Abstract: Type II diabetes (T2D) is characterized for insulin resistance in muscle, liver, and fat (1). Progesterone receptor membrane component 1 (Pgrmc1) is novel cell surface receptor which is associated with insulin receptor beta (IRβ) (2). Therefore, we speculated Pgrmc1 might be related to T2D. Using *Pgrmc1* KO mice reported in our previous study (3), we observed the decrease of body weight (BW) and increase of muscle weight per body weight. When blood glucose level in post-prandial state was lower, *Pgrmc1* KO mice showed improvements in glucose tolerance test (GTT) and insulin tolerance test (ITT). Though insulin level was low, insulin signaling genes were up-regulated in post-prandial *Pgrmc1* KO mice, especially in muscle. Regulations of blood glucose level and insulin signaling gene levels by *Pgrmc1* were also similarly observed in insulin-deficient state. To induce T2D, C57BL/6 mice were fed with high-fat diet for 8 weeks and injected by low dose of streptozotocin (30mg/kg). As a result, T2D-induced *Pgrmc1* KO mice increased lean mass per BW, decreased the blood glucose level, and improved GTT and ITT. The insulin signaling genes were also up-regulated, while cytoplasmic GLUT4 was decreased, but membrane GLUT4 was increased in T2D-induced *Pgrmc1* KO muscle. Glycolysis, TCA cycle, and oxidative phosphorylation genes were increased, suggesting energy metabolism was increased in T2D-induced *Pgrmc1* KO muscle. Present study suggests that *Pgrmc1* loss increases insulin signaling through induction of cytoplasmic IRβ and pAKT, and induces glucose uptake of muscle, thereby showing improvement in T2D progression. This has important clinical value because *Pgrmc1* modulation will evade hypoglycemia caused by classic insulin therapy for T2D (4).
References: (1) Fernandez, A. M., Kim, J. K., Yakar, S., Dupont, J., Hernandez-Sanchez, C., Castle, A. L., Filmore, J., Shulman, G. I., and Le Roith, D. (2001) Functional inactivation of the IGF-I and insulin receptors in skeletal muscle causes type 2 diabetes. Genes & development 15, 1926-1934. (2) Hampton, K. K., Anderson, K., Frazier, H., Thibault, O., and Craven, R. J. (2018) Insulin Receptor Plasma Membrane Levels Increased by the Progesterone Receptor Membrane Component 1. Mol Pharmacol 94, 665-673. (3) Lee, S. R., Kwon, S. W., Kaya, P., Lee, Y. H., Lee, J. G., Kim, G., Lee, G. S., Baek, I. J., and Hong, E. J. (2018) Loss of progesterone receptor membrane component 1 promotes hepatic steatosis via the induced de novo lipogenesis. Scientific reports 8, 15711. (4) Zammitt, N. N., and Frier, B. M. (2005) Hypoglycemia in type 2 diabetes: pathophysiology, frequency, and effects of different treatment modalities. Diabetes care 28, 2948-2961.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II

Patterns of Thyroid Disease in Basrah, Iraq. Retrospective Study

Abbas Ali Mansour, MD,FRCP,FACE, Ali Hussain Ali Alhamza, MD, Ammar Mohammed Saeed Abdullah Almomin, MD, Ibrahim Abbood Zaboon, MD, Nassar Taha Yaseen Alibrahim, MD, Rudha Naser Hussein, MD, Muayad Baheer Kadhim, MD, Adel Gassab Mohammed, MD, Dheyaa Kadhim Jabbar Al-Waeli, MD, Hussein Ali Nwayyir, MD, Haider Ayad Yassin Alidrisi, MD, Ibrahim Hani Hussein, MD, Samih Abed Odhaib, MD, Mahmood Thamer Jallod Altemimi, MD, Husam Jihad Imran, MD.
Faiha Diabetes Endocrine and Metabolism Center,Uinversity of Basrah, Basrah, Iraq.

