVES

To investigate the brain tissue of patients with type 2 diabetes mellitus who died from COVID-19.

METHODOLOGY

This study included 31 patients with type 2 diabetes mellitus who had a positive test for SARS-CoV-2 detected by qRT-PCR and eventually expired in 2021 in Lviv regional and city hospitals from complications of COVID-19. We studied macroscopic and microscopic changes in the brain with the use of common histological and immunohistochemistry staining for activated astrocytes (GFAP, Thermo Scientific), activated microglia (CD68, Clone Ab-4, Thermo Scientific), T lymphocytes (CD3, Clone SP7, Thermo Scientific) in the cortex, basal ganglia, brainstem and cerebellum.

RESULTS

In all the cases, arteriolosclerosis with perivascular rarefaction was present. Ischemic lesions in the brain with focal encephalolysis were documented in 15 (48, 39%) out of 31 patients with type 2 diabetes mellitus. Hemorrhagic infarctions were rare. The main cyto/angio-architectural manifestations of brain damage were diffuse alteration of the basement membranes and vascular endothelium, capillary fibrosis and hyalinosis, pericyte proliferation, congophilic angiopathy accompanied by a sharp disruption of transcapillary transport. The astrogliosis with positive GFAP was seen in all cases but showed variable degrees. The perivascular activation of microglia and the microglial nodules with CD68 positive cells were in the studied regions of the brain, but less in the cerebellum. Perivascular infiltration by CD3 was most pronounced in the brainstem.

CONCLUSION

The morphological changes associated with COVID-19 and type 2 diabetes mellitus include pathology of the microvasculature, ischemic infarction with encephalolysis, astrogliosis, microgliosis and perivascular infiltration by CD3 in different regions of the brain.

PP-D-04

ASSOCIATION OF CIRCULATING HYPOXIA-INDUCIBLE FACTOR 1 ALPHA WITH TYPE 2 DIABETES IN INDIVIDUALS WITH SEVERE OBESITY

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OBJECTIVES

Obesity and type 2 diabetes (T2D) are often attributed to hypoxia. Adaptive responses to hypoxia are regulated by hypoxia-inducible factor 1 α (HIF1α). The role of hyperglycemia in mediating HIF1α expression and activity remains unclear. This cross-sectional study aimed to evaluate the relationship between plasma HIF1α and T2D in individuals with severe obesity.

METHODOLOGY

The study involved adults with severe obesity recruited at the Khoo Teck Puat Hospital (N=252, age: 45±8 years, 38% men, body mass index: 41.1 ± 6.5 kg/m^2). The level of HIF1α in plasma was measured by immunoassay. Spearman's correlation and modified Poisson regression analysis were used to evaluate the association of HIF1α with glycated haemoglobin (HbA1c) and T2D, respectively.

RESULTS
Out of 252 subjects, 52 %(n = 131) of the subjects had T2D. A positive correlation was observed between HIF-1α and HbA1c (rho = 0.295, P<0.001). Individuals with T2D had markedly higher median HIF1α levels compared with their non-T2D counterparts [207.1 (IQR:180.4–246.1) vs 155.1 (IQR:132.0–189.6) pg/ml; P<0.001)]. The association between natural log-transformed circulating HIF1α and T2D (outcome) remained significant even after adjusting for age, gender, body mass index and HbA1c (risk ratio: 2.63, 95% CI: 1.85–3.74, P<0.001).

CONCLUSION
To our knowledge, this is the first study to demonstrate an association between circulating HIF1α and T2D in people with severe obesity. Our data suggest that hyperglycemia may result in the accumulation of HIF1α protein, which may contribute to the development of T2D-associated complications. Hence, inhibition of HIF1α expression may exert beneficial effects on T2D and its complications.

PP-D-05

THE EFFECTS OF ADVERSE CHILDHOOD EXPERIENCES (ACE) ON THE DEVELOPMENT OF DIABETES MELLITUS (DM) AND PRIMARY HYPOTHYROIDISM IN ADULTS

https://doi.org/10.15605/jafes.037.AFES.45

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OBJECTIVES
Globally, diabetes mellitus (DM) and hypothyroidism are the leading endocrine disorders. The etiology of DM and hypothyroidism is complex and the influence of toxic stress on their development is yet to be explored. Few studies report high scores of adverse childhood experiences (ACE) in DM patients. Our study aims to investigate the effect of ACE on DM, insulin resistance (IR) and primary hypothyroidism in a local population and to understand its effects on the risk of developing these diseases in adulthood.

METHODOLOGY
A cross-sectional web-based study was conducted. We investigated 123 adults over 21 years old who were clinically diagnosed with DM, IR and primary hypothyroidism in Georgia using an ACE (scores ranging from 0-4+) survey and the CDC guidelines for risk factors for ACE.

RESULTS
Analysis showed that 42 participants had only one of the three endocrine disorders: 27 with DM, 7 with IR and 8 with hypothyroidism. On the other hand, 81 patients had 2 out of 3 disorders: 27 had DM and hypothyroidism while54 had hypothyroidism with IR. ACE score of 4+ was associated with increased odds of DM (OR = 2.51, 95% CI 5.32, 1.18) and hypothyroidism (OR = 1.34, 95% CI 3.04, 0.59). The ACE was not associated with IR (OR = 0.65, 95%CI 1.34, 0.31). However, in patients with both IR and hypothyroidism, a high ACE score was observed (OR = 1.78, Cl 95% 6.28, 0.51). Participants with concomitant DM and hypothyroidism had the strongest association with ACE (OR = 3.26, 95% Cl 9.29, 1.14).

CONCLUSION
Results of the study suggest that a high ACE score increases the risk for DM, hypothyroidism and IR with hypothyroidism. This opens new avenues to develop preventive and management strategies for these diseases.

PP-D-06

MEDITERRANEAN DIET FOR DIABETES MELLITUS TYPE 2 PREVENTION, A LESSON FROM 751,161 SUBJECT: A SYSTEMATIC REVIEW AND META-ANALYSIS

https://doi.org/10.15605/jafes.037.AFES.46

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OBJECTIVES
An unhealthy diet including excessive caloric intake and physical inactivity are strongly associated with future risk for type 2 diabetes (T2D). A meta-analysis by Esposito et al. showed that adoption of a healthy diet will decrease the risk of diabetes by 20%. An example of diet modification is the Mediterranean diet. Hence, we would like to determine the effect of the Mediterranean diet on the prevention of T2D.

METHODOLOGY
Electronic searches from several electronic databases for cohort and randomized controlled trial (RCT) was carried out in May 2022 with the following keywords: "Diabetes Mellitus Type 2" and " Mediterranean diet" and "Prevention" and "Incidence." Pooled effect was calculated using the statistical software Stata version 13. Primary analyses included the incidence of T2D and was limited to prospective studies in the healthy and/or high-risk population.

RESULTS
From 546 studies published from 2007 to 2020, 4 RCTs and 18 cohort studies (751,161 subjects) were included in our meta-analysis. Subgroup analysis was performed based on health status and sex. From pooled analysis, Mediterranean diet will decrease the risk for T2D by 17.6% (RR 0.824 (95%CI 0.803-0.845, I2: 70.05, P<0.0001). This effect was greater in the high-risk population (27%) and females (9.98%). The Egger regression test showed no evidence of substantial publication bias (P=0.12).

CONCLUSION
The present study has shown the benefits of adopting the Mediterranean diet among the healthy and high-risk population. Diet modification is essential, especially in those at risk for T2D and CVD.

PP-D-07

THE DIAGNOSTIC VALUE OF FIBROSIS-4 SCORE (FIB-4) IN DETECTING NON-ALCOHOLIC FATTY LIVER DISEASE AMONG ADULTS WITH TYPE 2 DIABETES MELLITUS

https://doi.org/10.15605/jafes.037.AFES.47

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OBJECTIVES
This study aimed to determine the diagnostic value of Fibrosis 4 (FIB-4) index in detecting non-alcoholic fatty liver disease (NAFLD) among adult Type 2 Diabetes Mellitus (T2DM) patients.

METHODOLOGY
A single center, analytical cross-sectional study was conducted among adult T2DM patients with and without NAFLD at St. Luke's Medical Center, Quezon City. Medical history was obtained by reviewing charts of eligible patients. Liver ultrasound was used as the reference standard for the diagnosis of NAFLD. The FIB-4 index was calculated with the formula: age (years) x AST (U/L)/(platelets (10^9/L) x ALT (U/L)1/2.

RESULTS
A total of 305 patients with T2DM were included in the study. The prevalence of NAFLD based on ultrasound among diabetic patients is 76.07%. The median age, AST, and ALT were significantly higher in patients with NAFLD than those without. Platelet count was significantly lower in patients with NAFLD than those without. The proportion of patients with low platelet count, high AST and high ALT were significantly higher in patients with NALFD than those without. In this study, the FIB-4 index cut-off score for screening of NAFLD is ≥0.76, with an accuracy of 66.23%, sensitivity of 75%, specificity of 38.3%, PPV of 79.46% and NPV of 32.56% in detecting fatty liver.

CONCLUSION
A FIB-4 index value of ≥0.76 has acceptable sensitivity for screening NAFLD even in the absence of fibrosis among patients with T2DM. However, due to its low specificity, additional tests to establish a diagnosis of NAFLD may be required.

PP-D-08

ENDOTHELIAL DYSFUNCTION IS ALREADY PRESENT IN THE PRE-IMPAIRED GLUCOSE TOLERANCE (PRE-IGT) STAGE WITH NO SIGNIFICANT IDENTIFIABLE CARDIOVASCULAR RISK FACTORS

https://doi.org/10.15605/jafes.037.AFES.48

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OBJECTIVES

Hyperinsulinemia, which is observed at the pre-impaired glucose tolerance (pre-IGT) stage, is the earliest dysmetabolic signal in the course of type 2 diabetes mellitus. The increased C-peptide during this period has been demonstrated to be the culprit for the development of cardiovascular disease. This study aims to determine the prevalence of endothelial dysfunction among individuals with pre-IGT and to determine the cardiovascular risk factors contributory to the development of endothelial dysfunction.

METHODOLOGY

We screened adult patients at risk for diabetes mellitus (first-degree relative with type 2 DM, obesity, history of gestational diabetes, and polycystic ovary syndrome). Pertinent demographic, clinical, and laboratory results were determined and recorded. To test for endothelial dysfunction, brachial artery flow-mediated dilatation (FMD) was performed on pre-IGT patients. Binary logistic regression was used to determine significant risk factors affecting endothelial dysfunction and to compare risk factors between FMD (+) and FMD (-) patients.

RESULTS

Of the 67 patients screened, 41 have pre-IGT with a prevalence of 61%. Among the pre-IGT who had FMD done (31/41), seven were FMD (+) with a prevalence of 22.58%. FMD (+) patients were more obese and had higher total cholesterol and LDL, however, the finding was not statistically significant. Other CVD risk factors were comparable between groups. In addition, none of the risk factors significantly predicted the development of endothelial dysfunction among patients with pre-IGT ($p>0.05$).

CONCLUSION

At the pre-IGT stage, endothelial dysfunction is already present in 22% of patients. No significant identifiable CVD risk factors have been found so far.

PP-D-09

SEX DIFFERENCES IN CARDIOMETABOLIC RISK FACTORS IN A TYPE 2 DIABETES POPULATION: AN INTERIM ANALYSIS OF THE TARGET-T2D STUDY IN MALAYSIA

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OBJECTIVES

This study aimed to examine differences in the control and treatment of cardiometabolic risk factors between males and females with type 2 diabetes (T2D) in Malaysia.

METHODOLOGY

The TARGET-T2D study, an ongoing cross-sectional study (December 2021–June 2022), involves T2D adults treated with lifestyle modification with and without oral/injectable glucose-lowering drugs for ≥12 months in outpatient settings. We included 8 tertiary public hospitals in the Greater Kuala Lumpur region. In this interim analysis (13 December 2021–31 March 2022), we compared the attainment rates of ABC targets (HbA1c<7%, Blood pressure [BP]<130/80 mm Hg, LDL-Cholesterol <1.8 mmol/L) and use of cardiorenal-protective drugs (sodium-glucose co-transporter-2 inhibitors [SGLT2i], glucagon-like peptide-1 receptor analogues, renin-angiotensin system inhibitors [RASi], statins) by sex.

RESULTS

Among 2532 patients (mean HbA1c 8.2 ± 2.0%, mean body mass index 29.8 ± 6.4 kg/m^2, 54.4% females), females were younger and less likely to smoke than males. Of the entire cohort, 99.5% were at ESC high-/very high cardiovascular risk categories, wherein 70.3% of females and 78.6% of males were at very high-risk (p<0.001). Compared with males, more females attained BP <130/80 mm Hg (68.8% versus 62.2%; p<0.001), but not LDL-cholesterol <1.8 mmol/L (21.8% versus 31.5%; p<0.001) and all ABC targets (5.2% versus 7.3%; p=0.040). Fewer females were treated with SGLT2i (37.9% versus 44.2%; p=0.002), RASi (63.0% versus 69.6%; p<0.001) and statins (87.8% versus 92.6%; p<0.001) than males.

CONCLUSION

In this very high-risk T2D group, more males attained optimal risk factor control than females. Health services and mechanistic research are needed to explain the differences in risk profiles and treatment patterns.

PP-D-10

DEVELOPMENT AND EVALUATION OF AN ALTERNATIVE OBESE RAT ANIMAL MODEL OF TYPE 2 DIABETES

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OBJECTIVES

The aim of this study was to develop and evaluate of an alternative obese rat model for type 2 diabetes.

METHODOLOGY

Forty, 6-week-old, male Wistar rats were randomly divided into 5 groups as: Normal Control (NC), Diabetic Control (DC), Saccharin low 0.033% (SACL), Saccharin medium 0.067% (SACM) and Saccharin high 1.33% (SACH). The DC group was only given 10% fructose in water while the SACL, SACM and SACH groups were supplied with 0.03%, 0.067% and 0.13% saccharin respectively, in combination with 10% fructose in drinking water for 4 weeks only, while the animals in NC group were fed with normal drinking water. Thereafter, all animals were given normal drinking water for the remaining period of the study and fed with commercially available rat chow diet ad libitum for the duration of the study. The Body Mass Index (BMI) of the animals were measured weekly, with a BMI ≥0.69 g/cm2 considered obese. Once obesity was confirmed, all rats in DC and SAC groups were injected intraperitoneally with a low dose (40 mg/kg BW) of streptozotocin (STZ) dissolved in 0.1 M citrate buffer (pH 4.5), while the animals in NC group were injected with an equivalent volume of citrate buffer. One week after the STZ injection, animals with a non-fasting blood glucose level ≥200 mg/dl were considered diabetic.

RESULTS

After the 13-week experimental period, the SACL group demonstrated a sustainably higher BMI and obesity level, higher blood glucose level as well as better anti-diabetic drug sensitivity, more insulin resistance, lower glucose tolerance and partial pancreatic β-cell damage in comparison to the other diabetic groups.

CONCLUSION

Considering all above, the 10% fructose along with 0.033% saccharin fed and STZ (40 mg/kg BW) injected group could be a suitable animal model of obesity-related type 2 diabetes.

PP-D-11

EVALUATING HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH YOUNG-ONSET TYPE 2 DIABETES IN SINGAPORE USING EuroQol EQ-5D-5L

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OBJECTIVES

Despite multiple efforts to create awareness and reduce the rise of young-onset T2D (YT2D), the prevalence of YT2D remains high in Singapore. There is also limited information on how YT2D patients have been coping with their chronic condition. We hypothesize that YT2D patients face a myriad of challenges in their daily routine and aim to determine specific areas to focus on for providing patient-centred care.

METHODOLOGY
The 269 patients (onset age ≤35 years) enrolled were subjected to the EQ-5D-5L questionnaire upon recruitment. EQ-5D-5L consists of a descriptive page, which comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression with 5 response levels, and an EQ-VAS scale (0-100), which evaluates health status and health preference. Health states were validated against the Singapore valuation set.

RESULTS
Majority (72.1%) of the patients (mean ± SD age: 33.7 ± 13.8, diabetes duration: 10.5 ± 10.6) reported a full health state of "11111". Of the remaining patients, 15.2% and 14.9% reported problems of varying severity under pain/discomfort and anxiety/depression, respectively. Mean VAS score was 79.3 (range 30-100) with 29% reporting a score of ≤70. A longer duration of diabetes was found to be associated with lower VAS scores (≤70 or >70) (OR=1.04, 95% CI: 1.01-1.09, p=0.028) after adjusting for age, gender, ethnicity, BMI and HbA1c.

CONCLUSION
Our results suggest that patients with younger-onset and longer diabetes duration have lower self-rated quality of life. We identified pain/discomfort and anxiety/depression as two areas of concern that clinical care providers can focus on to better support patients in their diabetes care.

PP-D-12

RNA-SEQ ANALYSIS OF LIVER FROM NASH-HCC MODEL MOUSE TREATED WITH STREPTOZOTOCIN-HIGH FAT DIET

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OBJECTIVES
NASH is a chronic liver disease, often associated with type II diabetes, which sometimes progresses to more serious conditions such as liver fibrosis and hepatocellular carcinoma (HCC). The STAM™ mouse shows the same pathological progression as human NASH patients, and has been widely used for both drug efficacy and basic research. In this study, we analyzed the RNA-seq data of STAM™ mouse at each pathological stage (steatosis, steatohepatitis, liver fibrosis and HCC) and examined the clinical correlation at the genetic level.

METHODOLOGY
NASH was induced in male mice by a single subcutaneous injection of streptozotocin 2 days after birth and feeding with high fat diet after 4 weeks of age. The mice were sacrificed and livers collected at 6, 8, 12 and 20 weeks of age. For liver samples, the left lateral lobe was snap frozen in liquid nitrogen and stored at -80°C for RNA-seq analysis. Total RNA of the cells was isolated using RNeasy mini kit.

RESULTS
The gene expression of the canonical pathways in NASH progression from steatosis to HCC were analyzed, such as immune system process, oxidation-reduction process and lipid metabolic process. Moreover, since it has been reported that genetic traits are involved in the development of NASH-HCC, we subsequently analyzed the genetic mutations in the STAM™ mice. The number of individual genes showing mutations in mTOR involved in Insulin signalling increases as the disease progresses, especially in the liver cancer phase.

CONCLUSION
These results indicate that gene profiles in the STAM™ mouse are clinically correlated.

PP-D-13

CLINICAL EFFECTIVENESS OF ONCE-WEEKLY DULAGLUTIDE AS ADD-ON TO SGLT2i IN THAI PATIENTS WITH T2DM: RETROSPECTIVE STUDY IN A REAL-WORLD SETTING

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OBJECTIVES
Both GLP-1 receptor agonists (GLP-1 RA) and SGLT2 inhibitors (SGLT2i) reduce the risk of cardiovascular and renal complications when included as part of usual care in T2DM patients with established atherosclerotic cardiovascular disease (ASCVD) or multiple risk factors for ASCVD. Dulaglutide is a once-weekly GLP1-RA which became available in Thailand in 2018. This study aimed to show the real-world use of dulaglutide as add-on to SGLT2i among Thai patients with T2D in a specialized tertiary diabetes center.

METHODOLOGY
This retrospective cohort study included patients who were prescribed with dulaglutide for at least 1 month between 2018 and 2020 at Theptarin Hospital, Bangkok, Thailand. Primary (change in A1C) and secondary (including change in body weight, glycemic and weight-loss target achievement) endpoints were assessed at baseline and at follow-up visit.

RESULTS
A total of 41 patients (females 51.2%, mean age 56.9±13.4 years, duration of diabetes 15.7 ± 9.0 years, BMI 34.2 ± 5.8 kg/m^2, baseline A1C 8.5 ± 1.7%, SGLT2i-treated 48.8%, insulin-treated 51.2%, established ASCVD 9.8%) were included in the study. During a mean follow-up of 5.7 months after treatment initiation, the overall mean A1C reduction was 0.9% with weight loss of 2.3 kg. The proportion of patients who could achieve A1C < 7.0% increased from 12.5% to 31.4%. Among SGLT2i-treated patients, overall mean A1C reduction when compared with non SGLT2i-treated patients was 1.0 ± 1.3% and 0.8 ± 1.8%, respectively (p=0.716). Body weight reduction in SGLT2i users was -3.0 ± 4.7 kg while for non-SGLT2i users, it was -1.6 ± 3.4 kg (p=0.277). Reported adverse events were consistent with the known safety profile of GLP-1 RA.

CONCLUSION
In routine clinical practice among Thai patients with T2D, the combination of dulaglutide and SGLT2i was well tolerated and associated with sustained glycemic control and weight loss in a wide range of patients with T2D comparable with what has been observed in randomized clinical trials.

PP-D-14

ASSOCIATION BETWEEN ELEVATED PHASE ANGLE AND REDUCED RISK OF CHRONIC KIDNEY DISEASE PROGRESSION IN TYPE 2 DIABETES

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OBJECTIVES
Phase angle (PhA) is a bioelectrical impedance analysis parameter defined as the angle of the vector formed by the body's resistance and reactance. It indicates nutritional status, with higher levels signifying healthier cell membrane and higher muscle mass. Currently, the association between PhA and chronic kidney disease (CKD) progression is unknown. Pigment epithelium-derived factor(PEDF) has anti-oxidant, anti-angiogenic and anti-inflammatory properties, and its circulating level may be elevated in CKD. We investigated the association between PhA and CKD progression, and the possible mediation of PEDF in this association among Type 2 Diabetes(T2D) patients.

METHODOLOGY
We conducted a prospective study on 868 patients (mean age 58.1 ± 8.6 years) from SMART2D cohort. PhA was measured using bio-impedance analysis. CKD progression was defined as deterioration across KDIGO estimated glomerular filtration rate(eGFR) categories with ≥25% decrease from baseline. Enzyme-linked immunosorbent assay was used to quantitate PEDF. We examined the association between PhA and CKD progression using Cox proportional regression, adjusting for demographics, clinical parameters and medications. This research has been approved by an ethical committee.

RESULTS
After a follow-up period of 8.6 years, 40.3% of participants had CKD progression. PhA is inversely associated with CKD progression with a hazard ratio(HR) of 0.69 (95% CI 0.61-0.79; p<0.001). The inverse association persists in fully adjusted analysis with HR 0.78 (95% CI 0.67-0.91;p=0.001). Binary mediation analysis revealed that PEDF accounted for 13.7% of association between PhA and CKD progression (p=0.028).

CONCLUSION
Our findings have revealed a previously unobserved association between higher PhA and reduced risk of CKD progression. This may pave the way for future studies on the role of PhA in monitoring renal decline.

PP-D-15

EFFECT OF CITRAL ON NONALCOHOLIC STEATOHEPATITIS (NASH) VIA AMPK-MEDIATED AUTOPHAGY AND INFLAMMASOME PATHWAY IN TYPE 2 DIABETIC MICE

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OBJECTIVES
Nonalcoholic steatohepatitis (NASH) is the progressive form of non-alcoholic fatty liver disease (NAFLD), associated with lipotoxicity-induced autophagy defects and significantly increased inflammasome expression. Citral, a terpenoid and the main constituent of Lemongrass, is reported to have multiple biological activities. This study aimed to investigate the effect of citral on mechanisms underlying the relationship between the autophagy Inflammatory and lipid metabolism-related gene deregulation associated with NASH using an in vivo model of type 2 diabetes.

METHODOLOGY
Thirty male BALB/c mice were randomly divided into three groups: control (n = 10), model (n = 10), and treatment (citral) group (n = 10). Mouse models of NAFLD and diabetes were established using a high-fat diet and streptozocin.

RESULTS
The levels of fasting blood glucose (FBG), total cholesterol (TC), and triglyceride (TG) in the serum were significantly reduced after citral treatment. The levels of insulin, leptin and adiponectin were also corrected by citral treatment. Treatment with citral markedly reduced the levels of liver injury markers, malondialdehyde (MDA), alanine aminotransferase (ALT) and Aspartate transaminase (AST) and inflammatory markers like TNF-α and Caspase 3 and CRP levels. The expression of AMPK, LC3-II, Beclin-1 and Parkin were increased significantly, whereas mTor, ACC and NLRP3 and IL-1β proteins were suppressed after citral treatment.

CONCLUSION
These results suggest that citral stimulates activity of AMPK and inhibit the NLRP3 inflammasome by enhancing the autophagy pathway in liver, which makes it a promising candidate for a therapeutic agent for the management of NASH associated with diabetes.

PP-D-16

HIGH EXTRACELLULAR WATER TO TOTAL BODY WATER RATIO AND DIABETIC RETINOPATHY PROGRESSION IN TYPE 2 DIABETES

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OBJECTIVES
Excess extracellular water is associated with chronic kidney disease progression. It is not known if it is associated with diabetic retinopathy (DR) progression. We aim to investigate the relationship between the ratio of extracellular-water to total-body-water (ECW/TBW), an indicator of fluid balance, and DR progression in type 2 diabetes mellitus (T2DM), and elucidate its role as a potential mediator in the relationship between matrix metallo-proteinase-2 (MMP2) and DR progression.

METHODOLOGY
We conducted a prospective study on 1,041 patients (mean age 56.5 ± 10.7 years) from the SMART2D cohort. ECW/TBW ratio was measured using bio-impedance analysis. Digital colour fundus photographs were examined for DR in a masked fashion. DR progression was defined as increase in severity across categories - normal, non-proliferative DR and proliferative DR. This research has been approved by an ethical committee.

