Abstract Booklet

Generation of insulin-secreting beta cells from hiPSCs derived from diabetic and healthy individuals

Ahmed K. Elsayed[1], Bushra Memon[1,2], Maryam Aghadi[1,2], Yasmin Abu aqel[1,2], Idil Aigha[1,2], Mohammed Bashir[3], Essam M. Abdelalim[1,2*]

[1]*Diabetes Research Center, Qatar Biomedical Research Institute (QBRI), Hamad Bin Khalifa University (HBKU), Qatar Foundation (QF)*

[2]*College of Health and Life Sciences, Hamad Bin Khalifa University (HBKU), Qatar Foundation(QF)*

[3]*Department of Endocrinology, Qatar Metabolic Institute, Hamad Medical Corporation, Doha, Qatar.*

Induced pluripotent stem cells (iPSCs) are a promising alternative autologous source for beta cell replacement therapy, circumventing the hurdles of the donor shortage and immune rejection following allogenic islet transplantation. While the first clinical trial using hPSC-derived pancreatic progenitors is ongoing for evaluating the safety and efficacy of their therapeutic use in treating T1D, the effort is currently focused on generating functional beta cells *in vitro*. Therefore, in this study, our aim was to generate glucose-responsive pancreatic beta cells from different iPSC lines, including those generated from healthy and of diabetic individuals. In our study, iPSCs were generated from blood samples of healthy individuals and patients with T2D. The generated iPSCs were fully characterized for their pluripotency abilities. The iPSCs were differentiated into definitive endoderm (FOXA2$^+$/SOX17$^+$) with a high efficiency (~94%) and were further differentiated into pancreatic progenitors using our recently established protocol. hiPSC-derived pancreatic progenitors co-expressed PDX1 and NKX6.1, they key TFs required for beta cell functionality. These progenitors were further directed into endocrine progenitors (NGN3+) and finally into beta cells (INS+) either in adherent culture or 3D aggregates conditions. These iPSC-derived beta cells from diabetic and non-diabetic individuals co-expressed C-PEPTIDE and INSULIN (INS) with NKX6.1, which is crucial for beta cell functionality. Moreover, the hiPSC-derived beta cells were able to respond to glucose stimulation by secreting INS and C-PEPTIDE through glucose-stimulated insulin secretion (GSIS) assay. Some of the generated endocrine cells showed polyhormonal characteristics (INS+/GCG+ or INS+/SST+). Also, some cells did not express INS, but expressed other hormones (GCG+/INS- or SST+/INS-) with alpha and delta cell fates, indicating a heterogeneous endocrine population. In conclusion, we produced functional beta cells *in vitro* from different hiPSC lines established in our lab. Our ability to generate different stages of pancreatic development, including functional beta cells can be used to understand diabetes pathophysiology. Furthermore, hiPSC-derived beta cells can be used for drug screening and beta cell therapy.

Understanding genetic factors involved in the development of insulin resistance in patients with psoriasis using patient-specific iPSCs

Ahmed K. Elsayed[1,] Gowher Ali[1], Bushra Memon[1,2], Manjula Nandakumar[1], Mohammed Bashir[3], Ihab Younis[4], Yasmin Abu Aqel[1,2], Ramzi Temanni[5], Fadhil Abubaker[6], Shahrad Taheri[7], Essam M. Abdelalim*[1,2]

[1]*Diabetes Research Center, Qatar Biomedical Research Institute (QBRI), Hamad Bin Khalifa University (HBKU), Qatar Foundation (QF*

[2]*College of Health and Life Sciences, Hamad Bin Khalifa University (HBKU), (QF)*

[3]*Department of Endocrinology, Qatar Metabolic Institute, Hamad Medical Corporation, Doha, Qatar*

[4]*Biological Sciences Program, Carnegie Mellon University in Qatar, Qatar Foundation (QF)*

[5]*Biomedical Informatics Division, Sidra Medicine, Doha, Qatar.*

[6]*Computer Sciences Program, Carnegie Mellon University in Qatar,(QF)*

[7]*Department of Medicine and Clinical Research Core, Weill Cornell Medicine-Qatar,(QF)*

Insulin resistance is a precursor and accelerating factor for Type 2 diabetes (T2D) and cardiovascular diseases, two of the greatest health challenges facing Qatar and the world today. Cytokine-induced insulin resistance has been shown to be involved in epidermal dysfunction, a hallmark in the development psoriasis. A link between insulin resistance, psoriasis, T2D, and other metabolic disorders has been observed. Previous studies reported that patients with psoriasis for more than two years, regardless the severity of the disease, are at a very high risk of developing diabetes and insulin resistance. The debate on the genetic origin of the pathogenesis of psoriasis and insulin resistance remains unresolved due to lack of suitable *in vitro* human models mimicking the disease phenotypes. Here, we provide the first human induced pluripotent stem cell (iPSC) model for psoriasis carrying the genetic signature of the patients. iPSCs were generated from PBMCs of healthy donor controls (Ctr-iPSCs) and patients with psoriasis who also had insulin resistance and family history of psoriasis (PsO-iPSCs). The generated iPSC lines expressed the main pluripotency markers at mRNA and protein levels and were able to differentiate into all three germs layers upon spontaneous differentiation. Ctr-iPSCs and PsO-iPSCs were efficiently differentiated into keratinocyte (KC) progenitor and mature KCs that expressed specified markers for each stage. RNA sequencing of KCs derived from Ctr-iPSCs and PsO-iPSCs identified 361 commonly upregulated and 412 commonly downregulated genes. KCs derived from PsO-iPSCs showed dysregulated transcripts associated with psoriasis and KC differentiation, such as *HLA-C*, *KLF4*, chemokines, type I interferon (IFN)-inducible genes, solute carrier family, *IVL, DSG1, and HLA-DQA1* as well as transcripts associated with insulin resistance, such as *IRS2*, *GDF15*, *GLUT10*, and *GLUT14*. Glucose uptake assay showed no significant change in glucose uptaken by the mature KCs-PsO in response to insulin treatment; however, KCs-Ctr showed a significant increase in insulin-induced glucose uptake indicating that psoriatic KCs possess genetic defects that confer insulin resistance. Taken together, these findings highlight the substantial contribution of genetic predisposition in the development of psoriasis and insulin resistance. The iPSC model established in the current study can be used for further investigations to decipher the link between genetic insulin resistance and psoriasis.

Generation of a novel hiPSC-based model to understand the mechanisms underlying insulin resistance in the offspring of T2D parents

Bushra Memon[1,2], Ahmed K. Elsayed[1], Mohammed El-Allam[1], Gowher Ali[1], Maryam Aghadi[1,2], Eman Abdelsalam[1,2], Ilham Bettahi[3,4], Noor N. Suleiman[4], Abdul B. Abou-Samra[4], Essam M. Abdelalim*[1,2]

[1]*Diabetes Research Center, Qatar Biomedical Research Institute, Hamad Bin Khalifa University, QF*

[2]*College of Health and Life Science, Hamad Bin Khalifa University, QF*

[3]*Translational Research Institute, Hamad Medical Corporation.*

[4]*Qatar Metabolic Institute, Department of Medicine, Hamad Medical Corporation*

The development of insulin resistance (IR) in insulin target cells involves genetic and acquired factors. However, the molecular and genetic basis for the development of IR in insulin target tissues is not fully understood. Studying insulin resistant offspring of type 2 diabetic (T2D) parents, individuals at high risk of developing T2D, may facilitate our understanding of the genetic contribution in the development of T2D. Induced pluripotent stem cell (iPSC) technology can generate cells genetically identical to IR individuals, which can help in distinguishing between genetic and acquired defects in insulin sensitivity. Therefore, the aim of the current study was to generate hiPSCs from insulin-resistant offspring of T2D parents (IR offspring) and insulin sensitive (IS) individuals to establish *in vitro* models of IR. hiPSCs were generated from four subjects of each group (IR offspring and IS) and from each subject three iPSC lines were established. From a cohort of 60 individuals studied at HMC, who underwent a hyperinsulinemic euglycemic clamp, we selected the most insulin sensitive (insulin sensitive or IS, M>12 mg/Kg/min) and the least insulin sensitive (insulin resistant or IR, M<4 mg/Kg/min) individuals. Blood samples were collected from the IR and IS groups for hiPSCs preparation. All the subjects were lean, normoglycemic, and come from families with a strong history of T2D (both parents are diabetic), while the IS subjects were lean, insulin sensitive and come from families without a history of diabetes (neither parents have diabetes). iPSCs were generated from PBMCs of four subjects from each group using non-integrating Sendai virus. Three iPSC lines were established from each subject. All iPSCs lines were extensively characterized using different approaches, including immunostaining, alkaline phosphatase (AP) activity, RT-PCR, karyotyping, and embryoid body (EB) formation. The generated cell lines expressed a panel of pluripotency markers, such as OCT4, SOX2, NANOG, KLF4, c-MYC, TERT, amongst others, at mRNA and protein levels as well as exhibited a normal karyotype. We validated the ability of these iPSCs to differentiate into the three germ layers- ectoderm, endoderm and mesoderm spontaneously, as seen by the expression of germ layer-specific markers like NESTIN, SOX17, BRACHYURY and scorecard analysis. Since these IR-iPSCs carry genetic signatures of individuals with IR and ultimately T2D, they will be employed to study the impaired signaling pathways dysregulating metabolism, in the insulin-target tissues, such as the liver and skeletal muscle, that are key pathological characteristics of T2D. Thus, our PSC model will serve as a platform for dissecting the early events responsible for IR and T2D development, especially in the Qatari population at high risk of developing T2D and can be used for drug screening for T2D prevention.

PDX11-/NKX6.1+ progenitors derived from human pluripotent stem cells as a novel source of insulin-secreting cells

Bushra Memon[1,2], Fadhil Abubaker[3], Ihab Younis[3], Essam M. Abdelalim*[1,2]

[1]College of Health and Life Science, Hamad Bin Khalifa University, QF

[2]Diabetes Research Centre, Qatar Biomedical Research Institute, Hamad Bin Khalifa University, QF

[3]Biological Sciences Program, Carnegie Mellon University in Qatar, QF

Beta cell replacement strategies are a promising alternative for diabetes treatment. Pancreatic beta cells have been isolated or transdifferentiated from multiple sources, however, with limited application. Human pluripotent stem cells (hPSCs) serve as a scalable source for generating insulin-secreting cells for transplantation therapy. Generation of functional pancreatic beta cells from hPSCs have gained some success, however, the glucose-responsiveness of these cells still differ from the adult islet. Interestingly, clinical trial with hPSC-derived pancreatic progenitors, which are beta cell precursors, is underway. We previously demonstrated the generation of a novel population of pancreatic progenitors using hPSCs that expressed the transcription factor NKX6.1, exclusive to beta cells and critical for their functionality, independently of the master regulator of pancreatic development, PDX1 (PDX1-/NKX6.1+). Herein, we demonstrate their ability to differentiate into insulin-secreting cells *in vitro*, establishing them as a novel source of obtaining hPSC-derived beta cells. In order to characterize PDX1-/NKX6.1+ population, we performed RNA-Seq analysis of stage 4-derived PDX1+/NKX6.1+ (bona fide beta cell precursors) and PDX1-/NKX6.1+ (novel population) progenitors to identify differentially expressed genes between the two populations. RNA-Seq results revealed the downregulation of the main pancreatic developmental markers such as PDX1, FOXA1, FOXA2 and GATA6 as well as certain key tight junction proteins showing the loss of pancreatic epithelial identity and gain of mesenchymal nature. PDX1-/NKX6.1+ strongly co-express NESTIN, a pancreatic stem cell marker, indicating that this population is representative of the pancreatic mesenchyme. On further differentiation, we found that PDX1-/NKX6.1+ structures were able to differentiate into INSULIN, GLUCAGON and SOMATOSTATIN-expressing endocrine cells (reproducible in 4 cell lines: hESCs- H1, HUES8 and H9 & hiPSCs). Finally, we show that these PDX1-/NKX6.1+-derived beta cells are functional as they secrete C-PEPTIDE in response to increased glucose. Interestingly, transcriptome analysis for the PDX1-/NKX6.1+-derived beta cells revealed its similarities to pancreatic islet endocrine cells, specifically to the proliferative or regenerated beta cell subtype. Therefore, our novel PDX1-/NKX6.1+ pancreatic progenitors can serve as an alternative source of insulin-secreting cells for cell therapy for diabetes.

Scalable generation of mesenchymal stem cells and adipocytes from multiple human pluripotent stem cell lines

Manale Karam[1], Maryam Aghadi[1,2], Mohammed El-Allam[1], Ihab Younis[3], Essam M. Abdelalim*[1,2]

[1]Diabetes Research Centre, Qatar Biomedical Research Institute (QBRI), Hamad Bin Khalifa University (HBKU), Qatar Foundation (QF),

[2]College of Health and Life Sciences, Hamad Bin Khalifa University (HBKU), QF

[3]Biological Sciences Program, Carnegie Mellon University in Qatar, QF

Human pluripotent stem cells (hPSCs) can provide unlimited supply for mesenchymal stem cells (MSCs) and adipocytes that can be used for therapeutic applications. In this study, our aim was to enhance the generation of hPSC-derived MSCs and subsequently differentiate them into large number of adipocytes. Therefore, we modified previously published protocols by using different concentrations of retinoic acid (RA) at early stage of MSC differentiation. Embryoid bodies (EBs) derived from several hESC and hiPSC lines were treated with three different concentrations of RA from day 2 to day 5 of differentiation. On day 7 of differentiation, treatment of hPSCs with RA enhanced the generation of EBs by 3.3-fold (low concentration, RA-low) and 6.8-fold (high concentration, RA-high) in comparison to the untreated condition. This increase in the number of EBs generated from RA-high PSCs was associated with decreased apoptosis without any effect on cell proliferation. At day 16 of differentiation, most RA-untreated EBs formed fibroblast-like cells and 56% of them expressed the MSC specific marker CD73, while RA-treated EBs maintained their undifferentiated phenotype and only 9% of the cells expressed CD73. However, the dissociation of RA-treated EBs on day 12 induced their rapid differentiation into fibroblast-like cells and 90% of them expressed the MSC marker CD73 on day 16 of differentiation indicating the importance of cell dissociation for MSC differentiation of RA-treated cells. At day 25, all three RA-treatment conditions showed elongated MSC-like cells expressing the MSC markers CD44, CD73 and CD90. The number of these cells was significantly increased by 3.8-fold and 18-fold when the ESC-derived EBs were treated with RA-low and RA-high, respectively. Interestingly, RA-high effect on iPSC-derived EBs was more dramatic than on ESC-derived EBs; allowing 314 to 10700-fold increase in comparison to untreated cells. Importantly, the MSCs derived from RA-high treated EBs showed 3-fold increase in their proliferation rate and 2-fold increase in their differentiation potential towards adipocytes. These results indicate that short-term EB treatment with high RA concentration dramatically enhances the yield of differentiation towards highly proliferative MSCs with enhanced adipogenic differentiation potential.

Understanding the Role of NKX6.1 in Favoring Pancreatic Progenitors Development into Functional β cells

Idil I. Aigha[1,2], Bushra Memon[1,2], Ahmed Kamel[1], Essam M. Abdelalim*[1,2]

[1]_Diabetes Research Center, Qatar Biomedical Research Institute (QBRI), Hamad Bin Khalifa University (HBKU), Qatar Foundation (QF),_
[2]_College of Health and Life Sciences, Hamad Bin Khalifa University (HBKU), Qatar Foundation,_

The timely coordinated expression of certain transcription factors (TFs) is necessary for the development of a functional pancreas. The Co-expression of specific TFs in the multipotent progenitor cells (MPCs) is critical for generation of functional insulin producing β cells. Human pluripotent stem cells (hPSCs)-derived pancreatic progenitors co-expressing PDX1 and NKX6.1 (PDX1+/NKX6.1+) matured into functional β-cells when transplanted into immune-deficient mice and successfully reduced high glucose blood levels. On the other hand, progenitors lacking NKX6.1 expression (PDX1+/NKX6.1-) developed into poly-hormonal cells and failed to function properly _in vivo_. This highly suggests that NKX6.1 expression in PDX1+ MPCs is required for functional β cell generation. However, the mechanism by which NKX6.1 expressing in MPCs contributes to maturation of functional pancreatic β cells remains elusive. Henceforth, we aimed for enriching expression of NKX6.1 through the introduction of modifications into existing differentiation protocols and we have recently demonstrated the generation of a novel population of human pluripotent stem cell (hPSC)-derived MPCs that exclusively express NKX6.1, independently of PDX1 (PDX1−/NKX6.1+). This novel population was enriched using our recently established protocol, allowing their reorganization in three-dimensional (3D) structures. Since NKX6.1 induction in MPCs can direct them to endocrine and/or ductal cells in humans, we examined the co-expression of endocrine and ductal markers. We found that the expression of the pancreatic endocrine progenitor markers chromogranin A (CHGA) and neurogenin 3 (NGN3) was not detected in the NKX6.1+ 3D structures, while few structures were positive for NKX2.2, another endocrine progenitor marker, thereby shedding light on the origin of this novel population and its role in pancreatic endocrine development. Furthermore, SOX9 was highly expressed in the 3D structures, but cytokeratin 19, a main ductal marker, was not detected in these structures. These data support the existence of two independent NKX6.1+ MPC populations during human pancreatic development and the novel PDX1−/NKX6.1+ population may be involved in a unique trajectory to generate β cells in humans. Moreover, we examined the contribution of NKX6.1 in favouring functional mono-hormonal β-cells lineage. The effect of exogenous expression and knockdown of NKX6.1 notably demonstrated that NKX6.1 expression in MPC is necessary to prevent unsought early endocrine induction. Furthermore, NKX6.1 expression induces MPC proliferation and maintenance. Collectively, these data highlight the significant role of NKX6.1 in the development of MPC into functional insulin producing β-cells. Additionally, the identification of this novel population (PDX1− /NKX6.1+) opens the door to investigate an alternative path towards pancreatic islet cells development that is independent of PDX1.

