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A 2 cm plantar tumour causing severe systemic osteomalacia: a case of tumour-induced hypophosphataemia

Category: Clinical-Endocrinology

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Introduction: Tumour-induced osteomalacia (TIO) is a rare paraneoplastic disorder caused by fibroblast growth factor 23 (FGF23)–secreting mesenchymal tumours, leading to renal phosphate wasting, impaired skeletal mineralisation, and progressive osteomalacia. Delayed recognition of persistent hypophosphataemia may result in profound and irreversible skeletal morbidity.

History and Examination Findings: A 58-year-old man presented with a five-year history of progressive bone pain, multiple atraumatic fractures with a left femur fracture warranting hip arthroplasty, significant height loss, and worsening skeletal deformity. He had been evaluated across multiple services prior to referral. Examination revealed marked kyphosis, severe chest wall deformity with exertional dyspnoea and reduced effort tolerance resulting in restrictive chest wall mechanics (FVC 42%, FEV1 42%, DLCO 62%). A well-circumscribed 2 cm mass was palpable beneath the right first metatarsophalangeal joint.

Investigations: Biochemistry demonstrated persistent hypophosphataemia, serum phosphate 0.44 mmol/L (0.78–1.42), elevated alkaline phosphatase 307 U/L (42-98), normal serum calcium 2.45 mmol/L (2.15–2.5), and elevated parathyroid hormone 10.8 pmol/L (1.6–6.9). Twenty-four-hour urinary phosphate excretion was inappropriately normal 20.64 mmol/24 h, with reduced tubular maximum phosphate reabsorption (TmP/GFR: 0.42 (0.9–1.35), consistent with renal phosphate wasting. A hereditary cause was excluded on genetic testing. Serum FGF23 measurement was unavailable.

Spinal imaging demonstrated multilevel vertebral compression fractures (T12-L4) with vertebral height loss, bilateral fractures of the pelvic girdle, ischium and bilateral pubic bones with diffuse cortical thinning and demineralisation. MRI of the right foot identified a 2 cm non-enhancing subcutaneous fibrous lesion at the medial plantar surface beneath the first metatarsophalangeal joint with fractures of the first four metatarsals, first proximal phalanx, distal fibula and right calcaneus. The lesion was surgically excised, and histopathological examination demonstrated features compatible with a phosphaturic mesenchymal tumour. Postoperatively, serum phosphate improved to 0.62 mmol/L within two months, with improved renal phosphate wasting.

Conclusion: This case illustrates the severe systemic and respiratory consequences of prolonged, unrecognised hypophosphataemia caused by a small FGF23-secreting tumour. Early recognition is critical to prevent irreversible skeletal and respiratory morbidity. In TIO, biochemical correction is usually rapid after complete resection. Failure of phosphate normalisation should prompt consideration of residual or occult FGF23-secreting disease and warrants ongoing follow-up.

Maternal microRNAs as predictors of infant birth weight in a South African population

Category: Basic Science

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Background: Low (LBW, 4,000 g) birth weight are associated with increased perinatal complications and long-term risk of non-communicable diseases. Maternal circulating microRNAs are promising biomarkers of pregnancy outcomes. This study investigated maternal circulating microRNAs as predictors of infant birth weight among pregnant women in Soweto, South Africa.

Methods: MiRNAs associated with birth weight were identified using a dual approach. First, miRNAs were isolated from serum samples of age- and body mass index (BMI)-matched pregnant women at 28 weeks of gestation and profiled using LNA miRNOME PCR panels containing 179 unique miRNAs (HBW: $n = 5$; LBW: $n = 9$; appropriate birth weight [ABW]: $n = 10$). Second, a scoping review of the literature was conducted by searching Scopus, Web of Science, and MEDLINE/PubMed to identify maternal miRNAs previously reported to be associated with birth weight.

Results: LNA-based miRNome profiling using global Ct normalisation identified 25 differentially expressed miRNAs in mothers of LBW infants and 16 in mothers of HBW infants compared with ABW controls (≥ 2-fold change, $p \le 0.05$). In contrast, normalisation using GeNorm identified three differentially expressed miRNAs in the LBW group and nine in the HBW group compared with ABW. One miRNA in the LBW group and seven in the HBW group were consistently differentially expressed across both normalisation strategies. The scoping review identified 453 articles, of which 25 met the inclusion criteria. Eleven miRNAs, miR-16-5p, miR-17, miR-18a, miR-20b-5p, miR-21, miR-92a, miR-127-3p, miR-143-3p, miR-181a-5p, miR-221-3p and miR-520a-5p, were reported to be associated with birth weight outcomes. Of these, two studies reported downregulation of miR-18a in HBW compared with ABW, while miR-181a-5p was consistently associated with LBW. There was no overlap between the differentially expressed miRNAs identified in the miRNome profiling panels and those reported in the scoping review.

Conclusion: Differential miRNA expression was observed in mothers of LBW and HBW infants; however, findings varied by normalisation method and did not overlap with previously published literature. These results highlight population- and method-specific variability and the need for further validation. Current ongoing studies in a larger cohort will evaluate the potential of these miRNAs to serve as predictive biomarkers for adverse birth weight outcomes.

Oestrogen receptor alpha binding and drug interaction risk of aspalathin and nothofagin isolated from rooibos (*Aspalathus linearis*), with selective oestrogen receptor modulator therapy (SERM)

Category: Basic Science

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Background: Rooibos (*Aspalathus linearis*) tea is consumed daily by millions of South Africans, including patients on hormonal therapy such as selective oestrogen receptor modulator (SERM). Its two exclusive compounds, aspalathin and nothofagin, have been shown to have various effects, such as anti-inflammatory and antioxidant properties, but their phytoestrogenic effects via oestrogen receptor alpha (ERα) signalling remain poorly explored. This study aimed to determine the oestrogen receptor alpha (ERα) pharmacokinetic properties, binding affinity and potential interaction risk of aspalathin and nothofagin to interfere with SERM therapy.

Methods: The pharmacokinetic properties of aspalathin and nothofagin were determined with SwissADME and ProTox-3.0. The binding affinity to ERα was established with Schrödinger Maestro 13.6 suites. LigPrep was used to prepare the ligands (aspalathin, nothofagin, oestradiol and tamoxifen; www.pubchem.org), protein preparation wizard was used to prepare the 3D structure of ERα (PDBID:1A52, www.rcsb.org), and Glide was used for molecular docking analysis.

Results: Aspalathin showed a stronger binding affinity for ERα (-9.86 kcal/mol) compared with nothofagin (-8.73 kcal/mol). However, the reference compounds oestradiol and tamoxifen showed a higher binding affinity of -11.02 kcal/mol and -10.33 kcal/mol, respectively. Furthermore, although predicted LD50 of 2000 mg/kg for aspalathin and 1500 mg/kg for nothofagin, suggest low acute toxicity, their pharmacokinetic properties indicate low gastrointestinal absorption and low oral bioavailability.

Conclusion: These data suggest that oral consumption of rooibos is unlikely to affect efficacy of SERM therapy. Thus, since published mechanisms of action of rooibos suggest that it may contribute to management of known side-effects of SERMs, such joint pain, weight gain, fatigue and stroke - in addition to its well-established benefits in terms of inflammatory and oxidative stress outcome - we recommend the consumption of rooibos as a safe complimentary modality in SERM therapy.

Identification of a novel ChAT missense variant in a South African woman with gestational diabetes mellitus

Category: Basic Science

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Background: Gestational diabetes mellitus (GDM) is the most common metabolic complication of pregnancy and confers a substantial lifetime risk of type 2 diabetes. Despite its rising prevalence in Africa, the genetic contribution to GDM remains underexplored. Choline acetyltransferase (ChAT), a key enzyme in acetylcholine synthesis, plays a regulatory role in insulin secretion and glucose homeostasis. We hypothesised that deleterious variants in ChAT may contribute to GDM susceptibility in African populations.

Methods/History and Examination Findings: Placental DNA from 12 women diagnosed with GDM and 10 ethnically matched normoglycaemic controls was analysed. The protein-coding regions of ChAT were amplified and sequenced using Sanger sequencing. Variants were annotated using Ensembl VEP, gnomAD, RegulomeDB, CADD, PolyPhen2, and additional in silico prediction tools. Structural modelling was performed using the human ChAT crystal structure (PDB: 7AMD).

Results: We identified a novel heterozygous missense variant in exon 8 of ChAT (c.1213C > G; p.Leu405Val) in one GDM patient. The variant was absent in controls and not reported in gnomAD. In silico analyses suggest potential functional relevance, supported by gene constraint metrics indicating intolerance to loss-of-function and missense variation. Regulatory annotation demonstrated localisation within an epigenetically active region, including DNase hypersensitivity peaks in the placenta. Structural modelling did not predict major conformational disruption but suggested possible subtle functional effects.

Conclusion: This study reports the first investigation of ChAT in GDM in an African cohort and identifies a novel rare variant that may act as a disease modifier. These findings support further large-scale genomic and functional studies to elucidate the contributions of cholinergic pathways to GDM pathophysiology and to precision risk stratification in African populations.

Effects of endotoxin immune toleraised and polarised macrophage secretome in Serum Free - versus FBS containing Media on collagen production in wound healing

Category: Basic Science

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Background: Non-healing diabetic wounds are the leading cause of lower limb amputations globally. Dysregulation of pro-resolving mediators and failure of macrophages (M1) to switch towards a pro-regenerative (M2) phenotype causes persistent inflammation and lack of progression through the phases of healing. There are currently no effective treatments available. We previously demonstrated the effectiveness of combined tolerisation (Tol) and polarisation (Pol) of macrophage (MΦ) conditioned media (cultured in FBS) in improving collagen deposition, cell infiltration and displaying signs of angiogenesis in a diabetic mouse wound model. The focus of this study is adapting the Tol/Pol M2Φ CM therapy for use in humans by culturing these cells in Serum Free Media (SFM) instead of Foetal Bovine Serum (FBS) and validating its reproducibility.

Methods: THP-1 monocytic cells, initially cultured in standard growth media (GM, 10% FBS), were serially adapted to SFM (GM, 5% CTS serum replacement media) at confluence. The SFM adapted cells then underwent 1) M1Φ polarisation (10 ng/ml GMCSF, 1 week), followed by 2) M2Φ polarisation (10 ng/ml IL4, 24h) and final treatment group consisted of 3) Tolerised (100 ng/ml PamC3SK, 48h) and Polarised (10 ng/ml IL4, 24h) M2Φ (Tol/Pol M2Φ). Parallel GM experiments were conducted. Conditioned media (CM) collected was analysed via ELISA and multiplex (paracrine effect), fibroblast migration (scratch assay) and hydroxyproline production.

Results: Cells adapted well to SFM with significantly higher population doubling time (2.12 days) compared to GM cells (1.78 days). Although no differences in growth factor, chemokine, pro-inflammatory and interleukin expression was seen between treatments in GM and SFM, the Tol/Pol M2Φ showed increased TGF-β1, TGF-β2, MCP-1 and IL8 within the GM group. The Tol/Pol M2Φ CM in the SFM group displayed increased hydroxyproline, MMP-9, TIMP-1 and TIMP-2 expression which all play significant roles in collagen deposition.

Conclusion: Both SFM and GM Tol/Pol M2Φ CM treatments show increased expression of components promoting collagen deposition i.e increased hydroxyproline, MMP-9, TIMP-1 and TIMP-2 for SFM and, increased TGF-β1 and TGF-β2 for GM. Adapting this optimised therapy to SFM advances it towards clinical use for treatment of DFUs. Further analysis is needed to characterise and confirm the efficiency of the treatment in SFM.

Improving in vitro predictability using advanced cell culture models

Category: Basic Science

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Background: New approach methods (NAMs) are transforming the research landscape by rapidly improving the interspecies translatability of in vitro findings to humans; these include advanced cell/tissue-based methods, in silico modelling, organ-on-a-chip technology, omics technologies and, of course, artificial intelligence (AI). Advanced cell culture techniques provide researchers with sophisticated tools to replicate complex cellular processes and mimic physiological conditions and are useful in investigating public health priorities in communicable and non-communicable diseases, and the intersections thereof.

Methods: Both the predictive toxicology and pancreatic beta cell spheroid models were developed using the Celvivo ClinostarTM that allows for the creation of a microgravitational culture environment that facilitates the long-term (minimum 30 days) culture of the respective cells. For both models, viability was assessed using the ATP assay, and size morphometry was measured at defined time points. Glucose utilisation was also monitored over the course of the culture period. For the hepatic spheroids, HepG2-derived C3A cells were used and urea and cholesterol production was monitored. For the beta cell spheroid model, INS1E cells were used and insulin secretion was used as the key performance indicator. Cellular architecture was analysed using transmission electron microscopy.

Results: Both spheroid models were successfully established and shown to more closely mimic in vivo conditions than their conventional counterparts. Cellular turnover was reduced as spheroids reached days 18–23 and the constructs became more functional in nature, while still maintaining adequate glucose utilisation profiles. Cellular architecture reflected some tissue-like characteristics, including deposition of extracellular matrix as well as the presence of tight junction proteins.

Conclusion: Each of these models play a prominent role in understanding pathophysiology associated with diabetes and related metabolic disorders/diseases, and demonstrates the potential for more physiologically relevant in vitro models in pre-clinical testing. Both models will also provide valuable insights into drug efficacy, mechanism of action(s) and toxicological profiling.

Online nutritional disclosure of alcoholic beverages in South Africa is predominantly limited to alcohol by volume, with key nutrients omitted

Category: Clinical - Other

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Background: Excessive alcohol consumption is a risk factor for obesity due to its high energy content and effects on fat metabolism. However, alcoholic beverages in South Africa, and many other countries, are not required to disclose nutritional information other than alcohol by volume (ABV), limiting consumer awareness of energy and sugar intake.

Methods: This cross-sectional study is the first to assess the extent of online nutritional information disclosure for alcoholic beverages in South Africa. All data were collected between April and September 2025. Alcoholic beverages were identified from the top five retailers (based on market share). A total of 3 435 unique alcoholic products were analysed across six groups: beers, ready-to-drink beverages

(RTDs), red wines, white wines, sparkling wines and rosés, and spirits. Nutritional information was extracted from official brand websites, and a disclosure score was assigned based on nutrients reported. Data were analysed using chi-square and Kruskal–Wallis tests.

Results: Most beverages disclosed ABV (83.3%), while sugar was reported for only 33.0% and only <3% for other nutrients. Beers demonstrated the widest disclosure variability (median score = 1, IQR = 1–6), whereas RTDs scored the lowest (median = 1, IQR = 1–1), despite having the highest sugar (median = 5.65 g/100 ml, IQR = 3.28–7.28). Only 3.0% of all beverages included an ingredient list.

Conclusion: In conclusion, most alcoholic beverages sold in South Africa predominately disclose ABV and often omit disclosure of other key nutrients. These findings highlight an urgent need for regulatory reform mandating nutritional information disclosure for alcoholic beverages to support informed consumer choices and reduce risk of obesity-related diseases.

Exploring in utero exposure to teratogens in the development of risk susceptibility in adolescents from rural and urban low-income settings: a comparison study

Category: Basic Science

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Background: The rising prevalence of obesity, prediabetes and dyslipidaemia in adolescents exposed to nicotine and alcohol during pregnancy, particularly in low-income settings, is concerning. Comparisons between rural and urban settings and the clustering and prediction of cardiometabolic risk require further investigation. This study aimed to develop a predictive model for early identification and intervention among adolescents from rural and urban low-income settings exposed in utero to teratogens and presenting with obesity and/or dyslipidaemia and dysglycaemia.

Methods: We conducted a cross-sectional analytic sub-study of 92 adolescents participating in an ongoing cohort in the Western Cape, South Africa. Predictors included sociodemographic factors (age, sex), behavioural risk factors (tobacco, alcohol, physical activity, diet), and clinical measures (BMI, waist circumference, blood pressure, fasting blood glucose and HbA1C, lipid profile). Data was collected through questionnaires and clinical assessments. Dependent variables were BMI, waist circumference, skinfold thickness, lipid profile, and fasting blood glucose. Independent variables included prenatal exposures, diet, and physical activity, with sex and puberty as control variables. Multivariable logistic regression identified predictors of cardiometabolic risk, and prediction modelling assessed discriminative performance.

Results: Participants were equally urban and rural, mean age 12.2 years (SD 1.9), 55% female. In utero exposures: maternal smoking 68%, maternal alcohol 42% (overlap 38%). Prevalence: obesity 18% (95% CI 14–22%), dyslipidaemia 15% (13–18%), combined 10%. Obesity was significantly higher in urban settings. Independent predictors of the composite outcome included maternal smoking (AOR 2.2, 95% CI 1.7–2.9, $p = 0.004$), maternal alcohol (AOR 1.6, 95% CI 1.1–2.4, $p = 0.02$), low physical activity (AOR 2.2, 95% CI 1.5–3.3), poor diet (AOR 1.9, 95% CI 1.3–2.8), and low SES (AOR 1.5, 95% CI 1.0–2.2). The predictive model showed good discrimination (AUC 0.89, Sensitivity = 95.24 %, Specificity = 71.43 %).

Conclusion: Key prenatal and modifiable lifestyle factors predict adolescent cardiometabolic risk. The predictive model demonstrated good discrimination and calibration, supporting its potential for targeted prevention strategies.

Rapid review of Gender-affirming Healthcare for children and adolescents: evidence synthesis (2021–2025) and recommendations for South Africa

Category: Clinical – Endocrinology

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Background: The global evidence base on Gender-affirming Healthcare (GAHC) has expanded rapidly since the publication of the South African HIV Clinicians Society Gender-affirming Healthcare Guideline in 2021. An updated, locally grounded, evidence-informed assessment of health outcomes associated with GAHC for transgender and gender-diverse (TGD) young people will support South African stakeholders in their work. A rapid review synthesised the empirical evidence (January 2021–August 2025) across psychosocial, endocrine, surgical, policy, and non-medical gender-affirming interventions for TGD youth under 18, with attention to South Africa's social, legal, and health-system context. The focus of this presentation will be the endocrine findings.

Methods: A rapid review approach balanced rigour with timeliness. Searches were conducted across 12 databases, supplemented by targeted searches for recent systematic reviews, with date limits set to capture records indexed between 2021-01-01 to 2025-12-31. Eligible reports included peer-reviewed primary studies that reported outcomes of psychosocial, endocrine, surgical, non-medical, or policy/legal interventions involving TGD youth under 18 with $N \geq 5$. Systematic and grey-literature reviews with reproducible search protocols were included. Commentaries, opinion pieces, editorials, case series with $N < 5$, reviews lacking reproducible search strategies, and studies without intervention-related outcomes for TGD youth < 18 were excluded. Findings were synthesised narratively by intervention domain.

Results: Between 2021 and 2025, 117 original journal articles, 17 systematic reviews in academic journals and four grey literature reviews examined endocrine interventions for TGD adolescents. All reviews noted methodological constraints common in pediatric research with small populations and emphasised the need for larger, longer-term prospective studies. GnRHa and GAHT produce expected and desired physiological outcomes. Bone mineral density (BMD) reductions on GnRHa are largely transient and BMD increases after discontinuation of GnRHa or initiation of GAHT. Adolescents receiving endocrine care report high treatment satisfaction, and very low rates of regret. Mental-health outcomes are broadly stable or improved, while barriers to accessing GAHC are linked to poorer mental health outcomes.

Conclusion: Although the evidence base should improve and expand, the current evidence indicates that GAHC for TGD youth improves wellbeing, prevents harm, and supports healthier developmental and mental-health trajectories when delivered within supportive and affirming environments.

Gangrenous Digitis: is auto-amputation a viable primary management strategy in high risk diabetic foot disease in low-resourced countries?

Category: Clinical – Diabetes

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Background: ***Introduction:*** Diabetes mellitus is the most common cause of a lower limb amputation (LLA) worldwide. More than 1 million LLA's are performed on people with diabetes each year. For gangrene, surgical intervention remains the preferred treatment method; however, this may lead to longer hospital stays, increased deaths, and reduced rehabilitation, all of which places a fiscal burden on low-resourced countries. In select candidates with dry gangrene, auto-amputation of digits could be considered. This case highlights the management of an auto-amputation as an outpatient.