RESULTS
After 7.8 years' follow-up, 15.5% of 1,041 participants experienced DR progression. Logistic regression showed that Tertile 3 ECW/TBW ratio, indicative of higher ECW/TBW ratio, was associated with 129% higher odds of DR progression with unadjusted Odds Ratio (OR) 2.29 (95% CI 1.49-3.52, p<0.001) compared with Tertile 1 ECW/TBW ratio. Having adjusted for demographics, clinical co-variables and medications, the positive association persisted for Tertile 3 ECW/TBW ratio with OR 2.79 (95% CI 1.58-4.89, p<0.001). Binary mediation revealed that ECW/TBW ratio accounted for 41.5% of the relationship between MMP2 and DR progression (p=0.001).

CONCLUSION
The novel finding of the association between a higher ECW/TBW ratio and DR progression highlights the importance of extracellular fluid excess as a potential marker of DR progression for future studies and interventions.

PP-D-17

CHOREA HYPERGLYCEMIA BASAL GANGLIA SYNDROME: A CASE REPORT OF A RARE DIABETES COMPLICATION

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BACKGROUND
Chorea hyperglycemia basal ganglia syndrome (C-H-BG) is a rare sequelae of acute hyperglycemia with a predilection for Asians and elderly women. Cases are often misdiagnosed with the more common intracerebral hemorrhage. The purpose of this report is to present this rare condition in a relatively young Asian male and discuss the approach to such cases.

CASE
A single case of C-H-BG was closely followed and recorded.

A 53-year-old-male, Filipino, with type 2 diabetes mellitus and hypertension for more than 10 years, presented with sudden onset of hyperkinetic, involuntary, non-patterned, continuous movements of the left upper and lower extremities. Investigations revealed severe hyperglycemia (CBG 328 mg/dL; HbA1c 15.4%) without acidemia and ketonuria. Cranial computed tomography scan showed hyperdensity on the right caudate and lentiform nuclei. On cranial magnetic resonance imaging, there was T1-weighted hyperintense and T2-weighted hypointense signal involving the right putamen, globus pallidus and caudate. Cranial magnetic resonance angiography showed stenosis on the cavernous segment of the right internal carotid artery (ICA), left ICA and middle cerebral artery junction, the A1 segment of the left anterior communicating artery and proximal P2 segments of the bilateral posterior cerebral arteries. The patient was managed with a basal-bolus insulin regimen to control the blood glucose and haloperidol to manage the extrapyramidal symptoms. Consequently, there was complete resolution of the involuntary movements.

CONCLUSION
This case emphasizes the importance of early recognition of this rare diabetes complication. Manifestations of C-H-BG are debilitating but reversible through aggressive glucose control and haloperidol.

PP-D-18

PATIENT CHARACTERISTICS, GLYCEMIC CONTROL AND MANAGEMENT PATTERNS OF TYPE 2 DIABETES MELLITUS IN MALAYSIA

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OBJECTIVES
To highlight the real-world data on patient characteristics and management patterns among Malaysian type 2 diabetes mellitus (T2DM) patients based on the DISCOVER Global Registry.

METHODOLOGY
The DISCOVER Global Registry is a prospective, non-interventional, clinician-led study involving adults with T2DM. Data from January 2017 to May 2020 were analyzed which included demographic details, biochemical parameters, medication use and details of follow up.

RESULTS
A total of 332 patients were enrolled (51% males, mean age 50.7 years, DM duration 76 months, body mass index 29.5 kg/m^2, waist circumference 103 cm, blood pressure 132/76 mm Hg and co-morbidities (16% hypertension, 20% dyslipidemia). The mean HbA1c was 8.5%. The HbA1c value was <7% in 29% [88], 7-8% in 21% [65]) and >8% in 50% [150]. The mean fasting glucose level was 8.4 mmol/L, serum creatinine 80.5 µmol/L, eGFR 87 ml/min/1.73m^2, total cholesterol 7.7 mmol/L, triglycerides 2.2 mmol/L and low density lipoprotein 3.4 mmol/L. Majority of the patients (44% [147]) were on biguanides, followed by insulin (33% [110]), sulfonylureas (14% [47]), dipeptidyl-peptidase-4 inhibitors (8% [27]) and sodium-glucose cotransporter-2 inhibitors (6% [19]). At baseline, 36% (118) were on monotherapy, 21% (68) on dual, 14% (45) on triple, 6% (20) on quadruple therapies and 52% (171) were on cholesterol medication.

CONCLUSION
The percentage of poorly controlled DM remains high with majority of them being obese. Kidney function remains preserved while lipid levels are not on target. Metformin constitutes the most common diabetic agent used. Nearly half of patients are not on statin despite therapeutic necessities.

PP-D-19

MUTATION SPECTRUM OF MONOGENIC DIABETES IN SINGAPORE

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OBJECTIVES

Monogenic diabetes, a rare condition known to affect about 5% of young-onset diabetes, is not routinely investigated in our local population with diabetes. The NHG-KTPH Monogenic Diabetes Registry was set up in 2017 to study the prevalence of monogenic diabetes in Singapore as well as determine the underlying mutations responsible for this condition to facilitate the application of precision medicine to this group of individuals.

METHODOLOGY

Young-onset (≤35 years) individuals with atypical diabetes were enrolled into our monogenic diabetes study and subjected to genetic testing using 16-gene next-generation sequencing, mt.3243A>G TaqMan genotyping and multiplex-ligation dependent probe amplification (for HNF1A, HNF4A, GCK, HNF1B). Variants identified were annotated according to guidelines from American College of Medical Genetics and Genomics (ACMG). Likely pathogenic/pathogenic variants were validated using bi-directional Sanger sequencing.

RESULTS

Among 340 probands sequenced, 43 (12.6%) had a likely pathogenic/pathogenic variant in one of these 8 genes: HNF1A (27.9%), HNF4A (25.6%), GCK (16.3%), mt.3243A>G (16.3%), HNF1B (4.7%), ABCC8 (4.7%), PAX4 (2.3%) and NEUROD1 (2.3%). Most (95.3%) of the variants occurred in genes which are clinically actionable. Mutation-positive cases are mostly female (67.4% vs 49.8%, p=0.031), have lower BMI (median 24.9 vs 22.4 kg/m^2, p<0.001), lower waist circumference (74.0 vs 82.0 cm, p<0.001), higher HDL (1.41 vs 1.26 mM, p=0.003), lower triglycerides (0.95 vs 1.39 mM, p=0.005), lower C-peptide (506.2 vs 819.8 pM, p=0.013), lower hsCRP (0.70 vs 1.40 mg/L, p=0.007) and lower uric acid (5.45 vs 6.41 mg/dL, p=0.007) than mutation-negative cases.

CONCLUSION

Monogenic diabetes is non-trivial in our local population of young-onset atypical diabetes. The combination of clinical parameters and biomarkers can be explored to improve selection of individuals for genetic testing. This facilitates early and accurate genetic diagnosis of monogenic diabetes that can better inform clinical management.

PP-D-20

REGIONAL DISPARITIES IN THE PREVALENCE OF DIAGNOSED DIABETES IN RURAL VS. URBAN UNITED STATES, 2004–2019

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OBJECTIVES

United States (US) rural, compared to nonrural populations have less access to diabetes care. It is unknown if rurality also contributes to disparities in the prevalence of diabetes. The study objective was to evaluate the trend in US prevalence of diabetes from 2004–2019 by county-rurality and region.

METHODOLOGY

We used US Centers for Disease Control and Prevention (CDC) data on prevalence of diagnosed diabetes in adults aged ≥20 years, available for 97.6% of US counties (3147/3226) from 2004–2019. Trends in annual age-adjusted prevalent diabetes rate per 100 adults (AAPR) were assessed by weighted least squares regression. Year was fitted with a spline function, and AAPR change was tested by a model-based comparison of 2019 vs. 2004.

RESULTS

The overall AAPR increased from 6.5 (per 100) in 2004 to 8.4 in 2011 and 8.8 in 2019. The 2019 vs. 2004 percentage-increase (95% confidence interval) was present at all rurality levels: 33% (27%–40%) for noncore counties (most rural), 38% (37%–38%) for large fringe metro counties (second most urban), and 35% (35%–35%) for large central metro counties (most urban) (all, p<.001). Stratified by region, the AAPR percentage-increase was lowest in the Northeast (30% [28%–33%]; p<.001) and highest in the South (40% [39%–41%]; p<.001).

CONCLUSION

The US prevalence of diabetes increased from 2004 to 2019 across all county-rurality levels. This study revealed a worsening trend in the South vs. other regions, which may highlight areas for interventions to reduce diabetes incidence.

PP-D-21

THE EFFECT OF PROBIOTICS ON INSULIN SENSITIVITY, GLYCEMIC CONTROL AND LIPID PROFILE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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OBJECTIVES
Fermented kimchi, a traditional Korean food, which contains multi-strained probiotics (Innolac) is purported to have beneficial effects on glucose and lipid metabolism in patients with prediabetes and obesity. However, the effect of probiotics in patients with type 2 diabetes remains unclear. This study investigated the effect of probiotics on insulin sensitivity, glycemic control and lipid profile in patients with type 2 diabetes mellitus.

METHODOLOGY
This was a hospital-based, randomized controlled clinical study conducted in patients consulting at the diabetes clinic of North Okkalapa General and Teaching Hospital during January 2019 to October 2020. A total of 75 patients with HbA1c 7.0% to 8.0% were recruited and prospectively randomized. Eleven patients (14.6% of study population) dropped out, and 32 patients in each group were studied to receive either oral probiotics sachet daily (probiotics group n = 32) or usual medical care (control group n=32) for two months. Determination of HOMA-IR, HbA1c and fasting lipid profile (TC, HDL, LDL and TG) was done at baseline and after 2 months. Mean changes between both groups were compared and analyzed by per protocol analysis.

RESULTS
There was no significant difference in baseline clinical characteristics between the two groups. The probiotics group showed significant improvement of fasting insulin (-4.26 ± 1.87 mU/L reduction, P=0.02, 95% CI), insulin sensitivity (-1.53 ± 0.67 HOMA IR reduction, P=0.02, 95% CI) and TG level (-25.65 ± 9.68 mg/dl, P=0.01, 95% CI) compared with the control group. There was no significant improvement of glycemic control (FBG and HbA1c), TC, HDL and LDL in the probiotics group compared with the control group. No significant adverse event was seen in both groups.

CONCLUSIONS
In patients with inadequately controlled type 2 diabetes mellitus, supplementation of probiotics revealed improvement in insulin sensitivity (HOMA-IR), fasting insulin and triglyceride (TG) but did not show improvement in FBG, HbA1C and lipid profile (TC, HDL and LDL).

PP-D-22

IMPACT OF LIVER STEATOSIS ON GLYCEMIC IMPROVEMENT AT SIX MONTHS AFTER BARIATRIC SURGERY

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OBJECTIVES
Non-alcoholic fatty liver disease (NAFLD) is strongly associated with obesity and increases the risk of type 2 diabetes (T2D) development. This pilot prospective study aimed to determine whether the severity of liver steatosis/fibrosis was associated with glycaemic improvement after bariatric surgery in adults with T2D.

METHODOLOGY
Patients with T2D scheduled for either Roux-en-Y gastric bypass or sleeve gastrectomy were recruited (n = 15; age: 46 ± 8 years, 46.7% males, body mass index (BMI): 40.8 ± 6.1 kg/m^2). Transient elastography with controlled attenuation parameter (CAP) was performed before surgery to assess liver steatosis and fibrosis. The study outcomes included relative percentage change in glycated haemoglobin (HbA1c) at 6-month post-surgery from baseline (pre-op), and T2D remission defined as 6-month HbA1c<6.5% without glucose-lowering medications.

HbA1c levels reduced from 7.4±1.4% to 6.3±1.0% at 6 months after surgery. The median relative percentage decrease in HbA1c was 13.4% (interquartile range: -25.8 to -6.3). The baseline CAP score (mean: 342 ± 50 dB/m; reflecting liver steatosis), but not the liver stiffness measurement score (reflecting liver fibrosis), was correlated with the relative percentage change in HbA1c (rho = 0.64, P=0.034). Linear regression analysis shows that higher CAP value was associated with reduced magnitude of HbA1c reduction (B = 0.21, 95% CI:0.06–0.36, P=0.017) after adjustment for baseline age, sex, BMI and HbA1c. Similarly, lower CAP score independently predicted T2D remission (relative risk=0.96, 95% CI:0.94–0.97, P<0.001).

CONCLUSIONS
Increased liver steatosis is associated with poorer glycaemic outcome after bariatric surgery. Therefore, interventions to reduce liver steatosis prior surgery may improve post-surgical glycaemic control in people with T2D.

PP-D-23

GLUCOSE VARIABILITY AND DIASTOLIC DYSFUNCTION IN PATIENTS WITH TYPE 2 DIABETES

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OBJECTIVES

Diastolic dysfunction is one of signs of heart failure and could be associated with autonomic neuropathy. Glycemic variability could be one of the reason predisposing to heart failure in subjects with diabetes. We examined the relationship between glycemic variability and diastolic dysfunction in patients with type 2 diabetes mellitus without coronary artery disease.

METHODOLOGY

Seventy-eight patients with heart failure with preserved left ventricular ejection fraction and type 2 diabetes mellitus were examined. Diastolic function was assessed by echocardiography, glycemic variability was evaluated by continuous glucose monitoring. According to the glycemic variability, all studiypatients were divided into two groups: group I - SD>2 (high glycemic variability), n = 40; group II - SD≤1.9 (normal glycemic variability), n = 38.

RESULTS

Group I were older (49 (9) vs 46 (5); $p<0.05$, with a longer duration of DM (10 yrs (9.5) vs 6 yrs(5.5); $p<0.01$). In group I compared to group II there were more patients with grade 2 diastolic dysfunction (25 (62.5%) vs 10 (26.3), $p<0.05$). Patients in group I had more severe diastolic dysfunction. In group I patients insulin and sulfonylureas were used more often (11 (27.5%) vs 0 p = 0.0001; 25 (62.5%) vs 10 (26.3%); $p<0.01$, respectively); patients of group II were more often treated with SGLT2 (2 (5%) vs 13 (34.21%); $p<0.01$).

CONCLUSIONS

Increased glycemic variability is associated with diastolic dysfunction and in patients with type 2 diabetes.

PP-D-24

COMPARISON OF THE CLINICAL OUTCOMES OF HYPERGLYCEMIC CRISIS IN COVID-POSITIVE AND COVID-NEGATIVE PATIENTS: A RETROSPECTIVE COHORT STUDY

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OBJECTIVES

Since the start of the COVID-19 pandemic, there has been an increased incidence of hyperglycemic crisis in hospitals, involving both those with and without COVID-19 infection. Our objective was to compare the clinical outcomes between COVID-positive and COVID-negative patients who were admitted for hyperglycemic crisis from March 2020 to February 2022.

METHODOLOGY

We conducted a retrospective cohort study of adult patients with hyperglycemic crisis on admission from March 1, 2020 to February 28, 2022 at the St. Luke's Medical Center - Global City. They were divided into two groups: those with and without COVID-19 infection. Their medical records were reviewed to determine and compare their clinical background, presenting clinical manifestations, non-COVID acute conditions, biochemical and clinical parameters, treatment regimen, and clinical outcomes. Descriptive statistics were employed.

RESULTS

The COVID-positive group had significantly higher in-hospital mortality rate prior to resolution of hyperglycemic crisis ($p=0.008$) and had a significantly higher proportion of patients who developed acute respiratory failure ($p=0.000$) and multi-organ failure ($p=0.003$). They were also significantly older and had a significantly higher proportion of patients who had preexisting malignancy, presented with cough and dyspnea, and received concurrent steroid treatment. The COVID-negative group significantly had more patients who presented with abdominal pain, had urinary tract infection on admission, and developed acute kidney injury.

CONCLUSION

Patients hospitalized with hyperglycemic crisis who also had COVID-19 infection had higher in-hospital mortality rate before resolution of hyperglycemic crisis, compared to those who did not have COVID-19 infection.

PP-D-25

COMPARISON OF CLINICAL OUTCOMES OF TYPE 2 DM PATIENTS WITH OVERWEIGHT AND OBESITY VERSUS THOSE WITH NORMAL BMI

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OBJECTIVES
This study aimed to determine the difference in glycemic control, metabolic parameters (LDL, HDL, triglycerides, and blood pressure control) and the presence of retinopathy and/or nephropathy between overweight and obese versus normal body mass index (BMI) type 2 diabetes mellitus patients.

METHODOLOGY
This is an analytic cross-sectional study of type 2 diabetes mellitus patients from outpatient clinics at St. Luke's Medical Center, Quezon City. Available medical records and laboratory tests were reviewed. Data were analyzed and compared between those overweight and obese versus those with normal BMI based on Asia Pacific Guidelines.

RESULTS
A total of 248 patients with type 2 diabetes mellitus were included in the study. Patients who are overweight and obese have a significantly higher risk of having uncontrolled diabetes (p=0.011), low HDL (p=0.035) and albuminuria (p=0.027) compared to those with normal BMI. There were no significant difference between overweight and obese patients versus those with normal BMI with regard to BP control, high LDL, high triglycerides and retinopathy.

CONCLUSION
Type 2 diabetes mellitus patients who are overweight and obese have a higher risk of developing uncontrolled diabetes, low HDL and albuminuria compared to those with normal BMI.

PP-D-26

THE INFLUENCE OF RENAL FUNCTION ON EFFICACY AND SAFETY OF LUSEOGLIFOZIN ADDED TO EXISTING INTENSIVE INSULIN THERAPY

https://doi.org/10.15605/jafes.037.AFES.66

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OBJECTIVES
The primary objectives of this study were to determine the efficacy of luseoglifozin on reduction of blood glucose in different eGFR categories. The secondary objectives were to evaluate the changes in body weight, blood pressure, urine microalbumin and eGFR.

METHODOLOGY
This study is a multicenter, open-label, single arm, interventional cohort study. We assigned 105 type 2 diabetes patients on intensive insulin therapy. The patients were stratified to three groups according to baseline eGFR; normal/mild renal impairment group with eGFR >60 mL/min, mild-moderate impairment group with eGFR 45 to 60 mL/min and moderate-severe impairment group with eGFR 30 to 45 mL/min. All patients were treated with luseoglifozin and followed up for 24 weeks. This research was approved by an ethical committee.

RESULTS
There was significant HbA1c reduction at week 24 from baseline in normal/mild renal impairment group with median changes of -0.7% (± 1.4)(p<0.001). Fasting plasma glucose demonstrated significant reduction in normal/mild renal impairment group with mean difference of -1.69 mmol/L (-2.61, -0.77)(p<0.001) and in mild-moderate renal impairment group with mean difference of -1.69 mmol/L(-3.33,-0.06)(p 0.044). Body weight was significantly decreased in normal/mild renal impairment and mild-moderate renal impairment group with median change of -0.5 kg (±2.9)(p 0.011) and -0.75 kg (±2.0)(p 0.019) respectively. There was no significant change in blood pressure, urine microalbumin and eGFR. Hypoglycemia incidence was higher among patients in lower eGFR and all were mild hypoglycemia.

CONCLUSION
Significant improvement in glycaemic control and body weight reduction were observed after treatment with luseoglifozin, particularly in normal/mild renal impairment group.

PP-D-27

ASSESSMENT OF DIETARY INTAKE IN 400 WOMEN WITH GESTATIONAL DIABETES

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OBJECTIVE
Gestational diabetes (GD) is one of the most common complications in pregnancy, affecting nearly 14% of pregnancies Obesity in the mother-to-be, usually related to hypercaloric diet, is an important risk factor. Evaluation of the correlation between caloric intake and maternal-fetal complications.

METHODOLOGY
Retrospective study, concerning 400 pregnant patients with GD: fasting blood glucose or OGTT, between 2017 and 2019. Dietary intake was assessed by expert dieticians.

RESULTS
The mean age was 34.54 ± 5.51 years [19 -46]. A history of personal gestational diabetes was found in 16.8% of which 23% were complicated by macrosomia. Among the patients, 33.3% were obese before conception.

Dietary survey: the average caloric intake was 2732.17 ± 605.87 calories with a diet considered hypercaloric: 60.9%.

The average fat content was 34.35 ± 4.5% and protein 11.25 ± 3.35%. The average carbohydrate content was 54 ± 4.7% [39-69%] with a high-carbohydrate diet in 50.5% of patients.

A high-calorie diet at the time of diagnosis was significantly correlated with the occurrence of obstetric complications (p=0.043) but not with fetal complications, including macrosomia (p=0.407).

CONCLUSIONS
Carbohydrates are an important source of energy for the mother and her fetus; it is recommended that all pregnant women have at least 175 g of carbohydrates per day. During gestational diabetes, it is essential to pay attention to the quantity (less than 35-45% of daily caloric intake) and type of carbohydrate: low glycemic index and slow digestion, to promote glycemic control and prevent maternal-fetal complications.

PP-D-28

RETROSPECTIVE EVALUATION OF WEIGHT LOSS TREATMENT IN OVERWEIGHT AND OBESE PERSONS WITH DIABETES IN CLINICS IN LAGOS, NIGERIA

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OBJECTIVES
Attainment of ideal weight in diabetes is vital. This retrospective study aims to evaluate how much weight patients were able to lose and the determinants of successful weight loss.

METHODOLOGY
Records of obese (BMI >30 kg/m^2) type 2 patients of two clinics in Lagos (public and private) were retrieved and biodata and weight records were perused. Drugs used to ensure weight loss were also extracted.

RESULTS
We studied 152 patient records. Their mean height was 1.65 m and their mean weight was 108 kg (mean BMI of 39.7 kg/m^2). Weight loss management included non-structured dietary counsel given to all the patients, 1-3 weight-reducing drugs including orlistat, topiramate, SGLT-2 inhibitors, and GLP-1RAs. The mean weight loss was 4.96 kg (range -30 to + 28 kg) for those managed with weight loss drugs. The weight loss in 108 (71.4%) was over a period of 1-3 years. Sustained weight loss of range 1-30 kg was observed with a mean weight loss of 12.4 kg in this group. The 28.6% who did not lose weight gained 1-28 kg, a mean weight gain of 4.16 kg over the same period. Those who experienced the greatest weight loss were on dual, triple, or quadruple therapy in addition to the diet. Only 3 patients had bariatric surgery for weight loss which was beneficial in one (lost 31 kg), equivocal in one (only transient weight loss and regained most of the weight), and not measurable in the 3rd (lost to follow-up).

CONCLUSION
Obese DM patients require active and aggressive combination/multidisciplinary care for improved metabolic and obesity control.

PP-D-29

HISTOLOGICAL FEATURES OF VASCULAR COMPLICATIONS OF THE LOWER EXTREMITIES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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OBJECTIVES
The aim of the work was to investigate histological features of vascular complications of the lower extremity in patients with type 2 diabetes mellitus.

METHODOLOGY
We studied macroscopic and microscopic changes of lower extremitytissues of 7 cases of diabetic gangrene. We used common histological methods of staining with hematoxylin and eosin, Masson's trichrome and Hart's elastin stain.

RESULTS
The main histological features of the vascular complications of lower extremity in patients with type 2 diabetes mellitus were: atherosclerosis arteries and thrombus formation; calcification of the middle tunica of arteria, including large areas of calcification and many small areas and proliferation of endothelium; thinning of the epidermis; thickening and fragmentation of fibrous structures in the dermis; reduction in skin appendage; hyalinosis and vascular thrombosis. In diabetic gangrene, skin defects of various depths and areas are determined with microcirculatory disorders, stasis, thrombus formation, wall hyalinosis, accumulation of purulent exudate and tissue detritus in the interstitial tissue. Pathomorphological criteria for the viability of the lower extremity tissues in diabetic foot and gangrene are the patency of large vessels, the integrity and clear differentiation of tissue structures, the arterioles wall thickness in the range 18.5 ± 1.5 μm, the diameter – 29.7 ± 0.8 μm, Kernogan index – 0.67 ± 0.08.

CONCLUSION
The main cause of disability and mortality in patients with diabetes mellitus is late vascular complications, including diabetic micro- and macroangiopathy of the lower extremities. Timely diagnosis of and adequate treatment can prevent the development of diabetic foot syndrome.

PP-D-30

EFFECT OF DIET ON CONTINUOUS GLUCOSE PROFILE OF HEALTHY INDIVIDUALS WITHOUT DIABETES

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OBJECTIVES
It is essential to understand continuous glucose monitoring (CGM) data in healthy subjects without diabetes which could serve as useful reference for interpretations of glucose measurements in diabetic patients. However, little is known about dietary impact on CGM data in studies of CGM in healthy individuals. We aim to characterise the effect of diet on interstitial glucose levels in healthy individuals without diabetes.

METHODOLOGY
We conducted a cross-sectional on 95 healthy volunteers without diabetes (mean age 34.9 ± 10.0 years) who underwent flash glucose monitoring using Freestyle Libre. Nutrient data collected from a food diary were analysed using FoodWorks Professional nutrient analysis software. Linear regression was performed to examine association between nutrient contents with peak glucose and 4-hr post-absorptive glucose levels, adjusting for demographics, body mass index, fasting plasma glucose and exercise.

RESULTS
The mean peak glucose and 4-hr post-absorptive glucose levels were 6.9 ± 1.7 and 4.6 ± 1.0 mmol/l. Higher levels of calorie, fat, carbohydrates and starch intake were associated with peak glucose levels in crude and fully adjusted analyses with adjusted coefficients 0.39 (95% CI 0.26-0.51; p<0.001), 0.21 (95% CI 0.08-0.34; p=0.001), 0.39 (95% CI 0.26-0.51; p<0.001) and 0.41 (95% CI 0.12-0.38; p<0.001) respectively. Higher levels of calorie, carbohydrates and sugar were associated with 4-hr post-absorptive glucose levels in crude and fully adjusted analyses with adjusted coefficients 0.13 (95% CI 0.06-0.21; p=0.001), 0.12 (95% CI 0.04-0.20; p=0.002) and 0.10 (95% CI 0.02-0.17; p=0.012) respectively.