Generation of iPSCs from patients with MODY2 and neonatal diabetes due to glucokinase mutations

Yasmin Abu Aqel[1,2], Ali Gowher[2], Sarah Al Khawaga[1,2,3], Khalid Hussain[3], Essam Abdelalim*[1,]

[1]College of Health and Life Science, Hamad Bin Khalifa University, Qatar Foundation(QF).
[2]Diabetes Research Center, Qatar Biomedical Research Institute, Hamad Bin Khalifa University , QF.
[3]Division of Endocrinology, Department of Pediatric Medicine, Sidra Medicine, Qatar.

Glucokinase (GCK) is a member of the hexokinase family that gives liver cells and pancreatic beta cells with the capacity to increase or decrease their rates of glucose utilization when the plasma glucose level rises or falls respectively. Mutations in the GCK gene lead to altered glucose homeostasis causing either hyperglycaemia or hypoglycaemia, depending on whether. Heterozygous loss of function *GCK* mutations cause maturity-onset diabetes of the young (MODY2), a monogenic form of diabetes that characterized by mild fasting hyperglycaemia , while homozygous inactivating mutations lead to permanent neonatal diabetes mellitus (PNDM), which is characterized by severe hyperglycaemia . In the current work, we generated induced pluripotent stem cells (iPSCs) from the blood cells of two patients having heterozygous and homozygous mutations in GCK gene. The mutations were confirmed using whole exome sequencing and then by Sanger sequencing in patient samples. Three iPSC lines were established from each patient, in which the mutation was confirmed using Sanger sequencing. All iPSCs lines were extensively characterized using different approaches, including immunostaining, RT-PCR, karyotyping, and embryoid body (EB) formation. The generated cell lines expressed pluripotency markers at mRNA and protein levels and were able to differentiate into all three germs layers upon spontaneous differentiation. To generate isogenic controls, we used CRISPR-Cas9 knock-in approach to correct the mutation in patient-specific iPSCs. Two corrected patient-specific iPSC lines were established. Mutated and corrected iPSCs will be used to understand the role of GCK mutations in the development of MODY2 and neonatal diabetes. This human iPSC-based model can be for screening drugs and cell therapy.

Regulation of endocrine fibroblast growth factors by Intralipid and Insulin in healthy and PCOS women.

Manjunath Ramanjaneya[1], Jayakumar Jerobin[1], Ilham Bettahi[1], Milin Bensila[1], Raihanath Parammal[1], Myint Aye[3] , Meis Alkasem[1], Kodappully Sivaraman Siveen[4], Thozhukat Sathyapalan[3], Monica Skarulis [1], Stephen Lawrence Atkin[2†] and Abdul-Badi Abou-Samra[1†].

1. Qatar Metabolic Institute and Interim Translational Research Institute, Academic Health System, and Department of Medicine, Hamad Medical Corporation, PO Box 3050, Doha, Qatar.
2. Weill Cornell Medicine Qatar, Doha, Qatar.
3. Department of Academic Endocrinology, Diabetes and Metabolism, Hull York Medical School, Hull, United Kingdom.
4. Translational Research Institute, Academic Health System, Hamad Medical Corporation

Background:- PCOS is a hormonal and metabolic disorder that affects almost 5-10% of women. Fibroblast growth factors are metabolic hormones that regulate glucose and lipid metabolism. Endocrine FGF family includes FGF19, FGF21 and FGF23. FGF19 levels is lower in obese, T2D and NAFLD in contrast FGF21 was found to be higher in obesity, T2D and NAFLD subject and positively correlated with intrahepatic TG in NAFLD patients. The current study examined the response of FGF19, 21 and 23 lipids intralipid and insulin challenge in PCOS (n=11) and healthy women (n=10).

Methods:- All subjects underwent 5-hour intralipid infusion with a hyperinsulinemic euglycaemic clamp in the final 2 hours and 8 weeks of exercise intervention. Plasma endocrine FGFs were measured together with blood biochemistry. Repeated measures Annova and post-hoc analysis was performed to determine significance.

Results:-

Plasma FGF19, 21 and 23 levels were similar between PCOS and the controls both before and after exercise.
FGF19: Intralipid suppressed FGF19 in PCOS subjects (P<0.0001) and controls (P<0.01). Insulin administration predominantly reversed intralipid mediated suppression of FGF19 only in controls (P<0.01).
FGF21: Intralipid did not alter FGF21 in both groups. Administration of insulin along with intralipid significantly elevated FGF21 expression in control (P<0.0001) and PCOS subjects (P<0.0001).
FGF23: Intralipid did not alter FGF23 in both the groups. Administration of insulin along with intralipid significantly suppressed FGF23 expression only in control group (P<0.01). Additionally lipid induced rise in triglycerides and NEFA were suppressed with by insulin.

Conclusions:- FGF19, 21 and 23 were similar in PCOS and controls although exercise improved glucose disposal rate, this was not translated into significant alteration in endocrine FGFs changes in circulation. In conclusion this is the first study to show differential regulation of FGF family members by intralipids and insulin in PCOS and healthy women suggesting that FGF family members play key role in regulation of lipid and glucose metabolism.

Lipid and insulin inversely regulate C1Q Tumor Necrosis Factor-Related Protein 15 in healthy and women with PCOS.

Manjunath Ramanjaneya[1], Jayakumar Jerobin[1], Ilham Bettahi[1], Milin Bensila[1], Raihanath Parammal[1], Myint Aye[3] , Thozhukat Sathyapalan[3], Monica Skarulis [1], Abdul-Badi Abou-Samra[1†] and Stephen Lawrence Atkin[2†].
1. Qatar Metabolic Institute and Interim Translational Research Institute, Academic Health System, and Department of Medicine, Hamad Medical Corporation
2. Weill Cornell Medicine Qatar, Doha, Qatar.
3. Department of Academic Endocrinology, Diabetes and Metabolism, Hull York Medical School, Hull, United Kingdom.
4. Translational Research Institute, Academic Health System, Hamad Medical Corporation,

Background: C1Q Tumor Necrosis Factor-Related Proteins 15 (CTRP 15) also referred as myonectin/ erythroferrone is a nutrient-responsive myokine involved in regulation of fatty acid metabolism. Myonectin expression is elevated in obese subcutaneous adipose tissue of human and in rat skeletal muscle. Circulating levels were found to be higher obese and in diabetes subjects compared to control. The current study was designed to examine the response of myonectin to lipids (intralipid) followed by insulin in PCOS and healthy subjects.

Methods: All subjects (PCOS n=11 and control n=10) underwent 5-hour intralipid/saline infusion with a hyperinsulinemic euglycaemic clamp in the final 2 hours and 8 weeks of exercise intervention. Plasma myonectin was measured during clamp and following exercise using a commercial elisa kit.

Results: Plasma myonectin was higher in PCOS compared to controls (P<0.05). Intralipid decreased myonectin to 79±6% of basal in control 100% (P<0.01) and to 80±9% of basal in PCOS (P<0.05) subjects. Administration of insulin reversed intralipid mediated suppression of myonectin from 79±6% to 98±9% in control and from 80±8% to 108±22% in PCOS subjects.

Conclusions: This is the first study to show that myonectin is higher in PCOS subjects and exercise does not alter circulating myonectin levels. Intra-lipids suppress myonectin in both control and PCOS subjects. Lipid mediated suppression in myonectin was reversed by insulin. Lipid and insulin inversely regulate plasma myonectin suggesting that lipids and insulin play important roles in the regulation of myonectin.

The Expression of TBC1 Domain Family, member 4 (TBC1D4) in Skeletal Muscles of Insulin-Resistant Mice in Response to Sulforaphane.

Nasser M. Rizk, Amina Saleh, Abdelrahman El-Gamal, Dina Elsayegh , Isin Cakir, Masoud Ghamari-Langroudi.
 1 Qatar University, Doha, Qatar,
2 University of Michigan, Ann Arbor, MI, USA,
3 Vandrbilt University, Nashville, TN, USA.

Background: Obesity is usually accompanied by impaired glucose homeostasis. Decreased glucose transport to the peripheral tissue, mainly skeletal muscles, leads to reduced whole-body glucose uptake and hyperglycaemia. TBC1D4 gene is involved in the traffic of GLUT4 from the intracellular location to the outer cell membrane in skeletal muscle. Sulforaphane (SFN) has been suggested as a new potential anti-diabetic compound (1). The aim of this study is to investigate the effect of SFN on glucose homeostasis and its effects on TBC1D4 and GLUT4 gene expressions in skeletal muscles of DIO mice.

Methodology: C57BL/6 mice (n=20) were fed a high fat diet (60%) for 16 weeks to reach a bodyweight around 45-50 gm. Bodyweight and food intake were checked. SFN was injected via intraperitoneal route (5mg/kg BW) for four weeks to DIO mice, while another set of DIO mice received a vehicle and used as a control. Glucose tolerance test (1g/kg BW) of glucose solution via IP and insulin sensitivity were employed (1 IU insulin/ g BW, IP route) at the beginning and end of the third week of the study. At the end of 4 weeks, the blood samples and skeletal muscles of both hindlimbs were collected. Gene expression analysis for GLUT4 and TBC1D4 genes were performed by qRT-PCR. Blood was used for glucose, adiponectin and insulin assessment

Results: SFN-treated DIO mice had significantly lower blood glucose than vehicle-treated mice at fasting levels (194.16 ± 14.12 vs. 147.44 ± 20.31 mg/dL, vehicle vs. SFN, p value=0.0003). Furthermore, at 120 minutes after GTT, the blood glucose level in mg/dl was (199.83±34.53 Vs 138.55±221.78) for vehicle Vs. SFN with p values=0.0011 respectively. ITT showed that SFN treatment did not enhance insulin sensitivity in DIO mice SFN treatment as measured by glucose levels with p values >0.05. SFN treatment did not significantly change the expression of TBC1D4, and GLUT4 genes in skeletal muscles of SFN treated mice versus vehicle treatment in skeletal muscles. Furthermore, SFN treatment did not change the insulin (1.84±0.74 vs 1.54±0.55 ng/ml, p=0.436), and adiponectin (11.96 ±2.29 vs 14.4±3.33 ug/ml, p=0.551) levels significantly in SFN treated mice versus vehicle treated DIO mice, respectively.

Conclusion: SFN treatment improves glucose disposal in DIO mice, which is not linked to the gene expression of GLUT4 and TBC1D4 and its mechanism of glucose disposal in skeletal muscles. Furthermore, SFN treatment did not improve insulin level, and the insulin sensitizer hormone; adiponectin as potential players for enhancing insulin sensitivity.

Application of CRISPR-CAS9 genome editing in understanding the molecular mechanisms of dysglycaemia in Fanconi-Bickel syndrome

Sanaa Sharari [1,2], Mustapha Aouida[1], Faiyaz Khan[2], Sara Al-Khawaga[1,2], Idris Mohammed[1,2], Basma Haris[2], Saras Saraswathi[2], Khalid Hussain[2]

1: College of Health and Life Sciences, Hamad Bin Khalifa University (HBKU), Qatar Foundation, Doha, Qatar.
2 : Department of Pediatric Medicine, Division of Endocrinology, Sidra Medicine, Doha, Qatar

Background: Fanconi-Bickel syndrome (FBS) is a rare form of glycogen storage disease (GSD) inherited as an autosomal recessive r and caused by mutations in the *SLC2A2* gene. The *SLC2A2* gene encodes for GLUT2, a low affinity facilitative glucose transporter expressed in critical tissues involved in glucose homeostasis such as hepatocytes, pancreatic β-cells, and renal tubular cells. Dysfunctional and reduced expression of GLUT2 causes fasting hypoglycaemia, postprandial hyperglycaemia , hepatomegaly, glucose and galactose intolerance, rickets, and poor growth. The role of dysfunctional GLUT2 in the cause of dysglycaemia is still not clearly understood.

Objective(s): 1. To describe the clinical and genetic characteristics of a new case of FBS patient associated with dysglycaemia. 2. To understand the molecular basis of dysglycaemia in FBS .

Case report: A 22 months old Palestinian boy, born to first degree cousins, presented with severe proximal tubular dysfunction, hepatomegaly with stage 1 fibrosis, rickets, developmental delay, hypotonia, and failure to thrive. Biochemical tests showed high levels of random blood glucose but low C-peptide levels. In addition to severe metabolic acidosis with normal anion gap with low potassium, low magnesium and low phosphorous levels. Urine analysis showed proteinuria, glycosuria, phosphaturia and aminoaciduria.

Methodology: Genomic DNA and RNA of the patient and parents were isolated from peripheral blood samples, and analysed by Whole Exome Sequencing (WES) and Sanger sequencing. CRISPR/CAS9 system was used to do the functional analysis.

Results: A novel homozygous nonsense mutation (c.901C>T) in the *SLC2A2* gene (R301X, Arg at codon 301 to stop codon) was found and confirmed by Sanger sequencing. To investigate the impact of this mutation, CRISPR/Cas9 system was used to substitute the nucleotide C by T at position 901. HEK293T cells were co-transfect by a plasmid carrying Cas9, the specific gRNA to target GLUT2 and DNA oligo donor template to specifically substitute C by T at the position 901. Mutated GLUT2 cells will be used to understand the functional and structural characterisation of the disease.

Role of TMEM-143 in Glucose Homeostasis-Implications in the Pathogenesis of Type-2 Diabetes

Ilham bettahi[*], Manjunath Ramanjaneya[*], Jerobin Jaya Komar[*], Abdelilah Arredouani[†], Kodappully S. Siveen[$],
Mohamed Chikri[†], Michael Kulinski[$], Ramzi M. Mohammad[#], Abdul Badi Abou Samra[*], Martin Steinhoff[$],
Fouad Azizi[$]

[$]*Translational Research Institute, Academic Health System, Hamad Medical Corporation (HMC), Doha, Qatar;*
[*]*Qatar Metabolic Institute (QMI), HMC, Doha, Qatar;* [†]*Qatar Biomedical Research Institute, Qatar
Foundation, Doha, Qatar;*[#]*Department of Oncology, Karmanos Cancer Institute, Wayne State University,
Detroit, Michigan, USA*

Abstract:

TMEM-143 (Transmembrane protein 143) human gene is located in the Chr19q13.33 chromosomal region, which is known to be associated with risk of type-2 diabetes and cancer. TMEM-143 gene is translated into a protein of unknown function, predicted to contain a mitochondrial signal sequence and to reside as an integral membrane protein in the mitochondria. We sought to elucidate TMEM-143 expression pattern, sub-cellular localization, and function in undifferentiated and differentiated C2C12 (myoblasts) and 3T3-L1 (pre-adipocytes). RT-PCR and western blot revealed that TMEM-143 exhibited a differential expression profile during differentiation process into myotubes and adipocytes respectively. Drugs used for metabolic disorders modulated TMEM-143 expression level. Rosiglitazone induced 2.2 ($\pm$0.4)- and 2.6 ($\pm$0.4)-fold increases in TMEM-143 mRNA and protein levels, respectively. Similarly, AICAR and Metformin upregulated TMEM-143 mRNA and protein levels by 2.0 ($\pm$0.35)- and 2.5 ($\pm$0.42)-fold respectively. Insulin and BGP-15 increased TMEM-143 protein level by 2-fold. Confocal fluorescence imaging (CFI) revealed subcellular distribution of TMEM-143 with a predominant localization to mitochondria (Manders Overlap Coefficient, MOC:0.5$\pm$0.03 in myotubes vs. 0.3$\pm$0.02 in adipocytes) and plasma membrane (MOC:0.4$\pm$0.01 in myotubes vs. 0.3$\pm$0.02 in adipocytes). TMEM-143 also exhibited a nuclear localization (MOC:0.2$\pm$0.01 in myotubes vs. 0.33$\pm$0.02 in adipocytes). CFI uncovered changes in TMEM-143 trafficking induced by pharmacological agents that affected its expression. TMEM-143 co-localized with glucose transporter type 4 (GLUT-4) (MOC: 0.75$\pm$0.02). TMEM-143 silencing with siRNA did not induce cell death and mitochondria dysfunction, but induced a 2-fold decrease in GLUT-4 mRNA and protein, and a 2.4-fold decrease in pAKT protein. Subsequently, glucose uptake was reduced by >50%. TMEM-143 may play a physiological role in glucose homeostasis and merits further investigation.