Methods: ***History and Examination Findings:*** The patient is a 36-year-old man with a family history of diabetes and is a smoker of 10 cigarettes per day for the past 12 years. He was diagnosed with diabetes at Groote Schuur Hospital when he presented with sepsis of the 4th and 5th digits of the right foot (RF). At that time his HbA1C was 13.2% and he was initiated on a basal bolus insulin regimen for diabetes control in-hospital. He had a RF toectomy, but 4 months later there was a need for progression to a transmetatarsal amputation (TMA) due to wet gangrene. He presented again after 5 months with swelling, an open wound and distal edge dark purple discolouration of the 3rd digit of the contralateral limb, this time as an outpatient. Due to his history and previous surgical amputations, it was decided to facilitate auto-amputation.

Results: ***Management:*** Initially, an antimicrobial dressing (Actisorb 220 Ag) and a moisture control dressing (Drawtex) was applied to the wound, in order to facilitate auto-amputation. After 2 days, the wound was significantly less swollen, there was no sign of infection, and there was a clearly demarcated area proximal to the intermediate phalanx. The same dressings were reapplied with changes every 7 days. Auto-amputation of the distal 3rd digit was successfully achieved after 2 months.

Conclusion: Digital auto-amputation could be considered as a primary management strategy in select patients as it is fiscally viable for low-resourced countries and it prevents additional trauma to patient and limb.

Proteomic analysis of healed and non-healed diabetic wounds

Category: Basic Science

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Background: Non-healing diabetic wounds remain a major clinical challenge due to the complex pathophysiology of diabetes mellitus (DM). We previously evaluated anti-inflammatory tissue-based therapies, amniotic membrane (AmR) and umbilical cord blood serum (UCBS), which improved healing quality and tissue regeneration. However, a subset of wounds developed spontaneous infection and failed to heal. These wounds resembled the clinical presentation of diabetic wounds and enabled further investigation into mechanisms underlying impaired healing and infection.

Methods: Bio-banked tissue from diabetic murine full-thickness excisional wounds was analysed at day 14 post-injury. Wounds were classified as healers or non-healers (excessive slough and infection) based on percentage wound closure and SPOT score. Comparative proteomic profiling was performed using LC–MS/MS. Neutrophil (Ly6G) and macrophage (CD68) infiltration were assessed by immunohistochemistry.

Results: A total of 102 proteins were differentially expressed between groups (p 2), with 55 upregulated and 47 down-regulated in non-healed wounds. Upregulated proteins in non-healers were predominantly associated with innate immune cell recruitment. This corresponded with significantly increased neutrophil infiltration, while macrophage infiltration was unchanged. Notably, several mitochondrial-associated proteins were downregulated in non-healed wounds.

Conclusion: Despite enhanced immune cell recruitment and marked neutrophil infiltration, persistent infection in non-healed wounds suggests impaired immune functionality. Anti-inflammatory therapies may further attenuate an already compromised acute immune response, increasing susceptibility to opportunistic infection. Sustained infection likely perpetuates inflammation and tissue damage, hallmarks of diabetic foot ulcers. Additionally, downregulation of mitochondrial-associated proteins indicates that mitochondrial dysfunction and impaired cellular energetics may contribute to defective healing.

Maternal global DNA methylation as an early predictor of preterm birth in South African women

Category: Basic Science

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Background: Diabetes during pregnancy is associated with adverse maternal and neonatal health outcomes. Epigenetic mechanisms, particularly DNA methylation, have been implicated in mediating the effects of the intrauterine environment, and dysregulated DNA methylation signatures may serve as potential biomarkers of pregnancy and birth outcomes. The aim of the study is to investigate the association between global DNA methylation and birth outcomes in South African women with different types of diabetes in pregnancy.

Methods: A prospective study was conducted in pregnant women with/without diabetes, who were recruited at the antenatal clinic at Steve Biko Academic Hospital, South Africa. Global DNA methylation was quantified in peripheral blood cells at ≤ 28 weeks of gestation in women with type 1 (T1DM, $n = 26$), type 2 (T2DM, $n = 77$), gestational diabetes mellitus (GDM, $n = 58$) and normoglycemia ($n = 69$), using the Imprint DNA quantification kit. Associations between global DNA methylation and diabetes type, maternal characteristics, and birth outcomes were analysed.

Results: Global DNA methylation levels were 1.6-fold lower ($p = 0.019$) in women who delivered prematurely compared to term births. This association remained significant ($p = 0.031$) after adjusting for confounders, age, body mass index and gestational age. A decreased trend towards significance was observed with 5 min Apgar score 0.05. In addition, global methylation was positively correlated with maternal leptin concentrations (rho = 0.4; $p < 0.0001$).

Conclusion: Our results suggest that maternal global DNA methylation may serve as an early predictor of preterm birth in high-risk women. Studies focused on gene-specific DNA methylation are currently underway to elucidate the mechanisms underlying the development of preterm birth. Such studies may pave the way for targeted interventions or preventative strategies aimed at improving pregnancy outcomes.

A rare case of thyroid hormone resistance syndrome

Category: Clinical - Endocrinology

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Introduction: Thyroid hormone resistance (THR) is a rare clinical syndrome characterised by impaired sensitivity of target organs to thyroid hormones. It is caused by mutations in the thyroid hormone receptor alpha or beta genes. THR has a prevalence of 1:40 000 to 1:50 000 with no reported case studies in South Africa.

History and Examination Findings: A 31-year-old female presented with palpitations, anxiety and weight loss associated with fatigue, dysphagia and goitre of 3-year duration.

Investigations: Biochemical results demonstrated persistently elevated free T4 ranging from 25.5 to 37.2 pmol/L (reference range: 11.5-22.7 pmol/L) and an elevated free T3 ranging from 8.2 to 12.7 pmol/L (reference range: 3.5–6.5 pmol/L). However, thyroid-stimulating hormone (TSH) was consistently within the reference range of 0.55–4.78 pmol/L.

The patient had a trial of antithyroid drugs which resulted in hypothyroid symptoms and a marked increase in TSH levels. Thereafter, the hyperthyroid symptoms were controlled by a beta-blocker. TSH receptor and thyroid peroxidase antibodies were negative. No family history of abnormal thyroid function tests (TFT) were reported. A mass lesion was excluded on brain imaging, which made a TSH-secreting pituitary adenoma less likely as the differential diagnosis, and thyroid scintigraphy showed diffuse uptake making Grave's disease unlikely.

The patient underwent two thyroid suppression tests, firstly using 100 µg thyroxine 12 hourly and later 50 µg tertroxin daily for 3 days. These tests resulted in a suppressed TSH and 85.5% suppression of TSH, respectively. These findings were in keeping with THR where a decrease in TSH levels is expected when supraphysiologic doses of thyroid hormone are used. Further results in support of the diagnosis of THR were low creatine kinase and elevated steroid hormone binding globulin levels. Unfortunately, the patient was lost to follow-up before genetic testing could be performed.

Conclusion: This case illustrates that discordant TFT results require further investigations and that dynamic function tests play a key role in ascertaining the correct diagnosis and patient management.

Transcriptomic signatures of hypertension in a South African Population

Category: Basic Science

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Background: Hypertension is a complex medical condition characterised by persistently elevated blood pressure, and effects over 1.28 billion adults worldwide. Its exact aetiology is often unknown, making it a multifactorial health issue. With advances in next-generation sequencing (NGS), RNA sequencing (RNA-seq) has emerged as a powerful tool for identifying disease-associated genes and pathways. This study aimed to identify transcriptomic changes associated with the development of hypertension in a South African population.

Methods: RNA sequencing was performed on RNA extracted from whole blood samples of 46 participants with hypertension and 5 normal control participants. Library preparation was performed using the MGIEasy RNA Library Prep Set according to the manufacturer's guidelines. Samples were sequenced using PE100 chemistry on the DNBSEQ-G400 platform. Differential expression gene (DEG) analysis was performed to compare hypertensive group with normotensive group (DESeq2). This analysis was followed by functional enrichment using Gene ontology (GO), Kyoto Encyclopaedia of Genes and Genomes (KEGG), and Gene Set Enrichment (GSEA) to identify significantly enriched biological processes and pathways associated with the gene set.

Results: We identified 1 099 genes that were significantly associated with hypertension (*p*-value 2.0), including 507 genes were upregulated and 1 125 genes were downregulated in the hypertensive group compared with the normal control group. Functional enrichment analysis revealed significant enrichment of pathways related to calcium signalling and insulin signalling, among others. These findings are consistent with previously reported differentially expressed genes involved in inflammatory and TNF signalling pathways.

Conclusion: This study identifies key transcriptional changes associated with hypertension and highlight the implication of metabolic and inflammatory pathways that may be involved in the disease development. Future studies aim to focus on the validation of identified candidate genes in a bigger group and exploring their therapeutic potential for hypertension.

Insulin therapy and changes in weight in type 1 diabetes mellitus patients in a South African setting

Category: Clinical – Diabetes

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[1] *None*

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Background: There is limited data on the prevalence of overweight and obesity among type 1 diabetes mellitus (T1DM) patients in sub-Saharan Africa.. Overweight/obesity in T1DM is associated with increased rates of diabetes-related complications.

Methods: A retrospective clinical audit was conducted to investigate weight changes in relation to insulin dose in South African patients with T1DM mellitus over the first 5 years post-diagnosis, and to describe the demographics, treatment factors and comorbidities associated with weight gain. The following data was recorded: demographic details, weight, height, HbA1c, insulin dose and the presence of comorbidities, at diagnosis and years 1 and 5 post-diagnosis.

Results: This study included 213 patients with a median age at diagnosis of 23(15−29) years. There was a significant increases in BMI (baseline 21.7[19.1–26.3] kg/m^2, year 1 23.2[20.7–27.7] kg/m2, year 5 25.3[22.0–29.6] kg/m^2, $p < 0.001$)kg/m^2, year 5 25.3(22.0−29.6) kg/m^2, $p < 0.001$), and insulin dose (baseline 0.69[0.52-0.89] units/kg/day, year 1 0.78[0.55–0.98] units/kg/day, year 5 0.97[0.73–1.18] units/kg/day, $p < 0.001$ for both) at all time points. Glycaemic control was poor at baseline and, despite a significant improvement, remained poor at year 5 (baseline 12.5[10.3–14.0] % vs year 5 10.1[8.30-12.7] %, $p < 0.001$). Females had a higher median BMI at baseline, year 1 and year 5. At year 5, the median BMI was in the overweight and normal categories in females and males, respectively (27.7[22.9–32.2] kg/m^2 vs. 23.5[21.4–26.9] kg/m^2, $p < 0.001$). At year 5, the prevalence of hypertension was 15.0% ($n = 32$), HIV 5.6% ($n = 12$) and dyslipidaemia 4.23% ($n = 9$). There was a positive correlation between BMI and total insulin dose. In contrast, when the insulin dose was expressed as units/kg/day, it had a negative relationship with BMI throughout the study period.

Conclusion: This cohort of black African patients demonstrated poor glycaemic control throughout the study period. Despite poor glycaemic control, this population had a high prevalence of overweight and obesity as well as a significant increase in BMI in the first 5 years post-diagnosis. There was a positive correlation between BMI and total insulin dose, but a negative correlation with weight-adjusted insulin. This apparent paradox may be explained by possible poor compliance resulting in a discordance between the dose taken by the patient and the prescribed dose.

Characterising the senescence-associated secretory phenotype in diabetic ADSCs: evaluating senomorphic therapeutic potential

Category: Basic Science

Saiuree Govender; Kelly Petersen-Ross; Mari van de Vyver

Stellenbosch University

Background: Diabetes mellitus (DM) is a global health concern affecting over 569 million individuals, with premature cellular senescence playing a pivotal role in disease progression. Senescent cells secrete senescence-associated secretory phenotype (SASP) factors that promote chronic insulin resistance, chronic inflammation and tissue dysfunction. Adipose-derived stem cells (ADSCs) are central to metabolic regulation. Senescent ADSCs, however, exacerbate diabetic complications as a consequence of SASP factors mediated by extracellular vesicles (EVs). This study sought to profile the SASP in DM-induced senescent ADSCs and evaluate the therapeutic potential of senomorphics to identify interventions in addition to glycaemic control.

Methods: Primary human ADSCs (< passage 10) were pre-treated with ascorbic acid 2-phosphate (0.6 mM), N-acetyl cysteine (3.75 mM), and metformin (200 µg/mL) for 24 h. Senescence-inducing media containing high glucose (25 mM), advanced glycation end products (AGE-BSA, 400 ug/mL), and tumour necrosis factor alpha (TNF-α, 0.02 ug/mL) were then added for 3 days to mimic the diabetic microenvironment. The expression of 36 cytokines associated with SASP was assessed using multiplex analysis. Extracellular components that mediate SASP (EVs) and modulate tissue remodelling were investigated.

Results: Compared to control, the DM-induced senescent ADSCs demonstrated altered SASP profiles with significant expression of inflammatory mediators (TGF-β1, TGF-β2, TGF-β1, FGF basic, Eotaxin, G-CSF, GM-CSF, IFN-γ, IL-1β, IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-10, IL-12(p20), IL-13, IL-15, IL-17A, IP-10, MCP-1 (MCAF), MIP-1α, MIP-1β, PDGF-BB, RANTES, TNF-α, VEGF), matrix metalloproteinases, MMP9, and tissue inhibitor, TIMP2, across different treatment conditions. EV secretion showed notable differences.

Conclusion: These findings provide a comprehensive characterisation of SASP composition in DM-induced senescent ADSCs. Senomorphic interventions show promise for the modulation of certain SASP components.

A case of pancytopaenia secondary to thyrotoxicosis with underlying Grave's disease

Category: Clinical – Endocrinology

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Introduction: Pancytopaenia is an uncommon but recognised aematological manifestation of severe thyrotoxicosis. While isolated anaemia or cytopaenias are more frequently observed, these are usually mild and not clinically significant. We report a case of a patient presenting with a clinically important pancytopaenia.

History and Examination Findings: A 77-year-old female with no background comorbidities presented with a four week history of worsening dyspnoea, pedal oedema and fatigue. Clinical examination revealed a widened pulse pressure, tremor of the outstretched hands, diffuse, symmetrical grade 2 goitre and features of high output cardiac failure. She had no features of thyroid eye disease, acropachy and dermopathy.

Investigations: Thyroid function tests confirmed thyrotoxicosis (TSH of < 0.01 mIU/L, FT4 55.7 pmol/L and the presence of thyroid receptor antibodies). A full blood count noted pancytopaenia, with Hb of 4.5 g/dL, WCC of 2.38x109/L, ANC of 0.92x109/L and Platelets of 64x109/L. The Vitamin B12 level was normal at 401 pmol/L. A bone marrow was done to investigate an inappropriate RPI of 0.6 which showed trilinear haematopoiesis, and a hypercellular marrow with no cytogenetic or molecular abnormalities. The patient was initiated on carbimazole and underwent adequate diuresis with a clinical and biochemical improvement after one week and resolution of pancytopaenia with normalisation of thyroid functions noted at a 3 week follow-up visit.

Conclusion: Thyroid hormone exerts complex effects on haematopoiesis. Although thyrotoxicosis typically stimulates erythropoiesis through increased metabolic demand and elevated erythropoietin levels, ineffective erythropoiesis, shortened red cell survival, autoimmune mechanisms, and peripheral destruction may lead to cytopenias. Granulocytopenia may also occur in Graves' disease due to immune-mediated mechanisms, while thrombocytopenia has been attributed to splenic sequestration or platelet-directed antibodies. This case highlights thyrotoxicosis as a potentially reversible cause of pancytopaenia. Recognition of this association is important to avoid unnecessary invasive investigations and to ensure prompt treatment of the underlying thyroid disorder.

Comparative analysis: corrected calcium versus total and ionised calcium in clinical practice

Category: Clinical – Other

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Background: Ionised calcium (iCa) represents the biologically active fraction of serum calcium and is considered the gold standard for assessing calcium status. However, due to cost, technical requirements and pre-analytical limitations, ionised calcium measurement is not always routinely performed in clinical practice. Instead, total calcium (tCa) and albumin-corrected calcium (cCa) are frequently used as surrogate markers. These measures may be influenced by physiological and biochemical factors such as albumin concentration, renal dysfunction, magnesium abnormalities and pH disturbances, particularly in critically ill patients. This study aimed to evaluate the correlation and agreement between ionised calcium, total calcium and corrected calcium in determining calcium status in patients presenting to the emergency department (ED) and intensive care unit (ICU).

Methods: A retrospective observational study was conducted using laboratory data from adult patients presenting to ED and ICU settings in private hospitals serviced by PathCare laboratories in Gauteng, South Africa. Patients with simultaneous measurements of ionised calcium, total calcium, albumin, creatinine, magnesium and pH between December 2023 and May 2024 were included. Corrected calcium was calculated using the Payne formula, with additional comparisons using the Orrell, Berry and NHLS/GSH correction equations. Calcium status was classified using standard laboratory reference ranges. Descriptive statistics summarised demographic and biochemical characteristics. Pearson and Spearman correlation coefficients were used to assess associations between calcium measurements. Agreement in classification of calcium status was evaluated using weighted Cohen's kappa coefficients.

Results: A total of 2 388 patients were included, of whom 56.3% were admitted to ICU and 43.7% to the ED. The median age of participants was 63 years (IQR 47–77), and 53.4% were male. Hypoalbuminaemia was markedly more prevalent in ICU patients compared with ED patients. Both total calcium and corrected calcium demonstrated statistically significant correlations with ionised calcium ($p < 0.001$). Corrected calcium showed a slightly stronger correlation with ionised calcium ($r = 0.6946$) compared with total calcium ($r = 0.6701$). However, agreement between these measures in classifying calcium status was poor. Weighted Cohen's kappa demonstrated only fair agreement between ionised calcium and total calcium ($\kappa = 0.34$) and between ionised calcium and corrected calcium ($\kappa = 0.27$). Alternative albumin-correction formulas showed similarly weak correlations and poor agreement.

Conclusion: Despite statistically significant correlations, both total calcium and albumin-corrected calcium demonstrated poor agreement with ionised calcium in assigning calcium status. These findings suggest that reliance on total or corrected calcium may lead to misclassification of calcium abnormalities, particularly in critically ill populations. Measurement of ionised calcium should therefore be preferred in emergency and intensive care settings where accurate assessment of calcium status is clinically important.

The effect of the SREBP-1c rs2033690347 and NR1H3 rs2279238 gene polymorphisms on lipid accumulation in a human hepatocellular cell line

Category: Basic Science

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a growing global health burden characterised by excessive lipid accumulation in hepatocytes. Genetic variation in key regulators of lipid homeostasis (e.g. sterol regulatory element-binding protein-1c [SREBP-1c] and liver-X-receptor [LXR]) may contribute to susceptibility to MASLD. SREBP-1c and LXR regulate hepatic lipid metabolism by functioning as lipid-sensing transcription factors, inducing the expression of genes involved in de novo lipogenesis, fatty acid synthesis, and triglyceride production. Two polymorphisms, SREBP-1c rs2033690347 (Arg527Cys; the arginine is essential for SREBP-1c cleavage and translocation to the nucleus) and LXR rs2279238 (C > T; located in an exon splicing enhancer region), have previously been associated with altered lipid profiles, however, their effects on hepatic intracellular lipid accumulation (ICLA) remain unclear. Therefore, this study aimed to investigate the impact of these variants on ICLA in the HepG2 human hepatocellular cell line.