SUN-418

Background: Data on thyroid disease epidemiology in the Middle East are scanty and anecdotal. This study aimed to assess the pattern of thyroid disease seen in Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC) in Basrah,Southern Iraq.
Methods
Retrospective observational study of database retrieval from the FDEMC a tertiary care Center in Basrah for the period of September 2008 to January 2019. Included all adults non pregnant 18 years or older.
Results
Total enrolled patients 17878; of them 4174(23.3%) men and 13705(76.7 %) women. There were 2229(12.5%) patients with hypothyroidism (83.0% women), with subclinical hypothyroidism observed in 364 out of 2229 with hypothyroidism(16.3%).
We found 1087 (6.1%) patients with hyperthyroidism (67.7% women) and subclinical hyperthyroidism observed in 92 of 1087 hyperthyroidism (8.4%).
Thyroid nodularity was seen in 944 (5.2%) patients (807 women in 85.5%). Thyroidectomy was done in 776(4.3%). Differentiated thyroid cancer was seen in 77 (0.4%).
Conclusion: Hypothyroidism was double that of hyperthyroidism. Cross-sectional community-based study can give more information on the epidemiology of thyroid disease in Iraq.Iodine status needed studded in the future.
Keywords: Hyperthyroidism, hypothyroidism,autoimmune thyroid disease, Iraq.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

Mechanisms of Insulin Resistance in Skeletal Muscle in Women with PCOS

Alba Moreno-Asso, PhD[1], Luke C. McIlvenna, PhD student[1], Rhiannon K. Patten, PhD student[1], Andrew J. McAinch, PhD[1], Raymond J. Rodgers, MAgrSc,PHD[2], Nigel K. Stepto, PhD[1].
[1]Victoria University, Melbourne, Australia, [2]University of Adelaide, Adelaide, Australia.

MON-647

Abstract: Polycystic ovary syndrome (PCOS) is the most common female endocrine disorder affecting metabolic, reproductive and mental health of 8-13% of reproductive-age women. Insulin resistance (IR) appears to underpin the pathophysiology of PCOS and is present in approximately 85% of women with PCOS. This underlying IR has been identified as unique from, but synergistic with, obesity-induced IR (1). Skeletal muscle accounts for up to 85% of whole body insulin-stimulated glucose uptake, however, in PCOS this is reduced about 27% when assessed by hyperinsulinemic euglycemic clamp (2). Interestingly, this reduced insulin-stimulated glucose uptake observed in skeletal muscle tissue is not retained in cultured myotubes

(3), suggesting that environmental factors may play a role in this PCOS-specific IR. Yet, the molecular mechanisms regulating IR remain unclear (4). Previous work suggested that Transforming Growth Factor Beta (TGFβ) superfamily ligands may be involved in the metabolic morbidity associated with PCOS (5). In this study, we investigated the effects of TGFβ1 (1, 5ng/ml), and the Anti-Müllerian hormone (AMH; 5, 10, 30ng/ml), a novel TGFβ superfamily ligand elevated in women with PCOS, as causal factors of IR in cultured myotubes from women with PCOS (n=10) and healthy controls (n=10). AMH negatively affected glucose uptake and insulin signalling increasing p-IRS1 (ser312) in a dose-dependent manner in myotubes from both women with and without PCOS. AMH did not appear to activate the canonical TGFβ/BMP signalling pathway. Conversely, TGFβ1 had an opposite effect in both PCOS and control myotubes cultures, decreasing phosphorylation of IRS1 (ser312) and enhancing glucose uptake via Smad2/3 signalling. In conclusion, these results suggest that AMH may play a role in skeletal muscle IR observed in PCOS, however, further research is required to elucidate its mechanisms of action and broader impact in this syndrome. **References:** (1) Stepto *et al. Hum Reprod* 2013 Mar;28(3):777-784. (2) Cassar *et al. Hum Reprod* 2016 Nov;31(11):2619-2631. (3) Corbould *et al*., *Am J Physiol-Endoc* 2005 May;88(5):E1047-54. (4) Stepto *et al. J Clin Endocrinol Metab*, 2019 Nov 1;104(11):5372-5381. (5) Raja-Khan *et al. Reprod Sci* 2014 Jan;21(1):20-31.

Cardiovascular Endocrinology

FROM BEDSIDE TO BENCH AND BACK AGAIN: LIPID METABOLISM & VASCULAR DISEASE

Retinol Binding Protein 4 Predicts Functional Vascular Disease in Early Postmenopausal Women

ELENI ARMENI, MD, PhD[1], Meletios P. Nigdelis, MD[2], Areti Augoulea, MD, PhD[3], Asimina Chondrou, MD[3], Dimitrios Rizos, PhD[4], George Kaparos, PhD[4], Andreas Alexandrou, MD, PhD[3], Dimitrios G. Goulis, MD,PHD[2], Georgios Georgiopoulos, MD, PhD[5], Kimon Stamatelopoulos, MD, PhD[5], Irene Lambrinoudaki, MD, PhD[3].