Intralipid infusion increases C1Q TNF related protein-2 (CTRP2) concentrations in control subjects and women with polycystic ovarian syndrome

Jayakumar Jerobin[1], Manjunath Ramanjaneya[1], Ilham Bettahi[1], Raihanath Parammal[1], Siveen Kodapully Sivaraman[2], Meis Alkasem[1], Myint Aye[4], Thozhukat Sathyapalan[4], Monica Skarulis Young[1], Stephen L. Atkin[3] and Abdul Badi Abou-Samra[1].

1. Qatar Metabolic Institute, Department of Medicine and Academic Health System, Hamad Medical Corporation, Doha, Qatar
2. Interim Translational Research Institute, Academic Health System, Hamad Medical Corporation, Doha, Qatar
3. Weill Cornell Medicine Qatar, Education City, Doha, Qatar
4. Department of Academic Endocrinology, Diabetes and Metabolism, Hull York Medical School, Hull, UK

Background: Polycystic ovary syndrome (PCOS) is often associated with obesity and insulin resistance. Adipose tissue is an active endocrine organ, which plays an important role in lipid and glucose metabolism by secreting bioactive molecules named adipokines. C1Q/TNF related proteins (CTRPs), namely CTRP2 and CTRP9, are secreted glycoproteins belonging to the adipokine family, which contribute to glucose and lipid homeostasis. In this study we examined the effects of intralipids and insulin infusion on CTRP2 and CTRP9 in healthy controls and PCOS subjects.

Methods: Ten PCOS and nine healthy controls underwent one hour of moderate intensity exercise three times per week for 8 weeks. Before and after exercise all the study participants had infusion of either saline or intralipids for 3 hours followed by 2 hours of hyperinsulinaemic-euglycemic clamp (HIEC). Plasma samples were collected at 0, 3 and 5 hours for measurement of CTRP 2 and CTRP9 concentrations.

Results: The insulin stimulated glucose disposal rate (M value) during HIEC was decreased in PCOS subjects; this reflects reduced sensitivity to insulin. Infusion of intralipids dramatically increased TG levels in the control and PCOS subjects ($p < 0.0001$); this was not altered by insulin infusion. Before and after exercise, intralipid infusion significantly increased CTRP2 levels in both healthy controls and PCOS subjects; this increase was not influenced by insulin infusion. Intralipids infusion had no effects on CTRP9 levels.

Conclusion: CTRP2 is increased by lipids but unaltered by insulin infusion. This study suggests that CTRP2 might have a physiological role in lipid metabolism.

Characterization of Gut Microbiome in Type-1 Diabetic Children in Qatar Population

Farah El Assadi[1-2], Arun Prasath Lakshmanan[2], Dhinoth Kumar Bangarusamy[2], Shaikha Alabduljabbar[2], Sara Zaidan[2], Goran Petrovski[3], Annalisa Terranegra[2]

[1] College of Health and Life Sciences, Hamad Bin Khalifa University, Qatar.

[2] Research Branch, Sidra Medicine, Qatar.

[3] Paediatrics Department, Endocrine and Diabetes Division, Sidra Medicine, Qatar.

Background:- The prevalence of type 1 diabetes mellitus (T1DM) and obesity in Qatar is one of the highest rates among few countries worldwide. Microbiome is a potential factor in NCD's pathogenesis; however, no study has examined its pattern in T1DM children in Qatar. Interestingly, some of the T1DM children are obese, unlike the majority. Hence, the aim of this study is to characterize peculiar gut microbiome profiles in T1DM and T1DM-obese children in Qatar.

Methods:- This study involves 120 paediatric subjects recruited from Sidra Medicine. Inclusion criteria are: 6-12 years old, no recent antibiotic treatment, no chronic diseases other than T1DM and obesity, and not newly diagnosed for T1DM. The participants are divided into 4-categories: healthy control (HC), T1DM, T1DM-Obese and Obese. Anthropometric parameters, clinical biomarkers, treatments, and 24-hrs dietary recalls are collected. The microbiome characterization is based on 16S rDNA sequencing on Illumina Miseq. QIIME 1.9.0 pipeline, R package, LefSe and Picrust are used for microbial analysis. Dietary analysis is performed using ePhood software. Statistical analysis is performed using R-package with two-sided p-value <0.05.

Results:- We present here preliminary results of microbiome compositions in the four groups. The α-diversity is significantly lower in the 3 groups compared to HC ($p < 0.001$). LefSe showed peculiar microbiota profile in each group (particularly, T1DM – *Lachnospiracea, Collinsella, Blautia, Clostridium;* T1DM- Obese – *Klebsiella*). Nutrients strongly correlated with specific bacteria in T1DM (Phosphorus – *Bifidobacterium*, *Enterococcus*, *bifidobacteriaceae*, *Megasphera*; VitB1, VitB2, VitD – *Clostridiaceae* and *Escherichia*; soluble glucids – unclassified *Peptococcaceae*).

Conclusion:- The relative abundance of Bacteroidetes in T1DM is significantly higher (63.4%) while Firmicutes is significantly lower (29.2%) compared to the T1DM-Obese (29% and 55.2%).

We propose that dietary pattern is the culprit behind the taxonomy microbial differences between T1DM and T1DM-obese subjects.

Serum Nerve Growth Factor among Subjects with Diabetic Peripheral Neuropathy after Low Level Laser Therapy (LLLT) – A Pilot Study.

Anju M[1], Saleena Ummer V [1], Arun G Maiya[2], Manjunath Hande [3]

[1] Department of MLT. [2] Department of PT, MCHP, [3] Department of Medicine, KMC,

MAHE, Manipal, India.

Background: India is emerging to be the diabetic capital of world, currently effecting 8.8% (72.9 million) of adult population. Diabetic peripheral neuropathy (DPN) is the most distressing complication of diabetes causing disability due to foot ulceration, amputation. Treatment for DPN is mainly focused on relieving pain and controlling symptoms. LLLT works by inducing photobiomodulational effect on cell and there by manage nerve injury.

Objective: To understand the changes in serum levels of Nerve Growth Factor (NGF) after LLLT in patients with DPN.

Methodology: Pre post study was done on 30 patients with DPN after obtaining informed consent. DPN was confirmed using 10g Monofilament test, Vibration perception threshold (VPT) and Michigan Neuropathy Screening Instrument. All patients were provided with LLLT for 9 minutes on dorsal and plantar surfaces of foot with a dosage of $3.1J/cm^2$ for 10 days. A blood sample was collected at baseline and 4 weeks after LLLT for NGF estimation.

Result: A mild increase in mean serum NGF was seen after LLLT but this was not statistically significant (p=0.956). A decrease in the VPT (p=0.003) and numeric pain rating score (p<0.001) was observed along with improvement in neuropathic quality of life in all patients treated with LLLT.

Conclusion: No significant difference in NGF levels was observed in majority of patients after LLLT. Since previous reports are inconclusive with NGF levels in DPN at various severity levels, we need to confirm the effect of LLLT on NGF with a larger cohort of participants with DPN at known severity levels.

Role of TMEM-143 in Glucose Homeostasis-Implications in the Pathogenesis of Type-2 Diabetes

Ilham bettahi[*], Manjunath Ramanjaneya[*], Jerobin Jaya Komar[*], Abdelilah Arredouani[†], Kodappully S. Siveen[$], Mohamed Chikri[†], Michael Kulinski[$], Ramzi M. Mohammad[#], Abdul Badi Abou Samra[*], Martin Steinhoff[$], Fouad Azizi[$]

[$]Translational Research Institute, Academic Health System, Hamad Medical Corporation (HMC), Doha, Qatar; [*]Qatar Metabolic Institute (QMI), HMC, Doha, Qatar; [†]Qatar Biomedical Research Institute, Qatar Foundation, Doha, Qatar; [#]Department of Oncology, Karmanos Cancer Institute, Wayne State University, Detroit, Michigan, USA

Abstract:

TMEM-143 (Transmembrane protein 143) human gene is located in the Chr19q13.33 chromosomal region, which is known to be associated with risk of type-2 diabetes and cancer. TMEM-143 gene is translated into a protein of unknown function, predicted to contain a mitochondrial signal sequence and to reside as an integral membrane protein in the mitochondria. We sought to elucidate TMEM-143 expression pattern, sub-cellular localization, and function in undifferentiated and differentiated C2C12 (myoblasts) and 3T3-L1 (pre-adipocytes). RT-PCR and western blot revealed that TMEM-143 exhibited a differential expression profile during differentiation process into myotubes and adipocytes respectively. Drugs used for metabolic disorders modulated TMEM-143 expression level. Rosiglitazone induced 2.2 ($\pm$0.4)- and 2.6 ($\pm$0.4)-fold increases in TMEM-143 mRNA and protein levels, respectively. Similarly, AICAR and Metformin upregulated TMEM-143 mRNA and protein levels by 2.0 ($\pm$0.35)- and 2.5 ($\pm$0.42)-fold respectively. Insulin and BGP-15 increased TMEM-143 protein level by 2-fold. Confocal fluorescence imaging (CFI) revealed subcellular distribution of TMEM-143 with a predominant localization to mitochondria (Manders Overlap Coefficient, MOC:0.5$\pm$0.03 in myotubes vs. 0.3$\pm$0.02 in adipocytes) and plasma membrane (MOC:0.4$\pm$0.01 in myotubes vs. 0.3$\pm$0.02 in adipocytes). TMEM-143 also exhibited a nuclear localization (MOC:0.2$\pm$0.01 in myotubes vs. 0.33$\pm$0.02 in adipocytes). CFI uncovered changes in TMEM-143 trafficking induced by pharmacological agents that affected its expression. TMEM-143 co-localized with glucose transporter type 4 (GLUT-4) (MOC: 0.75$\pm$0.02). TMEM-143 silencing with siRNA did not induce cell death and mitochondria dysfunction, but induced a 2-fold decrease in GLUT-4 mRNA and protein, and a 2.4-fold decrease in pAKT protein. Subsequently, glucose uptake was reduced by >50%. TMEM-143 may play a physiological role in glucose homeostasis and merits further investigation.

Circulating MicroRNAs as potential biomarkers of hypoglycaemia in controls and diabetes subjects.

Manjunath Ramanjaneya[1], Jayakumar Jerobin[1], Ilham Bettahi[1], Milin Bensila[1], Ahmed Al-Qaissi[3], Thozhukat Sathyapalan[3], Monica Skarulis [1], Stephen Lawrence Atkin[2†] and Abdul-Badi Abou-Samra[1†]

1. Qatar Metabolic Institute and Interim Translational Research Institute, Academic Health System, and Department of Medicine, Hamad Medical Corporation.
2. Weill Cornell Medicine Qatar, Doha, Qatar.
3. Department of Academic Endocrinology, Diabetes and Metabolism, Hull York Medical School, Hull, United Kingdom.
4. Translational Research Institute, Academic Health System, Hamad Medical Corporation,

MicroRNAs (miRNAs) are small non-coding RNAs that are stably expressed in circulation and are considered as emerging non-invasive biomarkers for many pathological conditions. Comprehensive characterization of the circulating miRNA under hypoglycaemic condition has not been studied previously in human. Therefore, present study was designed to profile and validate abundance of differentially expressed miRNA in control and diabetes (T2D) subjects.

Methods: The expression levels of 754 miRNA were analysed using a Taqman OpenArray Real-Time PCR system from 5 pooled samples in 25 (5x5 plasma) controls and 25 (5x5 plasma) T2D subjects in fasted state and hypoglycaemia (<2.2 mmoL/L achieved by intravenous infusion of soluble insulin).

Results: We analysed the relationship between miRNA levels and glucose, at baseline we found 3 miRNAs in controls and 15 in T2D (table 1a) were significantly altered with more than 2-fold change, (p<0.05). Further 13 miRNA that were significantly altered were common between control and T2D. Under hypoglycaemic condition miRNA expression profile was different for controls and T2D subjects. In controls at baseline only 3 miRNAs (1 unique, 2 miRNAs commonly between baseline and hypoglycaemia) were significantly different compared to hypoglycaemia which induced significant changes of 5 miRNA. In T2D subjects at baseline about 27miRNA were unique and significantly different compared to hypoglycaemia which induced significant changes of 53 miRNA (table 1b).

Conclusion: Our pooled sample data show that circulating miRNA profile is different in controls and T2D subjects. Induction of hypoglycaemia imparts unique miRNA signatures in controls which is different from T2D. Limitation of our findings is these findings are based on pooled samples therefore further studies are ongoing to validate these findings in individual samples for differentially expressed miRNAs in our study groups.

Table 1A) Significant or uniquely expressed miRNA at baseline in control, T2D and common between control and T2D.

CT (control)	Common between CT and T2D	T2D
miR-486-5p	miR-484	miR-146a-5p
miR-92a-3p	miR-25-3p	miR-425-5p
miR-29c-3p	miR-22-3p	miR-93-5p
	miR-17-5p	miR-126-5p
	miR-223-3p	miR-30b-5p
	miR-16-5p	miR-335-5p
	miR-20a-5p	miR-199a-3p
	miR-15a-5p	miR-148a-3p
	miR-221-3p	miR-150-5p
	miR-27a-3p	miR-326
	miR-451a	miR-24-3p
	miR-145-5p	miR-23a-3p
	miR-652-3p	miR-30d-5p
		miR-1260a
		miR-320a

Table 1b. Significantly or uniquely expressed miRNA at baseline and hypoglycemia in control and T2D.

CT_BL	CT_HY	Common CT_BL|CT_HY	T2D_BL	T2D_HY	Common T2D_BL|T2D_HY
miR-517a-3p	miR-484	miR-486-5p	miR-409-3p	let-7e-5p	miR-146a-5p
	miR-25-3p	miR-221-3p	miR-885-5p		miR-140-3p
	miR-17-5p		miR-590-5p		miR-425-5p
	miR-92a-3p		miR-106b-3p		miR-101-3p
	miR-20a-5p		miR-215-5p		miR-194-5p
			miR-10a-5p		miR-93-5p
			miR-576-5p		miR-126-5p
			miR-431-5p		miR-16-2-3p
			miR-7-5p		miR-652-3p
			miR-425-3p		let-7d-3p
			miR-27a-3p		miR-29c-3p
			miR-181b-5p		miR-30b-5p
			let-7b-5p		miR-324-5p
			miR-365a-3p		miR-363-3p
			miR-221-3p		miR-191-5p
			miR-27b-3p		miR-122-5p
			miR-410-3p		miR-377-3p
			miR-99b-5p		miR-130a-3p
			miR-378a-3p		miR-145-5p
			miR-584-5p		miR-152-3p
			miR-495-3p		miR-186-5p
			miR-338-3p		miR-361-5p
			miR-378a-5p		miR-128-3p
			miR-210-3p		miR-660-5p
			miR-505-3p		miR-222-3p
			miR-483-3p		miR-148a-3p
			miR-181c-5p		miR-195-5p
					miR-423-5p
					let-7g-5p
					miR-143-3p
					miR-130b-3p
					miR-29b-3p
					miR-150-5p
					miR-484
					miR-326
					miR-185-5p
					miR-125a-5p
					miR-17-5p
					miR-181a-5p
					miR-369-3p
					miR-125b-5p
					miR-339-5p
					miR-26a-5p
					miR-30c-5p
					miR-24-3p
					miR-22-5p
					miR-424-5p
					miR-328-3p
					miR-23a-3p
					miR-15b-3p
					miR-151a-3p
					miR-223-3p
					miR-126-3p
					miR-148b-3p

Hepatokines Selenoprotein-P plasma 1 (SEPP1) is increased in Gestational Diabetes Mellitus compared to Gestational Diabetes Mellitus Diagnosed with Polycystic Ovary Syndrome.