Methods: HepG2 cells were plated at a density of 0.4x106/well and transfected with plasmids containing either the rs2033690347 C-allele, the rs2033690347 T-allele, the rs2279238 C-allele, the rs2279238 T-allele or an empty plasmid (control). ICLA was induced by adding 132 µL/mL oleic acid-BSA (2:1 ratio). Lipids were stained using Oil Red-O on days 1 and 4. ICLA was quantified spectrophotometrically and visualised microscopically. Statistical analyses were conducted using Student's unpaired t-tests for intraday comparisons and paired t-tests for interday comparisons.

Results: ICLA increased significantly from baseline to day 4 in the control experiment (100±0.0 vs. 372.8±25.5; $p = 0.003$). No significant differences were found in ICLA between cells expressing the rs2033690347 C and T-alleles on day 1 (282.3±165.5 vs. 267.7±253.9;

$p = 0.938$) or day 4 (198.2±68.4 vs. 183.5±117.9; $p = 0.863$). Similarly, no significant differences were found in ICLA between cells expressing the rs2279238 C and T-alleles on day 1 (169.2±27.8 vs. 137.41±20.5; $p = 0.192$) or day 4 (185.5±59.7 vs. 117.2±23.4; $p = 0.176$).

Conclusion: The two polymorphisms did not affect ICLA in HepG2 cells. Potentially, the effect of these polymorphisms on ICLA is small and endogenous expression of LXR and SREBP-1c is masking this effect. Future studies in cell lines lacking these proteins may be needed to elucidate the effects of these polymorphisms on ICLA and their potential role in MASLD.

Assessment of the behaviour, knowledge and opinion of micronutrient supplementation in post-bariatric surgery patients

Category: Clinical – Other

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Background: Bariatric surgery is an effective intervention for severe obesity but is associated with long term micronutrient deficiencies due to altered gastrointestinal anatomy and absorption. Lifelong micronutrient supplementation is therefore required to prevent nutritional complications and support sustained postoperative health. Despite established international guidelines, adherence to supplementation is inconsistent, and limited data exist within the South African private healthcare context. This study aimed to assess the behaviour, knowledge, and opinions regarding micronutrient supplementation among post-bariatric surgery patients attending private hospitals in South Africa.

Methods: A descriptive cross-sectional study with an analytical component was conducted among post-bariatric surgery patients in the South African private healthcare sector. Data were collected using a self-administered online questionnaire distributed via SunSurvey. A total of 150 questionnaires were distributed, and 80 fully completed responses were included in the analysis. Descriptive statistics summarised demographic, anthropometric, behavioural, knowledge, and opinion data. Inferential analyses included independent sample t-tests, Mann-Whitney U tests, and Spearman rank order correlation to explore associations between knowledge, behaviour, and opinion variables. Statistical significance was set at $p < 0.05$.

Results: Participants were predominantly female (86.3%) with a mean age of 46.75±10.19 years. Mean body mass index decreased from 45.45±7.40 kg/m^2 pre-surgery to 29.10±5.29 kg/m^2 post-surgery. Overall adherence to micronutrient supplementation was high at 85%; however, 41.3% reported occasionally forgetting to take supplements and 20% identified cost as a significant barrier. The mean micronutrient knowledge score was low at 24.3±22.1%, with more than one third of participants uncertain about essential postoperative vitamins and minerals. Supplement users demonstrated significantly higher positive opinion scores than non-users (mean difference = 0.35, 95% confidence interval [0.15, 0.55], $p < 0.001$). No significant association was found between knowledge and behaviour ($p = 0.069$), while a moderate positive correlation existed between knowledge and opinion (rho = 0.354, $p = 0.001$).

Conclusion: Post-bariatric surgery patients showed mostly high adherence and positive opinions on micronutrient supplementation, but limited knowledge. Persistent behavioural and financial barriers require improved education.

Ameliorative potentials of sulphated polysaccharides from *Gracilaria gracilis* in testicular tissues of type 2 diabetic rats

Category: Basic Science

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Background: Diabetes is one of the major global public health problems and seaweeds are wide consumed in many countries in the world, particularly in the far Easter countries. It is also slowly getting popular in South Africa not only due to its availability but also due to Eastern influence, particularly from China. Hence, the present study was conducted to examine the effects of sulphated polysaccharides (SPs) from *Garcilaria gracilis* in diabetes induced testicular abnormalities in rats.

Methods: Six weeks old male SD rats were randomly divided into 6 groups namely, Normal Control (NC), Diabetic Control (DBC), Low dose (150 mg/kg bw) SPs treated diabetic animals (DRL), High dose (300 mg/kg bw) SPs treated diabetic animals (DRH), Metformin (200 mg/kg bw) treated diabetic animals (DBM) and Normal animals treated with the high dose (300 mg/kg bw) of SPs (NRT). Animals in the treatment groups were given with respective dosages of SPs or metformin, when the animals in the NC and DBC groups were given with vehicle only. After 4 weeks intervention period, the urine and testes were collected from all animals for subsequent analyses.

Results: Induction of diabetes, significantly decreased the concentration of testicular insulin and IRS-1, GLUT4, FSH levels and the activities of hexokinase, glucose-6-phosphatase, glucose-6-phosphate dehydrogenase, glyoxalase 1, glutathione reductase, 13β- and 17β-hydroxysteroid dehydrogenase, reduced glutathione, ATP and increased the activities of glucose-6-phosphatase, fructose-1,6-bisphosphatase, glycogen phosphorylase, aldose reductase, polyol dehydrogenase, ATPase, ENTPDase, and glutathione reductase level compared to NC group. The ultrastructural morphology of testes was significantly deteriorated in the DBC group compared to the NC group as seen by histopathological and scanning electron microscopic examinations. In contrast, the treatment with SPs significantly ameliorated all diabetes-induced abnormalities, particularly with the high dose.

Conclusion: The results of this study suggest that SPs from *Gracilaria gracilis* has beneficial effects on insulin signalling, glucose metabolism and steroidogenesis in the testicular tissues of diabetic rats, so it can be considered for potential antidiabetic supplement.

Addition of natural or artificial alternative sweeteners to coffee with or without milk is better for diabetics or not: a comparative study

Category: Basic Science

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Background: Type 2 diabetes (T2D) is a chronic metabolic disorder characterised by persistent hyperglycaemia and increased oxidative stress, both of which contribute to insulin resistance and complications such as cardiovascular disease. Arabica coffee, rich in polyphenolic compounds, notably chlorogenic acid (CGA), possesses antioxidant and anti-diabetic properties that may help alleviate these effects. However, the addition of sweeteners and milk—common additives to enhance coffee's flavour—may alter its existing bioactivity, influencing its potential role in T2D management. The aim of this study was to examine the effects of the addition of natural or artificial alternative sweeteners to coffee with or without milk, particularly for diabetics.

Methods: The antioxidant and anti-diabetic properties of Arabica coffee with or without milk or natural or artificial sweeteners were examined through assays evaluating radical scavenging (DPPH, FRAP, NO), carbohydrate digesting enzyme (α-amylase) inhibition, and glucose uptake studies *in vitro*. Additionally, the binding of bioactive compounds from coffee with sucrose and/or milk were analysed by scanning electron microscopy (SEM). All analyses were done in triplicate and the data were analysed by using a statistical software package (SPSS).

Results: Results showed that natural alternative sweeteners, especially stevia, effectively preserved or enhanced coffee's bioactive properties. Artificial sweeteners, though beneficial, were generally less effective than natural options, with sucralose emerging as the most potent among them. On the other hand, sucrose, the most commonly used natural sweetener, significantly diminished coffee's bioactive effects, underscoring the advantages of using sucrose to maintain its health benefits. The addition of milk alone reduced coffee's antioxidant and anti-diabetic activity, likely due to interactions between milk proteins and coffee's CGA, which may lower the bioavailability. However, the introduction of sweeteners to coffee-milk mixtures—especially with stevia—led to a substantial recovery of bioactivity, indicating a synergistic effect that preserved and enhanced coffee's functional properties.

Conclusion: These findings support the use of natural alternative sweeteners over artificial sweeteners, preferably without milk, for individuals seeking to optimise coffee's health benefits while managing oxidative stress and blood glucose levels. The additional milk with natural alternative sweetener, stevia, may not impact the health benefits of coffee as impacts by the addition of artificial sweeteners.

A crude polyphenol-enriched extract of Cyclopia intermedia and its major polyphenol, mangiferin attenuate inflammation and excess lipolysis in dysfunctional 3T3-L1 adipocytes

Category: Basic Science

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Background: Obesity is associated with chronic low-grade inflammation in adipose tissue, which disrupts adipocyte lipid storage capacity and promotes excessive lipolysis, leading to impaired adipokine secretion. These alterations drive adipocyte dysfunction and contribute to the development of obesity-associated metabolic disorders. Previously, we reported that a crude polyphenol-enriched fraction of Cyclopia intermedia (CPEF) mediates its anti-obesity potential by reducing lipid content in 3T3-L1 adipocytes. In the present study, we aimed to investigate the anti-inflammatory and anti-lipolytic potential of CPEF and its major polyphenol, mangiferin, in dysfunctional 3T3-L1 adipocytes.

Methods: Adipocyte dysfunction in 3T3-L1 adipocytes was induced by tumour necrosis factor alpha (TNFα, 10 ng/mL), lipopolysaccharide (LPS, 100 ng/mL), and palmitic acid (PA, 0.75 mM) combination treatment for 24 hours, followed by treatment with CPEF (0.1–100 µg/mL) and mangiferin (0.1–100 µM) for 24 hours. Metabolic activity, lipid accumulation, lipolysis, interleukin 6 (IL-6), monocyte chemoattractant protein 1 (MCP-1), and adiponectin (AdipoQ) were assessed using the adenosine triphosphate (ATP) content, Oil Red O staining, glycerol release, and the enzyme-linked immunosorbent assays, respectively.

Results: TNFα, LPS, and PA combination treatment reduced metabolic activity ($p < 0.001$) and AdipoQ secretion ($p < 0.001$), while increasing glycerol release ($p < 0.001$), IL-6 ($p < 0.001$), and MCP-1 ($p < 0.05$) secretion. All concentrations of CPEF increased the ATP content ($v < 0.01$), while mangiferin increased ATP content at 100 µM ($p< 0.05$). Glycerol secretion was decreased by CPEF and mangiferin at 1, 10, and 100 µg/mL or µM ($p < 0.05$). All concentrations of CPEF and mangiferin increased lipid accumulation in dysfunctional adipocytes. IL-6 secretion was decreased by CPEF and mangiferin treatment at all tested concentrations ($p < 0.05$). Mangiferin decreased MCP-1 secretion at all tested concentrations ($p < 0.01$), whereas CPEF had no significant effects. Furthermore, CPEF and mangiferin increased AdipoQ secretion at 0.1 µg/mL or µM ($p < 0.05$).

Conclusion: This study demonstrates the potential of CPEF and mangiferin to alleviate excess lipolysis by decreasing glycerol release and mitigate inflammation by reducing IL-6 and MCP-1 secretion while increasing AdipoQ levels in dysfunctional 3T3-L1 adipocytes. Both treatments enhanced lipid accumulation, indicating suppression of excessive lipolysis. Further research to elucidate the molecular mechanisms that underlie these anti-lipolytic and anti-inflammatory effects of CPEF and mangiferin is warranted.

The great pretenders: unmasking hidden adrenal insufficiency in porphyria

Category: Clinical – Endocrinology

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Introduction: Adrenal insufficiency can result in significant patient morbidity and mortality, but due to the range of symptoms and variable clinical course and aetiologies, it can be a challenging condition to diagnose and manage. In this report, we describe hypoadrenalism is a patient known with porphyria.

History and Examination Findings: A 55-year-old female, known with hereditary erythropoietic porphyria, was hospitalised several times due to severe hyponatraemia (serum sodium 106 mmol/L). The admissions were accompanied by skin blistering, severe abdominal pain and vomiting. She remained euvolemic and normotensive. Due to the high urinary-sodium and urinary osmolality (U-Na 86 mmol/L and U-osmolality 641 mmol/kg), she was diagnosed with syndrome of inappropriate antidiuretic hormone (SIADH), which was likely precipitated by the porphyria attacks. Chest X-ray, thyroid function test and brain MRI were normal. Early morning cortisol was reduced (cortisol 86 nmol/L), however no further testing was done at that stage. During each admission, it was noted that the serum sodium levels normalised with the management of the porphyria attack.

She was now electively admitted to the endocrine unit for investigation of suspected hypoadrenalism. Clinically, she was well with no skin abnormalities and normal systemic evaluation. During this admission, the serum electrolytes and osmolality are normal. Laboratory investigations revealed serum 8 am cortisol 98 nmol/L with normal ACTH 3.0 pmol/L. A 250 mcg ACTH stimulation test was performed (serum cortisol 379 nmol/L at 30 minutes and 311 nmol/L at 60 minutes after Synacthen), demonstrating failure of cortisol levels to rise adequately. Unfortunately, 21-hydroxylase antibodies were not tested as the test is unavailable in the state sector. The patient was then discharged home on stress doses of glucocorticoid replacement therapy.

Investigations: Urinary-Na 86 mmol/L and U-osmolality
641 mmol/kg
Serum 8 am cortisol 98 nmol/L
ACTH 3.0 pmol/L
250 mcg ACTH stimulation test was performed: serum cortisol
379 nmol/L at 30 minutes and 311 nmol/L at 60 minutes after
synacthen

Conclusion: Porphyrias are a group of 8 inherited metabolic disorders of haem biosynthesis. They are often classified as hepatic or erythropoietic according to the organ in which haem precursors accumulate. Porphyria is rare and clinical disease is seen in only 10% of carriers. Porphyria attacks may present with severe abdominal pain, nausea, vomiting, constipation, excretion of red coloured urine and signs of increased sympathetic activity. Hyponatremia due to SIADH develops in 40% of patients and can lead to convulsions. Porphyria can be exacerbated by infections, several drugs, surgery and alcohol. Diagnosis is made by excess of urine porphobilinogen and 5-aminolaevulinic-acid. Treatment should include the avoidance of precipitating factors and the administration of haem infusions.

Adrenal insufficiency is a life-threatening condition. It can present alone, or in combination with other comorbidities. A variety of infective causes, particularly tuberculosis in sub-Saharan Africa, have been identified as the most common cause of adrenal insufficiency in our setting, though autoimmune causes are more prominent in international literature. A case-control study in Barcelona in 2014 showed that there an imbalance in adrenal steroidogenesis with subsequent reduction in cortisol biosynthesis in patients with acute porphyria. Primary adrenal insufficiency (PAI), an intrinsic adrenal defect in glucocorticoid and mineralocorticoid synthesis, is linked to mutations in more than 25 genes.

There is a link between porphyria and adrenal insufficiency, and testing adrenal function in porphyria patients and their families may be warranted. Porphyria and adrenal insufficiency are both rare conditions, both being characterised with similar clinical features, as well as the presence of hyponatraemia.

Predictors for remission of Grave's disease following radioactive iodine (131i)

Category: Clinical - Endocrinology

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Background: Radioactive iodine (RAI) therapy is an established definitive treatment for Graves' disease (GD). However, predictors of remission and timing of response remain inconsistent, and data from African populations are limited. This study aimed to determine the rate and timing of remission after first dose fixed radioactive iodine therapy in Graves' disease and to identify clinical predictors of remission after initial and repeat RAI treatment at a tertiary hospital in Johannesburg, South Africa.

Methods: A retrospective observational study was conducted at a tertiary academic hospital in Johannesburg. Patients with confirmed GD who received a fixed dose of 370 MBq (10 mCi) radioactive iodine between January 2016 and December 2023 were included. Clinical, demographic and biochemical data were extracted from medical records. RAI was offered according to institutional practice, including failure of antithyroid therapy after 12–18 months or earlier in cases of unstable thyroid control, severe disease complications or intolerance to carbimazole. Remission was defined as euthyroidism or hypothyroidism within 12 months following RAI without antithyroid drug use.

Results: A total of 102 participants were included (87.3% female; mean age 40.9 ± 12.5 years), most of whom were Black (80.4%). After the first fixed RAI dose, 83 patients (81.4%) achieved remission, most within 3 months (58, 69.9%), followed by 6 months (16, 19.3%), 9 months (5, 6.0%) and 12 months (4, 4.8%). Twenty-three participants required a second RAI dose following failure of the first treatment. The median interval between doses was 10.2 months (IQR 7.9–15.1). Following the second RAI dose, 21 of 22 patients (95.4%) achieved remission, most within three months (81.8%). Median BMI increased significantly from 26.1 to 29.0 kg/m^2 following RAI ($p < 0.001$). Ninety-five participants (93.1%) received antithyroid therapy before RAI for a median of 7.1 months (IQR 3.9–14.1), shorter than guideline recommendations.

Conclusion: Fixed-dose RAI therapy achieved high remission rates in this South African cohort, with most patients achieving remission within three months. Repeat RAI therapy was highly effective for persistent disease. Earlier use of RAI compared with guideline-recommended antithyroid therapy highlights the need for further studies evaluating prolonged medical therapy versus earlier definitive treatment in resource-limited settings.

Postoperative hypocalcemia with low parathyroid hormone and elevated alkaline phosphatase in primary hyperparathyroidism: hungry bone syndrome complicated by distal renal tubular acidosis

Category: Clinical – Endocrinology

<u>Cain Khosa</u>; Sadiya Nanabhya; Zareena Angamia; Zodwa Dire; Sumy Thomas; Nazeer Mohamed
University of Witwatersrand

Background: A 38-year-old male with well controlled HIV (RVD positive, viral load undetectable on TLD1) presented with primary hyperparathyroidism (PHPT) due to a left superior parathyroid adenoma. He had recurrent pancreatitis secondary to severe hypercalcemia (preoperative corrected calcium 4.10 mmol/L, magnesium 0.62 mmol/L, phosphate 0.89 mmol/L, PTH 169 pg/mL, ALP 494 U/L). Preoperative control with IV saline hydration and 40 mg of furosemide prior to zoledronic acid reduced calcium to 3.36 mmol/L. By Day 14 preop, calcium was 2.7 mmol/L. After parathyroidectomy, he developed profound hypocalcemia (Day 1 Ca 2.7, Day 3 Ca 1.96, Day 7 Ca 1.49, Day 21 Ca 1.36, Day 27 Ca 2.05 mmol/L) with undetectable PTH (1.2 pg/mL) and a marked rise in ALP

(769 U/L), consistent with hungry bone syndrome despite expected PTH suppression. Renal function remained stable, but urine pH 6.8 suggested distal renal tubular acidosis, contributing to impaired calcium handling. Management included intravenous calcium carbonate, oral calcitriol, and bicarbonate replacement initiated on Day 7 to address metabolic acidosis. By Day 27, calcium improved to 2.05 mmol/L, phosphate to 1.2 mmol/L, and magnesium to 0.8 mmol/L, indicating partial response to aggressive supplementation.

Methods: Hypocalcemia is this case was considered multifactorial. The contributing factors includes hungry bone syndrome, hypoparathyroidism, prior use of zoledronic acid and distal tubular acidosis. However, hungry bone syndrome was the primary driver of prolonged hypocalcemia post-parathyroidectomy, with bisphosphonate use as a contributing but not a dominant factor.

Results: Preoperative corrected calcium 4.10 mmol/L, magnesium 0.62 mmol/L, phosphate 0.89 mmol/L, PTH 169 pg/mL, ALP 494 U/L). Preoperative control with IV saline hydration and 40 mg of furosemide prior to zoledronic acid reduced calcium to 3.36 mmol/L. By Day 14 preop, calcium was 2.7 mmol/L . After parathyroidectomy, he developed profound hypocalcemia (Day 1 Ca 2.7, Day 3 Ca 1.96, Day 7 Ca 1.49, Day 21 Ca 1.36, Day 27 Ca 2.05 mmol/L) with undetectable PTH (1.2 pg/mL) and a marked rise in ALP (769 U/L), consistent with hungry bone syndrome despite expected PTH suppression. Renal function remained stable, but urine pH 6.8 suggested distal renal tubular acidosis.