CONCLUSION
Meals with higher calorie, fat, carbohydrates and starch intake induced higher peak glucose levels. Meals with higher levels of calorie, carbohydrates and sugar intake induced higher post-absorptive glucose levels.

PP-D-31

ASSOCIATION BETWEEN ALBUMINURIA AND SLOW GAIT SPEED IN MALES WITH TYPE 2 DIABETES

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OBJECTIVES

Chronic kidney disease is highly prevalent in older patients with type 2 diabetes (T2D). Albuminuria is a marker of vascular endothelial pathology that reflects increased inflammatory state of CKD. Such vascular pathology could contribute to skeletal muscle damage and poor physical performance. We aimed to investigate association between albuminuria and gait speed in males with T2D.

METHODOLOGY

We conducted a cross-sectional on 100 male patients (mean age 63.3±7.3 years) with T2D. Slow gait speed was defined as ≤0.8 m/s. Albuminuria was defined as urinary albumin-to-creatinine ratio (uACR) ≥ 30 mg/g. Logistic regression was performed to examine relationship between albuminuria and slow gait speed, adjusting for demographics, diabetes duration, blood pressure, haemoglobin A1c, estimated glomerular filtration rate (eGFR) and appendicular skeletal muscle mass.

This research has been approved by an ethics committee.

RESULTS

There were 51 patients with slow gait speed. The median uACR was 35 mg/g (IQR 10-174) and 50.6% of patients had albuminuria. Univariate analysis showed that albuminuria was positively associated with slow gait speed with odds ratio (OR) 2.80 (95%CI 1.20-6.57; p=0.017). The association persisted in the fully adjusted analysis with OR 4.56 (95% CI 1.24-16.77; p=0.022). Similar findings were observed using log-transformed uACR as a continuous variable with OR 1.67 (95% CI 1.19-2.36; p=0.003) in the fully adjusted analysis. There was no evidence of association between eGFR and slow gait speed.

CONCLUSION

Albuminuria was independently associated with slow gait speed in T2D. Hence, evaluation of albuminuria is a potential tool to identify older patients at risk of functional impairment.

PP-D-32

ASPALATHIN-RICH GREEN ROIBOS EXTRACT IN COMBINATION WITH GLYBURIDE AND ATORVASTATIN ENHANCES LIPID METABOLISM IN A db/db MOUSE MODEL

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OBJECTIVES

This study investigated the effects of combining an aspalathin-rich green rooibos extract (GRT) with glyburide and atorvastatin in a type 2 diabetic (db/db) mouse model.

METHODOLOGY

Db/db mice were treated orally with glyburide and atorvastatin and GRT as mono and combination therapies for 5 weeks. An intraperitoneal glucose tolerance test was conducted at 3 weeks of treatment. Serum was collected for lipid analyses and liver tissues were collected for histological examination and gene expression.

RESULTS

There was an increase in the fasting plasma glucose (FPG) of the db/db compared to the lean mice (from 7.98 ± 0.34 to 26.44 ± 1.84, p<0.0001). GRT reduced FPG levels in db/db mice when compared to untreated controls (from 26.44 ± 1.84 to 18.7 ± 4.4, p<0.001) without affecting bodyweight. Glyburide had no effect on FPG alone or in combination with GRT in db/db mice. Atorvastatin reduced cholesterol (from 4.00 ± 0.12 to 2.93 ± 0.13, p<0.05) and triglyceride levels (from 2.77 ± 0.50 to 1.48 ± 0.23, p<0.05). The hypo-triglyceridemic effect of atorvastatin was enhanced when combined with GRT and glyburide (from 2.77 ± 0.50 to 1.73 ± 0.35, p =0.0002). Glyburide reduced the severity and pattern of steatotic lipid droplet accumulation from a mediovesicular type across all lobular areas, whilst GRT

with glyburide reduced the abundance and severity of lipid droplet accumulation predominantly in the centri- and mediolobular areas. GRT, glyburide and atorvastatin reduced the abundance and severity of lipid accumulation as well as the intensity score.

CONCLUSION
GRT or glyburide in combination with atorvastatin had no effect on blood glucose or lipid profiles, but a significant reduction in lipid droplet accumulation was observed.

PP-D-33

COMPARISON OF THRICE-DAILY PREMIXED HUMAN INSULIN WITH BASAL-BOLUS THERAPY AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS

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OBJECTIVES
In Malaysia's public hospitals, 82.4% of insulin-treated type 2 diabetes mellitus (T2DM) patients were taking human insulin due to budget constraints. Twice-daily premixed human insulin (PHI) regimen was intensified to basal-bolus (BB) regimen when glycemic control was inadequate. We aimed to compare the efficacy and safety of thrice-daily (TDS) PHI with BB regimen.

METHODOLOGY
A cross-over study among T2DM patients was conducted in Penang Hospital between October 2020 and June 2021. Patients in Group A were assigned to TDS and crossed-over to BB at week-12, and vice versa for group B. Glycated haemoglobin (HbA1c), total daily dose (TDD) of insulin, weight, hypoglycaemia, and adherence to insulin injection were measured at baseline, week-12 and week-24.

RESULTS
Forty-four patients (75% female; baseline mean HbA1c 9.55%; mean duration of T2DM 16 years) were included. Mean HbA1c reduced significantly from baseline to week-12 for group A (-0.95%, p<0.001) and group B (-1.06%, p<0.001) respectively. No difference in HbA1c in group A (-0.25%, p=0.212) when switching to BB at week-12 to week-24 but HbA1c reduced significantly in group B (-0.49%, p=0.007) when switching to TDS and significant between the groups, p=0.026. In group A, no difference in TDD but weight reduced significantly at week-12 (-0.5 kg, p=0.002). TDD increased significantly in group B (p=0.042) from baseline to week-12 and between the groups (p=0.044). Meanwhile, no difference in hypoglycaemia and adherence were observed within and between the groups.

CONCLUSION
Thrice-daily PHI is an effective and safe alternative to BB regimen when intensifying insulin treatment.

PP-D-34

PREDICTORS OF WORSENING GLYCEMIC CONTROL INDICES AND VARIABILITY AMONG ADMITTED MODERATE TO CRITICAL COVID-19 PATIENTS WITH TYPE 2 DIABETES MELLITUS

https://doi.org/10.15605/jafes.037.AFES.74

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OBJECTIVES
It has been noted that COVID-19 infection increases the risk of poor blood glucose control in T2DM patients and since diabetes is associated with low-grade chronic inflammation, COVID-19 exacerbates this inflammatory condition leading to heightened insulin resistance and hyperglycemia. Invariably, mortality risk is increased with hyperglycemia and poor glycemic variability, hence, this study aims to identify the predictors associated with glycemic control and variability among patients with COVID-19 and T2DM.

METHODOLOGY
This is a retrospective cross-sectional analytical study involving 109 patients with the diagnosis of moderate to severe COVID-19 and T2DM. Records review was done from March 2020 to June 2021. Odds ratio from binary logistic regression were computed to determine predictors for worsening glycemic control indices and variability. This research has been approved by the UST Hospital Research Ethics Committee.

RESULTS
Of the 109 patients, 78% had worsening glycemic control and variability, and 22% had no worsening outcomes. Chronic kidney disease (OR 2.83, p=0.035) was associated with poor glycemic variability. In contrast, increasing eGFR level (OR 0.97, p=0.004) was associated with less likelihood of worsening variability. HsCRP (OR 1.01, p=0.011), HbA1c (OR 1.86, p=0.003), severe COVID-19 (OR 8.91, p=0.008) and critical COVID-19 (OR 4.42, p=0.003) were associated with worsening glycemic control. Steroid use (OR 71.17, p<0.001) showed the strongest association with hyperglycemia.

CONCLUSION
Potential clinical, laboratory and inflammatory profiles were identified as predictors for worsening outcomes. HbA1c, hsCRP, and COVID-19 severity are predictors of hyperglycemia. Likewise, chronic kidney disease is a predictor of poor glycemic variability.

PP-D-35

THE CORRELATION BETWEEN HYPERTENSION IN COMBINATION WITH PROTEINURIA AND HEART FAILURE EVENTS IN T2DM PATIENTS (BUITENZORG STUDY PRELIMINARY REPORT)

https://doi.org/10.15605/jafes.037.AFES.75

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OBJECTIVES
The contribution of proteinuria in combination with hypertension to heart failure events has been shown in previous study, but little information is available in developing countries, particularly in a low-resource setting. This pilot study aimed to evaluate the risk of a history of hypertension and proteinuria as a potential early recognition of heart failure in adults with type 2 diabetes mellitus.

METHODOLOGY
This study was a multicentre and observational study with cross-sectional design approach. A total of 153 T2DM were enrolled from three internal medicine clinics in Bogor, West Java, between January 2018 and March 2018. They had been controlled and treated with their routine glucose lowering drugs. Echocardiography was used to evaluate their heart function in a real-world setting. More data were collected from the integrated retrospective data reserve in electronic or written medical records of each clinic.

RESULTS
Correlative analysis between hypertension and heart failure events was analysed using Spearman test. The stratum analysis between hypertension, proteinuria and heart failure events was also conducted using Chi-Square. All the statistical analysis used the significance p value of <0.05.

CONCLUSION
There was significant correlation between hypertension in combination with proteinuria with heart failure events in type 2 diabetic patients.

PP-D-36

EVALUATION OF IN-PATIENT HYPERGLYCEMIA MANAGEMENT AMONG NON-CRITICALLY ILL PATIENTS AT THE UNIVERSITY OF SANTO TOMAS HOSPITAL (USTH): A PROSPECTIVE STUDY

https://doi.org/10.15605/jafes.037.AFES.76

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OBJECTIVES
Approximately 64% of in-patients with hyperglycemia had pre-existing diabetes. This study aimed to assess adherence to in-patient hyperglycemia management guidelines and outcomes in non-critically ill patients at the University of Santo Tomas Hospital

METHODOLOGY
A prospective analytical study of in-patients with hyperglycemia or diabetes mellitus type 2 from September-December 2021 was done. A checklist based on recent in-patient hyperglycemia recommendations was used to assess management and conformity to guidelines.

RESULTS
A total of 127 patients were included. HbA1c was measured in 57% of these patients. The incidence of in-patient hyperglycemia was 36% with highest proportion among admissions for infection. The most common (28%) regimen on admission was resumption of home medications with modified dose. Standard hospital glucose monitoring [USTH Point-of-Care (POC) testing] was applied, however, occasional delays in testing caused lack of coordination between insulin injections and meals. Eighty-eight percent of elective surgery patients received pre-admission treatment for hyperglycemia. Referral to endocrinologists was done in 76 patients. A shift to insulin therapy for persistent hyperglycemia (>180 mg/dL) was done in 15% of patients who were insulin naive. Overall, target capillary blood glucose (CBG) range of 140 to 180 mg/dL was achieved in 97% of patients. The median CBG of 145 mg/dl on admission was lowered to 132 mg/dL on discharge (p<0.00001). Compliance to discharge and follow-up instructions were poorer among non-endocrinologists (p<0.0001).

CONCLUSION
This study demonstrated prompt management upon admission according to guidelines but also showed delays in insulin initiation and endocrine referrals in response to persistent hyperglycemia, inconsistent timing of monitoring in relation to meals, and poor discharge practices among non-endocrinologists—areas which need improvement.

PP-D-37

PREDICTING AMPUTATION RISK AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS WITH DIABETIC FOOT ULCER USING PEDIS SCORES IN A TERTIARY HOSPITAL: A PROSPECTIVE STUDY

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OBJECTIVES
The study aims to determine the demographic profile (age and gender) of patients who have diabetic foot ulcer (DFU), the presence of comorbidities such as obesity, hypertension, cardiovascular disease, liver disease and renal failure, and the correlation of PEDIS scoring in predicting amputation.

METHODOLOGY
This was a prospective cohort study which included 50 patients who were admitted or seen at the outpatient department of CRMC from January to October 2021. The demographic data (age, gender and location) and comorbidities were obtained. Each patient had individual PEDIS scoring sheets. To assess for perfusion (P), an ankle brachial index (ABI) was done to determine if there was peripheral arterial disease (PAD) with or without critical limb ischemia. To describe the extent (E) of the wound, we graded them from 0 to +3 for skin intact, <1 cm2, 1–3 cm^2, and >3 cm^2, respectively. Depth (D) was evaluated by physical examination and foot x-rays. Infection (I) was assessed based on the presence of inflammation and secretions. Lastly, sensation (S) was evaluated using a 128-Hz tuning fork on the affected limb. Outcomes were documented, namely amputation, debridement and wound care.

RESULTS
There were no significance differences among subjects in terms of gender. However, age differences among patients were significant with a p value of 0.003 and was predictive of amputation among 41-60 age group with p value of 0.003. Hypertension was found to be a significant co-morbidity, with p value at 0.043. PEDIS scores among the participants were also significant with p value of <0.001 with 54% amputation rate for patients with PEDIS score >7.

CONCLUSION
Our findings indicate that patients with DFU aged 41 to 60 years, diagnosed with hypertension and PEDIS score >7 are likely to require amputation.

PP-D-38

REAL-WORLD SURVEY ON INSULIN INJECTION TECHNIQUES AMONG PEOPLE WITH DIABETES IN SEMI-URBAN AND VILLAGE POPULATION IN KERALA

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OBJECTIVE
The success of insulin therapy in diabetes depends on proper storage and correct injection technique. The objective of this study is to assess the current insulin injection technique among patients with diabetes mellitus in semi-urban and village population in Kerala.

METHODOLOGY
This observational study was conducted from June to December 2021 in Tirur and Pathanamthitta, Kerala. A total of 140 participants aged 25 to 60 years, using insulin pen or vial for at least 3 months were recruited. A survey questionnaire on key insulin injection practices was administered.

RESULTS
The abdomen was the most common (57.14%) site of insulin injection. Injection site rotation was followed by 92.85%. The practice of handwashing and cleaning of the injection site was practiced by 110 (78.57%) & 105 (75%), respectively. A total of 135 (96.42%) subjects were using the needle more than once. Majority (85.71%) were storing insulins at proper temperature. Pain and swelling at the injection site were reported by 52.14 % and 7.14%, respectively. The majority of patients (96.42%) threw the needle and syringes directly into the garbage and public drainage system.

CONCLUSION
Our study identified a significant gap between insulin administration guidelines and current insulin injection practice. Hence, diabetes education and counselling about proper insulin injection techniques should be provided to people with diabetes and their caregivers.

PP-D-39

ASSOCIATION BETWEEN BODY COMPOSITION AND BODY INDEX MASS AMONG GERIATRIC PATIENTS WITH TYPE 2 DIABETES MELLITUS IN SUMBAWA BESAR DISTRICT

https://doi.org/10.15605/jafes.037.AFES.79

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OBJECTIVES
Body distribution has been a new paradigm and more accurately to assess than body mass index. The body composted four molecular components: water, fat, proteins, and mineral. Body composition consists of cell or mass, extracellular water, skeleton, and connective tissue. This may highlight calculated fat and body composition more reliable for capturing real composition, especially for geriatrics with T2DM. This study compares body composition and BMI status among geriatric patients with diabetes in Sumbawa Besar district.

METHODOLOGY
This is an analytical study with an observational design conducted in Sumbawa Besar district. The data was taken using the consecutive sampling method; 41 samples of elderly T2DM were collected from primary data according to inclusion and exclusion criteria—the analysis using univariate and bivariate analysis.

RESULTS
The median age in this study was 67.6 (60-18) years old; BMI 23.16 (14.4-33.9) kg/m^2; visceral fat 9.43 (0.5-29) %; body waist 89.3 (80-110) cm. The mean several parameters between higher and normal BMI group was compared using an independent t-test. The mean of visceral body fat in the higher BMI group is significantly higher than the control group (p=0.000). Body waist circumference and fat percentage is not different between groups (p>0.05).

CONCLUSION
There is a relationship between high levels of visceral fat and BMI in the elderly with T2DM. However, there are disparities between several body composition and BMI status among geriatric patients with diabetic conditions.

PP-D-40

TYPE 2 DIABETES MELLITUS PATIENTS' COMPREHENSION OF HYPOGLYCEMIA: A LONG AND WINDING ROAD TO OPTIMAL CARE OF DIABETES

https://doi.org/10.15605/jafes.037.AFES.80

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OBJECTIVES
Recent study at our tertiary referral hospital showed that the rate of severe hypoglycemia among type 2 diabetes mellitus (T2DM) outpatients was 34%. Our study aims to examine patients' comprehension of hypoglycemia and its associated factors.

METHODOLOGY
This cross-sectional study used data from a study reporting rates of severe hypoglycemia conducted in our hospital. Patients' comprehension of hypoglycemia was defined as patients' ability to define cut-off value of hypoglycemia and mention at least 3 neuroglycopenic symptoms.

RESULTS
Out of 291 patients, 62.9% were women and the mean age was 59.9 (± 9.36) years. The median HbA1c was 7.5% (range: 5.1-14.3) and the median diabetes duration was 12 (range: 1-43) years. There were only 63 (21.7%) patients who had comprehension of signs and symptoms of hypoglycemia. Factors associated were poor comprehension of hypoglycemia were the following: 1. Age >60 years (OR 0.45; p=0.006; 95% CI 0.25, 0.80), 2. HbA1c ≤ 7.5% (OR 0.53; p=0.026; 95% CI 0.30, 0.93), 3. Education level ≤9 years (OR 0.39; p=0.013; 95% CI 0.18,0.84) and (4) Use of sulfonylurea only (OR 0.49; p=0.025; 95% CI 0.27,0.92).

CONCLUSION
The proportion of patients with comprehension of hypoglycemia was low. Older age, lower education level, poorer glycemic control, and use of sulfonylurea are associated factors of patients' comprehension of hypoglycemia. Our findings suggest the lack of effective diabetes education and further studies are needed to evaluate the need for a better diabetes education structure for our T2DM patients.

PP-D-41

EUGLYCEMIC DIABETIC KETOACIDOSIS AMONG FILIPINO PATIENTS WITH TYPE 2 DIABETES MELLITUS ASSOCIATED WITH SGLT2-INHIBITORS: CASE SERIES

https://doi.org/10.15605/jafes.037.AFES.81

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OBJECTIVES
Euglycemic diabetic ketoacidosis (EuDKA) is an uncommon but serious adverse effect of SGLT2-i. The use of SGLT2-i is likely to increase because of its beneficial effects on cardiovascular and kidney outcomes which may lead to an increase in the incidence of EuDKA. The study contributes to the body of knowledge on the present data regarding EuDKA.

CASE
This case series included adult patients diagnosed with EuDKA secondary to SGLT2-i in a tertiary training hospital from November 2021 to April 2022. Four patients were iincluded in the study.

The most common presenting symptoms include abdominal pain, nausea, vomiting and diarrhea. All patients had confirmed type 2 diabetes mellitus. All patients were prescribed with more than 2 oral hypoglycemic medications. Two (50%) patients had heart disease and hypertension. The median age was 67 years, and 2 (50%) were males. The median hemoglobin A1c (HbA1c) on presentation was 8.7% (range: 5.3% - 10.9%. The median BMI was 25 kg/m^2. All patients were admitted in the ICU. The median length of ICU stay and hospital was 5 days and 18 days, respectively. The median time to resolution of metabolic acidosis was 30 hours.

CONCLUSION
The diagnosis of EuDKA is elusive due to presenting generalized symptoms and the lack of awareness among patients. Normoglycemia in the setting of metabolic acidosis poses a challenge for diagnosis. Among patients with surgical procedures and history of intake of SGLT2-i, it is important to obtain serum or urine ketones during the post-operative period.

PP-D-42

A COMPREHENSIVE STUDY FOR THE IDENTIFICATION OF DIABETES MELLITUS TYPE 1 IN INDONESIA (ACROSS 21 STUDY PRELIMINARY REPORT)

https://doi.org/10.15605/jafes.037.AFES.82

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OBJECTIVES
Testing for islet cell autoantibody markers such as anti-GAD65, anti-IA2, anti-ZnT8, or IAA, for diagnosing diabetes mellitus type 1 (T1 DM) from other types of diabetes is underutilized in Indonesia. Comprehensive study of identifying T1 DM, involving the measurements of fasting sugar, HbA1c, glycated albumin, C-peptide, and 3 islet cell autoantibody markers: anti-GAD65, anti-IA2, and anti-ZnT8.

METHODOLOGY
Of 43 samples examined, 18 were classified as normal while 25 fulfilled the standard criteria for diabetes mellitus.

RESULTS
One out of 18 normal sugar samples and 9 out of 25 diabetic samples were found to have low C-peptide level. Evaluation using a combination of the 3 islet cell autoantibodies used in this study revealed 5 out of the 16 diabetic samples having measurable level of 1 or 2 autoantibodies. Two out of the 17 normal sugar samples with normal C-peptide level demonstrated measurable level of at least 1 autoantibody marker. Out of the 10 samples with low C-peptide level, only 5 samples demonstrated measurable level of 1 or 2 autoantibodies.

CONCLUSION
Islet cell autoantibodies could be present in normal sugar samples with normal C-peptide level. A low C-peptide does not automatically translate to the presence of islet cell autoantibodies. Measurement of islet cell autoantibody markers for a precise diagnosis of T1 DM in Indonesia is important.

PP-D-43

EUGLYCEMIC DIABETIC KETOACIDOSIS WITH REFRACTORY METABOLIC ACIDOSIS IN A PATIENT WITH T2 DM ON EMPAGLIFLOZIN AND INTERMITTENT FASTING

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BACKGROUND
Euglycemic Diabetic Ketoacidosis (EuDKA) is a clinical triad of normal blood glucose levels, ketonemia, and high anion gap metabolic acidosis. It is less commonly associated with the use of Sodium-Glucose Co-Transporter 2 inhibitors (SGLT2i) such as empagliflozin. Due to the introduction of SGLT2i in the treatment of T2DM and HF, there is an increasing incidence of EuDKA.

CASE
We report a case of a 28-year-old female recently diagnosed with diabetes mellitus type 2 (T2 DM) maintained on semaglutide 0.25 mcg subcutaneously once a week and empagliflozin 10 mg once daily presenting with a three-week history of easy fatigability, generalized body weakness, nausea, vomiting and loss of appetite. At the ER, the patient experienced abdominal pain, nausea, and vomiting. The patient was managed as a case of severe refractory metabolic acidosis secondary to EuDKA. The patient was intubated for 5 days. The management consisted of insulin drip, hydration, renal replacement therapy (RRT), and bicarbonate drip. Resolution of acidosis with a pH of 7.42 and anion gap of 10.1 was achieved on the 8th day of admission.

CONCLUSION
This case reports a rare complication of SGLT2i in a patient with T2DM with retractable severe metabolic acidosis that can be effectively managed with RRT and cessation of SGLT2i. It also highlights the importance of giving D5-containing IV fluid for continued insulin administration which is important to reverse ketoacidosis while preventing hypoglycemia. Monitoring of serum ketones and serum electrolytes levels are crucial in the management of a patient with intractable acidosis needing mechanical ventilation and renal replacement therapy.

PP-D-44

DOES TIME TO DEVELOP POST-TRANSPLANTATION DIABETES PREDICT TIME TO GRAFT LOSS? AN ANALYSIS OF PATIENTS 20 YEARS POST-KIDNEY TRANSPLANT

https://doi.org/10.15605/jafes.037.AFES.84

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INTRODUCTION
Post-transplantation diabetes (PTDM) is common after solid organ transplantation. There are data to suggest that this complication may influence the transplant outcomes, namely the risk of graft loss.

To analyze whether there is a relationship between age at diagnosis and time to graft loss.

METHODOLOGY
Retrospective study with patients transplanted between 1989-2001 who developed PTDM.

RESULTS
We included 41 patients who had transplantation 24.7 (± 2.4) years ago. Majority (68.3%) were males with a mean age at transplantation of 46.5 (± 11.3) years. The average (years) of diagnosis of DMPT was 4.3 (± 5.3). C-peptide was detectable in all patients. Diabetes autoimmunity was negative in 96.4% of patients, with 1 patient having low anti-GAD65 titers. All patients were treated with therapeutic lifestyle measures, 78.0% were started on insulin therapy (on average 6.5±7.3 years post-transplantation) and 14.6% were started on oral antidiabetics (22.7±6.1 years post-transplantation). The median HbA1c in the 1st 5 years of DMPT was 6.9 ± 1.5%, while the median Hba1c in the 2nd, 3rd, and 4th year was 6.9 ± 1.1% (n = 28), 7,2 ± 1.2% (n = 21) and 6.9 ± 1.1% (n = 12), respectively. To date, 73.2% had graft loss (mean 11.3 ± 6.1 years post-transplant) and 55.3% died (12.2 ± 6.2 years post-transplant). There was a weak but significant correlation between latency to develop DMPT and time to graft loss (r = 0.419, p=0.021).

CONCLUSION
Our study suggests a positive correlation between time to develop PTDM and graft loss. However, it is not possible to establish causality, as earlier appearance of DMPT may be influenced by the doses of immunosuppressants in patients at a greater risk of graft loss.

POSTER PRESENTATIONS

GROWTH HORMONE / GROWTH

PP-GH-01

THE ROLE OF GROWTH HORMONE IN MAINTAINING PANCREATIC ISLET MORPHOLOGY

https://doi.org/10.15605/jafes.037.AFES.85

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OBJECTIVES
Endoplasmic reticulum stress (ER stress) is one of the causes of decreased insulin secretion with aging. Since growth hormone (GH) secretion decreases with age, we hypothesized that decreased GH was related to ER stress. We investigated islet structure in GH-deficient spontaneous dwarf rat (SDR), and GH effects in BRIN-BD11 cells derived from rat pancreatic β-cells.