Ilham Bettahi[1,2], Manjunath Ramanjaneya[1,2], Jayakumar Jerobin[1,2], Milin Bensila[1], Mohammed Bashir[2], Monica Skarulis[2], Stephen L Atkin[3] and Abdul-Badi Abou-Samra[2].

[1]*Translational Research Institute, Hamad Medical Corporation, Doha, Qatar.*

[2]*Qatar Metabolic Institute, Department of Medicine, Hamad Medical Corporation, Doha, Qatar.*

[3] *Weill Cornell Medicine Qatar, Doha, Qatar.*

Background: Gestational diabetes (GDM) is defined as glucose intolerance that is first diagnosed during pregnancy and women with polycystic ovary syndrome (PCOS) are at increased risk for developing gestational diabetes mellitus (GDM) during pregnancy. Selenoprotein P (SEPP1) is a hepatokine, primarily synthesized from the liver and is responsible for Selenium (Se) transport from the liver to extrahepatic tissues. Circulating SEPP1 levels and hepatic expression of SEPP1 are elevated in patients with type2 diabetes and overweight/obese patients. Recently, it has been demonstrated that SEPP1 played an essential role in glucose metabolism and the regulation of insulin sensitivity as a new hepatokine. The purpose of this study was to measure plasma SEPP1 level in gestational diabetes with and without PCOS.

Methods: A cohort of 3 groups (N=64 pregnant women): 1) pregnant women with GDM (BMI=32.5 ±6.1); 2) pregnant women with PCOS-GDM (BMI=33.7 ±5.2); and 3) healthy pregnant women (BMI=28.8 ±7.4) (BMI: body mass index). Blood samples were collected from all subjects, and plasma SEPP1 were measured based on solid-phase sandwich Enzyme-linked Immunosorbent Assay technique.

Result: SEPP1 level was significantly higher in the GDM group compared to control. Further, SEPP1 was significantly lower in GDM with the PCOS group compared to the GDM group (*p<0.05*). Overall, there was a positive correlation between BMI (body mass index) and systolic blood pressure, also a correlation between cholesterol and high-density lipoprotein. In contrast, in the GDM group, there was no statically significant correlation between SEPP1 and BMI or HbA1c.

Conclusion: This result suggests a possible role for SEPP1 in the pathology of GDM, and SEPP1 may be a useful biomarker to differentiate GDM subjects from those with GDM- PCOS in the Qatari women population.

Gut Microbiome Shifts during Pregnancy Can Predict Gestational Diabetes Onset

Rola Salem [1,2], Shaikha Alabduljabbar [2], Arun P Lakshmanan [2], Mohammed Elanbari [2], Dhinoth K Bangarusamy [2], Sara Al Zaidan [2], Basirudeen Sa Kabeer [2], Tobias Brummaier [3,4,5], Karim Damji [3,6], Souhaila Al Khodor [2], Tomoshige Kino [2], Francois Nosten [3,6], Rose Mcgready [3,6], Damien Chaussabel [2] and Annalisa Terranegra[2]

[1]College of Health and Life Sciences, Hamad Bin Khalifa University, Qatar Foundation, Doha, Qatar
[2]Sidra Medicine, Doha, Qatar
[3]Shoklo Malaria Research Unit, Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Mae Sot, Thailand.
[4]Department of Medicine, Swiss Tropical and Public Health Institute, Basel, Switzerland
[5]Faculty of Medicine, University of Basel, Basel, Switzerland
[6]Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Old Road Campus, Oxford, United Kingdom

Background: Normal healthy pregnancy is considered a dynamic and transient process. During gestation the body undergoes substantial hormonal, immunological, and metabolic changes which lead to alteration in the anatomy and physiology of all the body systems. Microbiome profiling at multiple timepoints will allow us to better explore the underlying molecular mechanisms during pregnancy and its complications such as gestational diabetes (GDM).

Methods: Fifty six pregnant women (18-49 years age, viable singleton, and first trimester) were included in this study. Oral glucose tolerance test (OGTT) was performed at third trimester (TP3), as per clinical routine guidelines. Stool samples for 16S rDNA sequencing of gut microbiota and food frequency questionnaire at 4 time points: each trimester (TP1, 2, 3) and delivery (TP4) were collected.

Results: Since the beginning of the pregnancy, GDM subgroup of subjects revealed a peculiar microbiome profile with lower level of Bacteriodes at all TPs compared to normal pregnancies (72% vs 80% TP1, 69% vs 82% TP2, 71% vs 85% TP3, 78% vs 81% TP4); higher level of Firmicutes (18.7% vs 13.6% TP1, 19% vs 11% TP2, 15% vs 8.6% TP3, 14% vs 11% TP4); and Proteobacteria (6.2% vs 4.4% TP1, 11% vs 6.4% TP2, 9.8% vs 5% TP3, 6.5% vs 6% TP4). At the genus level, *Bacteroides, Succinovibrio* and *Lachnospiraceae*_NK4A136 showed double levels in GDM at TP1, TP2 and TP3. At TP4 the differences disappeared. GDM group also showed different food preferences that can correlate with microbiota (lower intake of vegetables, fish, poultry, fish paste, sugar at all TPs, $p < 0.05$).

Conclusion: This study provides insights into how the gut microbiota contributes to long-term gestational health complications. Also, it highlights that microbiome can be potentially used as early biomarker of GDM and can be targeted for preventive treatment of GDM.

Effects of Grape Skin Extract (GSE) on Glycemic Response in Prediabetic (PD) Subjects

Meis Alkasem, Ibrahim Abdulhakam, Noor N Suleiman, Tareq A Samra, Ahmad Iskandarani, Fayaz A Mir, Jerobin Kumar, Manjunath Ramanjaneya, Ramzi Mohamed, Kevin Zhou, Abdul-Badi Abou-Samra, Monica Skarulis

 Qatar Metabolic Institute, Hamad Medical Corporation
Translational Research Institute, Hamad Medical Corporation, Doha, Qatar.

Background: Prediabetes is the state of impaired fasting glucose and/or glucose intolerance and progresses to type 2 diabetes at a rate of ~10% annually. GSE decreases postprandial glycaemia through alpha glucosidase inhibition. This study aims to examine the effect of GSE on glucose metabolism in PD.

Methods: Blood glucose response to a standardized rice meal (35g uncooked weight) with or without GSE 600 mg (N=4), 1200 (N=8), 1800 mg (N=15) or 2400 mg (N=14) was determined.   Glucose area under the curve (AUC) was calculated and subjects were classified into "responders" or "non-responders" if AUC after GSE was reduced by at least 1 SD. The dose with the greatest effect was used in the randomized double-blind, placebo-controlled 3-month study of GSE before meals TID. Primary endpoint was glucose response during OGTT.

 Results: Forty-one (41) prediabetic subjects (83% male, age 29±8 years; BMI 23.2 %±5.9) were enrolled. 1800mg resulted in a small but significant decrease in glucose excursion in the single dose study. AUC was decreased by 2 SD in 9.7% and 1 SD in 24% of subjects. Participants were randomized to GSE (N=18) or placebo (N=17). After 3-months of GSE, insulin secretion was increased by 18%, HOMA-IR increased by 28% in GSE arm; there was no difference in glucose levels, lipid profile, blood pressure and inflammatory markers. BMI increased in the GSE group. GSE was generally well tolerated.

Conclusion: In conclusion, 3 months of GSE before meals did not improve glycaemia compared to placebo as originally hypothesized. Possible reasons for our findings: 1.) dose was not sufficient to decrease glucose absorption; 2.) adherence may not have been as reported; and 3.) the subjects showed significant increase in BMI. New formulations of GSE may be required for further study.

Non-nutritive sweetener stevioside increases glucose uptake via AKT pathway in adipocytes and myotubes

Jayakumar Jerobin[1], Manjunath Ramanjaneya[1], Ilham Bettahi[1], Siveen Kodappully Sivaraman[2], Raihanath Parammal[1],Fouad Azizi[2], Tareq Abousamra[1], Monica Skarulis Young[1] and Abdul Badi Abou Samra[1]

1. Qatar Metabolic Institute, Department of Medicine and Academic Health System, Hamad Medical Corporation, Doha, Qatar
2. Interim Translational Research Institute, Academic Health System, Hamad Medical Corporation, Doha, Qatar

Introduction: The metabolic syndrome is a major health risk in Middle Eastern countries including Qatar. Both nutritive and nonnutritive sweeteners (NNS) are consumed by people worldwide, and the consumption of sweeteners above the recommended level contributes to metabolic syndrome such as diabetes and NAFLD. The consumption of artificial NNS saccharin modulates the gut microbiota and promotes glucose intolerance. Currently the artificial NNS are replaced with natural NNS stevioside in foods and beverages since it has low caloric value. Studies have shown that stevioside possess antioxidant and antihyperglycemic properties which may have a potential role in type 2 diabetes mellitus treatment. This proposed study mainly focuses on the effect of NNS stevioside on glucose uptake in adipocytes and skeletal muscle myotubes.

Methods: The myotubes were formed by the addition of differentiation medium containing 2% horse serum in C2C12 myoblast. The 3T3L1 preadipocytes cells were cultured in DMEM medium, and the preadipocyte cells were differentiated in to mature adipocytes by the addition of IBMX, Insulin and Dexamethasone on 0th day. The maintenance media containing insulin was added till mature adipocytes was obtained. Steviosides (100 µM) were treated in adipocytes and myotubes for 2 hours. The glucose uptake was measured using glucose uptake assay kit. Western blot was done for GLUT-4 in plasma membrane and p-AKT(Ser473).

Results: In stevioside treated adipocytes and myotubes, phosphorylation of pAKT(ser473) was found to be significantly increased. We found a significant increase in glucose uptake when treated with stevioside in adipocytes and myotubes compared to controls. The plasma membrane expression levels of glucose transporter GLUT4 was found to be significantly increased in stevioside treated adipocytes and myotubes.

Conclusion: The stevioside showed increase in glucose uptake via AKT pathway indicating that stevioside may possess insulin sensitivity and glucose uptake properties in adipocytes and myotubes.

Difference between familial diabetes cases and healthy controls in terms of polygenic risk score and T2DM associated variants

Ibrahem Abdalhakam, Shaimaa Aroob , Meis Alkasem , Noor Suleiman, Puthen Jithesh, Omar Albagha, Abdul B. Abou-Samra

Qatar Metabolic Institute, Hamad Medical Corporation; Sidra Medicine & Qatar Biomedical Research Institute, Hamad Bin Khalifa University, Qatar Foundation

Introduction: The prevalence of type 2 diabetes (T2D) in Qatar is ~17% of adults and most T2D subjects have a family history of T2D. Clustering of T2D in certain Qatari families has been well recognized where 30-100% of siblings have diabetes. It is not clear if shared genetic, lifestyle or environmental factors are responsible for familial clustering of diabetes.

Aim: To investigate the genetic predisposition in familial diabetes in the Qatari population.

Method: A cross-sectional study involving a systematic genetic analysis of diabetes in a population of Qatari families (indigenous Qatari and long-term residents from Arab descendent) with a prevalence of T2D in more than 1/3 of siblings and of T1D more than 1/5th of siblings. 113 controls who were aged 55 years or above and with no history of HTN, DM or hypercholesteremia, were identified from Qatar genome project . Whole genome sequencing was performed and analysed to identify diabetes risk alleles in each family. Genetic risk score were calculated by the sum of the risk alleles of each case and control.

Results: Whole genome sequences of 20 individuals belonging to 6 different families were analysed. Analysis of the sequences for Type 2 diabetes associated risk alleles from GWAS catalogue was performed. This followed by the calculation of polygenic risk score for T2DM for each individual. Comparing the polygenic risk score for T2DM of cases with controls showed that cases have a significantly higher risk score than controls. Comparison of case and control groups based on the distribution of 'homozygous', 'heterozygous' and 'total' variants revealed variants that significantly different between cases and controls.

Conclusion: Polygenic risk score found to be higher in familial diabetes cases than controls. Also, specific variants were significantly different between cases and controls.

Assessment of Venetoclax Related Cardiotoxicity on Rat Cardiomyocytes H9C2 Cell Line: In-Vitro Study.

Shimaa Aboelbaha , Bodoor Aboujabal, Hesham M. Korashy

College of Pharmacy, Qatar University, Doha 2713, Qatar

Introduction: Venetoclax (VCX) is a newly approved anti-cancer agent for the treatment of chronic lymphocytic leukemia (CLL). It is a BH-3 mimetic that exerts its mechanism of action through inhibition of the anti-apoptotic Bcl-2 protein that is overly expressed in leukemia cells and contributes to their survival. Since most of the available anti-cancers cause cardiotoxicity with limited date on the safety profile of VCX on the heart, the possibility that VCX induces cardiotoxicity could not be rolled out.

Purpose: The aim of this study is to determine VCX potential cardiotoxicity effect through the following: assessment of VCX effect on hypertrophic (β-MHC, ANP) as well as apoptotic genes (Caspase-3, Bcl-2) on both translational and transcriptional levels.

Methodology: This study was conducted using rat cardiomyocyte H9C2 cell line as an in vitro model. Cell viability was determined using MTT assays. Quantification of mRNA and protein expression of tested biomarkers was conducted using Real Time Polymerase Chain Reaction (RT-PCR) and Western Blot analyses, respectively. Statistical tests used were one-way Analysis of variance (ANOVA) followed by Dunnett's. P-value was determined to be ≤ 0.05.

Results: Venetoclax at concentration of 10 µM and above was shown to cause H9c2 cytotoxicity and thus 10 and 25 µM concentrations were used in subsequent experiments. Results of both RT-PCR and Western Blot have shown that VCX treatment induced the expression of hypertrophic markers β-MHC and ANP. This was associated with induction of apoptosis as evidenced by increased caspase-3 protein and mRNA expression levels and decreased BCL-2 protein expression.

Conclusion: The current study demonstrates the first evidence of the ability of VCX to induce cardiotoxicity in rat cardiomyocytes through induction of apoptosis. Further research is warranted to assess the applicability of these results to humans.

Large-scale serological profiling of Qatari adult and pediatric population reveals association between obesity and humoral immunity to herpesviruses

Mahbuba Rahman[1#], Taushif Khan[1], Amira Saeed[2], Sathyavathi Sundaraju[2,] Fatima-Al-Ali[1], Stephen Ellegde[2,3,4]
, Sathyavathi Sundaraju[2], Patrick Tang[2,3], Mohammad Rubayet Hasan[2,3], Nico Marr[1,4]

[1]Department of Systems Biology and Immunology, Sidra Medicine, Doha, Qatar
[2]Department of Pathology, Sidra Medicine, Doha, Qatar
[3]Weil-Cornell Medical University, Doha, Qatar
[4]Department of Genetics, Harvard University, Boston, MA, USA
[5]Brigham and Women's Hospital, Boston, MA, USA
[6]Howard Hughes Medical Institute
[7]Hamad Bin Khalifa University, Doha, Qatar

Obesity is one of the most important health problems in Qatar, with more than 70% of its population being either obese or overweight. While obesity is predominantly caused by intake of high calorie diet and reduced physical activities, many other factors including infections or exposure to certain viruses have been reported to be associated with obesity in animal models and in human studies. However, these studies focused on the relationship of obesity with specific viral species only. Here, we used an unbiased high-throughput method, phage immunoprecipitation sequencing (PhIP-seq), for serological profiling of 800 Qatari adults and long-term residents of Qatar, and 200 Qatari children with the goal to identify associations between obesity and antibody specificities to protein antigen determinants of a wide range of microbial species. Our analysis revealed that there is a positive association between obesity and antibodies specific to a number of antigenic determinants of herpesviruses including herpes simplex viruses 1 and 2 (HSV-1/2), Epstein-Barr virus (EBV) and human cytomegalovirus (CMV) among Qatari adults. Conversely, we observed a negative association between obesity and antibody specificities to several genetically related species of the picornaviridae family, including human rhinoviruses 1B, 2, 14, 16 and 23 and coxsackievirus B5. A positive association of obesity with herpes viruses and a negative association with rhinoviruses were also noted in the paediatric population. The positive association between herpes virus-specific antibodies and obesity is consistent with previous reports on adipogenic properties of these viruses observed in cultured cells and animal models. The negative association of obesity with humoral responses to picornaviridae family in both adult and paediatric cohorts suggest a link between obesity and impaired immunity to particularly to this virus family and warrants further investigation.