Conclusion: This case highlights that hungry bone syndrome can occur with low PTH and elevated ALP post-parathyroidectomy, and that distal RTA may exacerbate hypocalcemia. Prolonged, high-dose calcium, vitamin D, and bicarbonate therapy, with close biochemical monitoring, are essential for management.

Sjogren's syndrome presenting as distal renal tubular acidosis with severe osteomalacia and primary hypothyroidism in a young Black female

Category: Clinical – Endocrinology

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University of Witwatersrand

Background: We present a 14 year old Black woman with a fragility fracture of the femoral neck following trivial trauma, associated with chronic diffuse bone pain and proximal muscle weakness.

Methods: Biochemical investigations demonstrated normal anion gap metabolic acidosis (pH 7.28, bicarbonate 9.5 mmol/L), hypokalaemia (potassium 3.4 mmol/L), hypercalciuria (24-hour urinary calcium 211 mg), elevated alkaline phosphatase (919 U/L), and secondary hyperparathyroidism (PTH 220 pg/mL) with sufficient 25-hydroxyvitamin D 30 ng/ml. Urine pH was inappropriately high at 6.5, consistent with distal renal tubular acidosis. Autoimmune screening revealed positive antinuclear antibody (speckled pattern, 3+), with Schirmer's test and labial salivary gland biopsy confirming Sjögren's syndrome. Thyroid function testing showed primary hypothyroidism (TSH 78 mIU/L, free T4 4.6 µg/dL) with elevated anti-TPO antibodies (480 IU/mL), consistent with Hashimoto's thyroiditis. Radiologic imaging demonstrated osteopenia, Looser's zones, and femoral neck fracture. Management with oral sodium bicarbonate, potassium chloride, calcium carbonate, and levothyroxine replacement led to correction of acidosis (pH 7.4, bicarbonate 20 mmol/L), normalisation of potassium (4.2 mmol/L), and marked clinical improvement in bone pain and muscle strength.

Results: Biochemical investigations demonstrated normal anion gap metabolic acidosis (pH 7.28, bicarbonate 9.5 mmol/L), hypokalaemia (potassium 3.4 mmol/L), hypercalciuria (24-hour urinary calcium 211 mg), elevated alkaline phosphatase (919 U/L), and secondary hyperparathyroidism (PTH 220 pg/mL) with sufficient 25-hydroxyvitamin D 30 ng/ml. Urine pH was inappropriately high at 6.5, consistent with distal renal tubular acidosis. Autoimmune screening revealed positive antinuclear antibody (speckled pattern, 3+), with Schirmer's test and labial salivary gland biopsy confirming Sjögren's syndrome. Thyroid function testing showed primary hypothyroidism (TSH 78 mIU/L, free T4 4.6 µg/dL) with elevated anti-TPO antibodies (480 IU/mL), consistent with Hashimoto's thyroiditis.

Conclusion: This case is notable for the rare presentation of Sjögren's syndrome in a young Black patient, highlighting the importance of considering autoimmune etiologies of dRTA and associated metabolic bone disease in atypical demographic groups.

Development and implementation of a scalable, modular digital health surveillance platform for low- to middle-income settings- The MaRooN Health Passport

Category: Basic Science

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Background: Low- to middle-income countries face a rising burden of non-communicable diseases (NCDs), yet surveillance systems remain fragmented and poorly integrated into routine care. In South Africa, health screening often occurs in isolated databases with limited capacity for real-time risk stratification or institutional planning. Scalable, context-appropriate digital infrastructure is required to support timely, actionable health intelligence.

Aim: To develop and implement a scalable, modular digital health surveillance platform (MaRooN Health Passport) suitable for low-resource settings, and to evaluate its capacity to characterise NCD and lifestyle risk patterns using advanced analytics.

Methods: MaRooN was developed using an implementation-focused approach and built on a secure REDCap-based architecture. The platform integrates validated instruments assessing lifestyle behaviours, mental health, cardiometabolic risk, and self-rated health, with automated scoring algorithms and branching logic to optimise data quality and reduce respondent burden. Modular design allows deployment across students, staff, athletes, and external community cohorts. Governance aligns with national data protection requirements. To date, the platform includes > 16 000 records from university and external research populations. Analyses include descriptive epidemiology, clustering techniques, and machine learning approaches to identify co-occurring behavioural and metabolic risk patterns and to characterise multimorbidity phenotypes.

Results: The MaRooN Health Passport has been successfully implemented across multiple cohorts, demonstrating high completion rates when embedded into routine workflows. The modular architecture enabled expansion without redevelopment of core infrastructure. Clustering and machine learning analyses identified distinct risk profiles characterised by co-occurring metabolic, behavioural, and psychosocial risk factors. These outputs support real-time risk stratification and institutional-level health planning.

Conclusion: The MaRooN Health Passport demonstrates that scalable digital surveillance infrastructure can be operationalised in resource-constrained settings using low-cost, interoperable systems. The integration of advanced analytics strengthens risk characterisation and supports evidence-informed decision-making. This platform provides a transferable framework for strengthening NCD surveillance and digital health infrastructure in South Africa and similar settings.

Association between genome-wide DNA methylation in peripheral blood and preterm birth in women with diabetes in pregnancy

Category: Basic Science

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Background: Preterm birth is the leading cause of neonatal morbidity and mortality worldwide, particularly among women with diabetes in pregnancy (DIP), who are at an increased risk. Epigenetic mechanisms, particularly DNA methylation, have emerged as potential biomarkers for preterm birth.

Methods: To investigate the association between maternal genome-wide DNA methylation at ≤ 28 weeks of gestation and preterm birth in South African women with DIP. This pilot study of Genome-wide DNA methylation profiling was conducted in peripheral blood samples collected at ≤ 28 weeks of gestation from women who delivered iatrogenic preterm birth prematurely (n = 15) and full-term (n = 16), including those with type 1 (T1DM, n = 8), type 2 diabetes (T2DM, n = 8) and gestational diabetes (GDM, n = 8) and controls (n = 7) using the Illumina Methylation EPIC beadchip arrays. Functional enrichment analysis of differentially methylated genes was conducted using Gene Ontology (GO) and Kyoto Encyclopaedia of Genes and Genomes (KEGG) pathway analyses.

Results: A total of 386 differentially methylated CpG sites (associated with 347 genes) were identified. Of these, 251 (65%) were hypomethylated, and 135 (35%) were hypermethylated in women with preterm compared to full-term births ($\Delta\beta > 10\%$; $p < 0.05$). Differentially methylated CpGs were located primarily in introns (51.7%) and promoter regions (19.9%). Functional enrichment analysis demonstrated that these changes occurred in genes associated with protein and ATP binding, lipid receptor activity, and histone-related kinase signalling and key cellular components. Two significant CpGs, cg11328284 and cg18638998, associated with the Serine/Threonine Kinase 39 (STK39) and Semaphorin6D (SEMA6D) genes, respectively, were commonly differentially methylated across all diabetes groups in women with preterm births compared to those with full-term births. Hypomethylation of cg11328284 was identified in T1DM ($\Delta\beta$ = -21%; p = 0,023), T2DM ($\Delta\beta$ = 18%; p = 0.040), and GDM ($\Delta\beta$ = 12%; p = 0.016), while cg18638998 was hypomethylated in T1DM ($\Delta\beta$ = 32%; p = 0.006), T2DM ($\Delta\beta$ = 26%; p = 0.008), but hypermethylated in GDM ($\Delta\beta$ = 25%; p = 0.012), and may play a role in inflammation, placental function, immune modulation and vascular signaling.

Conclusion: Differential genome-wide DNA methylation patterns are associated with preterm birth in South African women. Shared gene-specific methylation changes across diabetes subtypes suggest potential common biological pathways. Further work to validate and evaluate their potential as early biomarkers of preterm birth risk is warranted in this population.

The association of the rs709932 SERPINA gene polymorphism with dysglycaemia and metabolic syndrome in the South African black population

Category: Basic Science

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Background: Type 2 diabetes (T2D) is a major health concern in South Africa. In T2D, chronic low-grade inflammation contributes to insulin resistance and β-cell dysfunction, partly through dysregulation of anti-inflammatory proteins such as alpha-1-antitrypsin (AAT). AAT, encoded by the SERPINA1 gene, has recently been shown to have direct immunomodulatory properties, downregulating the expression of pro-inflammatory cytokines. Limiting chronic inflammation reduces insulin resistance (IR) and protects pancreatic β-cells from apoptosis, thus AAT activity has important metabolic consequences. Variation in the SERPINA1 gene may decrease the anti-inflammatory activity of AAT, predisposing individuals to the development of T2D. The SERPINA1 rs709932 (C > T) polymorphism results in an arginine-to-cysteine amino acid change. This change alters AAT structure and reduces its anti-inflammatory activity. Little is known about the association of rs709932 with metabolic dysfunction. Thus, this study aimed to investigate the association of the SERPINA1 rs709932 gene polymorphism with dysglycaemia and metabolic syndrome (MetS) in a South African black population.

Methods: Black South African participants (n = 240) were recruited from the greater Johannesburg region through convenience sampling. Anthropometric (BMI, waist circumference) and biochemical (HbA1c, lipid profiles) data were recorded. Participants were categorised as dysglycaemic if their HbA1c level was ≥ 5.7. MetS was diagnosed using established non-fasting criteria. Participants were genotyped for the rs709932 polymorphism using a TaqMan® allelic discrimination assay. Statistical analysis was performed using Statistica software v.13.

Results: The major allele for rs709932 was the C allele with a frequency of 0.90. In univariate analysis, participants with the rs709932 T allele had a significantly higher percentage of dysglycaemia (36.8 vs. 19.4%; p = 0.021) and MetS (34.2 vs. 14.2%; p = 0.004) compared to participants with the CC genotype. The associations of the rs709932 T allele with dysglycaemia and MetS remained when controlling for confounding variables in logistic regression analysis.

Conclusion: The rs709932 T allele is known to reduce AAT levels. Therefore, we hypothesise that in the presence of the T allele, AATs anti-inflammatory effects will be reduced. Thus, these individuals have increased inflammation, resulting in the development of metabolic complications such as dysglycaemia and MetS. Future studies should include AAT and pro-inflammatory cytokine quantification in larger cohorts.

Requirement for front-of-pack warning labels in South African porridges and cereals varies depending on preparation method and grain type

Category: Clinical – Other

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Background: The primary aim of the study was to determine the proportion of breakfast products requiring front-of-pack labels (FOPLs) according to R.3337 regulations and to compare nutritional content and FOPL requirements across grain types (modern grains, oats, and other ancient grains) and preparation method (ready-to-eat, instant, and cooking required).

Methods: A cross-sectional analysis of 271 products from leading South African supermarkets was conducted. Nutrient values per 100 g, including total energy, protein, carbohydrates, fats, dietary fibre, and sodium, were extracted from nutritional information tables. Ingredient lists identified grain types. Products were assessed against R.3337 FOPL thresholds for sugar, saturated fat, sodium, and artificial sweeteners. Products available from March to July 2024 were identified through online shopping platforms, supplemented by in-store visits where necessary.

Results: Breakfast products requiring cooking exhibited superior nutrient profiles (including higher protein and dietary fibre, and lower total sugar and sodium) compared to instant and/or ready-to-eat options ($p < 0.010$). Products containing ancient grains, particularly oats, showed more favourable nutritional profiles than those with modern grains ($p < 0.050$). While 73.5% of products required FOPLs, this varied by preparation method: 75.2% for ready-to-eat, 83.5% for instant, and none for cooking-required products. Similarly, FOPL requirements varied by grain type, with 50.0% of oat-based products requiring FOPLs compared to 81.9% of modern grain products and 75.4% of products containing other ancient grains.

Conclusion: Most porridges and cereals in South Africa required FOPLs due to high sugar, saturated fat, salt, and artificial sweeteners. However, products requiring cooking and those containing oats were less likely to need these warning labels.

The association of chromogranin A gene polymorphisms (rs9658638 and rs7159323) with chromogranin A concentrations in the South African population

Category: Basic Science

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Background: Chromogranin A (CgA), encoded by the CgA gene (CHGA), is a neuroendocrine prohormone that is proteolytically cleaved into functional peptides, including catestatin (CST), and plays a role in glucose regulation. Previously, we reported ethnic differences in CgA and CST levels, suggesting that genetic factors may influence CgA expression or processing. Polymorphisms in the CHGA gene have been associated with diabetes and hypertension. This study therefore investigated the association of the rs7159323 and rs9658638 CHGA gene promoter polymorphisms with levels of CgA, CST, and metabolic markers in healthy black and white South African women.

Methods: Normoglycaemic, normotensive black (n = 64) and white (n = 51) women were previously recruited from the greater Johannesburg area. Anthropometric measurements and fasting biochemical parameters (CgA, CST, C-peptide, leptin, and adiponectin) were available. Participants were genotyped for the rs7159323 and rs9658638 polymorphisms using PCR-RFLP. The association of CHGA genotypes with clinicopathological variables were determined in both ethnic groups. Multiple regression analyses were used to determine the relationship of the CHGA polymorphisms with CgA and CST levels after adjustment for possible confounding variables.

Results: There was no significant difference in rs7159323 (p = 0.067) and rs9658638 (p = 0.905) allelic frequencies between black and white women. In black women, the rs7159323 CC genotype was associated with higher C-peptide (0.7 [0.6–0.9] vs. 0.5 [0.5–0.6] nmol/L; p = 0.004) and adiponectin (1685 [854–7731] vs. 1159 [745–2090] ng/mL; p = 0.042) levels. The rs9658638 CT + TT genotype was associated with higher adiponectin levels in white women (10740 [8203; 11460] vs 3297.5 [1248; 10142] ng/mL; p = 0.007). In regression analyses, black ethnicity was associated with lower CST levels (p = 0.001). Furthermore, the main predictors of CgA levels were an older age (p = 0.007) and lower BMI (p = 0.019).

Conclusion: The association of the rs7159323 polymorphism with C-peptide and adiponectin levels in black women may be due to differences in linkage disequilibrium (LD) patterns with the rs7159323 polymorphism in LD with a nearby functional variant. The rs7159323 and rs9658638 polymorphisms do not explain the ethnic differences in CgA and CST levels in healthy South African women. Future studies should investigate polymorphisms in the CHGA gene that may disrupt CgA cleavage sites.

Optimising clonidine stimulation testing in children with suspected growth hormone deficiency: can sampling frequency be reduced?

Category: Clinical – Endocrinology

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Background: Diagnosis of growth hormone deficiency (GHD) is made using provocative tests due to the pulsatile nature of growth hormone (GH) secretion. The clonidine stimulation test (CST) is commonly used to rule out GHD. However, in resource-limited settings, the multiple blood sample collections required for CST makes it expensive and cumbersome. The aim of this study was to determine the diagnostic accuracy of samples collected at each time point and the most common GH peak time during a CST.

Methods: This was a retrospective analysis of records of children who have had CST at Charlotte Maxeke Johannesburg Academic Hospital Day Ward between 2019 to 2024. Patients were divided into two groups: GHD and non-GHD based on a clonidine stimulated GH peak ≥ 7 µg/L at any time point during the CST. GH was analysed on the Roche e602 analyser using electrochemiluminescence sandwich immunoassay. Data were analysed on MedCalc®, version 23.3.4 and R, version 4.5.2. Descriptive statistics were used to analyse demographic data whilst sensitivity and specificity were calculated to determine the diagnostic accuracy of the different sampling times during CST. A *p*-value < 0.05 was considered statistically significant.

Results: Out of 57 patients, 40 were male and 17, female, with 33 patients categorised as GHD and 24 as non-GHD. Most patients ($n = 51$) had sampling of GH up to 120 minutes, while only 11 patients had sampling at 150 minutes. GH measurements at all time points from baseline to 150 minutes (collected in 30-minute intervals) were found to be consistently lower in the GH deficient group ($p < 0.05$). Of those with non-GDH ($n = 24$), eight peaked (GH of ≥ 7 µg/L) at 90 minutes, five at baseline, four at 60 and 120 minutes, and three at 30 minutes. Sampling at 90 minutes demonstrated the highest diagnostic accuracy (90%), with a sensitivity of 100% and specificity of 77%. A combination of 90 and 120 minutes displayed improvement in diagnostic accuracy (100%) compared to 90 minutes alone.

Conclusion: In resource-limited settings, measuring GH at 90 minutes alone may be sufficient to exclude GHD during CST, with an additional 120-minute sample reserved for selected cases.

Hyperglycaemia and SARS-CoV-2 spike variants differentially modulate endothelial metabolic activity and bioenergetic pathways

Category: Basic Science

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Background: Hyperglycaemia is a key contributor to severe COVID-19 outcomes and may prime the vascular endothelium for enhanced viral-mediated dysfunction. Chronic high glucose alters endothelial metabolism, induces oxidative stress, and can modify glycosylation patterns, potentially influencing SARS-CoV-2 spike protein (S-protein) interactions and downstream signalling. Despite this, the interplay between hyperglycaemia and SARS-CoV-2 in endothelial cells remains poorly understood. This study aimed to elucidate how hyperglycaemia and S-protein variants modulate metabolic activity and ATP levels as potential mediators of downstream endothelial functional alterations, and viral entry-associated proteins in human umbilical vein endothelial cells (HUVECs).

Methods: HUVECs were exposed to 1) hyperglycaemic conditions (15 and 30 mM glucose) and 2) recombinant S-protein (WT, β, δ variants; 10–2 000 ng/mL) in separate experiments. Metabolic activity was assessed using WST-1 and ATP-based CellTiter-Glo assays, with glycolytic inhibition (2-deoxy-D-glucose, 2DG) and osmotic (mannitol) controls. Migration and protein expression analyses of viral entry receptors, endosomal trafficking mediators, and metabolic signalling regulators were evaluated by scratch assay and Western blotting, respectively.

Results: At 72 hours, hyperglycaemia significantly increased metabolic activity (15 mM glucose: WST-1 $p < 0.05$, ATP $p < 0.0001$; 30 mM glucose: WST-1 $p < 0.001$, ATP $p < 0.0001$), while mannitol elicited comparable effects ($p < 0.0001$), indicating partial osmotic contribution. Glycolytic inhibition caused marked reductions in viability at all timepoints ($p < 0.0001$). Spike variants modulated endothelial metabolism in a dose- and variant-specific manner: WT and β variants increased WST-1 and ATP activity across multiple concentrations ($p < 0.05$–$p < 0.0001$), whereas the δ variant decreased ATP ($p < 0.01$–$p < 0.001$) despite elevated WST-1 ($p < 0.05$), revealing differential bioenergetic responses.

Conclusion: These findings demonstrate that hyperglycaemia and SARS-CoV-2 S-protein variants differentially regulate endothelial metabolic activity and may influence viral entry pathways. Together, the data provide mechanistic insight into the metabolic-vascular interface underlying increased COVID-19 severity in diabetes and highlight endothelial bioenergetics as a potential therapeutic target to mitigate vascular vulnerability.

Distinct metabolic and inflammatory responses to lipotoxic and β-Adrenergic stimuli in 3T3-L1 and D16 adipocytes

Category: Basic Science

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Background: In vitro models of adipocyte dysfunction and beiging, the induction of a thermogenic and metabolically active adipocyte phenotype, provide insight into mechanisms underlying adipose tissue pathology and metabolic adaptability, respectively. 3T3-L1 adipocytes, derived from mouse embryonic fibroblasts, are the most widely used model, while D16 cells, derived from mouse inguinal adipose tissue, have been suggested to more accurately reflect beige adipocyte biology. This study investigated metabolic and inflammatory differences between these two adipocyte cell lines.

Methods: 3T3-L1 and D16 preadipocytes were differentiated for 8 days, whereafter, mature adipocytes were treated with 10 ng/mL TNFα, 0.75 mM palmitate or a combination of TNF α/palmitate to induce dysfunction, or with 1 or 10 µM CL316,243 to induce beiging for 24 and 48 hours. Metabolic activity was assessed using the MTT assay. Thereafter, both cell lines were treated with the optimal treatment conditions (TNF-α/palmitate and 10 µM CL316,243) for 24 hours. Lipid content was assessed using Oil Red O staining, lipolysis with the glycerol secretion assay and inflammation assessing by measuring adiponectin, MCP1, and IL-6 concentrations using ELISA. Data was analysed by one-way ANOVA using Dunnett post-hoc test.