METHODOLOGY
Overnight fasted 6- and 12-month-old male SDR and normal Sprague Dawley rats were used for collection of blood and pancreas samples. The mRNA expression of X-Box binding protein-1 (xbp-1), which is implicated in ER stress, was measured in BRIN-BD11 cells with or without GH treatment.

RESULTS
Serum concentration of glucose and proinsulin were higher in 12-month-old SDR than in age-matched normal rats. Islet structures of normal rats were oval, but the structures of 40% of islets were disrupted in 12 month-old SDR. The mRNA level of XBP-1 spliced form in the pancreas was increased with aging in normal rats, but not in SDR. Most XBP-1 antibody positive cells were in islets, and the positive cell number in islets was lower in 12 month-old SDR than in age matched normal rats. GH treatment increased mRNA levels of XBP-1s in BRIN-BD11 cells.

CONCLUSION
XBP-1 is known as the key factor in the unfolded protein response (UPR) following ER stress, and the UPR has been implicated in insulin secretion and β-cell survival. Our data suggested that GH might have a role in maintaining islet structure by increasing XBP-1 expression in β-cells.

PP-GH-02

ESTABLISHMENT OF GROWTH VELOCITY CHARTS FOR ASIAN INDIAN CHILDREN

https://doi.org/10.15605/jafes.037.AFES.86

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OBJECTIVES
Height velocity is a crucial anthropometric parameter for the evaluation of mild or recent onset short stature. The WHO recommends updating the growth references every decade. There is no data on height velocity among South Indian children. We therefore undertook this study to establish the normative data.

METHODOLOGY
This prospective longitudinal study included 3,327 apparently healthy children aged 3 to 18 years from government and private schools of Krishna district, Andhra Pradesh. Height and weight were measured at baseline and at three monthly intervals for one year (October 2018 to October 2019).

RESULTS
Age- and sex-specific height velocity percentiles were generated. The data was available in 1,627 boys and 1,700 girls. The mean peak height velocity was 7.18 ± 2.56 cm in boys observed at 12-12.9 years and 5.8 ± 2.56 cm in girls at 10-10.9 years.

CONCLUSION
Normative height velocity data for South Indian children has been presented. This is the first large scale study from South India evaluating height velocity data for children aged 3 to 18 years. The database for the study was derived from a heterogeneous population, by including children from rural and urban areas, thereby representative of data from diverse socioeconomic backgrounds. These charts can, therefore, be applied to the economically deprived and privileged alike, because a significant proportion of children catered to by paediatricians/endocrinologists in public hospitals belong to the former group.

PP-GH-03

ACHIEVING EQUILIBRIUM — GROWTH HORMONE (GH) DYSFUNCTION, THERAPY AND OBJECTIVE MEASUREMENT OF OUTCOME

https://doi.org/10.15605/jafes.037.AFES.87

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INTRODUCTION
Growth hormone (GH) derangement can impair physiological function and patient's quality of life (QoL). Until recently adult GH deficient (AGHD) patients have been undertreated in Australia due to prescribing cost limitations. Due to the relative rarity, adult acromegalic (AA) patient data has not been well documented across these domains.

This study aims to contribute to the clinical understanding of GH deficient and excess states once GH levels are normalised with therapy.

METHODOLOGY
This is a single-centre, mixed methods study and chart review (2012 to April 2022) of 28 AGHD and 15 AA patients enrolled from Macquarie University Pituitary Clinic. Diagnosis, work-up and management of the cause of AGHD or AA was as per the Society guidelines.

Clinical and psychosocial measures were taken at baseline and at each follow-up consultation. The primary outcome measure was insulin-like growth factor-1 (IGF-1). Secondary outcome measures included fasting blood glucose (FBG), glycated haemoglobin, lipid profiling, weight, body composition by SOZO bioimpedance (Impedimed) and QoL.

RESULTS
AGHD patients achieved normalisation of IGF-1 on therapy to the mid-upper range of normal. In AA patients, 85% achieved normalisation of IGF-1 on therapy. AGHD demonstrate improved metabolic profiles (lipid and glycaemic control), body composition, bone mineral density (BMD) and QoL with normalisation of GH levels, in keeping with the evidence base for pharmacotherapy. At the other end of the spectrum, AA patients, coming from excess status to normalisation of GH levels, had improved metabolic parameters, body composition and QoL. Untreated patients did not have any improvement across different parameters.

CONCLUSION
GH dysfunction has significant impact on patient well-being across multiple domains. Therapy reverses the deleterious clinical and psychosocial effects of GH dysfunction and successfully restores physiological equilibrium of the GH axis. Large long-term cohort follow up is needed to add to the literature.

POSTER PRESENTATIONS

HEALTH SYSTEMS / CARE

PP-HS-01

EDMONTON OBESITY STAGING SYSTEM IMPLEMENTATION AND EFFECTIVENESS IN AN AUSTRALIAN MULTIDISCIPLINARY WEIGHT MANAGEMENT CLINIC OVER A TWO-YEAR PERIOD

https://doi.org/10.15605/jafes.037.AFES.88

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INTRODUCTION

Multidisciplinary weight management clinics (MWMC) are being established globally to manage the ever-growing obesity epidemic. However, among Australian MWMC, there is a relative paucity of published clinical outcomes, particularly on assessing holistic patient outcomes. The Edmonton Obesity Staging System (EOSS) provides a framework based on metabolic, anthropometric and psychological factors for holistic obesity management, based on a 5-class scale [0-4 (highest-risk class)]. The EOSS has greater health and mortality predictability than traditional BMI or metabolic syndrome measures.

To evaluate the implementation and changes in patient outcomes based on an EOSS model in an Australian university hospital-based MWMC.

METHODOLOGY

A retrospective review of a cohort of patients (n=76) from the Healthy Weight Clinic, Sydney, over at least 2-year period of regular (<6 monthly) consults. All patients received intervention from at least an endocrinologist, dietitian and exercise physiologist.

RESULTS

Mean baseline EOSS class was 1.56 (SD 0.84) and after 24 months mean EOSS class statistically improved to 1.05 (SD 0.88) ($P<0.05$). Baseline mean BMI was 38.0 kg/m² (SD 7.1) and mean BMI at last follow-up was 33.4 kg/m² (SD 6.4), also statistically significant ($P<0.05$). All features of the EOSS scale, namely, anthropometric data, deranged liver function tests, dyslipidaemia and prediabetes state showed clinically significant reductions towards normal levels. Almost three quarters of our patients (72%) dropped reduced at least one EOSS class.

CONCLUSION

Care from MWMC can produce significant reductions in EOSS classes, leading to improved patient outcomes across multiple comorbidities over 2 years. Future studies should compare this framework across Australian MWMC, to establish a standardised approach to biopsychosocial obesity management.

PP-HS-02

BETTER METABOLIC OUTCOMES DELIVERED THROUGH A LIFESTYLE CARE PROGRAM IN PWD — EVIDENCE OF RETROSPECTIVE PILOT STUDY FROM URBAN INDIA

https://doi.org/10.15605/jafes.037.AFES.89

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OBJECTIVES

To assess the effect of a novel, personalized virtual diabetes care program, OneCare "IMPACT" program, on metabolic outcomes in PWD, among an urban south Indian cohort.

METHODOLOGY

A single-arm, retrospective, proof-of-concept study in PWD who enrolled in a 12-week virtual care program tailored to support diabetes self-management through personalized lifestyle education. The health coach remotely monitored patients through weekly scheduled calls to track progress. The patient's data, recorded by the coach, including HbA1c, weight, medications, and program engagement were used for the analysis.

RESULTS
A total of 41 patients with complete data were included for analysis. The mean age of the participants was 44.2 (± 12) years, 76% were male, median diabetes duration (years) of 1.3 (0.1–20), baseline HbA1c (%) of 9.5 (± 2.3), weight (kgs) of 74.6 (± 13.5). Decline in HbA1c (%) was 0.3 (SD 0.4, p <.001) with moderate effect size (d=0.53). HbA1c <7% was achieved in 54% while the clinician-decided target HbA1c was met in 61%. Mean weight (kgs) change was 2.5 (SD 2.7, p <.001) with large effect size (d=0.92). A significant short-term reduction in weight of ≥5% was achieved in 32% of patients. Majority (87%) had reduction in or continued same dose of diabetic medication at 12 weeks. The mean attendance was 83.6% and engagement fairly correlated with weight reduction, (-0.24, p=0.1) but not with decreasing HbA1c.

CONCLUSION
Clinically meaningful metabolic outcomes were achieved through the program with a high level of patient engagement in an urban Indian cohort. The study encourages well-designed RCT to confirm the effectiveness of the program.

PP-HS-03

COVID-19 LOCKDOWNS AND TELEHEALTH CONSULTATION IN WEIGHT MANAGEMENT OF PATIENTS ATTENDING THE HEALTHY WEIGHT CLINIC AT MACQUARIE UNIVERSITY HOSPITAL

https://doi.org/10.15605/jafes.037.AFES.90

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OBJECTIVES
Emerging literature suggests that the general Australian adult population experienced weight gain during the COVID-19 period. The primary aim of this study was to quantify changes to weight and body composition in an Australian Healthy Weight Clinic (HWC) over the COVID-19 period. Our secondary aim was to explore how lifestyle factors during periods of lockdown influenced anthropometric outcomes.

METHODOLOGY
The study period spanned December 2019 – December 2021. This period included two government-mandated lockdowns in March-June 2020 and June-September 2021. A retrospective chart review was conducted to extract weight and BMI outcomes from electronic patient records, while fat mass and skeletal muscle mass outcomes were extracted using SOZO bioimpedance spectroscopy. All outcomes were measured at three-month intervals. A patient survey based on current literature exploring lifestyle factors including eating and exercise, sources of stress and use of telehealth consultations was emailed to all currently enrolled clinic patients.

RESULTS
A total of 51 respondents were included in the quantitative arm and 229 survey responses were recorded. Weight decrease was linear and significant (p=<0.001) throughout the study period for the overall group. Average weight loss across the group was 15.7 kg (SD = 4.1 kg). No gender difference was observed. Fat mass % decrease followed a quadratic pattern (p=0.05). Among the most significant lifestyle factors were snacking, reduction in commute time and at-home childcare. Majority (65%) of participants who answered the questionnaire in full reported that telehealth consultations were useful in keeping them on track with prescribed diet and exercise regimes.

CONCLUSION
Despite disruptions to lifestyle and in-pehaven consultation, it appears that the implementation of telehealth appointments across our clinical services has been effective in assisting weight management at the clinical level. The efficacy of these services beyond the context of stay-at-home orders is promising and warrants further investigation.

PP-HS-04

REAL WORLD STUDY ON ORAL ESTRADIOL TREATMENT IN TRANSGENDER WOMEN

https://doi.org/10.15605/jafes.037.AFES.91

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OBJECTIVES
Treatment of transgender females (TGF) targets maintenance of physiological cisgender female hormone levels. This study evaluates dose effectiveness of oral estradiol valerate (EV) with (A) anti-androgens (spironolactone, finasteride), (B) post-orchiectomy or (C) GnRH-a/gonadotropin-releasing hormone agonists.

METHODOLOGY
We retrospectively evaluated Indian TGF on EV with (A), (B) or (C) with at least one year of follow-up. EV dose, changes in 17-β estradiol (E2) and testosterone (T) levels and achievement of target (E2>100 pg/ml; T<100 ng/dl) were assessed.

RESULTS
Overall cohort had 103 TGF: 41 were in group A, 22 were in group B, and 40 were in group C. In group A, 15% received spironolactone, 14 % received finasteride and 65% received both. Initial and final mean EV dose in overall cohort was 1.9 ± 0.58 mg and 3.22 ± 1.34 mg respectively, with significant increase in E2 (38.1 ± 21.1 to 92.7 ± 28.0 pg/ml) and decrease in T (587.2 ± 168.0 to 139.9 ± 164.1 ng/dl) from baseline. 32% of the overall cohort achieved target E2 levels and 56% achieved target T levels.

Groups B and C required significantly lower (P<0.0001) final EV dose of 2.73 ± 0.88 mg and 2.6 ± 0.78 mg respectively, compared to 4.1 ± 1.5 mg in group A. Relatively, groups B and C had significantly higher final E2 (P=0.0016), lower final T (P<0.0001) and a significantly greater proportion of subjects achieving target hormone levels: E2 (22%(B), 45%(C) versus 10% (A) and T [(93%(B) 100%(C) versus 2%(A)].

CONCLUSIONS
GnRH-a or orchiectomy, requiring significantly lower doses of EV, was more effective than anti-androgens in attaining target hormone levels in TGF. Spironolactone and finasteride did not help in testosterone suppression.

POSTER PRESENTATION

MECHANISMS

PP-M-01

PRIMARY MITOCHONDRIAL DISEASES AND ENDOCRINOPATHIES

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OBJECTIVES

Mitochondria are organelles in the cell involved in energy production by generating adenosine triphosphate (ATP). Primary mitochondrial diseases lead to the impairment of the mitochondrial respiratory chain and results in defective energy production. This review presents the endocrine disorders associated with primary mitochondrial diseases and describes the major genotypes and phenotypes in which they occur.

METHODOLOGY

A systematic search of literature was conducted using the search terms mitochondria, primary mitochondrial diseases, mutations, endocrine disorders, genotype and phenotype.

RESULTS

Primary mitochondrial diseases are due to defects in the mitochondrial or nuclear DNA. The defects can be inherited or sporadic (somatic mutations). The prevalence of primary mitochondrial diseases is at least 1 in 5,000. The most common mitochondrial DNA defect is the m.3243A > G mutation which is associated with several clinical syndromes including mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) and maternally inherited diabetes and deafness (MIDD). Diabetes mellitus (both type 1 and type 2) is the most common endocrine manifestation of mitochondrial DNA mutations mainly because of its association with the MELAS and MIDD phenotypes and the m.3243A > G mutation. Additional mitochondrial DNA mutations associated with diabetes mellitus include the m.14709T > C, m.8296A > G, and m.14577T > C mutations. Other endocrine disorders, although rarer, have also been reported in association with primary mitochondrial diseases. They include growth hormone deficiency (e.g., in MELAS with m.3243A > G mutation), hypothyroidism, hyperthyroidism, hypoparathyroidism, adrenal deficiency, and hypogonadism in both sexes.

CONCLUSION

Primary mitochondrial diseases, mainly due to mitochondrial DNA mutations, are important contributors to various endocrine disorders. The decrease in ATP production and/or increase in oxidative stress causes a failure in the synthesis and/or secretion of hormones, leading to multiple hormonal deficiencies. Through autoimmunity, several endocrinopathies can also occur. The most common endocrine dysfunction observed in primary mitochondrial diseases is diabetes mellitus.

POSTER PRESENTATION

ONCOLOGY

PP-O-01

HYPOTHYROIDISM AND HYPOPARATHYROIDISM SECONDARY TO METASTASIS OF BREAST CARCINOMA TO THE NECK

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BACKGROUND
Metastases to thyroid and parathyroid glands are uncommon. While both thyrotoxicosis and hypothyroidism have been reported in literature, hypoparathyroidism due to metastatic infiltration is very rare.

CASE
We report a female who developed hypothyroidism and hypoparathyroidism secondary to metastatic breast carcinoma.

A 57-year-old female was diagnosed with left breast infiltrative ductal carcinoma Stage 3 (T2N3aM0). She underwent left mastectomy and axillary clearance, followed by adjuvant chemotherapy and regional radiotherapy. She was treated with letrozole but defaulted. Two years later, she presented with progressive swelling over her anterior chest wall and neck, causing airway obstruction and requiring emergency tracheostomy. Biopsy of the neck mass reported metastatic high grade invasive breast carcinoma. Systemic chemotherapy (gemcitabine and cisplatin) was commenced. She complained of numbness over the extremities and was noted to have severe hypocalcemia with prolonged QTc (488ms) on ECG. Corrected calcium was 1.57 mmol/L (N 2.2-2.6), phosphate 0.81 mmol/L (N 0.81-1.45), magnesium 0.64 mmol/L (N 0.66-1.07), ALP 100 U/L (N 40-129), 25-OH Vitamin D 51.73 nmol/L and intact parathyroid hormone (iPTH) level was inappropriately normal at 2.5 pmol/L (N 1.6-6.0). Thyroid function showed hypothyroidism [fT4 <0.5 pmol/L (N 12.3-20.2), TSH 64.6 mIU/L (N 0.3-3.94)]. Anti-thyroid peroxidase was negative. She received intravenous calcium initially and was later commenced on oral levothyroxine, calcium carbonate and calcitriol, with normal calcium level and thyroid function on outpatient follow-up.

CONCLUSION
This case highlights the rare endocrine complications of hypothyroidism and hypoparathyroidism secondary to metastatic malignancy. Prompt recognition is important for timely treatment initiation to prevent life-threatening complications.

POSTER PRESENTATIONS

OBESITY / LIPIDS

PP-OL-01

HETEROZYGOTE FAMILIAL HYPERCHOLESTEROLEMIA – A NEW CHALLENGE FOR ENDOCRINOLOGISTS (PART 2)

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OBJECTIVE
Heterozygote familial hypercholesterolemia (HeFH) is a common genetic condition that causes high levels of low–density lipoprotein–cholesterol (LDL–C). This study aimed to determine the incidence of HeFH in a single-centre endocrinologist's clinical practice in Riga East Clinical University Hospital (RECUH) Outpatient Clinic.

METHODOLOGY
We collected data from medical records with HeFH (E78.01) from 2019 to 2021. Based on LDL–C, Apo–B, Apolipoprotein index (Apo Index), Lipoprotein(a)–Lp(a), Homocysteine, and DLCN score points, points were divided into 2 groups: the 1st group–definitive FH; the 2nd group–probable FH.

RESULTS
From a total of 3720 patients, 136 (3.7%) patients were included, 93 (68.4%) were females. The mean age was 49.96 ± 12.09 years old. 62 patients (45.6%) were included in the first group, 74 patients (54.4%) were in the second group. Only 20 patients (14.7%) received lipid-lowering therapy initially. The pretreatment laboratory findings in the 1st group were: LDL–C 4.48 ± 1.26 mmol/L; Apo–B 116.03 ± 26.14 mg/dL; Apo Index 0.77 ± 0.21; Lp(a) 78.66 ± 61.36 mg/dL. The laboratory findings in 2nd group were: LDL–C 4.09 ± 0.91 mmol/L; Apo–B 97.96 ±16.47 mg/dL; Apo Index 0.64 ± 0.11; Lp(a) 17.61 ± 23.36. In the 1st group, 40 (64.5%) patients received statins, 11 (17.7%) patients received statins and ezetimibe. In the 2nd group, 45 (60.8%) patients received statins, 10 (13.5%) patients received fibrates. In both groups, LDL–C, Apo–B, Apo Index, and homocysteine decreased at the end of the study ($p<0.001$). Lp(a) in both groups did not decrease ($p=0.552$;$p=0.889$). DLCN in the 1st group was 2.25 ± 2.0 points and 1.29 ± 1.4 points in the 2nd group.

CONCLUSION
HeFH is far more frequent than previously considered and its diagnosis and therapy must be improved.

PP-OL-02

CORRELATING THE CAROTID INTIMA-MEDIA THICKNESS WITH CARDIO-METABOLIC RISK FACTORS IS USEFUL IN ASSESSING SUBCLINICAL ATHEROSCLEROSIS PROGRESSION IN OBESE CHILDREN

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OBJECTIVE
Multiple risk factors can act as precipitant causes for atherosclerosis and analyzing them can offer a better understanding of the cardio-metabolic status of obese children and provide a better prediction of overall cardio-metabolic risk in adulthood. Our aim is to evaluate how the carotid intima-media thickness (CIMT) correlates to identifiable risk factors.

METHODOLOGY
We analyzed 85 patients aged 6–18 years old by measuring their CIMT using the Aixplorer MACH 30 echography machine - automatic measurement software. Three study groups were defined: obese, overweight and normal weight. The clinical examination included: BMI, waist circumference, puberty development, blood pressure measurements. Risk factors analyzed were: artificial postnatal nutrition, birth weight <2500 g or >3500 g, pregnancy-associated risk factors (>20 kg weight gain, gestational diabetes, gestational hypertension, autoimmune thyroiditis, smoking during pregnancy), family history (obesity, dyslipidemia, type 2 diabetes, coronary disease, stroke, autoimmune thyroiditis), smoking, sedentary lifestyle and abnormal sleeping habits.

RESULTS
CIMT values were significantly higher in adolescents. No difference was observed between sexes. CIMT values correlated positively with Tanner stages. More than 20 kg weight gain during pregnancy and other at-risk disorders during pregnancy (p=0.025), family history of cardiovascular risk (p=0.047), hypertension (p=0.01), and smoking (p=0.018) were linked to increased CIMT. Artificial postnatal nutrition, high/low birth weight and sedentary lifestyle were also linked to increased CIMT.

CONCLUSION
Childhood obesity predicts higher values of CIMT in young adulthood. Weight gain of >20 kg during pregnancy, family history of cardiovascular risk, high blood pressure and smoking are easily identifiable risk factors that are linked to increased CIMT. A medical history focused on risk factors is indispensable for assessing the cardio-metabolic risk status of patients.

PP-OL-03

CAROTID INTIMA MEDIA THICKNESS—A VALUABLE TOOL IN ASSESSING SUBCLINICAL ATHEROSCLEROSIS PROGRESSION IN OBESE CHILDREN

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OBJECTIVE
After the COVID-19 pandemic, the prevalence of obesity among children is higher than ever. The carotid intima-media thickness (CIMT), a predictor of atherosclerotic progression, correlates with most of the clinical and paraclinical parameters used for the assessment of obese patients. Our objective is to show that CIMT can be used in the assessment of subclinical atherosclerosis in obese children.

METHODOLOGY
We analyzed 85 patients aged 6–18 years old by measuring their CIMT using the Aixplorer MACH 30 echography machine - automatic measurement software. Three study groups were defined: obese, overweight and normal weight. The analysis focused on correlations between correlates and BMI, waist circumference, Tanner puberty stages and blood pressure as clinical tools, and to the usual blood parameters: lipid panel, triglycerides and fasting glucose.

RESULTS
Obesity and abdominal adiposity in children is linked to increased CIMT. Waist circumference and TG/HDL-C ratio are significant predictors of CIMT. Higher values for CIMT were detected in children with Tanner 4 and 5 development stages (p<0.041). Children with blood pressure values over the 95th percentile presented higher values for CIMT, regardless of their BMI. HDL-C, LDL-C, total cholesterol and triglycerides were correlated with CIMT; fasting glucose was not.

CONCLUSION
Expected values of the CIMT are influenced by the severity of the obesity. Abdominal adiposity of obese children is reliably correlated with CIMT values. High blood pressure is correlated to higher CIMT values, regardless of the patients' BMI. All evaluated blood parameters, except for fasting glucose, showed correlations with CIMT.

PP-OL-04

OVER-THE-COUNTER MULTIVITAMIN TRANSCUTANEOUS PATCH DOES NOT CORRECT NUTRITIONAL DEFICIENCIES IN PATIENTS UNDERGOING BARIATRIC SURGERY: A CASE REPORT

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BACKGROUND
Nutritional deficiencies of water-soluble vitamins are commonly seen following bariatric surgery and proper replacement is critical. The availability of over-the-counter (OTC) vitamin supplements has created challenges in appropriate vitamin replacement, given the potential for lower efficacy than typical prescription-strength formulations. We report a patient who developed lower extremity neuropathy following Roux-en-Y gastric bypass surgery (RYGB) despite using OTC skin patch multivitamins.

CASE

A 62-year-old female underwent RYGB for obesity and had an uneventful immediate postoperative course. She returned for follow-up 6 months later complaining of severe, recurrent vomiting along with lower extremity weakness, paresthesia, dizziness and ataxia. She reported sharp pain and numbness over bilateral anterior thighs. Medication review revealed an OTC multivitamin patch that she was taking to correct any vitamin deficiencies. Her BP was 101/62 mm Hg, HR was 60 bpm, BMI was 26.41, examination of heart, lungs and abdomen were normal. Neurological examination showed decreased sensation to touch on both feet, legs and 4/5 muscle strength on bilateral lower extremities. Laboratory examinations showed normal CBC, normal liver function, serum zinc 55 mcg/dL (ref 56-134), copper 115 mcg/dL (ref 72-166), vitamin B1 38.1 nmol/L (ref 66.5 – 200), vitamin B12 323 pg/mL (232-1245 pg/mL), 25-hydroxyvitamin-D 29 ng/mL (30-100 ng/mL). Cervical and thoracic MRI imaging were normal. After stopping the vitamin patch, she was treated with intravenous thiamine followed by 100 mg oral thiamine TID along with 1000 mcg oral cyanocobalamin once daily. She experienced complete recovery of her symptoms in 6 weeks.

CONCLUSION

Our patient relied on an OTC multivitamin patch which proved to be ineffective since it only contained 1 mg and the usual recommended dose is 50-100 mg orally daily. Symptoms will usually resolve with proper treatment. It is essential to pay attention to the nutritional status of post-bariatric surgery patients.