Assessment of histopathological prognosticators in diabetic nephropathy

Awais Nauman, Ahmed Khalaf, Rihab Elidrisi, Mohamad Alkadi, Adel A Aziz, Ahmed Hamdi, Omar Fituri,
Mohamad Asim, Mohammad Akhtar, Hassan Al-Malki, Essa Abuhelaiqa

Diabetic nephropathy (DN) is the leading cause of end stage kidney disease worldwide. Identification of clinical, laboratory and histopathological predictors of kidney failure in DN may improve outcomes.

We identified 45 kidney biopsies between 2017 to 2018 that were diagnosed with DN. Clinical, laboratory and histopathological variables were analysed to prognosticate 1-year kidney failure.

Sixteen of 45 patients with DN had kidney failure within 12 months of kidney biopsy while 29 patients did not. All patients who developed kidney failure had diabetic retinopathy as shown in table 1. Laboratory findings such a serum creatinine (597umol/L vs. 205umol/L, P<0.0001) and presence of haematuria (88% vs. 45%, P=0.01) prognosticated kidney outcome, while neither proteinuria or HBA1C did. IFTA score (2.4 vs. 1.8, P=0.02) and global glomerular sclerosis (52% vs. 32%, P=0.002) were the only histological findings that prognosticate kidney failure. Patients who have a second kidney diagnosis in addition to DN such as IgA, FSGS and MN had favourable outcomes [figure 1].

We identified serum creatinine, haematuria, IFTA and glomerular sclerosis as prognosticators of kidney failure at 1-year following DN diagnosis. Identification of patients at risk of kidney failure help individualize therapy and hence improve kidney outcomes.

Table 1. Predictors of kidney failure in diabetic nephropathy			
Variable	Kidney failure (n=16)	No kidney failure (n=29)	P value
Clinical Findings			
Age at biopsy	50±14	50±11	0.9
Female gender	3 (13%)	3 (10%)	0.7
Duration of diabetes mellitus (years)	13±7	13±9	0.9
Diabetic Retinopathy at biopsy	13/13 (100%)	13/18 (72%)	0.06
Indication of biopsy			
Proteinuria	7 (44%)	17 (59%)	0.4
Worsening CKD/AKI	5 (31%)	8 (28%)	0.9
Laboratory Finding			
Hemoglobin A1C at biopsy	7.4±1.6	7.6±2.2	0.7
Creatinine at biopsy	597±382	205±107	<0.0001
Urine protein/creatinine ratio at biopsy (mmol/g)	948±509	670±393	0.07
Hematuria at biopsy	14 (88%)	13 (45%)	0.01
Biopsy finding			
Interstitial fibrosis and tubular atrophy score (IFTA, 0-3)	2.4±0.8	1.8±1.0	0.02
Glomeruli with global sclerosis (%)	52±20	32±22	0.002
Nodular hyalinosis	11 (69%)	17 (59%)	0.5
Arteriosclerosis	16 (100%)	26 (90%)	0.5
Immunofluorescent deposition	13 (81%)	18 (62%)	0.3
Second diagnosis in addition to diabetic nephropathy	3 (19%)	11 (38%)	0.3
Focal Segmental glomerular sclerosis	0	3 (10%)	0.5
IgA nephropathy	0	1 (3%)	1
Acute interstitial nephritis (AIN)	2 (13%)	3 (10%)	0.3

Figure 1. Diabetic nephropathy and secondary diagnosis kidney outcome
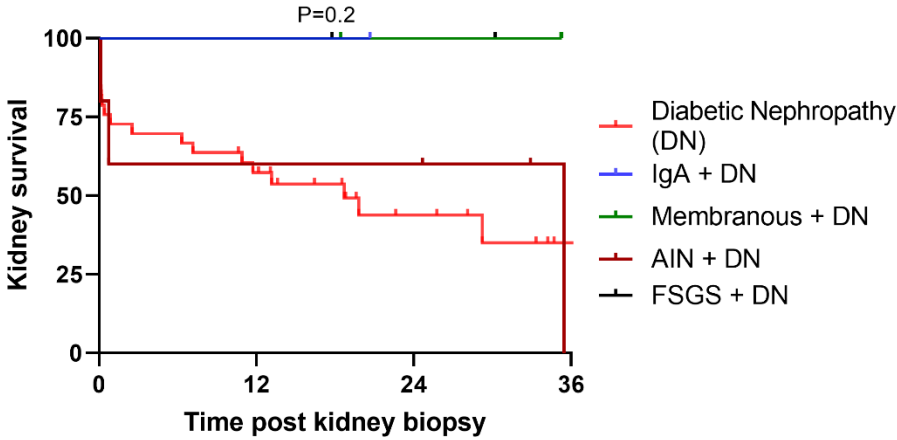
The Expression Of Retinal Micro RNA Evoked By Hyperglycaemia And After Adiponectin Treatment In Human Retinal Endothelial Cells

Duaa W. Al-Sadeq[1], Nasser M. Rizk[1]

[1] *Department of Biomedical Science, College of Health Sciences, Qatar University, Doha, Qatar*

Background: Diabetes mellitus is a chronic metabolic disease resulting in microvascular complications including diabetic retinopathy (DR). Adiponectin (ApN) is an adipokine hormone, and recent studies demonstrated that ApN could ameliorate critical biological process involved in the pathogenesis of DR. Micro-Ribonucleic acids (miRNAs) have been documented as novel biomarkers and are increasingly considered as molecules with significant modulatory action.

Aim: To characterize the miRNA profile and expression in human retinal endothelial cells (HRECs) exposed to hyperglycemic conditions (HG) and illustrate the effect of adiponectin on miRNA expression and related pathways in HRECs exposed to HG.

Methods: HRECs were treated with high glucose (30mM) for 96 hours duration followed by adiponectin (30µg/ml) for 24 h. Total RNA was extracted from HRECs. The gene panel array for both adhesion and angiogenesis molecules were performed using commercial RT2 Profiler PCR arrays. Furthermore, we utilized the small RNA sequencing for microRNA expression profiling of the HRECs.

Results: HG treatment increases the expression of different well-known adhesion and angiogenesis genes as well as predicted miRNAs involved in these pathways, which was counteracted by ApN. RNA-Seq for miRNA profiling revealed 13 differentially expressed miRNAs in HRECs exposed to HG. miR-146a-5p was differentially expressed in HRECs treated with ApN. Analysis pathway linked the significantly changed miRNAs induced by HG to essential pathways such as hypoxia signaling, inflammation, and oxidative stress.

Conclusion: HG induces expression of various adhesion and angiogenesis genes. Using RNA-Seq technology can accurately identify dysregulated miRNA profiles in HG retinal cells. MiR-146a was upregulated by adiponectin which targets different pathways involved in DR genesis.

Patients With Type-2 Diabetes Achieving Multifactorial Metabolic Targets In Secondary Care Diabetes Clinics In Qatar.

Mohammed Bashir[1], Tarik Elhadd[1], Zeinab Dabbous[1], Mashoud Siddique[1], Wajiha Gul[1], Obada Salameh[1], Gerorgios Ponirakis[2] & Rayaz A Malik[2]

Qatar Metabolic Institute[1], HMC, Doha, Qatar, Weill Cornell Medicine-Qatar[2], Doha, Qatar

Introductions: Optimal control of glycaemia, blood pressure and lipids is associated with a reduction in both micro- and macrovascular complications in patients with type 2 diabetes. However, studies from many countries have shown that a low proportion of patients achieve ABC (Hb**A**1c, **B**lood Pressure, **C**holesterol) targets.

Objective: To examine the proportion of patients with type 2 diabetes mellitus in secondary care in Qatar, who achieve the ABC targets.

Methods: This is a secondary analysis of a cohort of patients with type-2 diabetes enrolled to study the prevalence of diabetic neuropathy in Qatar.

Results: We have examined 1153 patients with type 2 diabetes (715 (62%) males and 438 (38%) females) with a mean age of 52.1 years ± 11.4 years and mean duration of diabetes of 10 ± 7 years. The proportion of patients achieving an HbA1c ≤ 7.0% was 35.1%; systolic blood pressure <140 mmHg was 70% and LDL ≤ 2.6 mmol/l was 54.1%; whilst the proportion achieving all three targets was 12.2%. Figure 1 shows the proportion of patients achieving different levels of ABC targets.

Discussion and Conclusion: This is the first report from Qatar showing that the proportion of patients with type 2 diabetes achieving ABC targets were comparable to Denmark (15%) and superior to Spain (2.6%). Further studies are required to understand the barriers in achieving ABC targets.
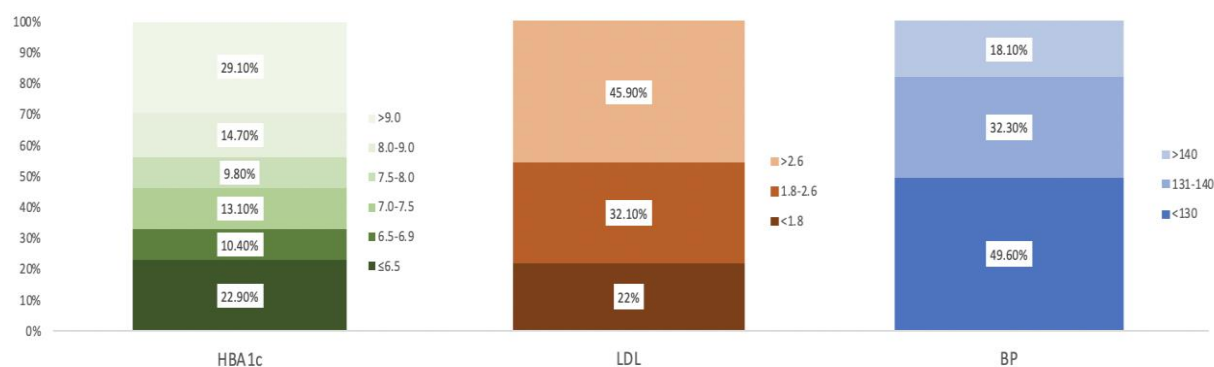
Fig 1. Proportion of patients achieving various ABC targets.

The Achievement Of Lower Cardiovascular Risk Factor Targets Is Related To A Higher Prevalence Of Painful Diabetic Neuropathy In Qatar

Tarik Elhadd[1], Mohamed Bashir[1], Zeinab Dabbous[1], Obada Salameh[1], Wajiha Gul[1], Mashhood Siddique[1], Georgios Ponirakis[2], Rayaz A Malik[2]

Qatar Metabolic Institute[1], HMC, Doha, Qatar, Weill Cornell Medicine-Qatar[2], Doha, Qatar

Background & Objective: Diabetic neuropathy is associated with poor glycemic control, hyperlipaemia and hypertension. However, painful diabetic neuropathy was associated with smoking, obesity and being female, but not glycaemic control, hypertension or proteinuria. We have assessed the prevalence of painful diabetic neuropathy in patients who did and did not achieve optimal levels for HbA1c, systolic BP, LDL cholesterol, ABC targets and ACR.

Patients & Methods: 1039 patients with type 2 diabetes, mean age 52.1 years ± 11.4 years and mean duration of diabetes 10 ± 7 years underwent assessment for painful diabetic neuropathy using the DN4 questionnaire in the Diabetes Centres in Hamad General Hospital and Al-Wakra.

Results: The prevalence of painful diabetic neuropathy (PDN) was 34.5%. The percentage of patients achieving an HbA1c of ≤ 7% was significantly lower (10% v 15.3%, P=0.02) in patients with painful diabetic neuropathy. The percentage of patients achieving a systolic BP ≤ 140 mmHg was significantly lower (12.0% v 18.5%, P=0.005) in patients with painful diabetic neuropathy. The percentage of patients with an elevated albumin creatinine ratio (15.2% v 8.0%, P=0.002) was higher in patients with painful diabetic neuropathy. The percentage of patients achieving an LDL ≤ 2.6 mmol/l did not differ significantly (12.6% v 15.3%, P=0.23) in patients with painful diabetic neuropathy. The percentage of patients not achieving all three ABC targets showed a non-significant trend to be higher (14.8% v 8.8%, P=0.07) in patients with painful diabetic neuropathy.

Conclusion: Our data confirms the importance of achieving optimal control of cardiovascular risk factors to prevent the development of painful diabetic neuropathy in patients with type-2 diabetes in Qatar.

Association of Vitamin B12 Deficiency and Metformin Use in Type 2 Diabetes Patients Treated at Hamad General Hospital, Qatar

Fahmi Yousef khan[1], Abdelmonem B. Yousif[1], Aasir Suliman[1], Ahmed Osman Saleh[1], Mohamed Magdi[1], Awni Alshurafa[1], Ebtihal Abdelmoneim Hassan[2], Ahmed Ghazy[1], Omar K. Salameh[1], Ahmed Abdallah[1.]

Department of medicine, Hamad general hospital, Doha, Qatar. 2- Department of accident & emergency, Hamad General Hospital, Doha, Qatar

Background: There is an accumulating evidence that suggest Metformin role in vitamin B12 deficiency among T2DM patients. However, there are limited data emphasizing this effect in the Middle East & Qatar.

Objectives: To assess the prevalence of vitamin B12 deficiency and its related factors among T2DM patients treated with metformin at Hamad General Hospital, Qatar.

Subjects and Methods: A retrospective cross-sectional analytical study was conducted at Hamad General Hospital (HGH). It involved T2DM patients treated with metformin. Out of 6420 identified patients, only 3124 were eligible. The mean age of the eligible patients was 56.6±10.2 years, where 72% were males and 28% were females. Table 1 describes the demographic and clinical characteristics of the patients involved in this study.

Results: The overall prevalence of metformin-induced vitamin B12 deficiency in T2DM patients was 30.7% (959 out of 2124 patients). There was a significant difference in vitamin B12 levels between normal B12 and B12-deficient groups. We also found the following as independent risk factors for metformin-induced B12 deficiency in T2DM patients: high daily dose of metformin (> 1000 mg), male gender, high BMI, smoking, sulfonylurea, Dipeptidyl Peptidase-4 inhibitor, H2 blockers/PPI, low fasting blood glucose, high HDL and low haemoglobin.

Conclusion: Based on our result, we advise for regular serum B12 screening in T2DM patients on metformin who have the risk factors mentioned above.

Table 1. Demographic and clinical characteristics of the 3124 patients involved in this study

Variables	Frequency	Percentage
Sex of the patients		
Female	888	28
Male	2236	72
Age (mean±SD)	56.6±10.2	
Nationality of the patients		
Others	2909	93
Qatari	215	7
Categorized BMI		
<25	455	15
25-<30	1246	40
=>30	1423	46
Duration of diabetes		
<4 Yrs	444	14
≥4 Yrs	2680	86
Duration of metformin use		
<4 Yrs	494	16
4-10 Yrs	1864	60
>10 Yrs	766	25
Daily dose of metformin	1842.19 ± 379.05	
≤1000 mg	26	0.9
>1000 mg	3098	99.1

Impact Of JCI Clinical Care Program On The Metabolic Parameters In Adults With Diabetes.

Khaled Dukhan, Bashar Alayash, Abdel Wahab Nofal, Duaa Alsmadi, Ragae Dughmosh, Mahmoud Zirie, Mohammed Bashir
National Diabetes Centre, Hamad General Hospital and Al Wakra Hospital – HMC

Introduction: JCI Clinical Care Program (CCPC) is a patient-centered program aims at improving patients' care quality through applying a standardized MDT care model. National Diabetes Centre is a certified CCPC Centre providing services in 3 sites: Hamad General Hospital (HGH), Al Wakra Hospital (AWH) and Women's Wellness and Research Center.

Aim: To measure impact of the CCPC program on the metabolic parameters in adult non-pregnant patients with diabetes in HGH and AWH.

Method: We included all patients enrolled in the CCPC program in HGH and AWH.