Results: Treatment with TNF-α/palmitate increased lipid accumulation (24.7%), lipolysis (75.0%), MCP-1 78.6%) and IL-6 (62.0%) secretion, and decreased adiponectin secretion (47.1%) in 3T3-L1 adipocytes. In D16 adipocytes, TNF-α/palmitate treatment had no effect on lipid content and lipolysis as well as MCP-1 secretion, however, increased IL-6 (14.2%) and adiponectin (79.5%) secretion. CL316,243 had no effect on lipid accumulation and MCP-1 secretion, but increased lipolysis (21.0%) and IL-6 secretion (81.1%) with suppressed secretion levels of adiponectin (43.0%) in 3T3-L1 adipocytes. In D16 adipocytes, CL316,243 increased lipid content (8.6%), lipolysis (113.1%) and adiponectin secretion (78,7%), decreased IL-6 (28.3%), and had no effect on MCP-1.

Conclusion: 3T3-L1 and D16 adipocytes show distinct metabolic and inflammatory responses to lipotoxic and β-adrenergic stimuli. TNF-α/palmitate induced lipid accumulation, lipolysis, and pro-inflammatory cytokines in 3T3-L1 cells, whereas D16 cells were largely resistant. CL316,243 increased lipolysis and adiponectin in D16 cells. These findings suggest 3T3-L1 adipocytes may be suited for modeling dysfunction and inflammation, while D16 adipocytes better reflect metabolic adaptability and beige-like responses.

The effect of the 14:10-hour time-restricted feeding regimen on selected markers of glucose homeostasis in diet-induced prediabetic male Sprague Dawley rats

Category: Basic Science

Sthembiso Msane; Andile Khathi; Aubrey Sosibo

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Background: Prediabetes is a condition that often precedes the onset of type 2 diabetes mellitus (T2DM). Literature evidence indicates that prediabetes is reversible, making it an important therapeutic target for preventing the progression to T2DM. Several studies have investigated intermittent fasting as a possible method to manage or treat prediabetes.

Methods: Twenty-four male Sprague Dawley rats were obtained and randomly divided into two dietary groups: group 1 ($n = 6$) received a standard diet and water, while group 2 ($n = 18$) was provided a high-fat, high-carbohydrate (HFHC) diet supplemented with 15% fructose for a period of 20 weeks to induce prediabetes. After confirming prediabetes, an intermittent fasting (IF) regimen was assigned to the rats while also having untreated and metformin-treated prediabetic rats serving as controls.

Results: Both IF and HFHC-Met groups yield significantly lower blood glucose, leptin and BMI results compared to the prediabetic group. The IF group yielded significantly lower insulin, HOMA-IR and HbA1C than both controls.

Conclusion: The study showed the potential of IF in alleviating prediabetes-induced dysregulation of glucose homeostasis and therefore warrants further investigations into its use in the management of prediabetes.

The effect of maternal methyl donor nutrient supplementation on metabolic health and intestinal regulatory T cells in a rat model of developmental programming

Category: Basic Science

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Background: Maternal methyl donor nutrient (MDN) supplementation during the perinatal period may influence metabolic health in offspring, however, literature reporting metabolic effects in offspring is inconsistent, presumably due to different composition of MDN. Metabolic health is closely linked to intestinal homeostasis and regulatory T cells, identified by Forkhead box protein 3 (Foxp3)-expression, which are key mediators of intestinal immune tolerance implicated in metabolic disease. This study investigated whether perinatal MDN supplementation alters the population of intestinal Foxp3+ cells in dams and whether this improves metabolic parameters and intestinal Foxp3+ cells in offspring fed an obesogenic diet.

Methods: Pregnant Sprague Dawley rats were fed either a control diet ($n = 7$) or an MDN diet ($n = 6$) for 6 weeks until weaning. The composition of the MDN diet was an AIN93G diet formulated to contain: 8.28 g L-methionine and 5.0 g choline, 10.0 mg folic acid, 35 mg vitamin B6, and 125 µg vitamin B12 per kg diet. Male offspring from control-fed (CON-HFD, $n = 10$) and MDN-fed (MDN-HFD, $n = 11$) dams were fed a high-fat diet (45% of kcal from fat) for 20 weeks. Metabolic parameters including body weight (BW), fasting blood glucose (FBG) and retroperitoneal fat weight (RFW) were measured in offspring. Immunohistochemistry was used to evaluate the expression of Foxp3 in the duodenum, ileum and colon of dams and offspring.

Results: Independent t-tests revealed that the population of Foxp3+ cells in the colon of dams fed the MDN diet was reduced ($p = 0.040$) compared to the control group. Maternal MDN supplementation did not alter BW, RFW and FBG in HFD-fed offspring (MDN-HFD). While maternal MDN supplementation did not affect Foxp3+ cells in the duodenum, they were reduced ($p = 0.005$) in the colon of offspring when compared to the CON-HFD group.

Conclusion: In this model, maternal MDN supplementation did not improve obesogenic-diet induced metabolic parameters in offspring, while reducing colonic Foxp3+ cell populations in both dams and offspring. This reduction in Foxp3+ cells may relate to shifts in gut microbiota, and future characterisation of gut microbiota composition and diversity may provide new insights to explain the lack of metabolic responses.

Analysis of genetic deletion on DARC-null-associated (rs2814778) and CXCL2 gene-associated (rs9131) ethnic neutropenia polymorphisms in multi-ethnic healthy population from Durban, South Africa

Category: Basic Science

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Background: Neutrophils are the major white blood cells (WBC) that are found in circulation, and they play different roles in an immune system and inflammation. Neutropenia due to inherited mutations has been reported in population from African and Europeans ancestry called ethnic neutropenia. Ethnic mutations of DARC-null (SNP rs2814778) and CXCL2 (SNP rs9131) genes has been associated with ethnic neutropenia in African ancestry. This study investigates if neutropenia reported in Durban (South Africa) is associated with inherited genetic mutations on SNP rs2814778 and SNP rs9131 in multi-ethnic healthy population from Durban (SA).

Methods: Upon ethics approval, study was carried out using human stored blood samples of 43 healthy patients, collected from King Edward Hospital (February 2021 to December 2022). The population consists of 31 Africans (9 males and 22 females), 9 Asians (2 males and 7 females) and 3 Europeans (3 males). Blood neutrophils, basophils and white blood cells (WBC) were measured using haemocytometer. TaqMan pre-designed SNP genotyping assay used in TaqMan genotyping experiment, SNP rs2814778 and rs913 were genotyped as per manufacturer's protocol. Quantstudio used for genotyping.

Results: Results showed that SNP rs2814778 of 42 healthy population had substitution of T→ C at nucleotide -46, homozygous to allele 1. However, one individual showed heterozygous genotype. Results showed that SNP rs9131 of all populations had substitution of C →T, homologous to allele 2. Furthermore, results showed that neutrophils for all populations were below normal range, while the WBC were on normal range. Basophils were shown to be above normal range.

Conclusion: Findings indicate that neutropenia reported in multi-ethnic population from Durban might be also due to mutations in SNP rs2814778 and SNP rs9131. High basophil count might indicate a compensatory mechanism of neutropenia. Therefore DARC-null trait is predominantly displayed in population of African ancestry. Additionally, reported absence of DARC and CXCL2 mutation has been associated with lower neutrophil counts in circulation but circulating WBC remains normal. However, factors such as environmental factors and diet can also be considered. These findings warrant further investigation of both genes as another potential contributing factor of ethnic neutropenia reported in Durban (SA).

A retrospective audit evaluating the impact of continuous glucose monitors on the quality of life and glycaemic control of people living with type 1 diabetes at Helen Joseph Tertiary Hospital

Category: Clinical – Diabetes

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University of Witwatersrand

Background: Continuous glucose monitoring (CGM) has demonstrated benefits in glycaemic control and selected psychosocial outcomes among people living with type 1 diabetes (T1D) in high-income settings. However, data from low- to middle-income countries (LMICs), particularly within public-sector health systems in sub-Saharan Africa, remain limited.

Methods: A retrospective descriptive pre- and post-clinical record audit was conducted at the Helen Joseph Tertiary Hospital Type 1 diabetes transition clinic. Adolescents aged 12–18 years with T1DM who were offered CGM as part of routine clinical care between August 2024 and April 2025 were included. Pre- and post-CGM laboratory glycated haemoglobin (HbA1c), CGM-derived metrics (time in range [TIR], time above and below range [TAR and TBR], and glucose management indicator [GMI]), and diabetes-related QOL measured using the Monitoring Individual Needs in Diabetes Youth Questionnaire (MY-Q) were analysed. Paired statistical analyses were performed with significance set at $p < 0.05$

Results: Fourteen adolescents (median age 16.2 years; 79% female) were included in the final analysis. Median HbA1c significantly improved following CGM use, decreasing from 11.4% (IQR 8.8–13.9) to 9.1% (IQR 7.8–12.6), representing a median reduction of 2.0% ($p = 0.021$). The proportion of participants with HbA1c > 10% decreased from 64% to 43%, although categorical changes did not reach statistical significance. A strong positive correlation was observed between laboratory HbA1c and CGM-derived GMI (Spearman's $\rho = 0.89$; $p < 0.001$), with GMI consistently overestimating laboratory HbA1c. No significant changes were observed in TIR, time above range (TAR), or time below range (TBR) over the study period. Overall, MY-Q scores did not change significantly (median 56 pre-CGM vs 54 post-CGM; $p = 0.58$); however, reductions in treatment-related worry and perceived treatment burden were noted at the domain level.

Conclusion: In this public-sector adolescent cohort with poor baseline glycaemic control, CGM use was associated with a clinically and statistically significant improvement in HbA1c despite no significant improvement in TIR. These findings support the feasibility and potential value of CGM implementation in low-resource settings and highlight the importance of combining glycaemic and psychosocial outcome measures when evaluating diabetes technologies in LMIC contexts.

Nitro Blue Tetrazolium (NBT) assay as a method of assessing neutrophil function in diabetes mellitus

Category: Basic Science

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Background: Neutrophils respond to invading pathogens through nicotinamide adenine dinucleotide phosphate (NADPH) oxidase–mediated respiratory bursts. Failure to preserve this immune response results in increased susceptibility to infection. In patients with diabetes mellitus, neutrophil dysfunction contributes to recurrent infections and the development of multiple complications. This study assessed the contribution of specific diabetic micro-environmental factors to the constitutive activation of neutrophils.

Methods: HL 60 (dHL 60) cells were exposed to either an induced diabetic micro-environment (iDME) or its individual components (high glucose, advanced glycation end products, TNFα) in culture. Standard differentiation media (1.3% dimethyl sulfoxide, DMSO) with phorbol 12 myristate 13 acetate (PMA) stimulation was used as positive control. The Nitro Blue Tetrazolium (NBT) reduction assay was performed to assess constitutive activation and the production of reactive oxygen species (ROS) assessed using a DCF-HA assay.

Results: Quantification of formazan positive and negative cells using microscopy indicated that 5−7 days of 1.3% DMSO differentiation followed by 90 minutes PMA stimulation induced neutrophil activation and granulation. A 2-fold increase in NBT staining was observed following PMA stimulation (HL-60 17%; HL-60+PMA 33%; diffHL-60 21%; diffHL-60+PMA 42%), confirming the sensitivity of the NBT assay to assess neutrophil responsiveness to stimulation under controlled conditions. Similarly, exposure to the diabetic micro-environmental factors altered neutrophil activation status and responsiveness to stimuli.

Conclusion: These findings support the use of the NBT reduction assay as a reliable method for assessing neutrophil function in the context of diabetes mellitus. With further refinement and expansion, this approach may contribute to the development of future therapeutic strategies and targeted treatment interventions.

The associations of childhood abuse with renal function in young South African women: a longitudinal study

Category: Clinical - Endocrinology

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Background: Evidence in high-income countries suggests that individuals with childhood abuse (CA) exposure have higher risk for developing chronic kidney disease (CKD). However, this relationship has not well studied in South African women who experience high rates of CA and CKD. Therefore, this study aimed to examine the associations of CA with the change in renal function over 3-years follow-up among baseline rape-exposed and rape-unexposed women aged 18–40 years in KwaZulu-Natal, using the data of the Rape Impact Cohort Evaluation longitudinal study.

Methods: Self-reported history of CA exposure (sexual, physical, emotional abuse, and parental neglect) was collected; renal function (serum creatinine and estimated glomerular filtration rate [eGFR]) was measured. Linear mixed effect models adjusted for age, employment, education, current smoking, current alcohol use, hypertension, and baseline-rape-exposure examined the CA-renal function associations, with the inclusion of the interaction term, "CA*rape-exposed".

Results: Among 1 613 women (median age, 24 years (IQR, 21–28)), 55.2% had experienced at least one type of CA. The most common was physical (41%), parental neglect (25%), emotional (21%) and sexual CA (12.5%). A quarter of women experienced a single CA type, and 30.2% were exposed to multiple CA types. Renal function data were collected at baseline ($n = 1\,613$), 12 ($n = 1\,178$), 24 ($n = 925$), and 36 months ($n = 571$). Any CA [coefficient=0.99 (standard error=0.32), $p = 0.001$], multiple CA type [0.37 (0.14), $p = 0.008$], and greater frequency of emotional CA [1.90 (0.35), $p < 0.001$] were associated with rising in S-creatinine over 3-years. There was evidence of an interaction effect of baseline rape-exposure with emotional CA ($p = 0.003$) but not with other CA types ($p \geq 0.192$ for interaction tests). Similarly, any CA [-0.82 (0.28), $p = 0.003$], multiple CA [-0.27 (0.12), $p = 0.025$], and greater frequency of emotional CA [-1.59 (0.31), $p < 0.001$] were associated with decreasing in eGFR over 3-years, with no evidence of an interaction effect of baseline-rape-exposure ($p \geq 0.146$ for all interaction tests). Other CA types were not associated with the changes in renal function over the period investigated.

Conclusion: CA is common in South Africa and associated with decreased renal function in young women. Prevention of CA should be included in strategies to address CKD risk in South African women.

Investigating the association between the gut microbiome and exercise-induced changes in insulin sensitivity in Black South African women

Category: Basic Science

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Background: The rising prevalence of type 2 diabetes in South Africa necessitates effective interventions to mitigate risk. While exercise is known to improve insulin sensitivity, the potential role of the gut microbiome in association with this effect remains understudied in African populations. This study aimed to investigate whether a 12-week exercise training intervention alters the gut microbiome and to determine if gut bacteria associate with exercise-induced improvements in insulin sensitivity.

Methods: We conducted a sub-study of a randomised controlled trial involving 28 women with obesity, assigned to an exercise intervention ($n = 16$) or control group ($n = 12$). The exercise group completed 12 weeks of supervised combined aerobic and resistance training while the control group maintained habitual activity levels. We assessed insulin sensitivity using a frequently sampled intravenous glucose tolerance test (IVGTT), body composition via dual-energy X-ray absorptiometry (DXA), cardiorespiratory fitness as peak oxygen consumption (VO2peak), and inflammatory markers. Faecal samples collected at baseline and post-intervention underwent 16S rRNA gene sequencing. We analysed alpha and beta diversity using ANOVA and PERMANOVA and employed linear mixed-effects models, to determine if specific genera were associated with the interaction between intervention group, time, and insulin sensitivity.

Results: Exercise significantly improved insulin sensitivity ($p = 0.035$), VO2peak ($p = 0.024$), and body mass index (BMI) ($p = 0.003$). Despite higher baseline diversity in the exercise group (Alpha $p = 0.03$; Beta $p = 0.012$), the intervention induced no longitudinal shifts in global diversity or the Prevotella-dominated community structure. Diversity metrics were unrelated to insulin sensitivity ($p > 0.05$), with composition driven primarily by socio-demographics rather than the intervention. However, linear mixed-effects modelling revealed a significant group-dependent association for Succinivibrio (FDR $p < 0.005$), which positively tracked with insulin sensitivity in the exercise group only.

Conclusion: A 12-week exercise intervention improved metabolic health without restructuring the global microbiome, which remained resilient and primarily driven by sociodemographics. Metabolic gains occurred independently of broad microbial diversity shifts. However, the specific coupling of Succinivibrio with insulin sensitivity in the exercise group suggests that targeted host-microbe interactions, rather than community-wide changes, underpin these adaptations.

Clinical profile, management and outcome of thyrotoxicosisin-pregnancy at Inkosi Albert Luthuli Central Hospital (IALCH): a 21-year tertiary centre experience

Category: Clinical – Endocrinology

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Background: Thyrotoxicosis affects 0.1–0.4% of pregnancies, commonly due to Graves' disease, and is associated with maternal complications and adverse perinatal outcomes. Data from sub-Saharan Africa on presentation, management and outcomes are limited. The objective was to describe the clinical spectrum, treatment strategies, and maternal, perinatal and foetal outcomes in women with thyrotoxicosis in pregnancy.

Methods: A 21-year (February 2002–August 2023) retrospective cohort study undertaken at Inkosi Albert Luthuli Central Hospital (IALCH). Data recorded included clinical features, laboratory results, and management; maternal outcomes were analysed per pregnancy and neonatal outcomes per infant (including twins).

Results: The analysis included 140 pregnancies, 98 deliveries and 103 neonatal outcomes. At presentation, median (IQR) age was 28.5 (25–34) years; 78.6% were African; Graves' disease accounted for 61% (n = 85); comorbidities included hypertension (36.4%), HIV (24.2%) and diabetes (12.1%). Mean gestational age at presentation was 33.7 ±8.14 weeks; mean serum free T4 32.72 ± 27.00 pmol/L and mean TSH 0.36 ± 0.95 mIU/L. TSH receptor autoantibody was positive in 80% (53/66) of tested women, with mean titre 12.4 ± 13.9 U/l. Maternal complications occurred in 30.7% of pregnancies, including pregnancy-induced hypertension (14%), heart failure (9%) and preterm labour (4%). Caesarean section delivery was undertaken in 76% (n = 74/98); and 69% (n = 51/74) were emergency procedures, and for foetal distress in 34%. Live birth rate was 98% (n = 101/103). Congenital anomalies were identified in 31% (32/103) of total births and included growth-related, neurological, cardio-respiratory, and cranio-facial anomalies. Carbimazole was prescribed in 74.3% of pregnancies (105/140); mean dose 21.49 ±17.49 mg/day and was not significantly associated with congenital anomalies (p = 0.085). Mean serum free T4 was 18.74 pmol/l, by delivery.

Conclusion: In this tertiary-referral cohort, thyrotoxicosis in pregnancy was characterised by late presentation, high multi-morbidity, and predominance of Graves' disease. Effective control of thyrotoxicosis was achieved in most women, with favourable perinatal outcomes. These findings add important regional evidence to guide clinical practice and support improved care pathways for women with thyrotoxicosis in sub-Saharan Africa.

Preference for and adherence to nutrition educational methods and materials among people living with diabetes: a qualitative study

Category: Clinical – Diabetes

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Background: Nutrition education is effective in diabetes management, yet adherence to dietary recommendations remains challenging. This study identifies preferred nutrition education methods and materials, as well as adherence levels to different educational approaches, among individuals living with diabetes in the Western Cape Province of South Africa, in both public and private healthcare facilities.

Methods: Using a multi-method approach, data was collected through questionnaires (n = 46) and six focus group discussions (n = 29). Participants were recruited from public and private healthcare facilities in the Cape Metropole and surrounding areas. Recruitment methods included both digital and physical posters, as well as leaflets. Quantitative data was analysed through descriptive statistics and qualitative data was analysed thematically using Atlas.ti software.