[1]Royal Free Hospital, LONDON, United Kingdom, [2]ARISTOTLE UNIV OF THESSALONIKI, Thessaloniki, Greece, [32]nd Department of Obstetrics and Gynecology, National and Kapodistrian University of Athens, Aretaieion Hospital, Athens, Greece, [4]Hormonal and Biochemical Laboratory, National and Kapodistrian University of Athens, Aretaieio Hospital, Athens, Greece, [5]Department of Clinical Therapeutics, Alexandra Hospital, National and Kapodistrian University of Athens, Athens, Greece.

OR17-07

Introduction: The impact of gender on the development of cardiovascular disease has long been recognized. The potential effect of sex-specific cardiovascular risk factors on molecular mediators of oxidative stress has received limited attention and the results remain conflicting.

Hypothesis: To assess the link between retinol binding protein 4 (RBP4) and menopause-specific cardiovascular risk factors, on indices of early subclinical atherosclerosis, in a sample of apparently healthy young, postmenopausal women.

Methods: This cross-sectional study included a total of 123 healthy postmenopausal women, recruited from a University Menopause Clinic. Participating women were, not on hormone therapy, antihypertensive or hypolipidemic treatment and had a menopausal age of up to 10 years. Fasting venous blood samples were obtained for hormonal and biochemical assessment, including levels of RBP4. Sonographical studies were performed on the same day and included carotid-femoral pulse wave velocity (PWV) and calculation of the carotid artery stiffness index (SI).

Major results: Univariate analysis showed that RBP4 values correlated positively with age, total cholesterol, triglycerides, LDL-cholesterol, testosterone-to-estrogen ratio; negatively with circulating estrogen and almost significantly with homocysteine levels. Levels of homocysteine were inversely associated with RBP4 (homocysteine: RBP4 <10.5ng/ml vs ≥10.5ng/ml: 11.2±2.81μmol/L vs 12.52±3.44μmol/L, p-value=0.049 ANCOVA, adjusted for age, BMI, HOMA-IR). Multivariate analysis showed that PWV values were predicted by RBP4 (b-coefficient=0.435, p-value=0.006), age, pulse pressure, homocysteine. S.I. beta was predicted independently by RBP4 levels (b-coefficient=0.324, p-value=0.039). Both models were adjusted for menopausal age, LDL-cholesterol, FEI, smoking, HOMA-IR.

Conclusion: RBP4 levels are linked with measures of local carotid and aortic arterial stiffness, in this sample of healthy postmenopausal women. This association seems to be mediated by higher levels of homocysteine, which may interfere with retinoic acid synthesis. Larger studies are required to further elucidate the significance of our findings.

References

1. Majerczyk M, Olszanecka-Glinianowicz M, Puzianowska-Kuznicka M, Chudek J: Retinol-binding protein 4 (RBP4) as the causative factor and marker of vascular injury related to insulin resistance. Postepy Hig Med Dosw 2016;70:1267-1275.

2. Smolders RG, van der Mooren MJ, Sipkema P, Kenemans P: Estrogens, homocysteine, vasodilatation and menopause: basic mechanisms, interactions and clinical implications. Gynecol Endocrinol 2003;17:339-354.

3. Limpach A, Dalton M, Miles R, Gadson P: Homocysteine inhibits retinoic acid synthesis: a mechanism for homocysteine-induced congenital defects. Exp Cell Res 2000;260:166-174.

Diabetes Mellitus and Glucose Metabolism

LIPIDS, OBESITY AND METABOLIC DISEASE

The Gut Microbiome Regulates Host Glucose Homeostasis via Peripheral Serotonin

Damien Keating, PhD.

Flinders University, Bedford Park, SA, Australia.

SAT-657

The gut microbiome is an established regulator of aspects of host metabolism, such as glucose handling. Despite the known impacts of the gut microbiota on host glucose homeostasis, the underlying mechanisms are unknown. The gut microbiome is also a potent mediator of gut-derived serotonin synthesis, and this peripheral source of serotonin