Results: We studies 140 patients, 60% were males, 40% Asians, 27% Qataris and 23% Arab. The mean age was 50 ±11.6 years, mean diabetes duration was 11.8 ±8.3 years, and the mean age at the onset of diabetes was 38.7 ±10.8 years. The mean HbA1c dropped from 9.6% to 8.6% at 6 months and was maintained at 12 months. The proportion of patients achieving HbA1c ≤ 8.0% was 38.5% at 6 months and 51.6% at 12 months; while 15.6% achieved HBA1c ≤ 7.0% at 12 months. Both the systolic and diastolic BP decreased by 3 mmHg at 12 months. The proportion of patients with systolic BP ≤ 140 mmHg was 74.3% at baseline, 77.6% at 6 months and 78.8% at 12 months. The mean BMI remained stable at 31 kg/m^2; however, the proportion of obese patients (BMI >30 kg/m^2) dropped from 56.4% to 55.8% and 53.0% at 6 and 12 months respectively. The mean LDL remained unchanged at 2.3mmol/l, but the proportion of patients with LDL ≤ 2.6mmol/l dropped from 75% to 70.1% and 65.4% at 6 and 12 months respectively.

Conclusion: The CCPC program has a positive impact on most metabolic parameters. A more in-depth evaluation is needed to understand the lack of improvement in the lipids profiles.

Diabetic Retinopathy Among Pregnant Women With Type 1 Diabetes Mellitus -NDC-WWRC

Zakara Afghan , Moufida Azek, Roshini Thomas, and Mohammed Bashir
Department of Ophthalmology, Hamad Medical Corporation. National Diabetes Centre, Women Wellness and Research Centre.

Background: - Pregnancy is associated with an accelerated rate of progression of diabetic retinopathy in women with type 1 diabetes (DM-1). Most of the progression occurs in the second half of pregnancy. Hence, both the national and international guidelines recommend screening for retinopathy in the first trimester OR at the first visit.

Aim: - This audit aims to examine the time to the first retina screening and describe the retinal findings.

Methods: - We included all the patients with DM-1 who attended the retina clinic from January 2019-November 2019.

Results: - Forty-one women with DM-1 were studied. The median age was 30 years (IQR 27-33), the median duration of diabetes was 12.2 years (IQR 7.6-20.2), and the median pre-conception HBA1C was 7.8% (IQR 7.1-8.7). The median time to the first retina screening visit was 16.6 weeks (IQR 13-23.4). Overall, 73.2% of the women had a normal screening in the first visit while 19.5% had NPDR (None-Proliferative Diabetic Retinopathy) and 7.3% had PDR (Proliferative Diabetic Retinopathy). In women with diabetes duration ≤ 5 years (7 women), there was no retinopathy detected in the first visit; while in those with diabetes duration > 5 years, 23.5% had NPDR and 8.8% had PDR.

Discussion and conclusion: - The average time for retina screening is within acceptable levels but could be improved further. The current rate of baseline diabetes retinopathy of 26.8% is higher than in other populations. Hence women with DM-1, with > 5 years duration, should be referred for retinal screening as soon as possible and should be prioritised. In the future, we will report on the rates of diabetic retinopathy progression in this high-risk cohort.

Diabetic Retinopathy Among Pregnant Women With Type 2 Diabetes Mellitus -NDC-WWRC

Moufida Azek, Roshini Thomas , Zakara Afghan, and Mohammed Bashir
Department of Ophthalmology, Hamad Medical Corporation. National Diabetes Centre, Women Wellness and Research Centre.

Background: - Pregnancy is associated with an accelerated rate of progression of diabetic retinopathy in women with type 1 diabetes (DM-1). Data in women with type 2 diabetes (DM-2) is quite scarce- especially in women with newly detected diabetes during pregnancy- but is assumed to be similar to DM-1. Hence screening for retinopathy is recommended in women with pre-existing DM-2 during pregnancy.

Aim: - This audit aims to examine the time to the first retina screening and describe the retinal findings.

Methods: - We included all the patients with DM-2 who attended the retina clinic from January 2019-November 2019.

Results: - We studied 262 women with DM-2; 148(56.5%) had pre-existing DM-2, and 114(43.5%) had newly detected DM-2 during pregnancy. In those with pre-existing DM-2, the median age was 35 years (IQR 32-39), the median duration of diabetes was 4.1 years (IQR 2-6.8), and the median pre-conception HBA1C was 6.6% (6.0 -8.1%). The median time to the first retina screening visit was 25 weeks (IQR 18-30). In women with pre-existing DM-2, 96% had a normal screening in the first visit, while 4.0% had NPDR (None-Proliferative Diabetic Retinopathy). In women with newly detected DM-2, no retinopathy was detected in the first screening visit.

Discussion and conclusion: - The average time for retina screening is in women with pre-existing type 2 diabetes is beyond the recommended gestational age. The gestational age at referral to the general diabetes service is the most likely influencing factor. Overall the rates of diabetic retinopathy in women with pre-existing type 2 diabetes is quite low and in keeping with data from other populations. As pregnancy seems to impact the rate of retinopathy progression for up to one year post-natal, more follow up data is required in this group.

Glycaemic Control In Pregnant Women With Type 2 Diabetes Enrolled In The CCPC-Program

Naglaa Al-Sharkaway, Eman Othman , Nahad Al-Alwai, Annama Joseph, Afrah Hussein Ahlam Alsaadi , Lubna Dagash, Aiswarya John , Riza Tupil, Salma Bashir & Mohammed Bashir

National Diabetes Centre-Women Wellness and Research Centre.

Background:- Achieving target glycaemic control is critical in improving pregnancy outcomes in women with type 2 diabetes (DM-2). The glycaemic control targets for women with DM-2 is HBA1c ≤6.5%.

Aim:- To measure the glycaemic control in pregnant women with DM-2.

Methods:- We included all women with DM-2 who were enrolled in the CCPC program since August 2018.

Results:- We are reporting on 258 women with DM-2, of which 154 (59.7%) had pre-existing DM-2, and 104 (40.3%) were newly detected DM-2 in the first trimester. In those with pre-existing DM-2, the median age was 35 years (IQR 32-39), the median duration of diabetes was 4.3 years (IQR 2.1-8.3); the mean pre-conception BMI was 32.1±7.5kg/m^2, and the mean pre-conception HBA1c was 7.2 ± 1.9%. The median age of women with newly detected DM-2 was 33 years (IQR 30-37), mean pre-conception BMI was 31.4±7.2kg/m^2 and mean HBA1c at diagnosis was 6.6 ± 1.2%. Metformin was used in 90.3% of the women while insulin was used in 81.4% of the women [89% in pre-existing DM2 and 70.2% in newly detected DM-2]. The median total daily doses(TDD) of insulin by the end of pregnancy was 0.5 units/kg (IQR 0.3-0.9) [0.6 units/kg(IQR 0.4-1.0) in pre-existing DM-2 and 0.3 units/kg(IQR 0.2-0.6) in newly detected DM-2.] The third-trimester target HBA1c of 6.5% was achieved in 79.7% of the women while 89.4% achieved HBA1c under 7.0%. Univariate regression analysis revealed that for each 1% increase in the first trimester HBA1c, the risk of not achieving glycaemic targets is increased by 1.7 folds.

Discussion and Conclusion:- The proportion of women with DM-2 achieving glycaemic targets (79.7%) is similar to the most recent national audit from the United Kingdom-2016 (74.5%). Pre-conception HBA1c influences the ability of the women to achieve glycaemic targets calling for better pre-pregnancy planning.

Glycaemic Control In Pregnant Women With Type 1 Diabetes Enrolled In The CCPC-Program

Eman Othman , Naglaa Al-Sharkaway, Nahad Al-Alwai, Annama Joseph, Afrah Hussein Ahlam Alsaadi , Lubna Dagash, Aiswarya John, Riza Tupil, Khaled Baagar, Mohammed Bashir

National Diabetes Centre-Women Wellness and Research Centre.

Background:- Achieving target glycaemic control is critical in improving pregnancy outcomes in women with type 1 diabetes (DM-1). Glycaemic control target is accepted as a HBA1c of ≤ 6.5%; however, in women at high risk of hypoglycaemia, the target HBA1c is <7.0%.

Aim:- To measure the impact on glycaemic control in pregnant women with DM-1

Methods:- We included all women with DM-1 who were enrolled in the CCPC program since August 2018. Women are enrolled into the program if they agree to receive all their obstetrics and diabetes care in the NDC-WWRC.

Results:- We are reporting on 33 women with DM-1 ; 60.6% were non-Qatari Arabs, and 30.3% were Qatari. The median age was 29 years (IQR 25-32), the median duration of diabetes was 11.7(6.1-19.1) years, mean pre-conception BMI was 23.6±7.2 kg/m^2. The mean pre-conception HBA1c was 7.8± 1.4% and only 25% of them had a HBA1C of ≤ 7.0%. All women were treated with multi-dose insulin injections. The median total daily dose of insulin was 0.9 units/kg (IQR 0.7-1.1). The mean third trimester HBA1c dropped to 6.9± 0.9%. The proportion of women, at the third trimester, who achieved a HBA1c ≤ 6.5% was 30% while those who achieved a HBA1C < 7.0% was 66.7%. Univariate analysis showed that, for every 1% increase in pre-conception HBA1c, the chances of not achieving glycaemic target is increased by 3 folds.

Discussion and Conclusion:- Managing DM-1 during pregnancy remains a challenge. We have shown previously that, in women with DM-1, pre-conception glycaemic control impacts pregnancy outcomes. While the number of studied women at this occasion is smaller, poor pre-conception glycaemic control seems to impede the ability to achieve glycaemic targets during pregnancy. Hence, pre-pregnancy planning appear to be critical for favourable pregnancy outcomes.

Gestational Weight Gain In Pregnant Women With Type 2 Diabetes Enrolled In The CCPC-Program

Ahlam Alsaadi , Lubna Dagash , Afrah Hussein , Naglaa Al-Sharkaway, Eman Othman, Nahad Al-Alwai, Annama Joseph, Riza Tupil, Aiswarya John , Salma Bashir, Mohammed Bashir

National Diabetes Centre- Women's Wellness and Research Centre.

Background:- Excessive gestational weight gain (GWG) is associated with worse maternal and fetal outcomes. We have previously reported that, in women with type 2 diabetes (DM-2), GWG was associated with a increased risk of poor neonatal outcomes. Hence, we actively target and manage weight gain during pregnancy.

Aim:- To report on the GWG in women with DM-2. Adequate GWG is defined based on the Institute of Medicine guidelines (IOM) and the Qatar national guidelines.

Methods:- We included all women with DM-2 who were enrolled in the CCPC program since August 2018.

Results:- We are reporting on 258 women with DM-2; median age was 34 years (IQR 31-38), the median duration of diabetes was 2 years (IQR 0.8-5), mean pre-conception weight was 80.5±16.4 kg and mean BMI was 31.9±7.4 kg/m^2 . The median GWG was 5.7 kg (IQR 0-9.9). Excessive GWG was seen in 30.9% and 33.6% of the women according to the IOM and the national criteria, respectively. Univariate analysis showed that for each 1 % increase in pre-conception HBA1c the risk of excessive GWG- using both criteria- is increased by 1.2 folds.

Discussion and conclusion:- The rates of excessive GWG is rarely reported in clinical studies. Excessive GWG was reported is 43% and 37% of women with DM-2 from two different cohorts (1,2). Pre-conception HBA1c is the leading risk factor for excessive GWG, likely as a result of intensification of insulin treatment. More stringent dietary approach is needed in women with DM-2 who conceive with poor glycaemic control.

Gestational Weight Gain In Pregnant Women With Type 1 Diabetes Enrolled In The CCPC-Program.

Lubna Dagash , Ahlam Alsaadi , Afrah Hussein,Naglaa Al-Sharkaway, Eman Othman, Nahad Al-Alwai, Annama Joseph, Aiswarya John ,Riza Tupil, Khaled Baagar, Mohammed Bashir

National Diabetes Centre- Women's Wellness and Research Centre.

Background:- Excessive gestational weight gain (GWG) is associate with poor maternal and fetal outcomes. We have previously reported that , in women with type 1 diabetes (DM-1), gestational weight gain is associated with increased risk of large for gestational age. Hence, we actively target and manage weight gain during pregnancy in women with DM-1.

Aim :- To report on the GWG in women with DM-1 enrolled in the CCPC program. Adequate GWG is defined based on the Institute of Medicine guidelines (IOM) and the Qatar national guidelines.

Methods:- We included all women with DM-1 who were enrolled into the CCPC program since August 2018.

Results:- We are reporting on 33 women with DM-1; The median age was 29 years (IQR 25-32) , median duration of diabetes was 11.7(6.1-19.1) years, mean pre-conception BMI was 23.6±7.2 kg/m^2 . The median GWG was 9 kg (IQR 6-15). Excessive GWG gain seen in 36.4% of the women according to both the IOM and the national guidelines criteria. Sensitivity analysis did not identify specific risk factors.

Discussion and conclusion:- The rates of excessive GWG in type 1 diabetes is rarely reported in clinical studies. Excessive GWG was reported in 50% and 51% of women with DM-1 in two different cohorts. Larger number of subjects are needed to explore factors associated with excessive GWG in women with DM-1 in Qatar.

Pregnancy Outcomes In Women With Pre-Existing DM Enrolled In The CCPC Program.

Afrah Hussein , Fatin Taha, Lubna Dagash , Ahlam Alsaadi , Naglaa Al-Sharkaway, Eman Othman, Nahad Al-Alwai, Annama Joseph, Aiswarya John , Riza Tupil, Mohammed Bashir

National Diabetes Centre-Women Wellness and Research Centre.

Background:- Pre-existing diabetes mellitus in pregnancy is associated with poor maternal and fetal outcomes. The main aim is to achieve near normal pregnancy outcomes in women with pre-existing diabetes and for this, multidisciplinary team approach is critical.

Aim:- To report on pregnancy outcomes in women with pre-existing DM who were enrolled in the CCPC program

Methods:- We included all women with DM-1 and DM-2 who were enrolled into the CCPC program since August 2018. We used the latest national audit from the United kingdom-2016-(Murphy et al- Diabetiologia *60:1668–77.)* for comparison due to its comprehensive nature

Results:- We are reporting on 258 women with DM-2 and 33 women with DM-1. We have reported on the base line demographics else-where. Table 1 shows the pregnancy outcomes in women with pre-existing diabetes in pregnancy and the UK results

Table 1:- Pregnancy outcomes				
	DM-1 (33)	UK-DM-1	DM-2 (258)	UK-DM-2
Life birth	33 (100%)	94%	254 (98.4%)	94.7%
IUFD	0	1%	1 (0.4%)	1%
Miscarriage	0	6%	3(1.2%)	5.3%
C-section	20(60.6%)	N/A	150(58.4%)	N/A
GA at delivery (weeks)	36.6 ± 2.2	36.4	37.1 ± 3.0	37.1
Pre-term delivery	11(33.3%)	39.7%	69(26.7%)	21.7%
Macrosomia	3(9.1%)	17.7%	14(5.4%)	10.5%
LGA	9(27.3%)	47.6%	48(18.8%)	22.9%

Discussion and Conclusion:- Pregnancy outcomes are similar to the most recent national audit from the United Kingdom-2016.

Mitigation Of Hypoglycaemia During Ramadan Detected By Flash Glucose Monitoring System Following Dose Adjustment Of Insulin And Sulphonyurea In Patients Taking Multiple Antidiabetic Agents (The PROFAST-IT Study)

Tarik Elhadd, Mohammed Bashir, Khaled Baager, Hamda Ali, Abdul Badie Abou Samra, for the PROFAST Study Group

Qatar Metabolic Institute, Department of Medicine, Hamad Medical Corporation, Doha, Qatar

Background & hypothesis: Patients with type-2 diabetes on multiple drug therapy who fast Ramadan are at increased risk of hypoglycaemia as shown in the PROFAST Study. We aimed to utilize the technology of flash glucose monitoring system to assess whether adjustment of doses of insulin and sulphonyurea agents will mitigate the risk of hypoglycaemia in these patients

Patients & Methods: We studied patients with type-2 DM on either basal insulin or a sulphonylurea agent plus at least 2 other anti-diabetic agents before and during Ramadan using the technology of flash glucose monitoring system (FreeStyle Libre), to assess the glucose variability and hypoglycaemia episodes. Patients received structured education and underwent dose adjustment of either insulin or sulphonyurea according to PROFAST Ramadan protocol.

Results: A total of 85 patients participated in the study. Full data were available only from 29 patients (24 males). There were 17 patients who were on SU+ and 12 patients were on basal insulin+. The average age of patients was 50 years, and diabetes duration of 10 yrs. Average blood glucose in the whole group before Ramadan was 156±34 mg/dl, with 70% of the group had levels within target range, and during Ramadan 160±36 mg/dl with 69.5% of patients were within target range. Total average episodes of hypoglycaemia were 3 before Ramadan and 2.2 during Ramadan. There was differential episodes of hypoglycaemia with those on SU+ having higher average episodes before Ramadan and lesser during Ramadan (3.7 vs 1.9), and the converse is true for those on basal insulin+ (1.8 vs 2.7). The difference was not statistically different either within or between the two groups (SU+ vs. Basal+). Hypos were mostly mild. Patients were of ethnic admixture.