Results: This study surveyed 46 participants with diabetes mellitus, predominantly type one (n = 36, 78.3%). The sample included 39.1% (n = 18) in full-time work, with the largest age group being 50+ years (n = 16, 34.5%). Most were managed by diabetes specialists (n = 31, 67.4%) and/or diabetes nurses (n = 11, 23.9%), and 65.2% (n = 30) used Continuous Glucose Monitoring (CGM). Nearly half had a family member with diabetes (n = 21, 47.8%). Significant gaps in nutritional care were identified: 60.9% (n = 28) never consulted with a dietitian after diagnosis, only 4.3% (n = 2) had regular quarterly consultations, and 39.1% (n = 18) last received nutrition education over two years ago, despite 87% (n = 40) expressing desire for additional resources. Five key themes emerged: dietitian experience, education methods preferences, education materials preferences, adherence, and new material development. Public facility participants faced severe consultation limitations and financial constraints including food insecurity, while both groups preferred personalised one-on-one counselling. Private sector participants favoured hybrid physical-digital materials; public sector participants preferred physical materials due to technology barriers and reliability. Essential design principles include cultural relevance with local South African foods, simple explanations, condensed information, visual aids, and acknowledgment of socioeconomic barriers.

Conclusion: Effective diabetes nutrition education must be accessible, affordable, practical, and culturally relevant, tailored to specific barriers and preferences of different socioeconomic groups. These findings provide critical insights for developing patient-centred, culturally sensitive strategies promoting sustained behavioural change in resource-constrained settings, with implications for healthcare practitioners, people living with diabetes, and health policy development.

The prevalence of diabetic complications and target organ damage among patients with type 2 diabetes mellitus attending a tertiary-care diabetic clinic

Category: Clinical – Diabetes

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Helen Joseph Tertiary Hospital

Background: Type 2 diabetes mellitus (T2D) is associated with significant micro- and macrovascular complications contributing to morbidity and mortality. Data describing the burden of diabetes-related target organ damage (TOD) in a South African setting remain limited. This study aimed to determine the prevalence of TOD and diabetes-associated complications among patients with T2D attending a tertiary diabetic clinic.

Methods: A retrospective clinical audit was conducted at the Diabetic Clinic of Helen Joseph Tertiary Hospital, Johannesburg. Records of patients aged ≥ 45 years with T2D were reviewed. Of 300 files audited from 1 January to 30 April 2020, 290 met inclusion criteria and were analysed. Documented microvascular and macrovascular complications and other diabetes-related TOD were extracted. Data were analysed descriptively; no inferential statistical testing was performed

Results: Overall, 223 participants (76.9%) had documented evidence of at least one form of TOD. Diabetic neuropathy was most prevalent, affecting 154 patients (53.1%). Nephropathy occurred in 97 patients (33.4%) and retinopathy in 59 patients (20.3%). Cataracts were documented in 53 patients (18.3%). Macrovascular complications included ischaemic heart disease in 35 patients (12.1%), cardiac failure in 34 patients (11.7%), and prior cerebrovascular accidents or transient ischaemic attacks in 25 patients (8.6%). Peripheral vascular disease was recorded in 14 patients (4.8%). Erectile dysfunction was documented in 14 male participants (14.4% of the male subgroup). The median [IQR] HbA1c levels of participants with TOD (9.5% [8.2-11.2%]) was significantly higher than those without TOD (8.4% [6.9–10.3%]; $p = 0.005$). Participant's HbA1c levels within the SEMDSA target range (45.8%) had a significantly lower prevalence of TOD than those with HbA1c levels not within target range (79.7%; $p < 0.001$)

Conclusion: This study illustrates a high prevalence of diabetes-related TOD among patients with T2D attending a tertiary specialist clinic, particularly neuropathy and nephropathy. Furthermore, it demonstrates an association between higher HbA1c levels and significant TOD. The lower reported prevalence of complications such as cataracts and erectile dysfunction, compared with published literature, likely reflects underdiagnosis and limitations in routine screening. This study emphasises the urgent need for structured screening programs, early referral pathways and adequate control of HbA1c levels within recommended targets to prevent significant TOD.

Synthesis, in silico and in vitro analysis of Schiff base sulfonamide derivatives as potential COX-2 inhibitors

Category: Basic Science

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Background: Cyclooxygenase-2 (COX-2) is a key enzyme in the regulation of inflammation, and its overexpression is implicated in various inflammatory conditions, including obesity associated adipose tissue inflammation. Sulfonamide-containing compounds such as sulfadiazine represent a privileged scaffold with a well-established COX-2 inhibitory activity and therapeutic relevance. Schiff base derivatisation is a widely employed medicinal chemistry strategy to enhance bioactivity and pharmacokinetic properties of compounds. This study integrates synthetic chemistry, in silico, and in vitro approaches, to evaluate four sulfonamide derivatives as potential COX-2 inhibitors.

Methods: Four compounds were synthesised via Schiff base condensation reaction of aldehydes and sulfadiazine (SDZ), and the structures were confirmed by fourier transform infrared (FT-IR) and (1H and 13C) nuclear magnetic resonance (NMR) spectroscopy. The absorption, distribution, metabolism, and excretion (ADME) and toxicity properties were profiled in silico using SwissADME and ProtoxIII, respectively. SwissTargetPrediction predicted COX-2 as a biological target for the compounds. Molecular docking was used to determine the compounds' binding poses and affinities at the COX-2 active site. All the compounds were subjected to 200 ns molecular dynamics (MD) simulations to evaluate complex stability and induced fit mechanisms. This was followed by free energy calculations to determine thermodynamic stability. In vitro COX-2 inhibitory activity was evaluated using a kinetic enzymatic assay.

Results: Schiff base derivatives (SR1-SR4) were successfully synthesised as indicated by the imine bond formation. The compounds exhibited favourable ADME profiles and reduced toxicity compared to celecoxib (COX-2 selective inhibitor) and SDZ. MD simulations revealed that SR1, SR2, and SR3 were well positioned on the active site of COX-2 throughout the simulations, while the binding free energy of SR3 was comparable to celecoxib (-41.01 kcal/mol vs -41.91 kcal/mol). In vitro analysis showed that SDZ, SR1, SR2, and SR4 at 1, 10, 50, 100, and 200 µM showed less than 50% COX-2 inhibitory activity, while SR3 induced 52% (50 µM), 59% (100 µM) and 73% (200 µM) COX-2 inhibition compared to celecoxib (73%).

Conclusion: In silico prediction and in vitro analysis suggests that SR3 has favourable pharmacokinetic properties and is a promising COX-2 inhibitor, indicating its potential to be further investigated for its anti-inflammatory properties.

Factors that lead to the hospitalisation of patients with diabetes mellitus and their management at a tertiary hospital in South Africa, Gauteng Province

Category: Clinical – Other

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Background: The increasing prevalence of diabetes around the world is a major health problem because of its associated morbidity and mortality. South Africa is among the countries with the highest burden of diabetes in Africa. Patients with diabetes have an increased demand for hospital services, particularly inpatient care. The aim of the study was to investigate the reasons for hospitalisation and the management of these patients.

Methods: The study was conducted prospectively over three months in internal medicine wards at a public tertiary hospital. Hospitalised adult patient's medical records were reviewed and analysed. A developed data collection tool was used to record demographics, reasons for hospitalisation, treatment, glycaemic outcomes and interventions done by a clinical pharmacist. Data analysis was done in consultation with a statistician.

Results: A total of 360 patients were hospitalised. The prevalence of diabetes was 25.0% ($n = 90$). From the sample of patients with diabetes ($n = 90$), the mean (SD) age was 58.5 (16.59), 54.4% were females and 85.6% had type 2 diabetes. Hypertension was a comorbidity in 58.9% of the patients. Acute metabolic complications of diabetes were the most prevalent factors for hospitalisation (30.0%) followed by infections, cardiovascular and renal complications, 24.4%, 23.3% and 11.1% respectively.

Hypoglycaemic agents commonly prescribed were metformin and insulin. Sliding scale insulin therapy was prescribed in 64.4% ($n = 90$) of the patients. In 70 interventions, 48.6% were directed to prescribers, 30.0% to patients and 21.4% to nurses. The most common interventions addressed untreated conditions (15.7%), medications not administered (14.3%) and directions not understood (25.7%), with a favourable acceptance rate. In terms of glycaemic outcomes, the mean (SD) fasting blood glucose was 10.0 mmol/l (4.90) and the an (SD) HbA1c was 9.8% (3.43). The overall inpatient mortality was 14.8% ($n = 90$).

Conclusion: The main factors for hospitalisation were poor glycaemic control and infections. Insulin remains the mainstay of therapy in inpatients, however, the use of only sliding scale insulin observed in some patients was found to be ineffective, contributing to poor glycaemic control. The significant hospitalisation burden of diabetes necessitates collaboration in reviewing or developing interventions and ongoing diabetes management strategies.

The association of G6PD variants with type 2 diabetes in a black South African population

Category: Basic Science

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Background: Oxidative stress contributes to the development of type 2 diabetes (T2D). Glucose-6-phosphate dehydrogenase (G6PD), the rate-limiting enzyme in the oxidative branch of the pentose phosphate pathway, catalyses the conversion of glucose-6-phosphate into 6-phosphogluconolactone while generating nicotinamide adenine dinucleotide phosphate (NADPH). NADPH is essential for maintaining cellular defence against oxidative damage. Two G6PD missense variants (MVs), rs1050828 (C > T) (MV1) and rs1050829 (T > C) (MV2), reduce G6PD activity by 20–88% depending on the allele present. G6PD-deficiency in erythrocytes results in a shorter cell lifespan thus lowering HbA1c levels via a non-glycaemic mechanism. Additionally, individuals with T2D have lower G6PD activity compared to non-diabetic controls, suggesting G6PD-deficiency is associated with impaired glycaemic regulation. Little is known about the effect of these polymorphisms on glycaemic changes. Thus, this study aimed to determine the association of the G6PD gene polymorphisms with T2D in the black South African population.

Methods: Black South African participants with T2D ($n = 93$) and non-diabetic control participants ($n = 87$) were recruited from the greater Johannesburg area to participant in a case-control study. Participants were genotyped for MV1 and MV2 using predesigned Taqman genotyping assays. As G6PD is an X-linked gene, the Clayton statistical method for X-linked associations was used as it accounts for random X-inactivation. Statistical analysis was performed using Statistica software.

Results: The frequency of the MV1 T-allele was 0.08 and the MV2 C-allele was 0.25. In a multivariate regression analysis T2D status ($p < 0.001$), and waist-to-height ratio ($p = 0.008$) were associated with higher, whilst the MV1 T-allele ($p = 0.003$) was associated with lower HbA1c levels. Male sex ($p = 0.001$), decreased age ($p < 0.001$), and the presence of the MV2 CC-genotype in females and C allele in males ($p = 0.030$) were associated with lower odds of having T2D.

Conclusion: The MV1 T-allele is known to result in lower HbA1c levels through non-glycaemic mechanisms and this association was observed in the current study. Thus, in T-allele carriers, HbA1c levels may not be a reliable marker of glycaemia. The MV2 C-allele was associated with lower odds of T2D however, it is not known whether this is mediated via changes in G6PD activity and mechanistic studies are therefore required.

Characterising real-world use of SGLT2 inhibitors in a South African tertiary diabetes clinic

Category: Clinical – Diabetes

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Background: Sodium-glucose co-transporter 2 (SGLT2) inhibitors confer glycaemic, cardiovascular, and renal benefits in type 2 diabetes mellitus (T2DM). However, real-world data from South Africa remains limited. This study aimed to characterise prescribing patterns, short-term efficacy, and safety of SGLT2 inhibitors in a diabetic clinic at a tertiary academic hospital.

Methods: A retrospective observational study of adults with T2DM initiated on empagliflozin or dapagliflozin between November 2022 and June 2023. Demographic, clinical, anthropometric, and biochemical parameters were extracted at baseline and at first follow-up, provided background glucose-lowering therapy remained unchanged. Outcomes included changes in weight, blood pressure, glycaemic control, renal function, lipid parameters, and adverse events. Analyses were descriptive, with results summarised as mean or median changes over time.

Results: Eighty-eight patients were included (median age 60 years; 58% male), predominantly of Black African ancestry, with a median T2DM duration of 11.5 years. Comorbidity burden was high, with prevalent hypertension, dyslipidaemia, established cardiovascular disease, and chronic kidney disease (CKD). Although 43% of patients had cardiorenal indications for SGLT2 inhibitor therapy, initiation occurred primarily within the diabetes clinic (73.8%), with fewer prescriptions initiated by cardiology (20.5%) or nephrology (3%) services. At a median follow-up of two months, mean reductions were observed in weight (–1.2 kg) and HbA1c (–0.6%). These changes were more pronounced in patients treated with empagliflozin, who demonstrated reductions in systolic [–5.9 mmHg] and diastolic [–3.3 mmHg] blood pressure (overall $p = 0.20$). Renal function improved in the empagliflozin group (eGFR +3.8%, creatinine –2.2%), while it declined in the dapagliflozin group (eGFR –9.4%, creatinine +17.9%); between-group differences in eGFR and creatinine were statistically significant ($p = 0.028$ and $p = 0.042$, respectively). No major adverse events or drug discontinuations were recorded during follow-up.

Conclusion: In this real-world South African cohort, SGLT2 inhibitors were associated with short-term improvements in glycaemic control, weight, and blood pressure, with an acceptable safety profile. Despite strong cardiorenal indications, prescribing remained concentrated within diabetes services, highlighting an implementation gap across specialties. Greater multidisciplinary engagement may enhance the clinical impact of SGLT2 inhibitors in resource-constrained settings.

Knowledge, attitudes and behaviours regarding diet and lifestyle related factors in South African males with osteopenia or osteoporosis

Category: Clinical – Endocrinology

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Background: Globally osteoporosis is seen as a silent disease causing pain, disability, poor quality of life, and loss of autonomy in many individuals. It is driven not only by non-modifiable risk factors, but also by modifiable risk factors like nicotine use, alcohol abuse, sedentary lifestyle, poor dietary habits, malnutrition and loss of muscle strength. Research on osteoporosis in men is lacking in the South African setting. This study was conducted to help fill the research gap. The main study aim was to describe the level of osteoporosis knowledge as well as the attitudes and behaviours regarding diet and lifestyle related risk factors amongst men who suffer from osteopenia or osteoporosis. Secondary objectives included the identification of any other associations between osteoporosis knowledge and attitudes, behaviours respectively.

Methods: This descriptive observational study with an analytical component used the Stellenbosch University (SUN) Survey platform to create an Osteoporosis Knowledge, Attitude and Behaviours Questionnaire (OKABQ) specifically adapted for South African men. Content and face validity was established and an electronic invitation to participate was sent to eligible candidates by an independent third party. Once data collection were completed, data cleaning and analysis was done and extensive assumption checks were conducted. Inferential statistics were applied to ensure result validity.

Results: One hundred and fourteen ($n = 114$) respondents participated, yielding an 80% study power with a significance level of $p < 0.05$. Respondents generally had insufficient osteoporosis knowledge, with a score below the classification threshold of 70%. No significant difference in osteoporosis knowledge and age ($p = 0.91$), ethnicity ($p = 0.053$), marital status ($p = 0.14$) and smoking status ($p = 0.056$) was found. The highest level of education ($p = 0.00$) and family history of osteoporosis ($p = 0.04$) were significant predictors of osteoporosis knowledge. Respondents' attitudes toward osteoporosis and behavioural adequacy exceeded the 70% threshold. Linear regression showed a statistically significant positive relationship between osteoporosis knowledge and attitude (R2 = 0.2, $p < 0.05$). Neither knowledge nor attitude were found to predict behaviour ($p = 0.07$, $p = 0.07$) respectively.

Conclusion: Low osteoporosis knowledge amongst the respondents call for osteoporosis education aimed at men. As per the Health Belief Model, improved osteoporosis knowledge may lead to positive attitudes and preventative behavioural changes.

Nutritional management of children and adolescents with type 1 diabetes at Tygerberg Hospital

Category: Clinical – Diabetes

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Background: Although adequate nutrition knowledge is essential for optimal blood glucose (BG) control, Tygerberg Hospital (TBH) does not employ a dietician, dedicated solely to the management of type 1 diabetes (T1D) children. To assess the knowledge of key T1D-related nutrition concepts of children and adolescents with T1D and of their caregivers, questionnaires were administered by an interviewer. In addition, nutritional management was evaluated against the recommendation of the 2018 ISPAD nutrition guidelines.

Methods: One hundred and thirty pairs T1D children/adolescents between 9 months and 18 years of age with T1D duration for > 1 year, and their caregivers, were recruited. Demographic data, HbA1c, BG monitoring technology, BMI, blood pressure, lipid profile and contact frequency with the dietician were recorded. The administered questionnaire assessed 9 key nutrition concepts. A score was calculated.

Results: Mean average score was 11.2/27 (95% CI 10.3/27–12.1/27) for adolescents and 13/27 (95% CI 12.2-13.7/27) for caregivers. Nutrition knowledge was adequate in two adolescents (2%), five caregivers (4%), and insufficient in 72 adolescents (77%) and 70 caregivers (55%). The adolescents recorded no correct responses for complex carbohydrates, two (2.15%) for carbohydrate counting, three (3.2%) for fibre. Label reading had the highest correct response (21; 22.6%). Six caregivers (4.7%) had correct responses for carbohydrate counting while micronutrients had the highest number of correct responses (34; 26.8%). If caregiver knowledge was adequate on saturated fats, the mean HbA1c of the participants was 9.0 (95% CI 8.0-9.9) %, while it was 10.4 (95% CI 10.0–10.8) % for those with caregivers of inadequate knowledge ($p = 0.02$). Highest scores were recorded in English speaking caregivers (15.6/27; 95% CI 14.1/27-17.1/27; $p = 0.00$) and in participants on continuous glucose monitoring (18.4/27; 95% CI 14.4/27-22.4/27; $p = 0.00$). Lowest scores were seen in caregivers with only primary education (11.4/27; 95% CI 10.4/27-12.4/27, $p = 0.00$). Adolescents with an HbA1c < 7.6% had a score of 17.2/27 (95% CI 14.2/27-20.2/27; $p < 0.001$). BMI, blood pressure, lipid profile and the contact frequency with the dietician had no impact on the score. Only 8 adolescents and 10 caregivers were seen at diagnosis, one month later and after one year.

Conclusion: Nutrition knowledge of adolescents and caregivers was poor. Dietary advice provided by dieticians was suboptimal.

Oral Presentation Abstracts

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Characteristics and outcomes of primary hyperparathyroidism: a single-centre retrospective review at a tertiary hospital in South Africa

Category: Clinical – Endocrinology

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Background: Primary hyperparathyroidism (PHPT) is a common endocrine disorder, yet local data describing its clinical profile and outcomes remain limited. We thus aimed to describe the clinical, biochemical and skeletal characteristics of adults with PHPT and evaluate surgical outcomes and the diagnostic performance of preoperative localisation imaging at a South African tertiary centre.

Methods: A retrospective single-centre observational study was conducted at Charlotte Maxeke Johannesburg Academic Hospital, including adults (≥ 18 years) with PHPT attending the endocrine clinic between January 2019 and January 2024. Pregnant patients and those with normocalcaemic or tertiary hyperparathyroidism were excluded.