PP-OL-05

A HIGH-FAT, HIGH-SUGAR DIET INDUCES INSULIN-LIKE GROWTH FACTOR 2 HYPER-METHYLATION IN MALE WISTAR RATS

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OBJECTIVE

The prevalence of obesity and insulin resistance (IR) has increased at an exponential rate worldwide. Although several mechanisms such as dysregulation of the epigenome have been implicated, the disease pathophysiology remains to be fully elucidated. The primary objective of this study was to elucidate DNA methylation profiles and gene regulatory networks that are altered in the skeletal muscle (SM) during the development of obesity and IR in male Wistar rats.

METHODOLOGY

Male Wistar rats (n=20) were fed either a high-fat, high-sugar (HFHS) or a standard diet (STD) for 12 weeks. SM was harvested for histology, gene expression measured using RT2 Profiler™ PCR arrays and Taqman® assays and global and gene-specific DNA methylation were quantified using pyrosequencing.

RESULTS

Rats in the HFHS group gained more weight (567.5 ± 8.8 vs 474.0 ± 10.5 g, $p<0.0001$) and had increased insulin concentrations (6.1 ± 0.9 vs 3.8± 0.6 ng/ml, $p<0.05$) compared to the STD-fed rats, while no histological differences were noted. Increased expression of Insulin-like growth factor 2 (IGF2) was associated with HFHS diet exposure. Whilst no global DNA methylation changes were observed, we identified hypermethylation of an intronic CpG site within IGF2 ($p<0.01$). In silico analysis identified binding sites for transcription factors CCCTC-binding factor (CTCF), myogenin and myoblast determination protein 1 (MYOD) within close proximity to the hypermethylated CpG.

CONCLUSION

This study provides information about dysregulated DNA methylation and gene expression signatures during the progression of obesity and IR in SM.

PP-OL-06

OBESITY AWARENESS AND ITS RELATIONSHIP TO SOCIODEMOGRAPHIC CHARACTERISTICS OF FILIPINO ADULTS: A SURVEY AMONG WORK-FROM-HOME EMPLOYEES IN METRO CEBU, PHILIPPINES

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OBJECTIVE
Worldwide prevalence of obesity has been increasing and is expected to worsen with the recent work environment restrictions brought about by the coronavirus disease pandemic. Awareness of obesity is an essential component in the prevention and treatment of obesity. However, there are no studies that have examined obesity awareness in the Philippines. This study aimed to determine the awareness on obesity and its relationship to various sociodemographic characteristics among Filipino adults working from home in Metro Cebu.

METHODOLOGY
This is a cross-sectional survey and was conducted in Metro Cebu, Philippines. Included were Filipinos aged 18 years old and above, non-healthcare professionals working from home. The research instrument used was the Obesity Awareness Questionnaire (OAC-20), covering different aspects of obesity.

RESULTS
A total of 458 respondents participated. The respondents were aware of majority of the important concepts on obesity with an average score of 79.18%. Despite having awareness on obesity, majority had a reported BMI above normal. Age (p=0.198), BMI (p=0.397), hours of work per day (p=0.101), and hours of physical activity per day (p=0.458) were not associated with obesity awareness among the studied population. Similarly, male and female (p=0.515), as well as single and married respondents (p=0.629) did not differ significantly in terms of their average obesity awareness scores. However, higher educational attainment (p=0.044) and higher socioeconomic status (p=0.002) were associated with higher obesity awareness scores.

CONCLUSION
The sampled population of Filipino adults working from home in Metro Cebu were aware of majority of the important concepts on obesity.

PP-OL-07

ASSOCIATION BETWEEN OBESITY PARAMETERS AND POOR OUTCOMES IN HOSPITALIZED PATIENTS WITH CONFIRMED MILD TO MODERATE COVID-19

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OBJECTIVE
This study aims to assess visceral fat values, waist circumference (WC), body mass index (BMI), and body fat percentage for their ability to predict poor outcomes during COVID-19 patients' hospitalization.

METHODOLOGY
This research has been approved by an ethical committee. This study is a prospective cohort of mild-moderate COVID-19 cases at Cipto Mangunkusumo Hospital who were hospitalized from December 2020 to March 2021. Patients were examined for visceral fat values and body fat percentage using a bioimpedance analyzer (BIA), WC and BMI at admission. Multivariate logistic regression analysis was performed to assess visceral fat, body mass percentage, BMI, and WC abilities in predicting poor composite outcomes of ARDS and mortality.

RESULTS
Two hundred and sixty-one patients were included. Visceral fat (RR 1.12 [95% CI 1.03-1.21], p=0.005) and waist circumference (RR 1.05 [95% CI 1.02-1.08], p=0.11) were associated with poor outcomes. Neither body percentage (RR 0.99 [95% CI 0.96-1.02], p=0.72) nor BMI (RR 1.05 [95% CI 0.99-1.12], p=0.11) were associated with poor outcomes. Based on multivariate logistic regression, WC was statistically significant as an independent risk factor influencing poor outcomes in COVID-19 patients (RR 1.04 [95% CI 1.01-1.08], p=0.003), which can be interpreted that each 1 cm increase in waist circumference was associated with a 4% increased risk of composite poor outcomes.

CONCLUSION
Visceral obesity parameters were significantly associated with poor outcomes in mild to moderate COVID-19 cases.

PP-OL-08

UNDERDIAGNOSIS OF CHRONIC METABOLIC DISEASES IN PATIENTS WITH NEWLY DIAGNOSED ISCHAEMIC HEART DISEASE

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OBJECTIVE
Despite community screening efforts for common modifiable risk factors, we observed that chronic diseases such as type 2 diabetes (T2DM) were often only detected at the point of ischaemic heart disease (IHD) diagnosis. We aim to investigate the prevalence of underdiagnosed modifiable risk factors in patients with IHD.

METHODOLOGY
We assessed the prevalence of previously undiagnosed cardiovascular risk factors among hospitalized patients with IHD (n=555) and compared the differences between patients with newly diagnosed IHD (IHD-N, 46.5%) and patients with known IHD (IHD-K, 53.5%).

RESULTS
The patients recruited were mostly males (82.5%) of Chinese ethnicity (49.1%). Overall, there was a high prevalence of newly diagnosed hypertension (13.3%), hyperlipidaemia (13.2%) and T2DM (4.9%). Compared with the IHD-K group, prevalence of previously undiagnosed hyperlipidaemia (26.0% vs 2.0%, p<0.001), hypertension (24.8% vs 3.4%, p<0.001) and T2DM (7.0% vs 3.0%, p<0.001) was higher in the IHD-N group. Prevalence of active smoking was high at ≈50% in both groups. The median concentration of total cholesterol and LDL-C were higher in the IHD-N group compared with the IHD-K group(p<0.001). Dietary habits of >50% of patients in both subgroups did not meet national recommendations for fruits, vegetables, whole grain and oily fish intake, although the IHD-K group had more regular omega-3 supplements intake (23.4% vs 10.4%, p=0.026) compared with the IHD-N group.

CONCLUSION
The high prevalence of previously undiagnosed chronic metabolic diseases among patients with newly diagnosed IHD underscores the importance of increased detection efforts as well as emphasis of a heart healthy diet and smoking cessation.

PP-OL-09

THE ASSOCIATION BETWEEN BETEL QUID CHEWING AND METABOLIC SYNDROME AMONG URBAN ADULTS IN THE MANDALAY DISTRICT OF MYANMAR

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INTRODUCTION
As the prevalence of the metabolic syndrome, obesity and diabetes increases worldwide, the need to identify modifiable lifestyle risk factors increases, especially those that may be relatively unique to a specific population.

To explore a possible association between betel quid chewing and metabolic syndrome (MS).

METHODOLOGY
This was a community-based cross-sectional study done in Dhamma Hall, a Buddhist temple. Participants were 391 adults residing in the Chan Aye Thar Zan Township in the Mandalay District of Myanmar. We interviewed the subjects and measured their triglycerides, HDL-Cholesterol (HDL), glucose, waist circumference, body mass index and blood pressure. The main outcome measures were betel quid chewing status and the presence of MS. Other risk factors for MS (age, sedentary lifestyle, family history of DM, hypertension, and cardiovascular disease, and risk factors for non-communicable disease such as sex, smoking, alcohol use), were adjusted through multivariate regression analysis.

RESULTS
The prevalence of MS was similar in chewers (n=182) and non-chewers, at about 50%. After controlling for other factors, the predictors for development of metabolic syndrome among betel chewers was the daily number of quids (Adjusted OR 1.47, CI 1.10- 3.30), age 40 years and older (AOR 2.23, CI 1.28 – 3.92), family history of hypertension (AOR 0.38, CI 0.21- 0.68), and family history of diabetes (AOR 0.10, CI 0.03- 0.32).

CONCLUSION
Betel quid chewing may represent a behavioral lifestyle target for approaches to reduce the incidence of metabolic syndrome.

PP-OL-10

EFFECTS OF GELESIS200, AN ORAL SUPERABSORBENT HYDROGEL, ON POSTPRANDIAL INSULIN RESPONSE IN PEOPLE WITH PREDIABETES: AN ANALYSIS OF THE LIGHT-UP STUDY

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OBJECTIVE
Postprandial hyperinsulinemia is associated with beta-cell dysfunction and development of type 2 diabetes. This analysis assessed the effect of Gelesis200 (GS200), an investigational oral superabsorbent hydrogel, on postprandial glucose and insulin response among people with prediabetes, in the LIGHT-UP study.

METHODOLOGY
The LIGHT-UP study investigated the safety and efficacy of GS200 vs. placebo over 25 weeks in 254 participants with prediabetes or type 2 diabetes and a body mass index of 27-40 kg/m^2. The analysis included participants with prediabetes who completed a 2-hr oral glucose tolerance test at baseline and at Week 25 (42 participants per arm). Plasma glucose and serum insulin were measured at 15–30-minute intervals. Area under the curve (AUC) was calculated using the trapezoidal method and differences were assessed using ANCOVA model with weight loss as a covariate.

RESULTS

Participants were 59.5% female, aged 47.1 ± 11.7 years, with a fasting glucose of 104.6±10.4 mg/dL. Baseline insulin AUC was 13,005.8 ± 6,895.2 μU/mL for GS200 and 13,233.8 ± 8,268.9 μU/mL for placebo. At week 25, insulin AUC was reduced by 17.0 ± 8.2% in GS200 and increased by 5.0 ± 8.0% in placebo arms (mean difference: -22.0 ± 10.5%, P=0.04). Participants on GS200 had a greater reduction in postprandial insulin at T60 (-35.0 ± 13.1 vs. -1.5 ± 12.8 μU/mL for placebo, P=0.05) and T120 (-30.9 ± 11.6 vs. 0.5 ± 11.4 μU/mL for placebo, P=0.04), and a greater reduction in insulin Cmax vs. placebo (mean difference: -47.3 ± 21.1 μU/mL, P=0.03). No significant differences were observed for postprandial glucose or HOMA-IR between arms.

CONCLUSION

Administration of GS200 in people with prediabetes significantly improved postprandial insulin secretion independent of weight loss.

PP-OL-11

RECURRENT HYPOGLYCAEMIA IN A PATIENT WITH TOTAL GASTRECTOMY

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CASE

A 56-year-old male hostel resident with a past history of spastic diplegic cerebral palsy was repeatedly admitted for hypoglycaemia since January 2021. Past medical history revealed that on August 2018 he had a 5 cm bleeding acute gastroduodenal ulcer which required total gastrectomy and duodenostomy. He had several admissions for severe symptomatic hypoglycaemia in 2021 (January, February, May, June, July). He denied history of over-the-counter medication or alcohol intake. He experienced hypoglycaemia after meals. Prolonged 75 g oral glucose tolerance test showed hypoglycaemia at 3 hours with a glucose level of 1.7 mmol/l and paired insulin of 4.3 mIU/l. Thyroid function test and 1 μg short synacthen test results were normal. Urine toxicology was normal. He was referred to a dietitian on September 2021 and was given a trial of 2 tablespoons uncooked cornstarch (UCS) with water. He did not have any hospital admissions for hypoglycaemia since then. The home sugar monitoring showed capillary glucose mostly at 4-5 mmol/l, occasionally down to 2.9 mmol/l but not requiring admission.

The patient suffered from late dumping syndrome which is also seen in post-bariatric surgery patients. After sleeve gastrectomy or bypass surgery, as the undigested food has rapid transit to the small intestine, it stimulates release of gut hormones including glucagon-like-peptide 1 which causes hypoglycaemia. Dietary modification includes small frequent meals and increasing dietary fibre intake. The UCS has a low glycaemic index. It slows down the absorption of glucose and rise in blood glucose. If the patient fails dietary measure, acarbose, diaxozide and somatostatin analogue are the next steps. If the patient fails medical treatment, he may need surgical re-intervention such as pyloric reconstruction.

PP-OL-12

BEMPEDOIC ACID (ETC-1002) AS A NEW ALTERNATIVE TO STATIN THERAPY: AN UPDATED META-ANALYSIS AND SYSTEMATIC REVIEW WITH GRADE APPROACH

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OBJECTIVES

Bempedoic acid inhibits ATP-citrate lyase (ACL) two steps upstream of HMG-CoA reductase and may be recommended for patients who have not achieved LDL-C targets despite maximally tolerated or high-intensity statin therapy. Until now, there is no meta-analysis performed and this study intends to answer this question and to provide additional trials.

METHODOLOGY

Studies were searched using keywords: Bempedoic Acid or ETC-1002 and lipid in several databases of the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, ScienceDirect, and OVID. All references were reviewed using the Centre for Evidence-Based Medicine critical appraisal checklist. The descriptions of the extracted data are guided by the Preferred Reporting Items for Systematic Reviews (PRISMA) statement with GRADE approach. 4385 papers were initially collected, and twelve studies were pooled and entered review synthesis.

RESULTS
Ten RCTs were identified with a total of 3754 patients, 2468 intervention and 1284 control, and followed up for 4 to 52 weeks. The combined data showed that the primary endpoint, percent changes in LDL-C MD -25.81 [95 CI% -29.56, -22.06], was statically significant. Secondary endpoints were to assess the percent change from baseline for non-HDL-C -20.19 [95 CI% -23.42, -16.95] and apolipoprotein B -15.43 [95 CI% -17.09, -13.76] with a p value of <0.00. Two studies revealed that when adding it to dual therapy, 90% of patients achieved LDL-C <70 mg/dL, and 95% of patients had ≥50% lower LDL-C from baseline to week 6;. One study showed that adding PCSK9i lowered LDL-C by 30.3% vs placebo (P<.001).

CONCLUSION
Bempedoic acid significantly decreased LDL-C, non-HDL-C, and apolipoprotein B levels.

PP-OL-13

CORRELATION OF TG/HDL-C RATIO AND TyG INDEX WITH C-REACTIVE PROTEIN IN IMPAIRED FASTING GLUCOSE SUBJECTS

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OBJECTIVES
Prediabetes is an insulin resistant (IR) condition. The TG/HDL-C ratio and TyG index were associated with prediabetes and IR which are related to cardiovascular disease (CVD). HS-CRP is a marker of inflammation that is closely related to CVD. The aim of this study is to determine the correlation between TG/HDL-C ratio and TyG index with HS-CRP as a marker of chronic inflammation in impaired fasting glucose (IFG).

METHODOLOGY
Research subjects were taken from Makassar Lipid and Diabetes Study, an observational study which involved 92 prediabetic subjects aged 18-70 years old in Makassar City, Indonesia between January to April 2022. Triglyceride, HDL-C, FPG, and HS-CRP were examined. Level of HS-CRP >3-10 mg/L defined as a high risk of CVD. Impaired Fasting Glucose defined as fasting plasma glucose 100-125 mg/dL. Statistical analyses used were Kruskal-Wallis and Chi-Square tests.

RESULTS
The mean TG/HDL-C ratio was 4.88, TyG index was 4.92, and HS-CRP level was 4.53 ± 2.91 mg/L. The Chi Square test showed that there was no significant difference between TG/HDL-C ratio and TyG Index with high risk group of CVD (HS-CRP >3-10 mg/dL) among IFG subjects with p= 0.383 and p=0.584, respectively.

CONCLUSION
Our results indicate that there is no statistically significant relationship between TG/HDL-C ratio and TyG index with HS-CRP in prediabetic IFG subjects.

PP-OL-14

OBESITY IN THE ASEAN REGION: INDONESIA'S PERSPECTIVE

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BACKGROUND
Obesity is a chronic, relapsing, multifactorial, treatable neurobehavioral disease in which an increase in fat mass causes adipose tissue dysfunction and physical fat mass abnormalities cause metabolic, biochemical, and psychosocial health problems. After smoking and armed violence, war, and terrorism, obesity is the third leading cause of social burden.

Indonesia, one of the countries with a large population of more than 270 million people, is the world's fourth most populous country. According to the Ministry of Health of the Republic of Indonesia's Basic Health Research, the prevalence of obesity in adults increased from 19.1 percent in 2007 to 26.3 percent in 2013 and 35.4 percent in 2018. Obesity is more prevalent in females than in males, at 44.4 percent and 26.6 percent, respectively. As a result, one in every three adults is obese. Overweight and obesity were prevalent in children at a rate of 20%, or one in every five children. According to the World Obesity Atlas (2022), Indonesia has 14 million females (14%) and 8 million males (8%) who are obese (BMI >30 kg/m^2)

The situation is a health burden as well as a financial burden for individuals and the state. The potential impact of rising obesity rates is an increase in the prevalence of prediabetes (IGT) and diabetes in Indonesia, which were 10.2 percent and 5.7 percent in 2007, 29.9 percent and 6.9 percent in 2013, and 30.8 percent and 10.9 percent in 2018. According to the 2019 IDF Atlas, Indonesia has the world's third largest adult population with prediabetes, with 29.1 million people and

more recently, according to the 2021 IDF Atlas, Indonesia has the world's fifth largest population of adults with diabetes, with 19.5 million people. Overweight and obesity also contribute to the prevalence of diabetes, hypertension, and ischemic heart disease, which are 5,020,2 thousand, 11,147.5 thousand, and 282.7 thousand, respectively. Another burden is the loss of 6-10 productive years. This consumes about 8% to 16% of national healthcare, and the total cost (direct and indirect) for obesity in 2016 is USD 2-4 billion.

CONCLUSION

The Indonesian government is well aware of the situation and has made obesity and prediabetes prevention a priority. Obesity and prediabetes prevention and intervention programs have been developed by the Ministry of Health in collaboration with professional associations.

PP-OL-15

SERVICE EVALUATION OF A REAL-WORLD, DIGITALLY ENABLED, TIME RESTRICTED EATING PROGRAMME FOR ADULTS IN THE UK

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OBJECTIVE

Obesity and type 2 diabetes (T2D) remain global health challenges. Continuous energy restriction enables weight loss, but recently time-restricted eating (TRE) has gained traction. Limited data exists about its effectiveness in a real-world setting. Reset Health is a technology-enabled programme for people living with obesity and T2D delivered by clinicians and mentors. The aim of this service evaluation was to assess the impact of the Reset Health programme on weight, metabolic parameters, and other health-related outcomes.

METHODOLOGY

We enrolled 653 adults (mean age 46.3 ± 10.8 yrs, mean BMI 35.2 ± 6.4 kg/m^2, HbA1c 42.4 ± 12.5 mmol/mol; 61% White Ethnicity) with 114 having pre- (n = 59; 9.0%) or T2D (n = 56; 8.6%). Data were analysed at 12 and 24-weeks of the 244 completers and reported using mean ± SD.

RESULTS

Members lost a significant amount of weight at 12- and 24-weeks, 7.7 ± 4.4 kg and 9.5 ± 5.9 kg respectively ($p<0.001$). Waist circumference decreased by 11 ± 7.5 cm at 24 weeks ($p<0.001$), with systolic blood pressure reducing by 6.6 ± 12.6 mm Hg ($p<0.001$) and diastolic blood pressure by 4.2 ± 10.5 mm Hg ($p=0.002$). HbA1c reduced by 4.5 ± 7.4 mmol/mol ($p=0.05$) in all participants and 8.7 ± 9.2 ($p=0.07$) in those with T2D. Quality of life improved over 24-weeks with significant reductions in depression (2.2 ± 3.4, $p<0.001$) and anxiety (1.9 ± 4.0; $p<0.001$) scores. Eating behaviour improved with a reduction in binge eating and emotional eating scores (5.9 ± 8.1; $p<0.001$; 0.69 ± 0.83, $p<0.001$, respectively), while restraint eating score increased (0.26 ± 0.62; $p=0.001$).

CONCLUSION

Evaluation of a novel service using a clinically led, digitally enabled time restricted eating programme within a real-world population shows significant improvements in weight loss, health-related outcomes and eating behaviour.

POSTER PRESENTATIONS

REPRODUCTIVE HEALTH

PP-RH-01

45, X/47, XY, +13 MOSAICISM IN A 15-YEAR-OLD GIRL

https://doi.org/10.15605/jafes.037.AFES.109

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BACKGROUND

Approximately 45% of postnatal Turner syndrome patients have a pure 45,X cell line. Other karyotypes that may be mosaic with 45,X most commonly include:46,XX,; 47,XXX; or 46,XY;The presence of a 46,XY cell line may occur in 5–10%. Only a few instances of mosaicism with X-monosomic and trisomic cell lines of 21, 18, 13 were described.

CASE

We report the case of a 15-year-old female consulting for pubertal delay. Physical examination revealed the following signs of Turner syndrome: short stature, cubitus valgus lack of secondary sexual signs, brachymetacarpia and cutaneous nevi while no features of trisomy 13 were present. She showed female type of external genitalia. LH and FSH were elevated (100 and 21.5 mUI/l), serum estradiol: <10 pg/ml, serum testosterone: 0.1 ng/ml. Chromosomal analysis revealed a complicated karyotype: 45,X/47,XY,+ 13 mosaicism. The culture of skin fibroblasts, however, showed only 45,X cells. The coelioscopy showed a hypoplastic uterus and the histological examination of the castrated gonads showed ovarian agenesis. Our patient had no complication of Turner syndrome nor of 13 trisomy except for the agenesis of her corpus callosum.

CONCLUSION

Despite her pathological karyotype, this patient had a Turner syndrome phenotype with no complication, no evidence of any androgen effect and no detected malformations. The phenotype in a 45,X/46,XY mosaic patient likely depends on the distribution of mosaicism percentage in different tissues. We suggest that additional cells should be analyzed and more molecular genetic studies should be conducted.

PP-RH-02

CLINICAL AND HORMONAL CHARACTERISTICS OF PATIENTS WITH POLYCYSTIC OVARY SYNDROME IN A PERUVIAN TERTIARY CENTER

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OBJECTIVES

To describe the clinical and hormonal characteristics of patients with PCOS in a Peruvian center.

METHODOLOGY

Descriptive study that evaluated the clinical, biochemical and ultrasound characteristics of patients with PCOS at the Hospital Edgardo Rebagliati Martins, Lima-Peru in 2019.

RESULTS

We evaluated 100 consecutive patients, age range between 14 to 43 years (x ± SD: 27.2±7.3). Menarche at 12.2 ± 1.5 years. Oligomenorrhea that began during adolescence was present in 84%. The most frequent reason for consultation was oligomenorrhea, obesity and infertility (primary in 11 and secondary in 4 women), 21% had a history of abortions. Hirsutism (modified Ferriman-Gallwey Score >8), nodular-cystic acne, and androgynous alopecia were present in 89%, 44%, and 21%, respectively. LH and FSH concentrations (early follicular phase) were 8.9 ± 5.7 and 4.4 ± 2.4 IU/L, respectively; LH/FSH ratio >2 in 61%. The mean concentration of free testosterone: 2.8 ± 1.2 (0.6 to 6.5 pg/mL), 47% had values above the upper limit of our laboratory (>2.6 pg/mL). Androstenedione was from 0.20 to 6.60 (mean value of 3.0 ± 1.1 ng/mL), 45% had values above the upper normal value of our laboratory (>2.7 ng/mL). On ultrasonography, 78% presented with the morphology of polycystic ovaries (follicular cysts >12, 2 – 9 mm in diameter, ovarian volume ≥10 mL); endometrial thickness >5 mm in 33%.

CONCLUSION

The most frequent reason for consultation was ovarian dysfunction, and hirsutism was the most prevalent clinical alteration. Hyperandrogenemia was present in 50% and polycystic morphology in 75%.

PP-RH-03

METABOLIC CHARACTERISTICS OF PATIENTS WITH POLYCYSTIC OVARY SYNDROME IN A PERUVIAN HOSPITAL

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OBJECTIVES
To describe the metabolic characteristics of patients with PCOS in the endocrinology service of a Peruvian hospital.

METHODOLOGY
Descriptive study that evaluated the clinical and metabolic characteristics of patients with PCOS in the endocrinology service of the Edgardo Rebagliati Martins National Hospital, Lima - Peru.

RESULTS
We evaluated 100 consecutive women; age 27.2 ± 7.3 years; 4% and 7% had DM2 and hypertension, respectively. 66% had a family history of DM2, 37% hypertension, 38% obesity, and 9% early cardiovascular disease. Twelve women had macrosomic children. Their BMI: 27.9 ± 6.4 g/m^2; 68% had a BMI >25 kg/m^2, 47% had a waist circumference > 88 cm, and 37% had acanthosis nigricans.

Fasting blood glucose: 91,9 ± 23,4 (range: 68–214 mg/dL); fasting insulin and 2 hours post-load: 15,8 ± 11,2 (range: 2,7–77,4) and 59,3 ± 59,7 (range: 8,4–400), respectively. Some 15% presented with basal hyperglycemia >100 mg/dL and 42% had basal hyperinsulinemia >12,5 uIU/ml.