Conclusion: Empowerment of type-2 diabetic patients by education and appropriate dose adjustments of drugs which are notorious in triggering hypoglycaemia will help to mitigate the risk of hypoglycaemia in such vulnerable patients. Our results will have implications for guidelines of management of patients with diabetes who fast the Holy month of Ramadan.

The Smart Utility Of Technology In Diabetes & Ramadan. A Model Using Pedometer And Freestyle Libre In Predicting Glucose Variability & Risk Of Hypoglycaemia In Type-2 Patients On Multiple Drug Regimens.

Raghvendra Mall[1*], Tarik Elhadd[2] , Mohammed Bashir[2], Joao Palotti[1, 3], Luis Fernandez-Luque[1], Faisal Farooq[1], Dahbia Al Mohanadi[2] & Abdul Badie Abu Samra[2]

Qatar Computer Research Institute (QCRI), Doha, Qatar[1], Qatar Metabolic Institute[2], Hamad Medical Corporation & CSAIL, Massachusetts Institute of Technology[3], USA;

Objective: To assess whether pairing the data from Fitbit-2 pedometer and glucose variability obtained from the flash glucose monitoring devices, Free-Style Libre, in diabetic patients fasting during Ramadan may help to predict glycaemic variability and risk of hypoglycaemia

Patients & Methods: We studied 35 patients from the PROFAST cohort for two weeks before and during Ramadan, complete data were available only from 13 patients (10 males and three females). Data were captured during physical activity and sleep. We formulated the data as a regression task and solved the same using *XGBoost*, an interpretable white-box non-linear machine learning technique. The machine learning model was trained with historical activity information (mean ± SD) of physical activity measured by number of steps performed in 1 hour intervals up to last 5 hours to predict the blood glucose level. The model included data of hour of the day, day of the week, part of the day and a binary indicator variable for Ramadan vs non-Ramadan day plus demographic and medication information from the Electronic Health Record (HER).The XGBoost model using just physical activity would achieve an R^2 of 0.548 and a mean absolute error (MAE) of 30.30. The R^2 of a model to be close to 1 for near perfect correlation and MAE to be closer to 0.

Results: There were ten patients on SU and three patients on basal insulin (plus at least two more agents), with age of (median and IQR) of 51 years (49-52); BMI, 33.2 kg/m2 (33.0- 35.9), & HbA1c 7.3% (6.7-7.8). The addition of EHR information helped to increase the R^2 to 0.636 and reduce MAE to 26.89. However, it was the time of the day features that helped to boost the performance of the model (R^2: 0.768, MAE: 20.55). Combining all the features together resulted in the optimal XG Boost model with R^2 of 0.836, MAE of 17.47. The optimal XGBoost model could accurately estimate hyperglycemic events (505 out of 623) and normal glucose levels (1,366 out of 1,450) but requires further improvement in identification of hypoglycemic events (28 out of 93). Since there were very few hypoglycemic events in our dataset, it was difficult for the machine learning model to correctly learn patterns in activity related to it. The optimal XG Boost model prioritizes features such as BMI, HBA1C, Gender, Age obtained from EHR as the most important features, followed by hour of the day, Ramadan day or not, week of the day features. Finally, features related to physical activity captured via Fitbit also gain some importance, albeit their significance is downgraded in the presence of EHR and time related features for CG level prediction. Interestingly, we observe that the blood glucose level prediction by our model is influenced by SGLT2i agents.

Discussion & Conclusion: By applying this novel model we were able to show that XGBoost is a non-linear machine learning model, achieves good performance in predicting the risk of glycemic variability and hypoglycaemia in patients who use multiple therapies while fasting Ramadan, when feeding the various clinical as well as physical activity variables to it. This model will further clinicians' effort to empower these patients to attain the goal of safe fasting.

SGLT2 Inhibitors Reduces Albumin Creatinine Ratio And ALT In Type 2 Diabetes: A Retrospective Descriptive Study

Silas Benjamin[1], Manjunath Ramanjaneya[2], Imran Janjua[1], Firjeeth Paramba[1], Jafer Palaki[1], Nasseer Massodi[1], Aisha Al Kubaisi[1], Prem Chandra[3], Monica Skarulis [2], Abdul-Badi Abou-Samra[2]

1. Department of Internal Medicine, HMC.
2. Qatar Metabolic Institute and Interim Translational Research Institute, HMC
3. Medical Research Center, Academic Health System, and Department of Medicine HMC

Introduction: SGLT 2 inhibitor is an insulin independent, therapeutic agent used in treatment of type 2 diabetes (T2D). It works by increasing renal excretion of glucose and its effects go beyond improvement in HbA1C, weight and blood pressure reduction.

Objectives: Impact of SGLT-2 inhibitor on albumin creatinine ratio and liver enzymes

Methods: Data was obtained from a retrospective cross sectional study on patients with T2D after adding Dapagliflozin (DAPA) to their anti-diabetic regimen between June 2017 – September 2018 in 40 T2D patients because they were not adequately controlled. Paired t-test was performed to assess the mean differences, fold changes following DAPA treatment and to calculate the significance between before and after the treatment.

Results: Whole group analysis showed there was reduction in BMI ($p<0.0001$), ALT ($p<0.0001$), ($p=0.0086$) and albumin to creatinine ratio ($p=0.0090$) following DAPA treatment. These patients were further subdivided into those who were on insulin plus DAPA and sulfonyl urea plus DAPA groups.

Subgroup analysis of patients who received insulin plus DAPA there was reduction in BMI ($p=0.0007$), HbA1c ($p<0.0001$), albumin to creatinine ratio ($p=0.0090$) and ALT ($p=0.0312$).

In patients who were on sulfonyl urea plus DAPA there was significant reduction in sulfonyl urea usage following DAPA therapy ($p=0.0116$), in addition other anthropometric measures including BMI ($p=0.0026$), HbA1c ($p<0.0001$), ALT ($p=0.0122$) and AST ($p=0.0362$). However, there was no significant changes in albumin to creatinine ratio ($p=0.814$).

Conclusion: our study demonstrates addition of DAPA to existing therapy reduces the requirement of sulfonyl urea dosage in these patients. Further lowers BMI, HbA1c, liver enzymes ALT, AST and reduced creatinine to albumin ratio. Our findings suggests addition of DAPA to existing therapy offers beneficial effects in T2D reduces risk for NAFLD and lowers cardiovascular risks in T2D patients.
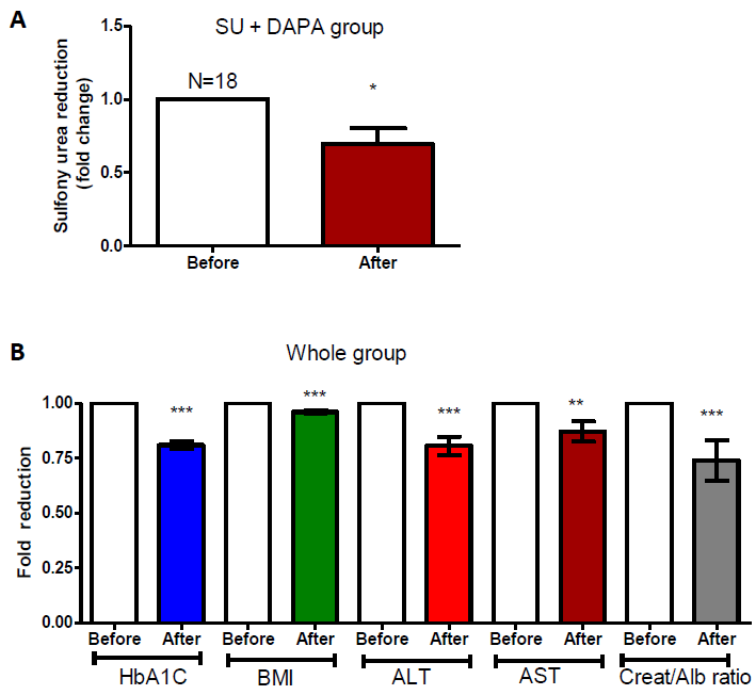
Figure 1: Whole group analysis of anthropometrics and biochemical measurements.

Empagliflozin Use Evaluation In Al Wakra National Diabetes Centre

Abdullah Abdu[1], Mahmoud Shafey [1], Eman Al Hmoud [1], Khaled Dukhan [2], Khaled Ashawesh[2].
1- Department of Pharmacy, 2- National Diabetes Centre (NDC)
Al Wakra Hospital, Hamad Medical Corporation

Background : Empagliflozin is a Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitor that reduces glucose reabsorption in the renal tubules, thereby reducing plasma glucose concentrations. It was recently added to Hamad Medical Corporation (HMC) formulary for the treatment of patients with type 2 diabetes mellitus.

Objectives: This audit evaluates empagliflozin utilization, efficacy, continuation of use and safety among patients following in the National Diabetes Centre (NDC), Al Wakra Hospital (AWH).

Methods: Data extraction from electronic health records for patients who started empagliflozin over 12 months in NDC - AWH (October 2018: September 2019). The first 3 months of that period was analysed – comprising 71 patients- to study glycated haemoglobin (HbA1c) change baseline and 2 follow up values- therapy duration and incidence of urinary tract infections, diabetic ketoacidosis and Fourneir's gangrene.

Results: 83% of the patients continued empagliflozin for more than 6 months, while 10% took it for less than 6 months. Only 7% stopped it in less than 3 months. Mean baseline HbA1c in this cohort was 8.8%, which dropped after an average of 4.3 months of empagliflozin use to become 8.4%. This improvement continued in the same pattern to reach mean HbA1c of 8% after an average of 7.6 months of empagliflozin use. 3% of the patients experienced urinary tract infections which led to discontinuation of empagliflozin. No incidence of diabetic ketoacidosis or Fourneir's gangrene was recorded in this cohort.

Conclusion: Empagliflozin utilization in the National Diabetes Center, Al Wakra Hospital showed good efficacy and continuation rate, with few reported side effects. Given this promising data, we expect increased use of empagliflozin in our center for patients with type 2 diabetes in the future.

Efficacy of Semaglutide by Background Sodium-Glucose Cotransporter 2 Inhibitor: A Post Hoc Analysis of SUSTAIN 9

Rayaz A. Malik[1] *(Presenting On Behalf Of The Authors Group)*, Bernard Zinman[2], Vaishali Bhosekar[3], Robert S. Busch[4], Ingrid Holst[5], Bernhard Ludvik[6], James Thrasher[7], Vincent C. Woo[8], Athena Philis-Tsimikas[9]

[1]*Weill Cornell Medical College, Al-Rayyan, Qatar;* [2]*Toronto, ON, Canada;* [3]*Bengaluru, India;* [4]*Albany, NY;* [5]*Søborg, Denmark;* [6]*Vienna, Austria;* [7]*Little Rock, AR;* [8]*Winnipeg, MB, Canada;* [9]*San Diego, CA.*

Background: The SUSTAIN clinical trials demonstrated the efficacy and safety of once-weekly subcutaneous semaglutide, a glucagon-like peptide 1 analog for the treatment of type 2 diabetes (T2D). SUSTAIN 9 investigated semaglutid 1.0 mg vs. placebo as add-on to a stable dose of sodium-glucose co transporter-2 inhibitor (SGLT2i) therapy, with or without metformin or a sulfonylurea. The primary and secondary endpoints were, respectively, change from baseline in HbA1c and body weight at week 30.

Methods: In this post hoc analysis, SUSTAIN 9 data were analysed by background SGLT2is (empagliflozin, canagliflozin, dapagliflozin or other [ipragliflozin, luseogliflozin and tofogliflozin; drugs available only in Japan]).

Results: In total, 302 subjects were randomized to semaglutide or placebo. Reductions in HbA1c and body weight were greater with semaglutide vs. placebo. There was no significant interaction between background SGLT2i and treatment effect (interaction p-value >0.05 for both endpoints), with a smaller observed weight reduction in the 'Other' group (Table). No safety concerns were identified when adding semaglutide to SGLT2i therapy. No diabetic ketoacidosis or lower limb amputation events occurred.

Conclusion: In subjects with T2D already receiving an SGLT2i, semaglutide generally resulted in superior HbA_{1c} and body weight reductions vs. placebo, regardless of background SGLT2i therapy.

Table. Efficacy endpoints in SUSTAIN 9 by background SGLT-2i therapy[‡]

Background SGLT-2i	Empagliflozin (N=102)		Canagliflozin (N=68)		Dapagliflozin[§] (N=106)		Other[¶] (N=25)	
	Semaglutide 1.0 mg (n=52)	Placebo (n=50)	Semaglutide 1.0 mg (n=39)	Placebo (n=29)	Semaglutide 1.0 mg (n=44)	Placebo (n=62)	Semaglutide 1.0 mg (n=15)	Placebo (n=10)
HbA$_{1c}$, %								
Baseline	8.0 (0.7)	7.9 (0.8)	7.8 (0.8)	7.8 (0.8)	8.1 (0.9)	8.2 (0.9)	8.5 (0.6)	8.3 (0.5)
Change from baseline at week 30	−1.4 (0.1)	−0.2 (0.1)	−1.4 (0.1)	+0.1 (0.2)	−1.5 (0.1)	−0.2 (0.1)	−2.2 (0.2)	−0.2 (0.2)
ETD [95% CI]	−1.3 [−1.58;−0.97]*		−1.5 [−1.89;−1.13]*		−1.3 [−1.65;−1.03]*		−2.0 [−2.62;−1.43]*	
p-value for interaction[†]	0.1687							
Body weight, kg								
Baseline	90.6 (17.2)	95.8 (23.4)	96.4 (20.9)	98.1 (20.0)	90.7 (16.9)	93.7 (21.9)	65.3 (13.2)	72.5 (12.9)
Change from baseline at week 30	−5.2 (0.5)	−1.3 (0.5)	−5.5 (0.6)	−0.2 (0.7)	−4.6 (0.6)	−1.1 (0.5)	−1.2 (0.9)	−0.2 (1.1)
ETD [95% CI]	−3.9 [−5.37;−2.40]*		−5.3 [−7.10;−3.47]*		−3.4 [−4.91;−1.97]*		−1.0 [−3.90;1.85]	
p-value for interaction[†]	0.0980							

*p<0.0001 vs placebo. [†]p-value for interaction of background SGLT-2i on treatment effect. [‡]302 subjects were randomized and 301 received trial medication; one subject was randomized but not included in this analysis due to not receiving SGLT-2i at screening. [§]Includes subjects receiving dapagliflozin or dapagliflozin propanediol monohydrate. [¶]Includes subjects receiving ipragliflozin L-proline, luseogliflozin or tofogliflozin. 'On-treatment without rescue medication' data analyzed using an analysis of covariance with treatment, subgroup and treatment by subgroup interaction, stratification factor and region as fixed factors, and baseline value as covariate. Baseline data are mean (SD); changes from baseline are mean (SE). CI, confidence interval; ETD, estimated treatment difference; SD, standard deviation; SE, standard error; SGLT-2i, sodium–glucose co-transporter-2 inhibitor.

Efficacy And Safety Of Semaglutide By Baseline BMI In SUSTAIN 1–5 And 7

Amin Jayyousi[1] *(presenting on behalf of the authors group)*, Adie Viljoen[2], Juan P Frias[3], Theis Gondolf[4], Jeff Unger[5].

[1]*Hamad Medical Corporation, Doha, Qatar;* [2]*Borthwick Diabetes Research Centre, Lister Hospital, Stevenage, UK;* [3]*National Research Institute, Los Angeles, CA, USA;* [4]*Novo Nordisk A/S, Søborg, Denmark;* [5]*Catalina Research Institute, LLC. Monclair, CA, USA.*

Background: SUSTAIN trials evaluated the efficacy and safety of semaglutide in subjects with type 2 diabetes and showed superior reductions in HbA1c and body weight vs placebo and all active comparators (sitagliptin, exenatide extended release, insulin glargine, dulaglutide), this *post hoc* analysis was conducted to evaluate if reductions in HbA1c were affected by baseline BMI in SUSTAIN trials.