Results: Ninety-six patients were included with a mean (SD) age of 64 (13.2) years and marked female predominance (89.6%). Most were asymptomatic at diagnosis (72.9%). Cardiometabolic comorbidities were common, including hypertension (56.3%), obesity (43.8%) and dyslipidaemia (31.3%). Baseline biochemistry demonstrated a median (IQR) corrected calcium of 2.71 (2.62–2.82) mmol/L, PTH 13.65 (9.1–20.1) pmol/L, mean phosphate 0.86 (0.23) mmol/L and 25-OH-vitamin D 70.84 (41.55–96.70) nmol/L. Skeletal and renal involvement were frequent: 74% had reduced bone mineral density (osteopenia 28.1%, osteoporosis 45.8%), while 20.8% had an eGFR < 60 ml/min/1.73 m^2. Parathyroidectomy was performed in 45 patients (46.9%), of whom 42 had single-gland disease. Ultrasound correctly localised the pathological gland in 76.2% (sensitivity 82.1%, PPV 91.4%), while technetium-99m sestamibi demonstrated higher accuracy (90.5%) with sensitivity and PPV of 95%. Combined imaging yielded the highest diagnostic performance (accuracy 95.2%, sensitivity 97.6%, PPV 97.6%), with excellent concordance between modalities ($\kappa = 0.83$; $p < 0.001$). Minimally invasive parathyroidectomy was performed in 64.4% of surgical cases. Histopathology confirmed single-gland adenoma in 93.3%. Surgical remission was achieved in 91.1%, with persistence in 6.7% and recurrence in 2.2%. Following surgery, significant reductions in calcium, PTH and alkaline phosphatase were observed with increases in phosphate and magnesium over 12 months (all $p < 0.05$). Bone mineral density improved significantly at all measured skeletal sites, with the greatest improvement at the lumbar spine.

Conclusion: Despite a predominantly asymptomatic presentation, skeletal involvement was common. Parathyroidectomy achieved high remission rates with sustained biochemical normalisation and improvement in bone mineral density. Dual-modality imaging demonstrated strong localisation performance for single-gland disease, supporting its role in surgical planning.

Diabetic complications among people living with type 2 diabetes in sub-Saharan Africa: a systematic review and meta-analysis

Category: Clinical - Other

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Background: Diabetic complications (DC) are a public health concern and are rising rapidly globally. The burden is high among adults living with type 2 diabetes mellitus (T2DM) in sub-Saharan Africa (SSA). Therefore, this review aimed to determine the pooled prevalence and associated factors of DCs among adults living with T2DM in SSA.

Methods: A systematic and comprehensive search was conducted across databases, including PubMed, Scopus, Web of Science, Cochrane Library, EBSCOhost, ScienceDirect, and SABINET African Journals. Articles reporting any information on the prevalence or associated factors of DC (retinopathy, neuropathy, nephropathy, peripheral arterial disease, foot ulcer, and cardiovascular disease) from January 2012 to August 2025 were included. A Bayesian random-effects meta-analysis was performed to estimate the pooled prevalence of DC and its associated factors.

Results: A total of 79 articles were included, with 28,881 adults living with T2DM, and 53.78% of the participants were female. The pooled prevalence of DC was 36.97% (95% CrI: 32.51, 41.46) with between-study variation 0.89. The largest pooled prevalence was recorded in West Africa (41.87%) and Southern Africa (37.78%). The most prevalent DC type was neuropathy (39.57%), followed by retinopathy (27.28%). The most significant risk factors for DC were age, body mass index, hypertension, duration of living with T2DM, and poor glycaemic control.

Conclusion: This review found that the high burden of DCs among adults living with T2DM in SSA underscores its major contribution to healthcare strain, disability, and premature mortality. Targeted interventions addressing metabolic risk factors integrated with early screening for DCs and timely, sustained glycaemic control are needed to reduce disease progression. Promoting physically active occupations and lifestyles should be prioritised to mitigate DCs. Future research should focus on predictive modelling to facilitate early detection of complications and enhance personalised T2DM management in SSA.

Indel variants associated with HPA axis suppression and ACTH sensitivity in corticosteroid-treated children with asthma

Category: Clinical - Endocrinology

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Background: Inhaled corticosteroids are central to asthma management but may lead to hypothalamic–pituitary–adrenal axis suppression (HPAS). Altered adrenocorticotropic hormone (ACTH) sensitivity may either contribute to or mitigate HPAS, and genetic susceptibility is thought to vary between individuals. This study aimed to identify insertion–deletion variants (indels) associated with HPAS and ACTH sensitivity in corticosteroid-treated children with asthma.

Methods: A genome-wide association study was performed using exome sequencing data from saliva-derived DNA of 95 asthmatic children aged 5–18 years receiving corticosteroid therapy, recruited from paediatric respiratory clinics at the Lung Institute, Tygerberg Hospital, and Red Cross War Memorial Children's Hospital in Cape Town, South Africa. Basal ACTH and cortisol (C), and post-metyrapone ACTH, 11-deoxycortisol (11DOC), and C levels were measured. HPAS was defined as serum C < 83 nmol/L or post-metyrapone ACTH < 106 pg/mL, 11DOC 3), and functional impact scores.

Results: For HPAS, one indel remained significant after association testing and permutation correction: rs398088143 in WNK1 (OR 5.35, 95% CI 1.09–26.33, $p = 0.041$). For ACTH sensitivity, three indels showed significant associations: rs1334333976 in SLC3A1 ($\beta = 0.42$, 95% CI 0.21–0.63, $p = 0.000152$), rs138226842 in ADCY8 ($\beta = 0.39$, 95% CI 0.17–0.60, $p = 0.000691$), and rs200903316 in PDE11A ($\beta = 0.29$, 95% CI 0.07–0.51, $p = 0.0127$). Functionally, the HPAS-associated variant maps to WNK1, a regulator of ion transport and cellular stress responses, while ACTH–sensitivity–associated variants map to genes involved in cAMP signalling (ADCY8, PDE11A) and amino acid transport (SLC3A1), implicating disrupted intracellular signalling and metabolic regulation in altered adrenal responsiveness.

Conclusion: This study identifies indels in WNK1, SLC3A1, ADCY8, and PDE11A as genetic markers of HPA axis suppression and altered ACTH sensitivity in asthmatic children receiving corticosteroid therapy, supporting improved risk stratification, earlier clinical intervention, and more personalised asthma management strategies in paediatric care.

Vitamin D Metabolites Trigger Apoptosis via Non-Genomic Mitochondrial and Survival Signalling Pathways in VDR-Deficient C33A Cervical Cancer Cells

Category: Basic Science

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Background: Vitamin D is classically recognised for its anti-proliferative and pro-apoptotic effects mediated through the vitamin D receptor (VDR). However, cervical carcinoma C33A cells, which reportedly lack functional VDR, continue to undergo apoptosis following vitamin D exposure. This study investigated whether vitamin D induces apoptosis in C33A cells via ROS-mediated mitochondrial perturbation and membrane-associated signalling pathways.

Methods: C33A cells were cultured under standard conditions, with all assays performed in triplicate across three independent experiments. Cells were treated with physiological and supraphysiological concentrations of 25-hydroxyvitamin D_3 (25(OH) D_3) and calcipotriol (a synthetic 1.25-dihydroxycholecalciferol analogue). Flow cytometry assessed cell viability, mitochondrial membrane potential, oxidative stress, Annexin V binding, and caspase-3/7 activation. Antioxidant responses were evaluated by measuring total superoxide dismutase (T-SOD) and catalase activity. Apoptotic morphology was examined using PlasDIC and brightfield microscopy. Regulation of MAPK, PI3K/AKT, and NF-κB signalling pathways was analysed by Western blotting. Statistical analysis was performed using one-way ANOVA with Bonferroni correction (significance = $p < 0.05$).

Results: Exposure to supraphysiological concentrations of vitamin D (25(OH)D_3 5000 nM; calcipotriol 100 µM) elicited pronounced apoptotic responses. Both compounds significantly disrupted mitochondrial membrane potential ($p < 0.0001$) and increased intracellular ROS accumulation (25(OH)D_3 $p < 0.0001$; calcipotriol $p = 0.0306$). Antioxidant enzyme activity declined in a dose-dependent manner, with reduced T-SOD and catalase activity at higher treatment concentrations, accompanied by reduced viable cell counts (25(OH) D_3 $p = 0.0005$; calcipotriol $p < 0.0001$).

Consistent morphological hallmarks of apoptosis—including cell rounding, membrane blebbing, karyorrhexis, and apoptotic body formation—were observed. Apoptosis was further confirmed by increased Annexin V positivity (25(OH)D_3 $p = 0.0176$; calcipotriol $p = 0.0002$) and robust caspase-3/7 activation for both compounds ($p < 0.0001$). Western blotting demonstrated significant down-regulation of key proteins within the MAPK, PI3K/AKT, and NF-κB pathways.

Conclusion: In conclusion, vitamin D induces apoptosis in C33A cervical carcinoma cells through non-genomic mitochondrial dysfunction and redox-sensitive signalling pathways, suggesting therapeutic potential even in cervical tumours lacking functional VDR.

The effects of continuous glucose monitoring on glycaemic control in people with type 1 diabetes: a randomised controlled clinical trial in South Africa (ACCEDE)

Category: Clinical - Diabetes

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Background: Continuous glucose monitoring (CGM) is an alternative to self-monitoring of blood glucose (SMBG) for individuals with type 1 diabetes (T1D). The clinical impact of CGM was evaluated in a pragmatic randomised controlled trial conducted in public sector clinics in South Africa.

Methods: Eligible participants were > 4 years old, with T1D and HbA1c of ≥ 10% within the past 3 months, and no HbA1c < 8% within 9 months. 248 participants were enrolled and randomised to: Arm 1 (continuous CGM), Arm 2 (periodic CGM use for 2 weeks every

3 months), or Arm 3 (standard of care, SMBG). HbA1c was assessed 3-monthly over the 9-month intervention period and 6 months after end of intervention (follow-up). Analyses included the intention-to-treat population (ITT) and a fully compliant (FC) subgroup (complete visit attendance and ≥ 70% adherence to CGM use).

Results: For the ITT population (248 participants), mean HbA1c declined across all arms from baseline (Arm 1: 12.3%, Arm 2: 11.9%, Arm 3: 12.3%) to 9 months (Arm 1: 11.3%, Arm 2: 11.1%, Arm 3: 11.4%). Statistically significant differences were observed at 3 months and 6 months, between Arms 2 and 3.

For the FC population (138 participants), mean HbA1c declined across all arms from baseline (Arm 1: 11.6%, Arm 2: 12.0%, Arm 3: 12.2%) to 9 months (Arm 1: 10.5%, Arm 2: 10.8%, Arm 3: 11.4%). Statistically significant differences were observed at 6 months between Arm 1 and 3, and between Arm 2 and 3.

Arm 2 spent more time in range (30.2%, 29.0%, 31.5% at 3, 6 and 9 months) and less time "very high" above range (42.6%, 44.2%, 39.3% at 3, 6 and 9 months) than Arm 1, for the ITT population (similar results for the FC). Arm 1 participants (FC population) spent markedly reduced "very low" time below range compared to Arm 2 participants (FC and ITT populations) and Arm 1 participants (ITT population).

Conclusion: Improvements across all arms suggest that diabetes education and strengthened clinical follow-up contributed to outcomes. Periodic CGM use showed higher time in range, supporting its potential use as a pragmatic strategy in resource-constrained settings.

Protein biomarkers for the future development of dysglycaemia in sub-Saharan African and European populations

Category: Clinical – Diabetes

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Background: The pathogenesis of dysglycaemia (incorporating type 2 diabetes, impaired fasting glucose, and impaired glucose tolerance) differs by ancestry and environment. This study aimed to identify plasma proteins predictive of incident dysglycaemia in European and sub-Saharan populations.

Methods: The study employed a nested case–control design including participants from two prospective cohort studies: Middle-Aged Soweto Cohort (MASC) in South Africa and the Swedish CArdioPulmonary bioImage Study (SCAPIS). Participants who developed dysglycaemia during follow-up were matched to normoglycemic controls by age, sex, and BMI. Plasma proteins were quantified using targeted proteomics (Olink Cardiovascular II and III panels). Nested penalised conditional logistic regression was used to identify predictive proteins for dysglycaemia, adjusting for education and fasting glucose.

Results: The median (25–75th percentile) baseline age and follow-up time were 53 (48–59) and 6.8 (6.3–7.2) years for MASC, and 40 (40–50) and 18 (11–24) years for SCAPIS, respectively. In the case-control design, 178 participants in MASC and 347 in SCAPIS developed dysglycaemia. Four proteins (IGFBP-2, IL-4RA, PON3, and tPA) were consistently associated with incident dysglycaemia in both MASC and SCAPIS. IGFBP-1 was additionally associated with dysglycaemia in MASC but not SCAPIS and Galectin-4, FGF21, FGF23, LDLR and FABP4 were unique to SCAPIS.

Conclusion: The substantial overlap in predictive proteins in MASC and SCAPIS suggest common inflammation, lipid metabolism, and insulinsignalling pathways contributing to dysglycaemia in these populations. However, differences in proteomic signatures indicate that the biological drivers of dysglycaemia may differ by ancestry, environment, or gene–environment interactions. Accordingly, dysglycaemia may develop through both shared and populationspecific biological pathways, meaning that biomarker-based prediction tools must be tailored to ancestry and environmental context rather than assuming universal applicability.

Bridging clinic and community care: interim mixed-methods evaluation of a lifestyle intervention for type 2 diabetes in South African primary healthcare

Category: Clinical – Diabetes

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The Noakes Foundation / Eat Better South Africa

Background: Under-resourced South African communities experience a high burden of type 2 diabetes (T2D) alongside comorbid conditions such as hypertension, HIV, and tuberculosis, within contexts of food insecurity, constrained healthcare resources, and limited access to sustained lifestyle support. The Eat Better South Africa (EBSA) program, developed by The Noakes Foundation, is a structured 6-week community-based nutrition education intervention emphasising practical dietary education, therapeutic carbohydrate restriction, whole-food choices, and peer support. While EBSA has previously been evaluated in community settings, this study represents the first evaluation of the program delivered within a public primary healthcare clinic. This paper presents interim findings from an ongoing mixed-methods evaluation of EBSA implemented at Dunoon Community Health Centre, Cape Town.

Methods: A single-arm mixed-methods study was conducted among adults with T2D or prediabetes and comorbidities. Quantitative assessments were completed at baseline and immediately post-intervention, with follow-up at 3, 6, and 12 months. Measures included anthropometry, blood pressure, random blood glucose, HbA1c, dietary intake, and validated psychosocial instruments. Qualitative data were collected through focus group discussions conducted pre- and post-intervention, with additional discussions planned at later follow-up points. Findings were integrated to examine convergence between measured outcomes and participant experiences.

Results: Twenty-three participants completed the intervention. Post-intervention analyses demonstrated improvements across metabolic indicators, including reductions in body weight (−2.0 kg), waist circumference (−9.3 cm in women; −11.9 cm in men), systolic (−2 mmHg) and diastolic blood pressure (−3 mmHg), and random blood glucose (−1.5 mmol/L). Improvements were also observed in diabetes self-management (DES-SF: 32.5 to 35.1), medication adherence (MARS: 21.6 to 22.1), and depressive symptoms (PHQ-9:8.4 to 3.5). At 3-month follow-up, HbA1c decreased by a mean of 0.5%. Mixed-methods integration demonstrated convergence between quantitative improvements and qualitative reports of increased nutritional literacy, confidence in food choices, motivation, and perceived control over health. Qualitative findings further highlighted the value of clinic-based delivery, regular feedback, and peer support, while contextualising structural barriers such as financial constraints.

Conclusion: EBSA shows promise as a feasible clinic-linked, community-informed intervention for chronic disease management in low-resource settings. Ongoing follow-up will inform sustainability and scalability within public health systems.

Diabetes duration, hypercalcaemia and anaemia are strong predictors of poor healing outcomes in diabetic patients

Category: Basic Science

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Background: Hard-to-heal (HTH) wounds pose a substantial challenge for patients and healthcare systems, causing persistent pain, immobility, infection and prolonged healing times, which significantly reduce patients' quality of life. Early identification of individuals at risk of developing HTH ulcerative wounds is essential to prevent complications. Although multiple risk factors for poor wound healing have been described, reliable predictive markers that distinguish whether a chronic ulcer may progress to a recurring/HTH wound are lacking.

Methods: This retrospective descriptive study included 161 individuals who had at least one chronic ulcerative wound and were receiving the appropriate standard of care (SoC) at a specialised wound care clinic in KwaZulu-Natal, South Africa, between January 2018 and September 2025. Of these, 87 patients (54%) had chronic ulcers that responded to SoC and healed within 12 weeks of continuous treatment. Recorded parameters included population demographics, metabolic and biochemical blood profiles, medical history, chronic medication use, wound characteristics and healing trajectories, clinical signs of infection, and microbiology wound swab cultures where clinically indicated.

Results: Receiver operator curve (ROC) analysis was used to assess the predictive value of baseline variables for HTH wound development. The prevalence of diabetes, diabetes duration > 12 years (AUC 0.7800, $p = 0.0025$), serum calcium > 11.86 mmol/L (AUC 0.8298, $p = 0.001$), haemoglobin (Hb) > 12.15 g/dL (AUC 0.6532, $p = 0.0199$), mean corpuscular haemoglobin (MCH) levels of 20 mm/hr (AUC 0.8011, p=0.0287), and mean corpuscular volume (MCV) of < 89.35 fL (AUC 0.6469, $p = 0.0389$) were identified as potential predictive markers of HTH wounds. More than 90% of ulcers exhibited clinical signs of infection, with 22/36 (61%) of HTH wounds displaying multidrug resistance.

Conclusion: The study found that, in addition to diabetes duration, hypercalcaemia (> 11.86 mmol/L) and anaemia were strong predictors of poor healing outcomes and the development of HTH wounds.

Diabetes-associated disruption of intracellular mitochondrial networks and structure

Category: Basic Science

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Background: Diabetes mellitus is characterised by persistent hyperglycemia that leads to oxidative stress which disrupts cellular metabolism and accelerates mitochondrial dysfunction, a critical driver of diabetic complications. Mitochondria regulate oxidative phosphorylation, redox signaling, and apoptotic pathways; thus, their impairment significantly alters cellular homeostasis.

Methods: The study investigated the effects of a diabetic microenvironment on mitochondrial integrity, morphology, function and evaluated the prophylactic efficacy of antioxidants. This was done by comparing healthy control C3H10T1/2 mesenchymal stem cells to cells that were exposed to the diabetic microenvironment (iDME) (high glucose, AGE-BSA, TNFα) in culture for a period of 3-days. Antioxidant pretreatment consisted of a combination of N-Acetylcysteine (NAC, 7.5mM) and ascorbic acid-2 phosphate (AAP, 0.6mM)) for a period of 24h. Cell viability (crystal violet assay), onset of premature senescence (SA-β-Galactosidase assay), mitochondrial morphological changes (transmission electron microscopy, TEM) and disruption of the intracellular mitochondrial network (Mitotracker, confocal microscopy) were assessed. The parameters of interest investigated through TEM included number of mitochondria per surface area, circularity/shape, length, width, as well as the cristae surface area, volume and score.

Results: The ultrastructural analysis of the cells exposed to the diabetic microenvironment (iDME) revealed swollen mitochondria with fragmented cristae and increased vacuolisation, consistent with structural disruptions. These changes were associated with impaired cell viability and the activation of stress response pathways, indicating an early transition toward mitochondrial-driven dysfunction. In the pretreatment group, the results showed improved cell energetics and viability, however, the mitochondrial morphological integrity remained compromised.

Conclusion: Collectively, the data support that sustained exposure to a diabetic microenvironment compromises mitochondrial morphology and function in C3H10T1/2 cells, driving oxidative imbalance and energetic failure. Given the central role of progenitor cells in tissue repair, such dysfunction may underscore impaired regeneration in diabetic microenvironments.

Characteristics and biochemical determinants of diabetic kidney disease: Findings from the Kalafong Diabetes Cohort Study

Category: Basic Science

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Background: Diabetic kidney disease (DKD) remains one of the most severe microvascular complications of diabetes and a major contributor to chronic kidney disease and cardiovascular mortality. Early identification of clinical and biochemical risk factors is essential for improving diagnostic stratification and guiding preventative strategies. This study aimed to characterise demographic and biochemical profiles of patients with diabetes and to compare renal function and biochemical biomarkers between patients with and without DKD in a South African cohort.

Methods: A cross-sectional analysis nested in the Kalafong Diabetes Cohort Study was conducted. Participants were categorised according to the KDIGO classification of estimated glomerular filtration rate (eGFR). Demographic and biochemical parameters were analysed. Non-parametric and comparative statistical tests were applied to evaluate differences across renal function categories.