Forty six percent had HOMA-IR >2,5; 66% had QUICKI <0,357 and 22% had a Glucose/Insulin ratio <4,5. HOMA-%B fluctuated between 30,9 and 928.8%; 28% had HOMA-%B <100% and 23% HOMA-%B >300%. 62% had OGIS method <405 and 32% ISI-composite <3.

HDLc and triglyceride concentrations were 45 ± 11,4 (range: 20–79 mg/dL) and 123 ± 75,3 (32–390 mg/dL), respectively. 54% had HDLc <50 mg/dL and 25% had triglycerides >150 mg/dL.

CONCLUSION
Increased weight, positive family history and metabolic alterations are frequent in PCOS. The different surrogates for establishing insulin resistance, both fasting and during oral glucose load, are variable. It is important to establish the PCOS phenotype present in each patient.

PP-RH-04

PRIMARY AMENORRHEA IN AN ADOLESCENT FEMALE AS A PRESENTING FEATURE OF BOUCHER-NEUHÄUSER SYNDROME

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BACKGROUND
Primary amenorrhea has multiple aetiologies, encompassing disorders of ovaries, outflow-tract, pituitary/hypothalamus and genetic conditions. Hypogonadotropic hypogonadism refers to secondary hypogonadism due to deficiency in gonadotrophins, resulting in lack of estradiol stimulation, commonly due to pituitary or hypothalamus lesions, but can be due to genetic causes.

CASE
We describe a 16-year-old female who presented with primary amenorrhea and lack of secondary sexual characteristics, with no underlying medical conditions. Her sister and mother attained menarche at age 14. On examination, her BMI was 25 kg/m^2 and height was 151 cm (mid-parental height 155 cm). She had no syndromic features, no anosmia, and no hirsutism or features of virilization, and no visual or neurological abnormalities. External genitalia was consistent with infantile labia with intact introitus. Tanner-staging for her breast was 2/5 and 1/5 for genitalia and pubic hair.

Her hormonal profile showed hypogonadotropic hypogonadism, with undetectable estradiol (<36.7 pmol/L) and low gonadotrophin levels: Luteinizing-hormone 1.14 IU/L (2.4–12.6) and Follicular-stimulating-hormone 2.61 IU/L (3.5–12.5)]. Her bone age was delayed at 14 years, compared to a chronological age of 16. Karyotyping was 46,XX. Pelvic MRI showed hypoplastic uterus with normal vagina and ovaries. A pituitary MRI revealed a normal pituitary gland. Genetic testing confirmed 2 variants of PNPLA6 gene in keeping with Boucher-Neuhäuser syndrome

CONCLUSION
Boucher-Neuhäuser syndrome (BNS) is a rare genetic disorder characterized by cerebellar ataxia, chorioretinal dystrophy, and hypogonadism. We illustrate an interesting case presenting with isolated hypogonadotrophic hypogonadism with genetic screen suggestive of BNS, underlying the importance of considering genetic causes of primary amenorrhea even when presentation is in adolescence.

TESTOSTERONE LEVELS IN MEN WITH TYPE 1 AND TYPE 2 DIABETES MELLITUS AFTER TRANSPLANTATION OF AUTOLOGOUS MESENCHYMAL STEM CELLS

https://doi.org/10.15605/jafes.037.AFES.113

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OBJECTIVES
To study the effect of autologous mesenchymal stem cells transplantation (AMSCT) on testosterone levels in men with Diabetes Mellitus Type 1 (T1DM) and Type 2 (T2DM).

METHODOLOGY
5 male DMT1and DMT2 patients (39-50 years old) who received AMSCT intravenously were compared to 5 male DMT1and DMT2 patients (32-56 years old) as the control group. Mesenchymal stem cells were obtained from the iliac crest of DMT1 and DMT2 patients, the cells were cultured for 3-4 weeks and infused (95-97 × 106). Glycated hemoglobin (HbA1C,%) and testosterone (ng/ml) levels in both groups were analyzed before and 3 months later after the AMSCT.

RESULTS
The baseline mean testosterone and HbA1C levels in men with DMT1 and DMT2 with AMSCT were -5.31 + 2.12 ng/ml and 9.45 + 1.24 % respectively. Three months after the AMSCT, the mean testosterone and HBA1c became -6.33 + 2.12 ng/ml (p=0.82) and 8.53 + 1.08% (p=0.25). The baseline mean testosterone and HbA1C levels in DMT1 and DMT2 men in the control group were 5.27 + 1.8 ng/ml and 8.84 + 2.2% respectively. Three months after, the testosterone was -3.69 + 1.18 ng/ml (p=0,179) and the HBA1c was 8.64 + 1.41% (p=0.19). After 3 months, the average testosterone level in men with DMT1 and DMT2 who underwent AMSCT significantly increased compared to the mean testosterone level in men of the control group: 6.33 + 2.12 ng/ml versus 3.69 + 1.18 ng/ml (p=0.015).

CONCLUSION
An increase in testosterone levels in men with DMT1 and DMT2 after 3 months of the AMSCT compared with the control group of men with DMT1 and DMT2 can serve as a confirmation of the effectiveness of AMSCT for the prevention of diabetic erectile dysfunction and hypogonadism in men with diabetes mellitus.

POSTER PRESENTATIONS

PITUITARY / NEUROENDOCRINE

PP-PN-01

SURVIVAL OF TRANSGENIC MICE WITH PANCREATIC NEUROENDOCRINE TUMORS IS DETERMINED MORE BY HYPOGLYCEMIA SEVERITY THAN METASTATIC BURDEN

https://doi.org/10.15605/jafes.037.AFES.114

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OBJECTIVES
The purpose of this study was to compare the blood glucose and survival profiles of two strains of transgenic mice that develop pancreatic neuroendocrine tumors (PanNETs) with contrasting functionality and metastatic potential.

METHODOLOGY
Two strains of RIP1-Tag2 (RT2) transgenic mice that develop spontaneous PanNETs were compared: (1) RT2 mice in the C57BL/6J background (RT2;B6), and (2) hybrid RT2 mice (RT2;ABF1) generated by crossing RT2;B6 males to wild-type A/J females. Blood glucose, survival, and incidence of liver metastasis were compared in the two strains from age 8 to 17 weeks.

RESULTS
Blood glucose profiles and survival were similar in C57BL/6J mice and B6;A/J mice that lacked the RT2 transgene and did not develop PanNETs. By comparison, mean blood glucose values in RT2;B6 mice that had largely benign but functional PanNETs were 50% lower (44 mg/dL) over the survey period than in RT2;AB6F1 mice (87.4 mg/dL) that had aggressive but non-functional PanNETs. Importantly, survival of RT2;B6 mice, which had only a 4% incidence of liver metastasis, was significantly less (35%) over 17 weeks than in RT2;AB6F1 mice (84%) that had a 47% incidence of liver metastasis.

CONCLUSION
Survival of transgenic mice with PanNETs is determined more by hypoglycemia severity than metastatic burden. PanNET insulin secretion is greater and survival shorter in RT2;B6 mice with rare metastases than in RT2;AB6F1 mice with frequent metastases. Tumor insulin secretion and hypoglycemia limit survival in RT2;B6 mice at an earlier age- more than the impact of liver metastases on increased mortality in RT2;AB6F1 mice.

PP-PN-02

CITRAL AMELIORATES ISCHEMIC BRAIN DAMAGE IN STREPTOZOTOCIN INDUCED DIABETES IN RATS THROUGH AUTOPHAGY ACTIVATION

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INTRODUCTION
Focal cerebral ischemia is one of the leading causes of death and disability worldwide, and more than 30% of stroke patients are known to be diabetic. Accumulating evidence indicates that autophagy can contribute to cell death processes under pathological conditions. Citral, a monoterpene found in the essential oil of several plants, such as *Cymbopogon citratus*, has been reported to have antioxidant and anti-inflammatory activity.

The aim of this study was to examine the neuroprotective effects of citral against ischemic stroke in diabetic rats and co-relate its probable effects on autophagy.

METHODOLOGY
Streptozotocin (STZ) stimulation-induced diabetic rats were subjected to 1 h ischemia followed by reperfusion. The diabetic rats received different dosages of citral vehicle at baseline and 24 h after the middle cerebral artery occlusion (MCAO). Neurological deficit, lipid profile, blood glucose, and molecular biological tests (expression of PI3K/AKT/mTOR pathway-related proteins) were then performed to demonstrate the neuroprotective effects and mechanism in I/R injured diabetic rat.

RESULT
The results showed that citral markedly attenuated IL-1β, IL-6, and TNF-α levels. Meanwhile, treatment with citral retained serum GSH levels, led to a lower MDA level and also ameliorated neurologic outcome in rats. Citral treatment significantly decreased serum glucose level, serum TG, TC and LDL. Citral administration dramatically upregulated the expression of p62, and downregulated the level of LC3, beclin-1.

CONCLUSION
All data reveal that citral could effectively ameliorate cerebral ischemia/reperfusion injury via ameliorating inflammatory response, oxidative stress, and improving autophagy through PI3K/Akt/mTOR signaling pathway in diabetic rats.

PP-PN-03

PREVALENCE, CLINICAL PRESENTATION AND TREATMENT OUTCOMES OF ACROMEGALY: A DESCRIPTIVE STUDY FROM THE MALAYSIAN ACROMEGALY REGISTRY

https://doi.org/10.15605/jafes.037.AFES.116

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OBJECTIVES
The Malaysian Acromegaly Registry aimed to improve utilization of health care resource of this rare disease. Prior analyses were performed between 2013 - 2016, which reported 140 patients from 12 hospitals.

METHODOLOGY
Demographic, clinical and imaging data of all adult acromegaly patients from 23 public and university hospitals were collected and entered into an online database from September 2020 - April 2021. Disease control was defined by normal age- and gender-specific IGF-1.

RESULTS
We analysed 247 patients [median age 56 years (44.0-65.5), 50.6% male, 42% Malays, disease duration 7 years(3.8 – 14.0)]. An estimated acromegaly prevalence of 7.6 per million Malaysian population was derived. The more common presentations were acral enlargement (84.6%), prognathism (79.8%) and headache (44.5%). Hypertension (57.5%), diabetes (46.6%) and sleep apnoea (18.2%) were the most frequent co-morbidities. The mean IGF-1 at diagnosis was 711.1 ± 293 ng/ml. Majority had macroadenoma (70.4%) with up to 22.7% having optic chiasm impingement. Out of 195 patients who underwent primary surgery, only 22.1% achieved disease control. A second surgery failed to achieve control in 75%. Two-thirds (65.8%) of the 117 patients who failed the first surgery received somatostatin receptor analogue (SSA) and/or dopamine agonist. Although 43.7% experienced uncontrolled disease after medical therapy, less than one-fifth underwent radiotherapy or radiosurgery during their course of illnesses. Pituitary hormone deficiency occurred in up to 15.4%, with hypocortisolism being most frequent.

CONCLUSIONS
The low prevalence compared to global figures reflect under-recognition of acromegaly in Malaysia. The high rate of disease persistence after surgery has made SSA second line therapy of choice. The use of radiotherapy in acromegaly was low.

PP-PN-04

HIGHER FOLLICLE STIMULATING HORMONE WAS ASSOCIATED WITH POOR HANDGRIP STRENGTH AND GAIT SPEED IN OLDER MEN WITH TYPE 2 DIABETES

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OBJECTIVES
Sarcopenia is characterised by age-related loss of muscle mass, strength and physical performance. It is accelerated in type 2 diabetes mellitus(T2DM). Higher follicle-stimulating hormone(FSH) reportedly contributes to muscle mass decline. The association between FSH with muscle strength and physical performance remains unknown. We aimed to investigate association between FSH and handgrip strength and gait speed in men with T2DM.

METHODOLOGY
We conducted a cross-sectional on male patients with T2DM. Serum FSH was measured using electrochemiluminescence immunoassay. Handgrip strength was measured using hand dynamometer and was low if <28 kg. Slow gait speed was defined as ≤0.8 m/s. Modified Poisson regression was used to examine relationship between FSH with handgrip strength and gait speed, adjusting for age and clinical covariates.

This research has been approved by an ethical committee.

RESULTS
There were 100 patients with mean age 63.3 ± 7.3 years. Forty percent had low handgrip strength and 51% had slow gait speed. Univariate analysis showed that Tertile 3 FSH was associated with low handgrip strength and slow gait speed with corresponding relative risk (RR) 1.96 (95% CI 1.07-3.57; p=0.028) and 1.74 (95% CI 1.06-2.85; p=0.027) compared to Tertile 1 FSH. The association persisted in fully adjusted model with RR 1.88 (95% CI 1.02-3.43; p=0.042) and 1.80(95% CI 1.03-3.16; p=0.040) for low handgrip strength and slow gait speed respectively.

CONCLUSION
Elevated FSH, likely indicative of subclinical primary hypogonadism, was independently associated with low handgrip strength and slow gait speed. Hence FSH may potentially be used to identify risk of poor muscle strength and physical performance in men with T2DM.

PP-PN-05

OSILODROSTAT IS EFFECTIVE AND WELL-TOLERATED IN ASIAN AND NON-ASIAN PATIENTS WITH CUSHING'S DISEASE: RESULTS FROM LINC 3 (PHASE III STUDY)

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OBJECTIVES
Osilodrostat, a potent oral 11β-hydroxylase inhibitor, normalised mean urinary free cortisol (mUFC) in most patients with Cushing's disease (CD) during a Phase III study (LINC 3; NCT02180217). We describe outcomes for Asian and non-Asian patients enrolled in LINC 3.

METHODOLOGY
CD patients with mUFC>1.5x upper limit of normal (ULN) received osilodrostat during the 48-week (W) core phase. Patients benefiting from osilodrostat at W48 could enter an optional extension. Dose adjustments were permitted (maximum dose 30 mg bid). Data are reported separately for Asian and non-Asian patients.

RESULTS
Twenty eight percent of patients were Asian (39/137) and enrolled in Korea (n = 14), Japan (n = 9), India (n = 7), Thailand (n = 5) and China (n = 4). Most non-Asian patients were Caucasian (n = 89/98;91%). Median (range) osilodrostat exposure from baseline to study end was 115 (1–194) weeks in Asian patients and 141 (4–245) weeks in non-Asian patients, median (range) osilodrostat dose was 3.7 (1–18) and 10.1 (1–47) mg/day, respectively. The mUFC was ≤ULN in 62% (24/39) of Asian and 68% (67/98) of non-Asian patients at W48, increasing to 68% (21/31) and 87% (65/75), respectively, at W72. Improvements in cardiovascular parameters were observed in both groups during osilodrostat treatment. Hypocortisolism-related adverse events, mostly of mild or moderate severity, occurred in 64% (25/39; n = 2 discontinued) of Asian and 50% (49/98; n = 3 discontinued) of non-Asian patients.

CONCLUSION
Beneficial effects of osilodrostat were similar in Asian and non-Asian patients in terms of biochemical control and clinical improvement, although Asian patients generally received lower doses. Osilodrostat was well tolerated in both groups.

PP-PN-06

SUCCESSFUL USE OF RITUXIMAB TO TREAT GLUCOCORTICOID RESISTANT LYMPHOPLASMACYTIC HYPOPHYSITIS: A CASE REPORT

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BACKGROUND
Lymphoplasmacytic hypophysitis is very rare and due to that its treatment is unclear. We present a case of glucocorticoid resistant lymphoplasmacytic hypophysitis successfully treated with rituximab.

CASE
A 34-year-old Sri Lankan male, presented with subacute onset severe headache and right sided visual impairment over 2 weeks without fever. He experienced nocturia with polydipsia since late adolescence which worsened with the onset of current symptoms. Later, he developed right sided parotitis. His height was 153 cm, BMI was 22.4 kg/m^2. There was complete vision loss in right visual field and bilateral optic nerve atrophy with more severe involvement on the right. He lacked secondary sexual characteristics. Hormonal evaluation demonstrated secondary hypothyroidism, hypoadrenalism, hypogonadism, low IGF-1, and normal prolactin levels. Osmolality studies confirmed the presence of diabetes insipidus. Brain MRI showed hypoplastic pituitary with contrast enhancing stalk, infiltration in the sellar, suprasellar and parasellar regions with optic nerve and cavernous sinus invasion. Parotid biopsy was normal. Inflammatory markers were elevated. Complete blood count was normal except for mild anemia. Tuberculosis, HIV, Aspergillosis, vasculitis, sarcoidosis and Langerhans Cell Histiocytosis were excluded.

Lymphocytic hypophysitis was presumed and was started on methyl prednisolone pulses with pituitary hormone replacement. Due to poor response and progression of disease, he underwent transsphenoidal biopsy which showed lymphoplasmacytic infiltration with sclerosis suggesting possible IgG4 disease. IgG4 staining was not available. Serum IgG4 levels were normal. Intravenous rituximab pulses (1 g) were given 2 weeks apart

There was marked response to rituximab. His headache settled, nasal desmopressin was tailed off and resulted in slight improvement of the vision of blind eye. Follow-up MRI scans after 5 months revealed no progression from baseline.

CONCLUSION
Rituximab may give promising results in the presence of glucocorticoid resistant lymphoplasmacytic hypophysitis.

PP-PN-07

DIAXOZIDE INDUCED THROMBOCYTOPENIA IN TREATMENT OF INSULINOMA

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BACKGROUND
Insulinoma is a rare neuroendocrine tumor. Hypoglycaemia due to insulinoma is be managed by diaxozide, a benzothiadiazine derivate with antihypertensive and hyperglycemic activities prior to definitive surgery.

CASE
A 65-year-old female was admitted with hunger pangs, sweating and giddiness after a large carbohydrate meal and weight gain of 14 kg in 2 years. On fasting, she developed symptomatic hypoglycaemia within 2 hours with random blood glucose 2.1 mmol/L, serum insulin 1213 pmol/L (N 17.8-173), C-peptide 7784 pmol/L (N 367-1469) and cortisol 598.5 nmol/L. CT pancreases showed a 5 x 5.1 x 5.3 cm irregular walled lesion with coarse calcifications at the tail of pancreas (HU 13-15) with no septation- likely insulinoma.

She was started on diaxozide for endogenous hyperinsulinemic hypoglycaemia with dose titrated up to 400 mg/day. One week after diaxozide initiation, she developed symptoms of diazoxide overdose, fever and thrombocytopenia (nadir level 10 x 10^9/L) with no source of infection. Diaxozide was stopped and she was switched to subcutaneous octreotide 100 mg TDS. Symptoms of overdosage, fever, and thrombocytopenia resolved after 4 days of stopping diaxozide. She then underwent distal pancreatectomy which was curative.

Thrombocytopenia is a rare complication of diaxozide and occurs due to platelet destruction from antibody formation. It is dose dependent and occurs 13-23 days after initiation of diaxozide and resolution will occur after discontinuing diaxozide.

CONCLUSIONS

Although thrombocytopenia is a rare complication of diaxozide, close monitoring of platelet count is needed to prevent complications.

PP-PN-08

DELAY IN GROWTH HORMONE THERAPY IS NOT DETRIMENTAL

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BACKGROUND

Pituitary hypothyroidism with growth hormone deficiency is often missed in primary care due to scarce health resources in developing countries. Well-meaning primary care with thyroxine for misdiagnosed primary hypothyroidism may be detrimental. However, the initial use of thyroxine in neonatal central hypothyroidism and growth hormone deficiency prevented long term intellectual decline even when it was inappropriately diagnosed as primary hypothyroidism.

CASE

Twin male siblings born to second degree consanguineous parents were managed by a pediatric specialist as primary hypothyroidism, requiring unusually high thyroxine doses. T4 was used to guide therapy. After consultation with an endocrinologist, the associated growth hormone deficiency was diagnosed. Pituitary structures on magnetic resonance imaging were normal.

The dose of thyroxine was beyond age-matched norms, with free T4 and free T3 values significantly high at 4 years of age. Confirmation of growth hormone deficiency was guided by hormone assay and auxology. Assistance from a growth hormone manufacturing company and government support helped manage both siblings from age 4 up to 18 years, notwithstanding limitations in periodic monitoring. The siblings are now in graduate technical college with respectable height gain.

CONCLUSION

Appropriate and timely diagnosis of pituitary hypothyroidism and associated growth hormone replacement, even in poor socioeconomic situations, can help nurture productive citizens.

PP-PN-09

AUTOIMMUNE POLYGLANDULAR SYNDROME (APS) TYPE 2 WITH CENTRAL DIABETES INSIPIDUS

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BACKGROUND

APS involves functional abnormalities in several endocrine and non-endocrine glands. Deficits may manifest over time. Screening for other manifestations is important. The major components of the syndrome are adrenal insufficiency, thyroid autoimmunity and type 1 diabetes. It is very rarely described with central diabetes insipidus (DI).

We present a very uncommon presentation of APS-2 with the onset of Addison's at age 7, developing other polyglandular associations over time and central DI in adulthood.

CASE

A 31-year-old woman with a history of Addison's disease diagnosed and treated with dexamethasone at age 7 presented with acute polyuria and polydipsia. She had negative water deprivation test according to the North Bristol protocol. Due to persistent symptoms, she was empirically commenced on desmopressin (Minirin) with good response. Testing finally diagnosed central DI: magnetic resonance imaging (MRI) demonstrated absence of the posterior pituitary bright spot and a 3 mm stalk thickening thought to be pathognomonic and possibly related to arginine vasopressin antibody status. Antibodies to thyroglobulin, thyroid receptor, ZnT8, GAD and IA2 were negative. TSH and HbA1c were normal.

CONCLUSION

APS-2 as an evolving polyglandular disease may be associated with other endocrine deficiencies, including central DI. Loss of pituitary bright spot and stalk thickening on MRI supports the diagnosis of central DI and should be considered in the work up of patients.

PP-PN-10

A CASE REPORT ON PITUITARY APOPLEXY FOLLOWING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY AND LAPAROSCOPIC CHOLECYSTECTOMY

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BACKGROUND

Pituitary apoplexy is a rare neurosurgical emergency increasingly being precipitated by minor surgical procedures.

CASE

A 49-year-old male underwent ERCP and laparoscopic cholecystectomy for acute cholangitis. Two days post-operatively, he complained of dizziness with horizontal diplopia and slight left eye ptosis. Five days postoperatively, he became drowsy, with complete ptosis and blurred vision of the left eye and decreased motor strength on all extremities. Cranial CT Scan showed a sellar/suprasellar ovoid soft tissue focus. Pituitary MRI confirmed a sellar/suprasellar heterogeneous mass measuring 1.5 cm x 2.5 cm x 1.8 cm, hyperintense on T1 and hypointense on T2. Hormonal workup showed low IGF-1 [63.50 ng/mL, reference value (RV) 74-196], GH (0.60 ng/mL, RV 0-0.97), LH (0.16 mIU/mL, RV 1.5-9.3). total testosterone (<10 pg/mL, RV 164-753), ACTH (<5 pg/mL, RV 5-46), 0800H cortisol (<1.00 µg/dL, RV 3.7-19.4), PRL (1.11 ng/mL, RV 2.1-17.7), TSH (0.23 uIU/mL, 0.55-4.78) and FT3 (2.23 pg/mL, RV 2.3-4.2). He was managed as panhypopituitarism (secondary adrenal insufficiency, hypothyroidism, hypogonadism) secondary to pituitary macroadenoma with pituitary apoplexy. He was given hydrocortisone and underwent endoscopic transsphenoidal pituitary mass excision. He was discharged improved on prednisone 7.5 mg/day and levothyroxine 100 µg/day.

CONCLUSION

Pituitary apoplexy should be considered in patients with abrupt neuro-ophthalmological deterioration even after minor gastrointestinal surgeries. Early diagnosis allows immediate intervention to preserve vision and provide hormonal replacement.

PP-PN-11

A CONCURRENT FINDING OF A GROWTH HORMONE-PRODUCING PITUITARY ADENOMA AND A RADIOLOGICALLY-CONFIRMED SYMPTOMATIC RATHKE'S CLEFT CYST

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BACKGROUND

We present a case report describing a rare finding of concurrent growth hormone (GH)-producing pituitary adenoma and a radiologically confirmed symptomatic Rathke's cleft cyst (RCC) in a 65-year-old female patient.

CASE

Hormonal studies showed elevated insulin-like growth factor (IGF) [43.3 nmol/L, reference range (RV) 6.2-24 nmol/L and 51.3 nmol/L] taken two months apart. Other assays were normal (PRL 213 mIU/L, RV <700; 1000H cortisol 222 nmol/L, RV 14-690; TSH 1.3 mIU/L, RV 0.27-4.2; FT4 12 pmol/L, RV 12-22 pmol/L). OGTT revealed a failure to suppress serum GH to <1 µg/L, with nadir GH 2.3 µg/L. Pituitary meatus magnetic resonance imaging scan showed a 6.5 mm x 9 mm non-enhancing cyst in the pituitary sella which appeared to be displacing the normal pituitary tissue superiorly and slightly posteriorly. The optic chiasm was preserved, with no supra- or parasellar extension. After transphenoidal surgery, histolopathologic studies revealed a strongly GH-positive adenoma, also positive for PIT1, SF1; and Ki67 1-2%. PRL, FSH and LH staining were negative.

CONCLUSION

Clinicians are reminded about increasing evidence of the concurrent occurrence of symptomatic RCC(s) and pituitary adenoma(ta). More explanations beyond case reports or case series evidence are needed to explain their seeming concurrence.

PP-PN-12

TRANSIENT DIABETES INSIPIDUS: A COMPLICATION FOLLOWING TRANS-SPHENOIDAL SURGERY

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BACKGROUND
Central diabetes insipidus (DI) is one of the complications of trans-sphenoidal surgery caused by the damage of vasopressin-secreting neurons. While some patients develop permanent DI, most patients fully recover.

CASE
A 26-year-old female was referred to the endocrinology clinic for a suprasellar tumor. She presented with a chief complaint of hemianopsia two months prior to the admission. She also noted amenorrhea for about six months. Physical examination only showed bitemporal hemianopsia. She had normal free T4, TSH, LH, FSH, and cortisol levels. Brain MRI revealed cystic pituitary macroadenoma in the sellar-suprasellar region with optic chiasm compression. A day following transphenoidal surgery, she experienced polydipsia and polyuria. The patient was treated with desmopressin which improved symptoms in two days. After discontinuing desmopressin, her urine volume remained within normal limits.

DI as a complication of trans-sphenoidal surgery occurs in 18 to 30%, but the risk factors are not well established. It can be transient, permanent or triphasic, depending on the damage of vasopressin-secreting neurons. Postsurgical DI is diagnosed by excluding other forms of polyuria, such as excess intravenous fluids or mannitol administration. Key diagnostic clues are increased thirst, hypotonic polyuria and hypernatremia and/or hyperosmolality. Majority of cases are transient and resolve after two to three doses of desmopressin.

CONCLUSION
Urinary excretion and water balance following trans-sphenoidal surgery should be monitored closely. Increased diuresis might indicate postsurgical DI despite the amount of intravenous fluid administration.

PP-PN-13

AN UNUSUAL OCCURRENCE OF HYPOPITUITARISM IN MOSAIC TURNER SYNDROME: A CASE REPORT

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BACKGROUND
Turner syndrome (TS), the most common chromosomal anomaly in females, is characterized by short stature, hypergonadotropic hypogonadism and various congenital malformations. We report a case of concomitant multiple pituitary hormone deficiencies and gonadal dysgenesis.

CASE
An 18-year-old female was referred to our hospital for evaluation of short stature and primary amenorrhoea. Examination revealed severe short stature (height 131 cm, -4.2 SD), weight 27 kg with a BMI 15.7 kg/m^2, high arched palate, hypertelorism, increased facial naevi, camptodactyly with wide sandal gap. She had a female phenotype with female external genitalia and Tanner stage 1 for both breast and pubic hair development. Hormonal evaluation showed growth hormone (GH) deficiency and relative adrenal insufficiency after the clonidine and ACTH stimulation tests, respectively; low basal gonadotropin levels; low-normal prolactin levels; and intact thyroid axis. Abdominal ultrasonography showed pre-pubertal uterine and ovarian dimensions. Pituitary MRI revealed features suggestive of pituitary hypoplasia. Cytogenetic analysis pattern showed mosaic TS: mos 46,X,del(X)(q24)[17]/45,X[13]. The patient was diagnosed with concomitant hypopituitarism and mosaic TS. She was started on hydrocortisone and sex hormone replacement therapy, as financial constraints affected the decision on recombinant human GH therapy.

CONCLUSION
Mosaic TS with pituitary hormone deficiency is a very rare occurrence, probably the first case report from Indian literature. Combined gonadotropin, corticotropin and somatotropin deficiencies were previously not reported. In multiple pituitary hormone deficiencies, karyotyping should be performed even in presence of the slightest stigmata of TS.

PP-PN-14

PITUITARY APOPLEXY AND PROLACTINOMAS: A CASE SERIES

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BACKGROUND
Pituitary apoplexy describes the ischemic or hemorrhagic phenomenon that occurs in a pituitary adenoma. It may be the first manifestation of a pituitary gland adenoma.

CASES
Case 1 is a 31-year-old female with macroprolactinoma treated irregularly with cabergoline for three months. She had amenorrhea since age 14, and subsequent decreased visual acuity and oppressive headache. MRI revealed pituitary apoplexy. She was discharged with cabergoline and prednisone. Days later, she had vaginal bleeding and was found to be pregnant at 12 weeks.

Case 2 is a 40-year-old male with sexual dysfunction for six months. He had a two-month history of bitemporal hemianopsia, headache and nausea. Tests revealed prolactin >1000 ng/dL and low pituitary hormones. MRI revealed pituitary apoplexy in a 3.5 cm adenoma.

Case 3 is a 53-year-old male who presented with visual acuity deterioration and bilateral gynecomastia. Tests revealed elevated prolactin and pituitary gland adenoma on MRI. At 6 months on cabergoline, he had improvement in visual acuity, and decreased prolactin levels and tumor size. At 8 months, he experienced intense headache, vomiting and sensorium deterioration. MRI revealed extensive area of necrosis and intratumoral hemorrhage.

CONCLUSION
We present 3 cases of prolactinomas that presented with apoplexy associated with pregnancy, large adenoma size and treatment with cabergoline. Pituitary stimulation by estrogens in the pregnant state was likely. Pituitary apoplexy in large tumors is generally more frequent in non-functioning adenomas. Rarely, dopaminergic agonists increase the risk for pituitary apoplexy from lactotroph apoptosis.

POSTER PRESENTATIONS

THYROID

PP-T-01

PATTERN OF WEIGHT CHANGES FOLLOWING RADIOIODINE TREATMENT IN THAI PATIENTS WITH HYPERTHYROID GRAVES' DISEASE

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OBJECTIVES
The average weight gain following radioiodine (RAI) treatment is reported at 5 to 7 kg. We determined the extent of weight gain and associated risk factors for becoming obese in a cohort of Thai patients with RAI-treated Graves' disease (GD).

METHODOLOGY
A five-year retrospective study of RAI-treated GD patients at Theptarin Hospital was performed. Weights taken at initial presentation, RAI administration and follow-up were compared. The proportion and associated risk factors for weight gain ≥5% compared to weight at RAI administration were analyzed.

RESULTS
Between 2016 and 2020, 347 patients with GD (females 81.0%, mean age 34.0 ± 11.9 years, mean BMI 22. 9 kg/m^2) were treated with RAI (median dose 20 mCi). Almost all (91.9%) had hypothyroidism. During the median follow-up of 25 months, 71.2% had a median weight change of +2.1 kg compared with weight at RAI administration, and +3.0 kg compared with premorbid weight. Men gained more weight (2.9 versus 2.0 kg, p=0.277). Those with obese class I (BMI 25.0 to 29.9 kg/m^2) and class II (BMI ≥30.0 kg/m^2) increased (25.7 to 28.3%, and 6.2 to 9.1%, respectively). Weight loss upon diagnosis of GD and before RAI administration were the only factors associated with weight gain ≥5%.

CONCLUSION
Weight gain post-RAI treatment is common, with a significant proportion eventually becoming obese. Discussion of the risk of weight gain and the need for early intervention with comprehensive weight management support should be done in patients at risk.

PP-T-02

RELATIONSHIP OF MALIGNANCY IN THYROID NODULES WITH REPEAT BETHESDA III CLASSIFICATION ON FINE NEEDLE ASPIRATION BIOPSY

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OBJECTIVES
There is no consensus regarding treatment options available for patients with repeat Bethesda III Classification. This may cause anxiety regarding additional procedures and possible delay in definitive diagnosis and management. This study aimed to evaluate the risk of malignancy as well as the predictors of malignancy for repeat Bethesda III nodules on fine needle aspiration biopsy (FNAB).

METHODOLOGY
A single center, ambispective cross-sectional study of adult patients with thyroid nodules who underwent both initial and repeat fine needle aspiration biopsy at the Diabetes, Thyroid and Endocrine Center of St. Luke's Medical Center Quezon City was conducted. The Thyroid Registry was utilized to collect each patient's demographic and clinical characteristics, ultrasonographic features of thyroid nodules, and cytopathologic and histopathologic results. Subclassification of atypia/follicular lesion of undetermined significance (AUS/FLUS) were retrieved from cytopathology reports using the electronic Healthcare-Results Management System of the same institution.

RESULTS
A total of 59 adult patients with thyroid nodules were included. Thirty-eight patients were malignant based on histopathology, having an incidence of 64.41% (95% CI: 51.22-75.72%). There were no significant differences in clinical, ultrasonographic and cytopathologic features of malignancy between benign and malignant nodules.

CONCLUSION
A second FNAB result of AUS/FLUS carries a 64% risk of malignancy. This suggests an elevated risk of malignancy compared with a single FNAB result of Bethesda III (5-15%). This supports surgical intervention (lobectomy/thyroidectomy) as a reasonable option after a second Bethesda III classification on FNAB.

PP-T-03

UNDERSTANDING THE COMPLEX RELATIONSHIP BETWEEN TSH AND FREE THYROXINE

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OBJECTIVES
Guidelines suggest screening for thyroid disease using TSH first before FT4 due to their inverse log-linear relationship. The signal favours TSH over FT4 in a ratio of >100:2. We reassessed this FT4 to TSH relationship following the third-generation TSH assay from Roche.

METHODOLOGY
Consecutive paired TSH/FT4 from ambulatory non-hospitalized subjects assayed on Cobas e801 (Roche) between October 2020 to July 2022 were retrieved from our Laboratory Information System. For duplicate/multiple values from the same individual, the earliest values were retained. Reference intervals for the Roche assays were TSH 0.4-4.0 mIU/L and FT4 10-20 pmol/L. Descriptive statistics, linear and nonparametric (kernel) regression and cross-validation of the results (n = 7484) were performed using the statistical software packages in R 4.2.0.

RESULTS
Linear regression of logTSH against FT4 gave an r = -0.26. Nonparametric regression revealed two negative sigmoid curves merging into the euthyroxinemic region. Three different segments were determined: hypothyroxinemic (FT4<10): logTSH = 1.75-0.15fT4 (n = 144; r = -0.34, P<0.0001), euthyroxinemic (FT4 10-20): logTSH = 0.51-0.02fT4 (n = 6886, r = -0.10, p<0.0001), and hyperthyroxinemic (FT4>20): logTSH = 1.89-0.09fT4 (n = 454, r = -0.45, P<0.0001).

CONCLUSION
The relationship between FT4 and TSH is complex. The widely accepted view of a constant gradient of logTSH against FT4 over the whole range of thyroid test values is inaccurate. While the TSH-first strategy is applicable for thyroid dysfunction, two tests may be preferred for euthyroxinemic states in a hospital-based practice.

PP-T-04

CURRENT STATUS AND CHALLENGES IN THE MANAGEMENT OF POST-ABLATIVE HYPOTHYROIDISM DUE TO GRAVES' DISEASE AMONG THAI PATIENTS

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OBJECTIVES
Up to 40% of patients on levothyroxine (LT4) replacement have out-of-range TSH. This study aimed to evaluate TSH and daily LT4 dosage according to body mass index (BMI) in Thai patients with post-ablative hypothyroidism.

METHODOLOGY
We reviewed the medical records of Thai patients treated with radioactive iodine (RAI) for Graves' disease from 2016 to 2020 at Theptarin Hospital. Patients who received LT4 for at least 6 months were included. Serum TSH, FT4 and self-reported compliance were retrieved at the last visit. Daily LT4 dose was calculated based on actual body weight (ABW) compared with estimated lean body mass (LBM) by Hume formula.

RESULTS
A total of 271 patients (female 81.2%, mean age 36.7 ± 7.6 years, LT4 treatment duration 27.1±14.6 months, LT4 1.4±0.5 μg/kg ABW/day, LT4 2.0 ± 0.7 μg/kg LBM/day) were analyzed. Only 55.5% of patients achieved within-range TSH on last follow-up. TSH values were above reference range (>4.2 mIU/L) in 15.1% and below (<0.3 mIU/L) in 29.9%. Only 3.3% of all patients frequently missed dose of LT4 more than 15%. Within-range TSH was seen in 46.2% of obese patients (BMI ≥30 kg/m^2). There were no differences between daily LT4 doses based on ABW and LBM between within-range and out-of-range TSH groups. Obese patients required a lower daily LT4 dose relative to ABW and LBM to attain euthyroidism (ABW 1.1 ± 0.4 μg/kg/day and LBM 1.8 ± 0.6 μg/kg/day).

CONCLUSION
Almost 50% of patients with hypothyroidism had out-of-range TSH values. In obese patients, both ABW and LBM could be used to guide appropriate LT4 replacement dose.

PP-T-05

FOLLICULAR THYROGLOBULIN ANTAGONIZES THE ACTION OF TSH AND REGULATES THE EXPRESSION AND LOCALIZATION OF THE NOVEL IODIDE TRANSPORTER SLC26A7

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OBJECTIVES
Thyroglobulin (Tg) stored in the follicular lumen serves as a potent negative feedback regulator of follicular function that controls the expression of thyroid-specific genes. Recently, SLC26A7, a novel gene responsible for congenital hypothyroidism, was identified as an apical iodide transporter of thyrocytes. In this study, we examined the effects of TSH and follicular Tg on the expression and localization of SLC26A7.

METHODOLOGY
Rat thyroid FRTL-5 cells were stimulated by TSH or follicular concentrations of Tg. SLC26A7 mRNA and protein expression levels were evaluated using real-time PCR and Western blotting, respectively. Changes in subcellular localization of SLC26A7 in FRTL-5 cells and rat thyroid tissue sections were analyzed using confocal laser scanning microscopy.

RESULTS
TSH suppressed both mRNA and protein levels of SLC26A7, while it translocated SLC26A7 from the perinuclear area to the cell membrane. Tg also suppressed mRNA and protein levels of SLC26A7. However, Tg inhibited the ability of TSH to induce the plasma membrane localization of SLC26A7. In rat thyroid sections, SLC26A7 localization was inversely correlated with that of follicular Tg.

CONCLUSION
We have demonstrated that both TSH and follicular Tg suppressed the expression of SLC26A7. However, Tg inhibited the action of TSH to localize SLC26A7 to the plasma membrane both in vitro and in vivo. These results corroborate our hypothesis that the function of individual follicles is strongly regulated by the level of Tg accumulated in the follicular lumen.

PP-T-06

LANDSCAPE OF THYROID CARCINOMA: DIAGNOSTIC VALUE AND MANAGEMENT. RETROSPECTIVE STUDY OF A SINGLE CENTRE 2019-2021 (PART 2)

https://doi.org/10.15605/jafes.037.AFES.133

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OBJECTIVES
Ultrasound imaging and fine-needle aspiration (FNA) are the mainstays in evaluating thyroid nodules. There is a substantial lack of recent data on thyroid carcinoma.

This study aimed to determine the effectiveness of the Green Corridor and to collect the data on the diagnosis of thyroid carcinoma by FNA and confirmation after surgical intervention.

METHODOLOGY
We conducted a retrospective observational study on patients sent to the Green Corridor (code Z03.173) RECUH between 2019 to 2021. Data on FNA, treatment, thyroid cancer types and comorbidities were collected after surgery. We compared the efficiency of cytological (starting from Bethesda III, atypia of undetermined significance or follicular lesion of uncertain significance) and histological thyroid cancer diagnoses and analyzed the efficiency of the Green Corridor. Statistical analysis was conducted using IBM SPSS.

RESULTS
We included data from 563 patients. Thyroid cancer was confirmed in 153 (27.2%, women 80.4%). Surgical intervention (total thyroidectomy or hemithyroidectomy) and histologic confirmation of thyroid cancer was done in 147 patients. Four patients (2.6%) underwent radiation therapy, and two (1.3%) received palliative care due to an inoperable condition. FNA results of malignancy coincided with histological analysis in 114 patients (77%). In 84 (73.7%) patients, FNA malignancy type coincided with the histological analysis.

CONCLUSION
The Green Corridor has been shown to be effective based on the histological confirmation of thyroid cancer. FNA has proven its high diagnostic value in combination with cost-effectiveness and minimal invasiveness.

PP-T-07

NEW ONSET GRAVES' DISEASE AFTER SARS-CoV-2 VACCINATION

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BACKGROUND
There are increasing number of reports of thyroid dysfunction after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination. We report a case of new-onset Graves' disease following vaccination with adenovirus-vectored Vaxzevria (Oxford-AstraZeneca).

CASE
A 29-year-old female with no prior history of endocrine or autoimmune disease presented with a week of palpitations, heat intolerance and excessive sweating starting three days after her second dose of Vaxzevria. She was asymptomatic after her first dose given two months earlier. Her father and sister have Graves' disease. She had a diffuse goitre and no orbitopathy. Tests showed suppressed TSH [<0.01 mIU/L, normal range (NR) 0.27-4.2], elevated free T4 (>100 pmol/L, NR 12-22) and positive TSH receptor antibody (>40.00 IU/L, NR <1.75). Ultrasonography revealed a hypervascular, diffusely enlarged goitre. Oral carbimazole and propranolol were commenced. Five months later, free T4 normalized and TSH remained undetectable. To date, she remains hesitant to receive her booster dose.

SARS-CoV-2 infection and vaccination have been associated with subacute thyroiditis and autoimmune thyroid disease. While there are reports of new-onset Graves' disease after mRNA and adenovirus-vectored vaccines, it has not been associated with inactivated virus vaccines. The prevailing postulation is that the adjuvants in the vaccines can trigger an autoimmune event.

CONCLUSION
Physicians should be aware of the possibility of thyroid dysfunction after SARS-CoV-2 vaccination, especially in those with strong family history. More studies are required to establish causal relationship.

PP-T-08

LONG-TERM FOLLOW-UP OF THREE PATIENTS WITH PERIODIC PARALYSIS

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BACKGROUND
Periodic paralysis (PP) is a disorder of muscle ion channels, often precipitated by heavy exercise, fasting or high-carbohydrate meals.

CASES
Case 1: A 28-year-old male with hyperthyroidism had severe lower extremity weakness progressing to the upper extremities after high-intensity exercise, with serum K 1.7 mmol/L. Examination showed normal vitals, palpable thyroid and no neurological deficit. Methimazole, propranolol and KCl wer given. KCl was discontinued after 4 weeks with normalization of serum K. He developed hypothyroidism three months later and was prescribed levothyroxine. He is currently euthyroid without recurrent PP for six years.

Case 2: A 29-year-old male presented with severe exertional muscle weakness for 1.5 years. Examination showed normal vitals, thyroid, muscle and neurologic exam. Results revealed normal TFT, serum K, creatine kinase and decreased amplitude of compound muscle action potential with reduced motor unit recruitment or electrical silence on electromyography. Genetic testing found CACNA1S mutation consistent with hypokalemic PP. He was prescribed eplerenone and acetazolamide with resolution of symptoms for ten years.

Case 3: A 72-year-old male presented with episodes of flaccid paralysis, occurring an hour post-dinner, with serum K 3.2 mmol/L. Symptoms resolved after taking potassium. Examination during the episode showed stage 1 hypertension, proximal muscle weakness and hyporeflexia. Results revealed normal TSH (2.03 μIU/mL) and K (4.3 mmol/L). He continued to perform normal daily activities without any PP symptoms for nine years.

CONCLUSION
Limited information is available regarding the long-term follow up of patients with PP. Our patients illustrate a relatively benign long-term course with appropriate treatment.

PP-T-09

FLEAS AND TICKS: A CASE OF SIMULTANEOUS DIAGNOSIS OF PAPILLARY THYROID CANCER AND SYSTEMIC MASTOCYTOSIS

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BACKGROUND
There is no known association between systemic mastocytosis and thyroid cancer. Here, we report a woman diagnosed with papillary thyroid cancer (PTC) and systemic mastocytosis, simultaneously.

CASE
A 43-year-old female presented with cervical lymphadenopathy for 3 weeks. She denied any fever, night sweats, flushing, or skin rash. CT scan showed bilateral enlarged cervical lymph nodes with bilateral thyroid nodules. Imaging also revealed multiple lytic lesions in her spine and pelvis. On physical examination, she had palpable cervical lymph nodes with a hard left-sided thyroid nodule. Neck ultrasound revealed a 2.1 cm left hypoechoic thyroid nodule with microcalcifications and cervical lymph nodes. Fine needle aspiration of the thyroid nodule and lymph nodes confirmed PTC. The patient underwent total thyroidectomy with neck dissection, histology confirmed classic PTC (pT3N1bM0). Postsurgical serum thyroglobulin was 17.0 ng/mL and I131 scan showed no metabolic activity in the axial skeleton. Subsequent bone marrow biopsy of the pelvic lytic lesions revealed systemic mastocytosis. The patient was treated with intravenous 4 mg zoledronic acid every 3 months with improvement.

PTC is an indolent malignancy with an excellent 10-year survival rate with rare bone metastases (<4%). Systemic mastocytosis is a proliferation of mast cells that has a wide clinical spectrum from indolent disease to mast cell leukemia. The axial skeleton is affected in up to 50-70% of patients. The most common malignancies known to be associated with systemic mastocytosis are melanoma and non-melanoma skin cancers.

In our patient, initial findings of multiple lytic lesions raised concern for thyroid cancer metastasizing to the bones. However, there was no functional radiographic evidence of metastases. correct diagnosis of concurrent systemic mastocytosis required bone biopsy. Our patient is currently doing well with a good prognosis for both conditions.

CONCLUSION
This is the first known case report of a patient being simultaneously diagnosed with PTC and systemic mastocytosis.

PP-T-10

VAN WYCK GRUMBACH SYNDROME INDUCED BY PRIMARY HYPOTHYROIDISM

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BACKGROUND
We should always consider the possibility of partial or complete forms of premature puberty when dealing with primary hypothyroidism, particularly if the hypothyroidism diagnosis is delayed. Conversely, one should always keep in mind the possibility of primary hypothyroidism causing precocious puberty of the peripheral type.

CASE
An 8-year-old female was brought to the endocrine clinic due to short stature. She stands at 110 cm and weighs 31 kg. Her bone age was delayed by more than 2 years. Her TSH and anti-TPO antibodies were elevated. Following therapy with thyroxine 88 mcg daily, she was urgently brought to the clinic by her mother due to vaginal bleeding noted on the 25th day of thyroxine intake. She was noted to have thin-walled ovarian cysts and a thin endometrium on ultrasound indicating a peripheral type of precocious puberty. The serum estradiol and LH levels were in the prepubertal ranges. The parents were reassured and were asked to bring their daughter after 2 months for follow-up.

CONCLUSION
Her peripheral precocious puberty is likely due to the high TSH which can bind to the FSH receptors leading to the formation of thin-walled cysts and subsequent estradiol rise causing threshold bleeding which mimics menarche. The subsequent withdrawal of estradiol due to degenerating cysts may also trigger a random bleed. Unless there is heavy menorrhagia, specific therapy is not needed as the cysts tend to disappear spontaneously.

PP-T-11

CARDIAC TAMPONADE IN MYXEDEMA CRISIS – AN UNCOMMON PRESENTATION OF A RARE ENDOCRINE EMERGENCY

https://doi.org/10.15605/jafes.037.AFES.138

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BACKGROUND

Myxedema crisis is a state of severe hyperthyroidism with end-organ decompensation. Pericardial effusion is an uncommon manifestation of hypothyroidism. As large effusions are rare and typically accumulate slowly, cardiac tamponade rarely occurs. We present a rare case of cardiac tamponade from a large pericardial effusion in a patient with myxedema crisis.

CASE

Our patient was referred to our Endocrinology service for evaluation of severe hypothyroidism. A diagnosis of myxedema crisis was made due to the presence of biochemically-proven severe hypothyroidism {fT4 2.0 pmol/L [normal range (NR) 8-16], fT3 <2 pmol/L (NR 3.5-6), and TSH 82.27 mIU/L (NR 0.45-4.5)}, with features of end-organ decompensation (congestive heart failure, hypotension, bradycardia, and altered mental status). Transthoracic echocardiography revealed a large pericardial effusion with small ventricular size and reduced tricuspid inflow velocity suggestive of a partially compensated tamponade.

The patient received an intravenous thyroxine loading dose of 200 mcg followed by 100mcg daily maintenance doses. Despite improvement of the manifestations of hypothyroidism and normalisation of serum thyroxine levels, she remained persistently hypoxemic and could not be weaned from supplemental oxygen.

Hence, bedside pericardiocentesis was performed with diagnostic and therapeutic intent. Pericardial fluid analysis did not reveal any secondary cause. She demonstrated good clinical improvement post-pericardiocentesis and was eventually discharged.

CONCLUSION

Cardiac tamponade is a life-threatening severe manifestation of myxedema crisis. As pericardiocentesis may be lifesaving, we recommend screening for cardiac tamponade in patients with myxedema crisis who demonstrate poor cardiorespiratory improvement despite adequate thyroid hormone therapy.

PP-T-12

RE-ASSESSMENT OF THE TSH-FREE T4 RELATIONSHIP WITH ELECTROCHEMILUMINESCENCE ASSAY

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OBJECTIVES

In the initial assessment of thyroid function, Thyroid Stimulating Hormone (TSH) is often employed first followed by free T4 (fT4), since small changes in fT4 are accompanied by a much larger change in TSH from the time 3rd-generation TSH assays were introduced in 1990. This inverse TSH-fT4 log-linear relationship has been confirmed with many different assays. Roche Diagnostics, a popular automated immunoassay platform based on electrochemiluminescence, improved the sensitivity of their TSH assay from 0.01 to 0.005 mIU/L in late 2020. We studied the TSH-fT4 relationship with the new Roche assay on their Cobas e601 analyzer.

METHODOLOGY

All samples received from the primary health clinics with requests for both TSH and fT4 in 2021 were retrieved from the Laboratory Information System. Children (<18yo) and pregnant subjects were excluded. Where patients had repeat testing, only the earliest results were included to ensure that the thyroid tests were probably at their stable state. The assay measuring ranges are as follows: TSH 0.005-100 mIU/L and fT4 0.5-100 pmol/L. Statistical analyses were performed using MedCalc Statistical Software v20.106 (Ostend, Belgium).