Results: The study included 511 participants (mean age: 47.9 ± 15.1 years; 53.2% female). Type 2 diabetes was the most common phenotype (46.2%), followed by type 1 diabetes (43.2%). Mean HbA1c was 10.3 ± 3.2%, reflecting poor glycaemic control. Median BMI was 29.4 kg/m^2 (IQR 24.4–33.6). Mean eGFR was 89.1 ± 29.4 ml/min/1.73m^2 and median uACR was 1.7 mg/mmol (IQR 0.6–6.3); however, there was a progressive increase in uACR in keeping with worsening in renal function (from stage 1 to 4), respectively 12.4 to 19.9 to 38.8 to 124.8 mg/mmol ($p < 0.001$). Hypertension affected 48.3% of participants. Longer duration of diabetes was strongly associated with progressive renal impairment ($p = 0.001$). BMI also demonstrated significant variation across eGFR stages ($p < 0.001$). Lipid parameters were not significantly associated with renal function.

Conclusion: Poor glycaemic control, increased adiposity, and longer diabetes duration were associated with reduced renal function. These findings support the investigation and development of markers for DKD and risk stratification.

Insulin dynamics predict the development of dysglycaemia 6 years later: Sex-specific findings from the Middle-Aged Soweto Cohort

Category: Basic Science

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Background: Key defects in insulin sensitivity, secretion, clearance and β-cell function (insulin dynamics) underlie the development of dysglycaemia (impaired fasting glucose, impaired glucose tolerance and/or type 2 diabetes), yet their relative contributions remain poorly defined in African populations. We therefore investigated the sex-specific associations between insulin dynamics and 6-year incident dysglycaemia in middle-aged Black South Africans.

Methods: This prospective study of the Middle-Aged Soweto Cohort included 501 normal glucose tolerant participants (264 men, 237 women) with serial oral glucose tolerance tests (OGTT) at baseline (2017–2018) and at follow-up (2023-2025), to assess incident dysglycaemia. At baseline, glucose, insulin and C-peptide were measured during an OGTT, from which insulin sensitivity (Matsuda index), early (C-peptide index) and total insulin secretion, β-cell function (disposition index, DI), basal and total insulin clearance were derived. Anthropometry and dual x-ray absorptiometry (DXA)-derived body composition were assessed. Sex-stratified logistic regression examined associations between baseline insulin dynamics (log-transformed and standardised) and incident dysglycaemia; adjusted for age, HIV status and adiposity (fat mass index in men and visceral adipose tissue in women).

Results: The median baseline age of men and women was 51 and 53 years, respectively. After a median follow-up time of 6.9 years (IQR 6.3–7.1), 98 men and 77 women developed dysglycaemia. In men, DI ($\beta = -0.82$; $p = < 0.001$) and Matsuda index ($\beta = -0{,}82$; $p = 0.001$) showed the strongest inverse associations with incident dysglycaemia, followed by the C-peptide index ($\beta = -0.52$; $p = 0.005$). In women significant U-shaped associations were observed for total insulin secretion, basal insulin clearance and DI, with higher dysglycaemia risk seen at the low and high values and lower dysglycaemia risk across the middle ranges.

Conclusion: Baseline predictors of dysglycaemia differed by sex, with predominantly linear associations observed in men and nonlinear (U-shaped) associations in women. In men, risk was primarily associated with insulin sensitivity and β-cell function, whereas in women risk was linked to insulin secretion and basal insulin clearance, but not insulin sensitivity, supporting sex-specific approaches to dyglycaemia risk assessment in African populations.

Fatty Liver Index poorly discriminates MRI-measured hepatic steatosis in African adults

Category: Basic Science

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Background: The Fatty Liver Index (FLI) is widely used as a non-invasive proxy for hepatic steatosis, but its performance against magnetic resonance imaging (MRI) is unknown in African populations. We therefore examined the discriminatory performance of FLI for detecting hepatic steatosis in United Kingdom (UK) men and South African (SA) women.

Methods: This cross-sectional study included 57 European (EM) and 55 West African men (WAM) from the UK, and 45 Black South African women (BSAW). Hepatic fat was quantified by MRI using standardised acquisition and analysis by a single operator, with hepatic steatosis defined as liver fat ≥ 5%. FLI was calculated from anthropometric (body mass index and waist circumference) and clinical biomarkers (triglycerides and gamma-glutamyl transferase), with hepatic steatosis defined as a FLI > 60. Discriminatory performance was assessed using correlation analyses and receiver operating characteristic area under the curves (AUROC).

Results: The median (25–75th percentile) ages were 54 (34–58) years in EM, 49 (34–58) years in WAM, and 23 (21–27) years in BSAW. The prevalence of hepatic steatosis assessed by FLI and MRI was comparable in EM (54.4% vs. 53.7%) but differed markedly in WAM (44.4% vs. 24.0%) and BSAW (56.3% vs. 43.2%). FLI correlated strongly with MRI-measured liver fat and showed good discrimination for hepatic steatosis in EM (rs = 0.74, $p < 0.0001$; AUROC: 0.89 [0.81–0.98]), but weakly or not at all in WAM (rs = 0.31, $p = 0.030$; AUROC: 0.65 [0.46–0.85]) and BSAW (rs = 0.20, $p = 0.17$; AUROC: 0.57 [0.40–0.75]). Within the UK cohort, FLI performed significantly better in EM than in WAM ($p = 0.027$).

Conclusion: FLI accurately detects hepatic steatosis in Europeans but performs poorly in Africans when validated against MRI, highlighting the need for population-specific diagnostic tools.

Fatty liver indices, fibrosis scores, and serum testosterone levels in men with type 2 diabetes at two outpatient clinics in Durban

Category: Clinical – Diabetes

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Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) affects up to 70% of individuals with type 2 diabetes (T2DM). Male hypogonadism is also common in T2DM and may contribute to hepatic steatosis via adverse metabolic and inflammatory mechanisms. Non-invasive fatty liver indices including the fatty liver Index (FLI), hepatic steatosis index (HSI), and fibrosis scores, provide pragmatic tools for liver risk stratification. However, data in African populations are limited.

Methods: Retrospective analysis of data from a cross-sectional study of men with T2DM attending two outpatient clinics. Demographic, clinical, anthropometric, biochemical data were extracted from health records; laboratory tests including serum total testosterone (TT) and free testosterone (FT). Androgen deficiency symptoms were assessed using the Ageing Male's Symptoms questionnaire. Steatosis was assessed using FLI; fibrosis risk was estimated using FIB-4, AST-to-platelet ratio index (APRI), NAFLD Fibrosis Score (NFS). Low testosterone was defined as TT < 12 nmol/L and/or FT < 180 pmol/L. Associations were assessed using univariate analysis, receiver operating characteristic curves, and multivariable logistic regression.

Results: Analysis included 114 men (mean age 58.4 ± 11.7 years; mean diabetes duration 13.2 ± 9.1 years). Hepatic steatosis prevalence was 66.7% by FLI and 82.1% by HSI. Higher steatosis indices were associated with greater adiposity, including higher BMI, waist circumference, waist–hip ratio, triglycerides, and higher prevalence of metabolic syndrome (all $p < 0.05$).

Low TT was present in 38.1% and was associated with higher weight, BMI, waist circumference, and higher steatosis indices. Fibrosis scores did not differ by TT status. ROC analysis showed modest discrimination of FLI and HSI for low TT (AUC 0.65 and 0.66), while fibrosis scores were non-discriminatory (AUC ≤ 0.53). Discrimination for low FT was weak across all indices.

On multivariable logistic regression, higher hepatic steatosis was independently associated with lower TT (FLI OR 0.98, 95% CI 0.964–0.997, $p = 0.019$; HSI OR 0.91, 95% CI 0.852–0.967, $p = 0.003$). No consistent associations were observed with AMS scores.

Conclusion: In men with T2DM, non-invasive hepatic steatosis indices—but not fibrosis scores—are independently associated with lower total testosterone levels, with modest discrimination. These findings suggest steatosis indices may serve as pragmatic risk markers in resource-limited settings.

An audit of congenital adrenal hyperplasia in paediatric patients treated at Chris Hani Baragwanath Academic hospital, Charlotte Maxeke Johannesburg Academic hospital and Rahima Moosa Mother and Children's hospital in Johannesburg

Category: Clinical - Endocrinology

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Background: Objectives: To describe the clinical presentation, growth and skeletal maturation, pubertal features, biochemical control and management of paediatric congenital adrenal hyperplasia (CAH).

Design: Retrospective descriptive audit.

Setting: Paediatric endocrine clinics at tertiary hospitals in Johannesburg, South Africa

Subjects: Forty-one children with CAH seen from 2011 to 2023.

Outcome measures: Presentation, phenotype, height-for-age Z-score (HAZ), bone age, pubertal staging, 17-hydroxyprogesterone (17-OHP) and testosterone measurements, and treatment/adherence.

Methods: A multi-Centre retrospective audit was conducted of pediatrics patients with congenital adrenal hyperplasia (CAH) managed at three tertiary hospitals in Gauteng. Medical records for eligible patients were reviewed over the study period, and demographic, clinical, biochemical, treatment and outcome data were extracted using a standardised data collection tool. CAH phenotype/classification was determined from documented clinical features and available laboratory results. Data were captured in a secure database and analysed using descriptive statistics; continuous variables were summarised using medians and interquartile ranges and categorical variables using frequencies and percentages.

Results: Salt-wasting and simple virilising CAH accounted for 39% and 27%, respectively. Presenting features were ambiguous genitalia (80.5%) and salt-wasting crisis (39%). Median age at presentation was 1.4 months (IQR 0–18; min-max 0–113); 80.0% were female. Mean baseline HAZ was −0.26±2.20 ($n = 33$), short stature in 24.2% and tall stature in 15.2%. Bone age correlated with chronological age ($r = 0.786$; $p < 0.001$) but remained advanced in those assessed. Premature secondary sexual characteristics were documented in 73.9% (17/23) before age 8 (girls) and 9 (boys) with predominantly premature pubarche. 17-OHP and testosterone showed marked longitudinal variability. Poor adherence was documented in 62.5%–85.7%. CYP21A2 mutations detected in 14.6%.

Conclusions: Classic CAH predominated with frequent virilisation. Heterogeneous growth and skeletal maturation with variable hormone profiles, alongside poor adherence and limited genetic confirmation, support standardised longitudinal monitoring and adherence-focused care.

Metabolomics driven stratification of Type 2 Diabetes risk through integrative metabolomics and genetics – results from the Durban Diabetes Study (DDS)

Category: Basic Science

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Background: Type 2 diabetes (T2D) is a complex cardiometabolic disorder characterised by progressive metabolic dysregulation that often precedes clinical diagnosis by many years. Metabolomic profiling offers a powerful approach to capture intermediate biochemical phenotypes reflecting early pathophysiological changes in glucose metabolism, insulin resistance, and cardiometabolic risk. Integrating metabolomics with genetic data further enables the identification of molecular quantitative trait loci that drive variation in metabolite levels, providing insights into the biological mechanisms underlying T2D susceptibility and progression. The Durban Diabetes Study (DDS) was a cross-sectional population-based study in urban black South Africans.

Methods: Untargeted metabolomics was performed on data of 191 participants (119 normal glucose-tolerant controls, 72 with diabetes [cases]), quantifying 305 circulating metabolites. Differential metabolite abundance between cases and controls was assessed, alongside regression analyses of metabolites with cardiometabolic traits, including body mass index (BMI), waist circumference (WC), glycated haemoglobin (HbA1c), and systolic and diastolic blood pressure. Unsupervised k-means clustering was applied to control individuals to identify subclinical risk groups. We further integrated genome-wide genetic data to identify metabolite quantitative trait loci (molQTLs) using a metabolome-wide association approach.

Results: Several metabolites were significantly associated with cardiometabolic traits. HbA1c was inversely associated with 3-methylene-1,4-bis(oxy) butane ($\beta = -0.018$, FDR $= 3.74 \times 10^{-6}$) and positively associated with 2-ethyl-1,3-bis(oxy)propane ($\beta = 0.014$, FDR $= 5.20 \times 10^{-5}$). Differential expression analysis identified metabolites overexpressed in cases, including 1,2-ethenediol, gluconolactone, and glycerol, while L-threonine and related metabolites were underexpressed. Clustering of controls using 260 metabolites identified low-risk ($n = 62$) and high-risk ($n = 57$) subgroups. High-risk controls exhibited higher BMI, HbA1c, and triglyceride levels and showed intermediate metabolic profiles between low-risk controls and cases. Integration with genetic data identified independent molQTLs at rs149375457 ($p = 5.28 \times 10^{-11}$), rs944987634 ($p = 6.67 \times 10^{-12}$), and rs146168382 ($p = 1.47 \times 10^{-12}$).

Conclusion: This integrative metabolomic–genetic analysis identifies genetically regulated metabolites associated with cardiometabolic traits and reveals a high-risk metabolic phenotype among ostensibly healthy individuals. These findings support the potential of metabolomics-informed risk stratification to identify individuals at elevated cardiometabolic risk before clinical disease onset, enabling earlier intervention and precision prevention strategies.

The performance of a novel, diabetes-specific cognitive screening tool against the MoCA in older adults with type 2 diabetes

Category: Clinical - Diabetes

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Background: Older adults with type 2 diabetes mellitus (T2DM) are at a significantly greater risk of cognitive impairment than those without T2DM. Existing screening tools, such as the Montreal Cognitive Assessment (MoCA), are not tailored to the vascular cognitive profile characteristic of T2DM. To address this gap, we designed the Diabetic Cognitive Assessment Tool (DCAT), a simplified instrument for efficient screening of cognitive impairment in older adults with T2DM, and assessed its performance against the MoCA. The associations of glycaemic control, frailty, depression, education, age, and T2DM duration with cognitive performance were also assessed.

Methods: A cross-sectional study was conducted among 103 adults aged 65 years and older with T2DM attending a tertiary hospital diabetic clinic in Johannesburg, South Africa. Additionally, 55 age- and sex-matched controls without T2DM were recruited. Cognitive function was assessed using the DCAT and MoCA, whereas frailty and depression were assessed using the FRAIL scale and Geriatric Depression Scale. DCAT performance relative to the MoCA was evaluated using the receiver operating characteristic (ROC) analysis curve and Youden's index identified the optimal cut-off. Associations between clinical and cognitive measures were analysed using Spearman's correlation, and Cohen's *d* quantified domain-specific effect sizes.

Results: The DCAT's area under the curve was 0.81. Using a cut-off score of 13, the DCAT achieved a sensitivity of 78.4% and specificity of 78.7%, with positive and negative predictive values of 89.2%, and 56.9%, respectively. Among participants with T2DM, HbA1c levels correlated negatively with MoCA scores, and depression scores correlated negatively with both DCAT and MoCA scores. In both groups, years of education correlated positively with both cognitive measures. Age and T2DM duration did not correlate significantly with cognitive measures in either group. The executive function and memory domains exhibited large and medium effect sizes, respectively.

Conclusion: The DCAT demonstrated good discriminative ability in detecting cognitive impairment among older adults with T2DM. Poorer glycaemic control and depressive symptoms were associated with lower cognitive performance, whereas greater educational attainment was linked to better outcomes. The DCAT effectively assesses key cognitive domains, particularly executive function and memory. Further validation in larger, more diverse cohorts is warranted.

The relationship between phosphopenic rickets and bone age in South African children treated at a single clinic between 2006 and 2023

Category: Clinical – Endocrinology

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Background: Phosphopenic rickets impairs growth. Its impact on bone age is unclear. Understanding the relationship between phosphopenic rickets and bone age may help assess patients' remaining growth potential.

Methods: To assess the relationship between phosphopenic rickets and bone age. This was a retrospective descriptive study of children with phosphopenic rickets, attending the Metabolic Bone Clinic at Chris Hani Baragwanath Academic hHospital between January 2006 and December 2022. Bone ages from the initial clinic visit radiographs and on subsequent follow-up visits during treatment were assessed by Greulich-Pyle method. Hand-wrist and knee radiographs taken at initial presentation were assessed for the radiological severity of rickets using the Thacher score.

Results: Seventy-five patients' records diagnosed with phosphopenic rickets were reviewed. Ten ($n = 10/49$; 20%) patients presented with delayed bone age at diagnosis. The Thacher score at the initial presentation was higher in the delayed bone age group compared to the normal bone age group ($p = 0.04$). There was a negative correlation between the Thacher score and height for age z-score (HAZ) at presentation, thus children with more severe Thacher scores had lower HAZ scores ($r = -0.36$; $r2 = 0.13$; $p = 0.013$).

Conclusion: Phosphopenic rickets negatively impacts stature and bone age which is associated with a higher rickets radiological severity score. The clinical application of bone age assessments in addressing the short stature observed in this condition and mitigating possible associated risk factors is warranted to improve the management, quality of life and outcomes for these affected patients.

Genetic Predictors of Hypothalamic-Pituitary-Adrenal Axis Suppression in Asthmatic Children on Corticosteroids

Category: Clinical – Endocrinology

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Background: Hypothalamic-pituitary-adrenal axis suppression (HPAS) was documented in 16% of asthmatic children treated with corticosteroids (CS) in Cape Town hospitals. A suitable screening test for HPAS is not available. Thus, a cross-sectional study was conducted in asthmatic children on CS to identify genetic predictors of HPAS and establish their functional impact.

Methods: 95 asthmatic children 5–18 years on inhaled, nasal and topical CS were recruited from Cape Town hospitals. HPA axis function was assessed by using the early morning serum cortisol (C) and metyrapone test. HPAS was diagnosed if the serum C < 83 nmol/L or post-metyrapone (PM) ACTH < 106 pg/mL & PM 11-deoxycortisol (11DOC) < 208 nmol/L, & PM 11DOC + C < 400 nmol/L). Whole exome sequencing was performed from saliva DNA using Ion Torrent sequencing. Single nucleotide polymorphisms (SNPs) were analysed for association with the categorical phenotype, adjusted for age, sex, BMI z-score, CS dose and population. Functionality was assessed by the Combined Annotation-Dependent Depletion (CADD) and Regulome data base (RDB) scores, and identification of expression quantitative loci (eQTL). Only SNPs with high effect sizes were considered.

Results:

Table 1: SNPs associated with HPAS

rsI^{D1}	Gene	OR$^{2)}$	95% CI	p-value	CADD score	RDB score	eQTL
rs7023244	*FREM1*	14.14	1.74-114.8	3.6x10^{-3}	25.70	6	
rs10810249	*FREM1*	10.95	1.32-90.4	1.52x10^{-2}	7.48	6	
rs55634318	*PDGFB*	6.91	1.44-33.26	1.41x10^{-2}	0.35	2b	
rs1546124	*CRISPLD2*	5.09	1.87-13.81	1.27x10^{-3}	6.49	4	
rs9622979	*PDGFB*	4.59	1.38-15.29	1.63x10^{-2}	0.97	5	
rs28529127	*AVPR1B*	4.51	1.17–17.42	3.93x10^{-2}	5.50	5	
rs3741843	*TAS2R14*	4.29	1.51-12.16	8.20x10^{-3}	11.00	NA	✓

1) Reference SNP cluster identification, 2) odds ratio

Table 2: SNPs associated with protection against HPAS

rsID	Gene	OR	95% CI	p-value	CADD score	RDB score	eQTL
rs3742945	*TTC5*	0.06	0.01-0.27	1.33x10^{-}5	14.9	NA	✓
rs2318864	*TTC5*	0.16	0.06-0.46	5.39x10^{-4}	11.52	1f	✓
rs2286562	*PRKAR1A: FAM20A*	0.19	0.04-0.92	4.91x10^{-2}	13.17	1f	
rs3744160	*TBCD*	0.25	0.08-0.77	2.14x10^{-2}	4.86	NA	✓

Conclusion: The results suggest HPAS and its protection are inherited in a polygenetic manner. All identified SNPs were novel. Protective SNPs had more functional impact, particularly those of TTC5. Functional validation studies are required to confirm findings.