RESULTS

11369 subjects (Male = 2465, Female = 8904) aged 18-95 years (mean 48.8 ± 17.4) were studied. Excluding TSH values <0.005 and >100 mIU/L from the calculations (n=633), a significant inverse TSH-fT4 log-linear relationship was seen on regression analysis (log TSH = 1.104 - 0.0534 fT4; r = 0.38; p<0.001); TSH 0.006-99.9 mIU/L, fT4 0.88-100 pmol/L.

CONCLUSION

The assay is sensitive to changes in circulating fT4 and affirms the utility of TSH in thyroid function testing.

PP-T-13

UNUSUAL DERMATOLOGICAL MANIFESTATION OF GRAVES' DISEASE IN AFRO-CARIBBEAN PATIENTS

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OBJECTIVES
To describe an unusual skin manifestation of Graves' disease in Afro-Caribbean patients.

METHODOLOGY
Seven patients referred to a private endocrine clinic for management of hyperthyroidism between 2000 and 2021 are described. They all had laboratory confirmation of a thyrotoxic state by demonstration of suppressed TSH and elevated Free T4. Graves' disease was identified as the aetiology by the presence of at least one of the following: exophthalmos, diffuse goitre with bruit, elevated TSH-receptor antibodies or diffuse uptake on a technetium scan. At the time of consultation, the patients were noted to have unusual skin lesions, which were photographed either with their consent (six adult patients) or with the consent of the parent (one child).

RESULTS
The patients ranged in age from 9 to 52 years at the time of presentation. They were of Afro-Caribbean origin. They were all markedly thyrotoxic. They were noted to have skin lesions in areas other than the typical pre-tibial area. The lesions were non-pruritic and non-erythematous and were not in keeping with urticaria. The appearance in each of the patients was similar and was either papular or nodular. Areas involved included the chest, back, forearm, hand and foot, thigh and face. One patient (the first one identified) had biopsy that showed a perivascular lymphocytic infiltrate in the mid-dermis.

CONCLUSION
Nodular dermopathy in areas other than the pre-tibial region should be recognized as a dermatological manifestation of Graves' disease in Afro-Caribbean patients.

PP-T-14

A CASE OF SYNCHRONOUS MALIGNANT STRUMA OVARII AND PAPILLARY THYROID CARCINOMA

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BACKGROUND
We report a female presenting with synchronous malignant struma ovarii and papillary thyroid carcinoma.

In this case study, we reviewed the presentation, evaluation, diagnosis, and management of malignant struma ovarii presenting synchronously with papillary thyroid carcinoma. We also reviewed the differential diagnoses to be considered and approaches in the management of malignant struma ovarii after surgery.

CASE
A 32-year-old Filipino female presented with profuse vaginal bleeding associated with left hypogastric pain. Transvaginal ultrasound revealed 3.09 x 2.99 x 2.73 cm and 4.96 x 4.63 x 3.7 cm cystic masses with solid components on the right and a 6.56 x 6.54 x 4.76 cm complex mass on the left. Her thyroid function tests were normal: FT4 14.65 pmol/L (12-22 pmol/L), FT3 4.57 pmol/L (2.80-7.10 pmol/L), TSH 1.170 iUI/mL (0.27-4.2 iUI/mL). Serum thyroglobulin level was also normal. Her neck ultrasound and PET CT scan were unremarkable. She underwent emergency exploratory laparotomy with bilateral oophorectomy due to ovarian torsion. Histopathology of the right ovarian mass revealed a malignant struma ovarii (papillary thyroid carcinoma) without lymphovascular invasion, while the left ovarian mass was found to be a mature cystic teratoma. She subsequently underwent total thyroidectomy with histopathology revealing papillary thyroid microcarcinoma, infiltrative follicular variant, 0.1 cm in widest diameter, limited to the left lobe. Postoperatively, she underwent radioactive iodine and levothyroxine suppressive therapy.

CONCLUSION
Struma ovarii is a rare type of teratoma with no universally accepted criterion for diagnosis and management. Our case demonstrates that struma ovarii should be suspected in a woman presenting with an ovarian teratoma and should involve a multimodal treatment approach, including surgery, radioactive iodine treatment, and thyroxine therapy.

PP-T-15

GRAVES' DISEASE COMPLICATED BY POST-OPERATIVE GRAVES' OPHTHALMOPATHY AND PRETIBIAL MYXEDEMA

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BACKGROUND
The prevalence of Graves' Ophthalmopathy (GO) and pretibial myxedema is 0.15/10,000. We report a rare case of Graves' disease (GD) with development of GO and pretibial myxedema post-thyroidectomy which improved following treatment with teprotumumab.

CASE
A 51-year-old female presented with tachycardia, heat intolerance, and weight loss. She had undetectable TSH, elevated free T4 (6.1 ng/dL), total T3 (332.4 ng/d), TSI (19.50 IU/L), and TRAb (27 U/L; normal value <1.0 U/L). She denied any eye symptoms and did not have exophthalmos. She has an enlarged, hypervascular thyroid on neck ultrasound. She was treated with atenolol and methimazole to achieve euthyroidism. She eventually elected total thyroidectomy. Within 3 months after thyroidectomy, she developed exophthalmos and pretibial myxedema characterized by hyperpigmentation with the presence of firm papules and scattered coalescent plaques on the anterior aspects of both lower extremities. Skin biopsy confirmed pretibial myxedema. She was treated with teprotumumab with significant improvement of both GO and pretibial myxedema.

CONCLUSION
The occurrence of GO and pretibial myxedema in a patient with GD post-thyroidectomy is uncommon. Pretibial myxedema occurs because of the deposition of glycosaminoglycans (GAG) secreted by fibroblasts which have been found to express thyroid stimulating hormone receptors (TSHR) leading to deposition of mucin in the papillary and reticular dermis. Despite thyroidectomy, the thyroid antibodies themselves may lead to the accumulation of GAG. In fact, thyroidectomy does not affect the course of GO. Pretibial myxedema management depends on the symptomatology. Topical or intralesional glucocorticoids are used to treat symptomatic cases, though there is a 30% chance of recurrence. Teprotumumab has been approved to treat GO and only case reports of its use leading to improvement of pretibial myxedema have been described. More data are needed to determine its efficacy as a treatment option for pretibial myxedema.

PP-T-16

THYROID HEMIAGENESIS ASSOCIATED WITH POSSIBLE HASHIMOTO'S THYROIDITIS IN THE REMAINING LOBE PRESENTING AS LATE-ONSET HYPOTHYROIDISM IN ADULTHOOD

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BACKGROUND
Thyroid hemiagenesis is a very rare abnormality, usually discovered incidentally during the evaluation of unrelated thyroid disorders. In thyroid hemiagenesis, the left lobe tends to be absent with concomitant compensatory enlargement of the opposite lobe. Thyroid hemiagenesis *per se* is typically not associated with hypothyroidism. Here, we present an unusual case of thyroid hemiagenesis associated with possible Hashimoto's thyroiditis.

CASE
A 36-year-old Thai female with no known underlying disease presented with fatigue, chills, and weight gain for 6 months. She was given levothyroxine 75 µg/day based on results of her thyroid function tests at the previous hospital. However, her symptoms persisted. She denied family history of thyroid disorders and had no history of neck radiation. Initial blood tests at our hospital showed subclinical hypothyroidism (slightly elevated TSH level at 4.86 mIU/L; reference range 0.27-4.20 mIU/L) with negative thyroid auto-antibodies. Physical examination showed nonpalpable thyroid gland.

Her thyroid ultrasound revealed absent left thyroid lobe and atrophic right thyroid lobe with heterogeneous echotexture, compatible with possible Hashimoto's thyroiditis. FNA was no longer done to confirm the Hashimoto's thyroiditis. Levothyroxine was increased to 100 µg/day to keep her TSH level in the mid-normal range. During a 3-year follow-up period, the patient remains in a stable condition.

CONCLUSION
Thyroid ultrasonography should be performed in all patients with spontaneous hypothyroidism. Individuals with thyroid hemiagenesis are prone to develop additional thyroid pathologies. Close monitoring is required to detect concomitant disorders.

PP-T-17

PROPORTION AND FACTORS ASSOCIATED WITH THYROID DYSFUNCTION AMONG INDIVIDUALS REFERRED TO A TERTIARY CARE FACILITY IN KABUL, AFGHANISTAN

https://doi.org/10.15605/jafes.037.AFES.144

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OBJECTIVES
We aimed to determine the proportion and identify factors associated with thyroid dysfunction among individuals coming to a tertiary care facility in Kabul, Afghanistan.

METHODOLOGY
A cross-sectional study design was conducted from July to September 2018. Serum TSH levels were measured, and the patients were divided into three diagnostic categories according to their serum TSH concentrations: 1) Hypothyroidism 2) Hyperthyroidism 3) Normal thyroid function.

RESULTS
A total of 127 individuals were included. Majority of the study participants (77%) were females. Most of the participants (92%) did not have family history of thyroid dysfunction and majority of the female participants, (85%) were not pregnant in the last two years. Furthermore, 98% of participants were non-smokers.

CONCLUSION
The findings of the current study showed a high prevalence of thyroid dysfunction in individuals coming to FMIC for thyroid functions tests. The findings also indicated that age and smoking are the factors associated with thyroid dysfunction.

PP-T-18

TOWARDS EXCELLENCE IN THYROID SERVICE: AN ACCREDITED THYROID HOSPITAL

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OBJECTIVES
We described our experience at Theptarin, the first hospital in Thailand to achieve an accreditation in thyroid service from Thailand Healthcare Accreditation Institute in 2021.

METHODOLOGY
Our infrastructure fit the criteria of specific disease accreditation. The important components were availability of thyroidologists and multidisciplinary specialists in related fields, a large volume of patients with long-term follow-up, supporting facilities which include surgery and radioactive iodine ablation.

Key Performance Indexes (KPI) and evidence-based Clinical Practice Guidelines (CPG) for 3 common thyroid disorders (Graves' disease, thyroid nodule, and differentiated thyroid cancer) were created. Patient service was redesigned to be patient-centered and lean. Educational activities were organized for both healthcare professionals and the public. Patients' satisfaction was assessed. Research activities were also committed.

RESULTS
KPIs were set for 16 indicators. The consensus was reached for 7 CPG's. There were 12,150 visits by patients with thyroid disorders in 2021. The follow-up rate increased from 88.6% in 2019 to 98.5% in 2021. The rate of ultrasonography increased in patients with thyroid nodules (94.4% in 2019 to 98.5% in 2021). In patients with thyroid cancer, neither permanent hypoparathyroidism nor permanent recurrent laryngeal nerve injury occurred after surgery. Patients reported 86.9% satisfaction in 2021. Posters were displayed on world thyroid day and a multidisciplinary thyroid conference was organized. Eight researches in thyroid disorders were published in 2020-2021.

CONCLUSION
Accreditation for thyroid service is a testimony of excellence in patient care. It also serves as a model and set the stage for continuous improvement in outcome and safety of patient care.

PP-T-19

MYXEDEMA COMA AS AN EARLY MANIFESTATION OF HASHIMOTO'S THYROIDITIS: A CASE REPORT

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BACKGROUND
Myxedema coma is a rare, life-threatening endocrine emergency with a high mortality rate that needs early recognition and proper treatment. Most often, this condition can be found in patients with Hashimoto's thyroiditis or after total thyroidectomy.

CASE
A 39-year-old female was brought to Emergency Department due to delirium and general weakness. Upon examination, edema, weight gain, dry skin and amenorrhea were also present.

There was no history of thyroid disorders. She had hypotension, bradypnea, bradycardia, and was eventually intubated. Laboratory values included TSH 73.17 IU/L, T4 <10.23 nmol/L and anti-TPO 284 IU/mL. A diagnosis of myxedema coma and Hashimoto's thyroiditis was established, and the patient was treated with levothyroxine and hydrocortisone. Her condition rapidly stabilized.

The estimated incidence rate of myxedema coma is 0.22 per million people per year. It is 10 times more common in women. Clinical symptoms include altered mental status, hypothermia, bradycardia, hypotension, and hypoventilation. Physical findings may show a myxedematous facies, which is characterized by generalized puffiness, macroglossia, and a coarse facial appearance. Thyroid hormone measurement clinches the diagnosis. Popovenioic and Chiong also developed a scoring system to help diagnose it. The mortality rate may be as high as 20-60%. Protocols with high doses of thyroid hormone and supportive measures may improve the prognosis.

CONCLUSION
This case highlights that myxedema coma not only occurs in patients with a prior medical history of thyroid disease but can also be a first manifestation of hypothyroidism.

PP-T-20

PREDICTIVE FACTORS FOR RECURRENT GRAVES' DISEASE AFTER TREATMENT WITH HIGH FIXED-DOSE RADIOACTIVE IODINE THERAPY

https://doi.org/10.15605/jafes.037.AFES.147

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OBJECTIVES
Failure rates of radioactive iodine (RAI) for treatment of Graves' disease range from 10% to 40% depending on the region, patient characteristics and other factors. The purpose of this study was to investigate the predictive factors for RAI failure after treatment of Graves' hyperthyroidism with fixed-dose RAI.

METHODOLOGY
Ninety-six patients with Graves' disease who received 10 mCi or higher doses of RAI after failure of initial anti-thyroid drug (ATD) treatment with either propylthiouracil (PTU) or methimazole (Tapazole), were enrolled in this study. All patients had typical clinical presentation. RAI treatment was considered successful which euthyroidism or hypothyroidism was found after 1-year follow-up, without anti-thyroid drug usage.

RESULTS
The success rate of RAI therapy was 68% (65 out of 96 patients), while the failure rate was 32% (32 of total 96 patients). There was no significant difference between the success and failure groups regarding age, gender, thyroid functional status, and TSH receptor antibody. On the other hand, the failure group had a younger age at initial diagnosis, longer disease duration, and larger thyroid volume (all $p < 0.05$). In addition, we noticed that patients on PTU before RAI had a significantly higher failure rate (9 out of 15, 60%) than those on methimazole (22 out of 80, 28%).

CONCLUSIONS
We found age at diagnosis, duration of Graves' disease, and thyroid volume as significant factors affecting the outcome of RAI treatment, which were consistent with observations of previous studies. Our study showed that treatment with PTU prior to RAI led to a significantly higher failure rate than treatment with methimazole.

PP-T-21

EVALUATING THE KINETICS OF SODIUM-IODIDE SYMPORTER UPREGULATION IN RE-DIFFERENTIATION THERAPY CLINICAL TRIAL FOR ADVANCED THYROID CANCER

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OBJECTIVES
MAPK hyperactivation, such as via BRAFV600E mutation, is commonly detected in radioactive iodine (RAI)-refractory thyroid cancers with suppression of sodium-iodide symporter (NIS). We hypothesize that short treatment course with MAPK blockade could suffice in upregulating NIS, while sustained 4-6 weeks treatment in current regimens could predispose to resistance.

METHODOLOGY
We conducted a phase II trial using BRAF and MEK inhibitors, dabrafenib and trametinib (DT) to examine the kinetics of NIS upregulation in RAI-refractory thyroid cancer with MAPK signaling pathway mutation. Iodide uptake was assessed using I-124 PET-CT scan at baseline, after 1-2 weeks and 4 weeks of DT. If there was adequate iodide retention, RAI was administered.

The primary outcome was the proportion of patients attaining tumour lesional dosimetry of ≥20 Gy with I-131 dose of ≤300 mCi. Secondary outcomes included safety, response rate, progression-free survival, and thyroglobulin response.

This research has been approved by an ethics committee.

RESULTS
Seven patients with activating BRAF and RAS mutations were recruited. Five out of 7 patients (71%) attained iodine uptake: 2 after 1-2 weeks, 3 after 4 weeks of DT. Adverse event (AE) was seen in 6 out of 7 patients (86%). Most had grade 1-2 AE, except 2 with grade 3 AE (neutropenia, severe lethargy). At 6-month time point, 80% (4/5) had thyroglobulin reduction, and 5 patients had repeat scan; 3 had partial response (60%).

CONCLUSION
In our patients who responded to re-differentiation therapy, 40% responded with only 1-2 weeks of DT. Identification of early response predictors could guide treatment duration.

PP-T-22

VALIDATION AND CULTURAL ADAPTATION OF THYPRO (THYROID PATIENT REPORTED OUTCOME) QUESTIONNAIRE IN *BAHASA* (INDONESIAN LANGUAGE): A PRELIMINARY STUDY

https://doi.org/10.15605/jafes.037.AFES.149

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OBJECTIVES
The Thyroid Patient Reported Outcome (ThyPRO) questionnaire is a specific tool to assess health-related quality of life of patients with thyroid diseases. The aim of this study is to determine the validity and reliability of ThyPRO questionnaire among patients with Graves' disease in *Bahasa* (Indonesian language).

METHODOLOGY
This is a preliminary study among patients with Graves' disease in Cipto Mangunkusumo Hospital, a national referral hospital in Jakarta, Indonesia. After a systematic two-way translation process, the questionnaire was adapted and culturally validated. Internal reliabilities of the ThyPRO scales were assessed using Cronbach's α coefficient.

RESULTS
Twenty patients with Graves' disease completed the questionnaire process. Internal consistency and reliability of the ThyPRO scales were good. Test-retest reliability was done by calculating intraclass correlation coefficient (ICC) for each of the items and domains of the ThyPRO questionnaire. The ICC was moderate (ICC between 0.5 – 0.75) and reliability was good (ICC score >0.75).

CONCLUSION
The ThyPRO may be a useful, valid, and reliable tool for measuring health-related quality of life among patients with Graves' disease in Indonesia.

A MALE WITH GRAVES' DISEASE AND PAPILLARY THYROID CANCER WITHIN A THYROGLOSSAL DUCT CYST

https://doi.org/10.15605/jafes.037.AFES.150

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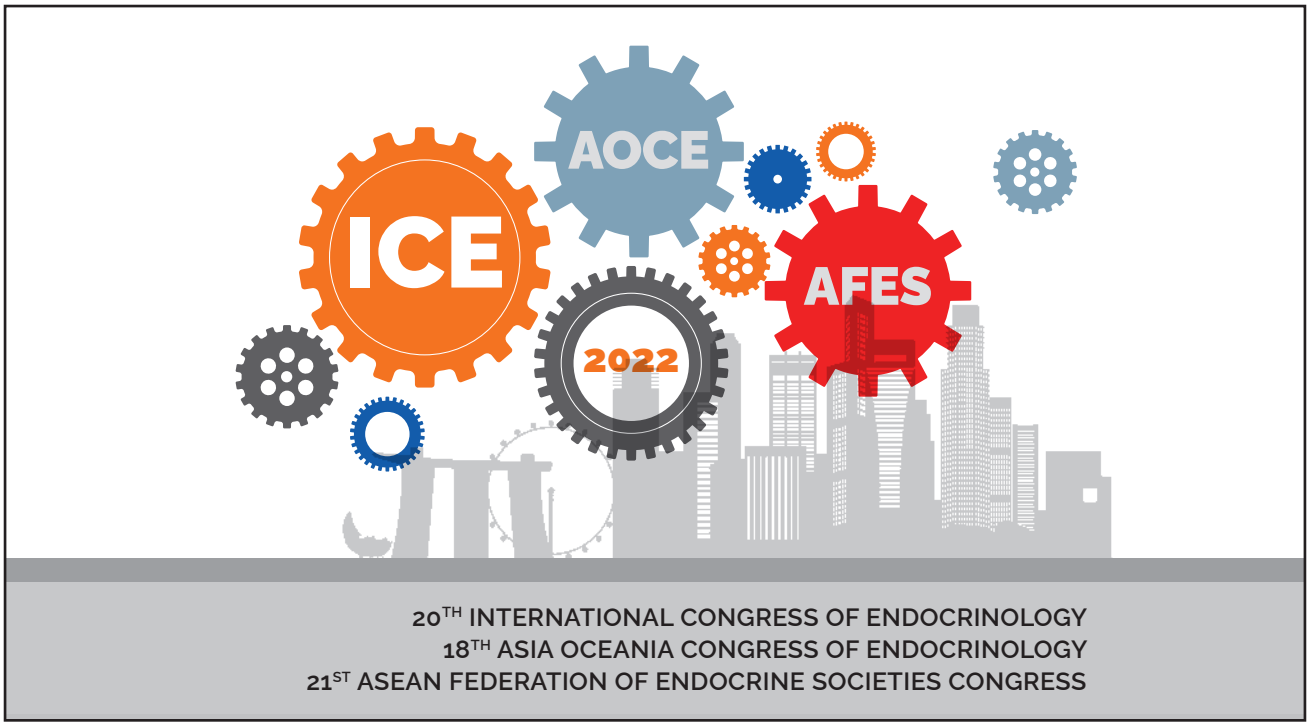
BACKGROUND

Malignancy within a thyroglossal duct cyst is infrequent, accounting for only 0.7 to 1% of thyroglossal duct cysts. It predominantly occurs in women. Majority are euthyroid, though some may have associated Hashimoto's thyroiditis.

CASE

A 42-year-old male presented with a 5-year history of a large anterior neck mass. He was previously diagnosed with Graves' disease and thyroid orbitopathy. Neck ultrasound showed a right submandibular mixed tumor measuring 36 x 30 mm with nonspecific lateral cervical lymph nodes and multiple mixed oval images with well-defined borders measuring less than 13 mm in diameter. He has moderate quiescent orbitopathy on ophthalmologic exam. He received treatment with high doses of methimazole and lithium carbonate for severe hyperthyroidism with difficult stabilization. Sistrunk surgery and total thyroidectomy were eventually performed. Histology report showed a 1.5 cm papillary thyroid carcinoma within a thyroglossal duct cyst.

In the literature we reviewed, there has been no other case involving a papillary thyroid carcinoma in a thyroglossal cyst with concomitant Graves' disease. Due to the low frequency of papillary thyroid carcinoma in a thyroglossal duct cyst, consensus has not been reached regarding the most appropriate treatment and follow-up. The management approach is currently based on the existing guidelines for differentiated thyroid cancer, with Sistrunk surgery and total thyroidectomy as the most appropriate initial treatment.



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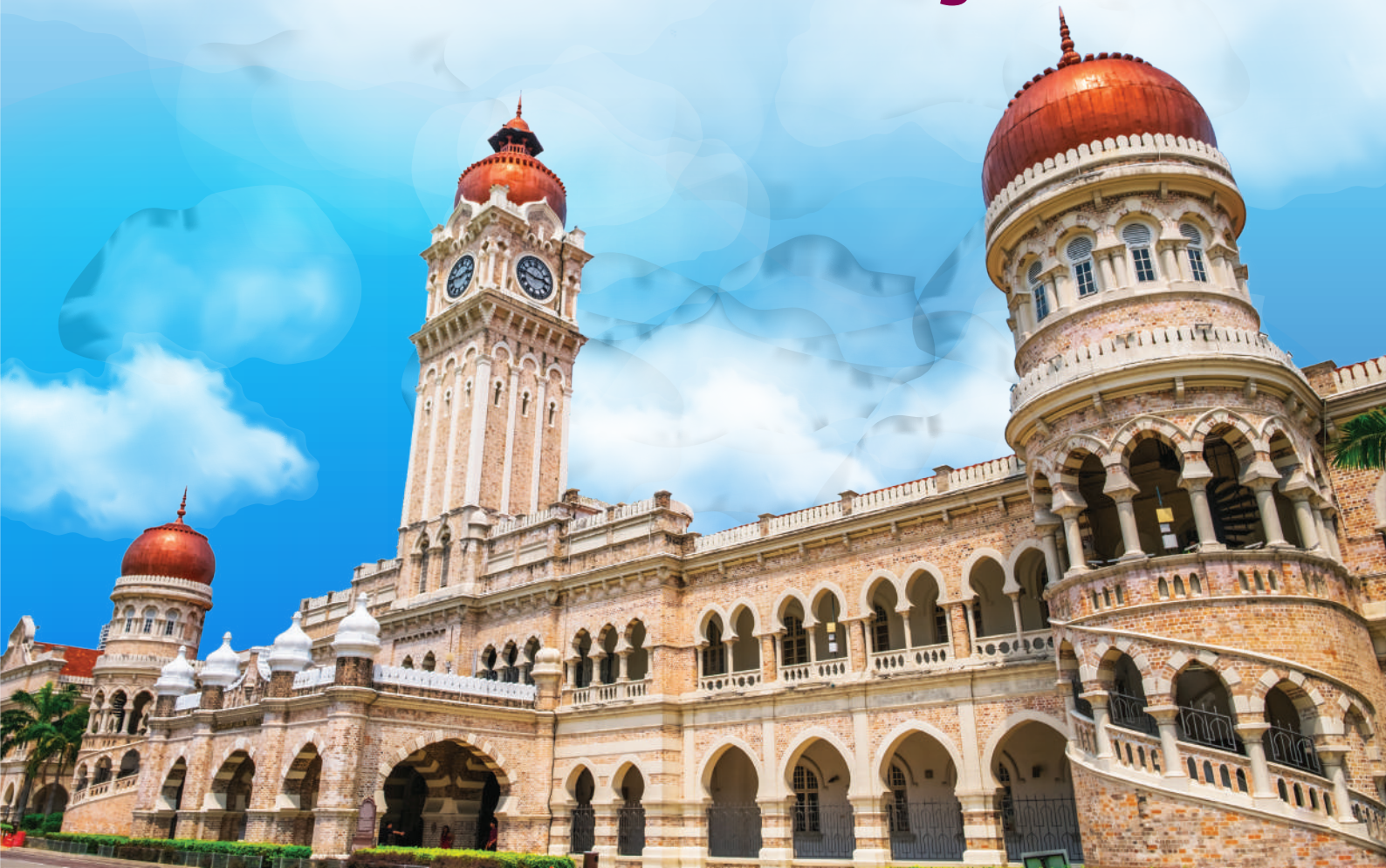

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