Methods: Change in HbA1c was evaluated by baseline BMI (<25, 25–<30, 30–<35 and ≥35 kg/m2) for semaglutide vs comparators by trial for SUSTAIN 1–5 and 7 in a mixed model for repeated measurement, with treatment, BMI subgroup and baseline HbA1c as covariates, and interaction between treatment and BMI subgroups at baseline. Safety data were pooled and analysed by a Cochran-Mantel-Haenszel analysis stratified by trial.

Results: There were no significant interactions between treatment and BMI, except for semaglutide 0.5 mg in SUSTAIN 7, indicating a consistent effect of semaglutide vs comparator on change in HbA1c across BMI subgroups. Reductions in mean HbA1c (%) from baseline were greater in all BMI subgroups with semaglutide vs all comparators except for the <25 kg/m2 BMI subgroup for semaglutide 0.5 mg vs insulin glargine and semaglutide 0.5 mg vs dulaglutide 0.75 mg (Figure).

Adverse events (AEs) were similar in all treatment arms across BMI subgroups. Gastrointestinal AEs were higher with semaglutide, but decreased with increasing baseline BMI, vs comparators (semaglutide: <25 kg/m2=48.8%, 25–<30 kg/m2=43.0%, 30–<35 kg/m2=39.4% and ≥35 kg/m2=39.3% vs comparators range: 21.2–28.9%).

Conclusion: The estimated treatment differences in mean HbA1c (%) for semaglutide vs placebo or active comparators do not appear to be influenced by baseline BMI. Semaglutide had an acceptable safety profile in all BMI subgroups.

Figure: Change in HbA1c (%) by baseline BMI (kg/m^2) in SUSTAIN 1–5 and 7
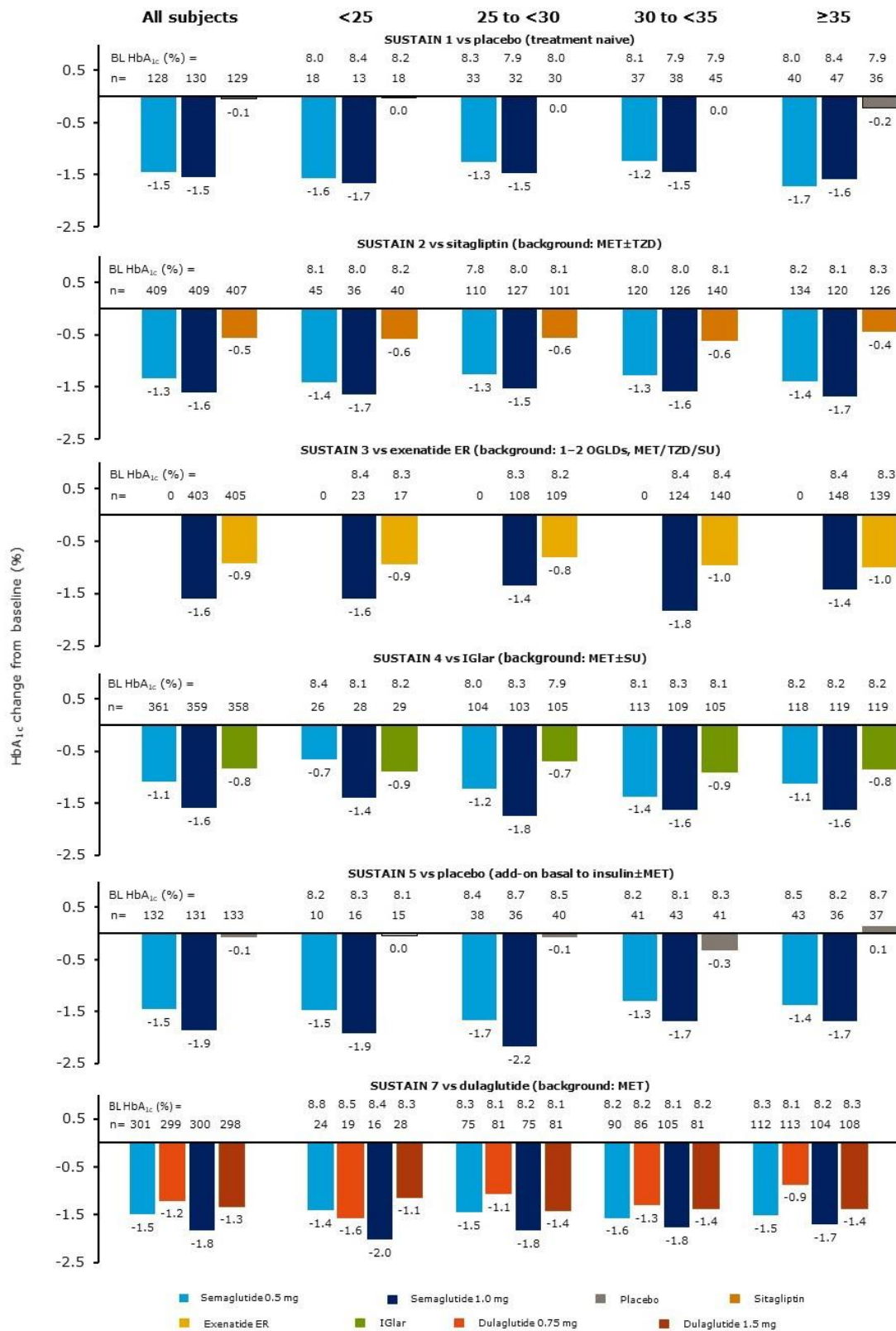
Values shown are estimated mean changes from baseline for subjects on treatment without rescue medication. BL, baseline; BMI, body mass index; exenatide ER, exenatide extended release; IGlar, insulin glargine; MET, metformin; OGLD, oral glucose-lowering drug; SU, sulphonylurea; TZD, thiazolidinedione.

The Effect Of Semaglutide Once Weekly On MACE and Blood Pressure By Race And   Ethnicity: SUSTAIN 6 Post Hoc Analysis

Malek Arjoub[1] *(Presenting on behalf of the authors group)*, C Desouza[2], SC Bain[3], T Gondolf[4], T Hansen[4], I Holst[4], RR Rea[5], J Seufert[6].

[1]*Novo Nordisk A/S – Doha – Qatar,* [2]*University of Nebraska Medical Center - Omaha - United States of America,* [3]*Swansea University, School of Medicine - Swansea - United Kingdom of Great Britain & Northern Ireland,* [4]*Novo Nordisk A/S - Søborg - Denmark,* [5]*Hospital de Clínicas da Universidade Federal do Paraná - Curitiba - Brazil,* [6]*University of Freiburg Medical Center, Faculty of Medicine - Freiburg - Germany.*

Background: In SUSTAIN 6, subcutaneous semaglutide once weekly added to standard of care significantly reduced major adverse cardiovascular events (MACE: non-fatal myocardial infarction, non-fatal stroke or death) vs placebo over 2 years in T2Dsubjects.

Purpose: Assess the effect of semaglutide vs placebo on MACE and blood pressure (BP) by race and ethnicity in a post hoc analysis of SUSTAIN6.

Methods: Subjects were randomised to semaglutide 0.5 mg, 1.0 mg or volume-matched placebo. Data for the two semaglutide-dose groups were pooled and compared to the pooled placebo groups. Time-to-event data were analysed with a Cox proportional hazards model. Changes from baseline to week 104 were analysed using analysis of covariance. The interaction between treatment and subgroup was added to the models.

Results: Overall, 3,297 patients received treatment. Subgroups included Caucasian, Asian, Black/African American, Other (race), and Hispanic, non-Hispanic (ethnicity). Mean baseline characteristics were similar across subgroups (age 64.7 years, HbA1c 8.7%, diabetes duration 14.2 years). Time to composite MACE and individual components were improved with semaglutide across all subgroups. Semaglutide affected BP similarly across race and ethnicity, except for systolic BP in Black/African American subjects (Table).

Conclusion: Overall there was no evidence of a differential effect of semaglutide on risk reduction in MACE and its components and on BP across race and ethnicity subgroups in this post hoc analysis.

	Race					Ethnicity		
Semaglutide (n) Placebo (n)	Caucasian 1,384 1,352	Asian 121 152	Black/African American 108 113	Other 35 32	Interaction p-value	Hispanic 256 254	Non-Hispanic 1,392 1,395	Interaction p-value
MACE and individual outcomes								
MACE HR [95% CI]	0.76 [0.58; 1.00]	0.58 [0.25; 1.34]	0.72 [0.23; 2.28]	0.46 [0.08; 2.50]	0.8793	0.67 [0.33; 1.36]	0.74 [0.57; 0.96]	0.7978
CV death HR [95% CI]	0.98 [0.63; 1.50]	0.32 [0.04; 2.85]	1.01 [0.06; 16.20]	n/a[†]	0.8089	0.79 [0.31; 2.00]	1.00 [0.63; 1.59]	0.6521
Non-fatal MI HR [95% CI]	0.69 [0.45; 1.07]	0.97 [0.36; 2.60]	1.37 [0.31; 6.12]	0.31 [0.03; 3.00]	0.6637	0.65 [0.18; 2.31]	0.74 [0.50; 1.10]	0.8562
Non-fatal stroke HR [95% CI]	0.70 [0.42; 1.16]	0.31 [0.04; 2.77]	n/a[‡]	n/a[‡]	0.9176	0.73 [0.16; 3.27]	0.60 [0.36; 0.99]	0.7995
Blood pressure at week 104								
Systolic BP* ETD (mmHg) [95% CI]	-1.92 [-3.09; -0.74]	-4.98 [-8.61; 1.35]	4.47 [0.15; 8.79]	-11.02 [-18.45; -3.60]	0.0008	-3.22 [-5.93; -0.51]	-1.81 [-2.98; -0.64]	0.3489
Diastolic BP* ETD (mmHg) [95% CI]	0.36 [-0.32; 1.04]	-1.31 [-3.43; 0.80]	-0.07 [-2.56; 2.43]	-3.41 [-7.73; 0.92]	0.1871	-0.18 [-1.75; 1.39]	0.16 [-0.52; 0.83]	0.6981

*Treatment difference between semaglutide and placebo (pooled 0.5 and 1.0 mg values for each treatment group) at week 104.

†No events in the placebo group; ‡No events in the semaglutide group. BP, blood pressure; CI, confidence interval; ETD, estimated treatment difference; HR, hazard ratio; MACE, major adverse cardiovascular event; MI, myocardial infarction.

Quality Of Life In Hemodialysis Diabetic Patients: A Multicenter Cross-Sectional Study From Palestine

Sohaib T. Khatib,[1] Mohammad K. Hemadneh,[1] Samer A. Hasan,[1] Emad Khazneh,[2] and Sa'ed H. Zyoud[3,4]

[1]Department of Medicine, College of Medicine and Health Sciences, An-Najah National University, Nablus, 44839 Palestine

[2]Nephrology Unit, Internal Medicine Department, An-Najah National University Hospital, An-Najah National University, Nablus, 44839 Palestine

[3]Poison Control and Drug Information Center (PCDIC), College of Medicine and Health Sciences, An-Najah National University, Nablus, 44839 Palestine

[4]Department of Clinical and Community Pharmacy, College of Medicine and Health Sciences, An-Najah National University, Nablus, 44839 Palestine

Background: Both diabetes and hemodialysis can seriously impair patients' health related quality of life (HRQOL). This study seeks to obtain data which will help to address the factors associated with impaired HRQOL in hemodialysis patients with diabetes in Palestine.

Methods: A cross-sectional study was performed in multiple centers in the period from November 2016 to June 2017. We utilized the Arabic version of EuroQoL 5 Dimensions 5 Levels (EQ-5D-5L) scale and EuroQol-visual analogue scale (EQ-VAS) to measure patients' HRQOL. The study was conducted in six dialysis centers in the North of West Bank, Palestine. Descriptive and comparative statistics were used to describe clinical and socio-demographic features of patients. Multiple linear regression analysis was used to determine the association between clinical and socio-demographic factors and HRQOL score.

Results: One hundred and forty-one diabetic patients undergoing hemodialysis were enrolled in our study. Overall, 52.5% of them (74 patients) were males; the patients had a mean age of 60.32 with 52.5% of them aged below 60. The mean ± standard deviation of EQ-5D-5L index and EQ-VAS score was 0.314 ± 0.4 and 50.85±22.43, respectively. The findings of this study suggest that female patients, uneducated patients, unemployed patients, unmarried patients, and patients with more chronic diseases and comorbidities had a significant poor HRQOL scores (p values <0.05). Variables such as marital status and occupational status were significantly ($p < 0.05$) associated with the QOL score. More specifically, married status and employed patients positively associated with QOL score ($\beta = 0.22$; $p = 0.016$ and $\beta = 0.27$; $p = 0.013$, respectively).

Conclusions: Among diabetic patients undergoing hemodialysis, married status and being employed were associated with modestly higher scores of QOL. We recommend that healthcare providers give more attention to diabetic dialysis patients who are unemployed and unmarried, as they are at a higher risk of having impaired HRQOL.

Effect Of Innovative Non-Weight Bearing Exercise During Hemodialysis On Diabetic Patients With Depression: A Randomized Controlled Trial

Fadwa Al‑Ali[1] Abdullah Hamad[1], He Zhou[2], Bahaa[1] ,Mincy Mathew[1] , Rania Ibrahim[1], Talal Talal[3], Bijan Najafi[2]

[1] *Department of Nephrology, Hamad General Hospital, Doha, Qatar*

[2] *Interdisciplinary Consortium on Advanced Motion Performance (iCAMP), Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Texas, USA*

[3] *Diabetic Foot and Wound Clinic, Hamad General Hospital, Doha, Qatar*

Background: Depression affects one third of hemodialysis (HD) patients. Untreated depression could negatively impact physical health, quality of life and outcomes. Face to face supervised exercise can reduce depression but are hard to achieve in HD patients because of dialysis schedule, post HD fatigue and transportation. In this study, we examined whether a non-weight bearing (NWB) foot and ankle supervised exercise program during hemodialysis session is effective to reduce depression. In addition, we compared supervised exercise with an innovative gamification of the exercise (Exergame) on reducing depression.

Methods: Eighty-one HD adults (age=64.2± 8.6 years, BMI=31.4± 7.5, female=55.6%) were recruited and randomized (ratio=1:1) into a virtually supervised exercise group (VSEG: n = 44) or a supervised exercise program (SEG: n = 37). Both groups underwent a 4-week NWB ankle and foot exercise program (30-min per session, 2 sessions per week) during HD process. The VSEG received exercise via an innovative Exergame program, which uses foot-worn sensors enabling them to play game-like exercise tasks by rotating their feet in dorsiflexion, plantarflexion, or internal-external rotations. The Exergame platform enables computerized coaching exercise (virtual supervision) and gamification features such as rewarding (audio and visual) when each exercise task is successfully completed. The SEG received similar NBW foot and ankle exercise. However instead of virtual supervision, the exercise tasks were coached by a nurse and no gamification feature was used except verbal encouragement by the nurse. The effect of exercise on depression was quantified by Center for Epidemiologic Studies Depression (CES-D) scale.

Results: Five subjects in the VSEG and 1 subject in SEG dropped from the study either because of health complication, travelling, or lack of interest. According to the CES-D score, 36% of subjects were depressed before the exercise program. Results suggest that both groups had significant reduction in the CED-D score (39% in the VSEG and 43% in the SEG, $p<0.001$) after 4-week exercise program. Similarly, percentage of depressed patients dropped by approximately 40% irrespective of group assignment. The effect size of change in depression scale in response to exercise was slightly larger in the VSEG (Cohen effect size d=0.68 in the VSEG vs. 0.66 in the VSEG), however no significant difference was observed between groups (p=0.165).

Conclusions: Our innovative trial suggests that NWB foot and ankle exercise is practical during HD process and is effective to reduce depression. Results demonstrated that virtually supervised exercise could be as effective as supervised exercise to reduce depression. Using virtually supervised exercise improve adherence and reduce burden of administrating exercise during HD therapy. Results showed slight benefit of gamification provided by computerized exercise, but the benefit was not significant in our sample.

Treatment Burden And Its Impact On Quality Of Life Among Chronic Kidney Disease Patients In Qatar

Asmaa Al-mansouri[1], Abdullah Ibrahim Hamad[2], Fadwa Saqr Al-Ali[2], Rania Abdelaziz Ibrahim[2], Mohamed Izham Mohamed Ibrahim[1], Nadir Kheir[3], Muna AlBakri[4], Ahmed Awaisu*[1]

[1]*College of Pharmacy, Qatar University;* [2]*Fahad Bin Jassim kidney Centre, Hamad Medical Corporation;* [3]*School of Pharmacy, University of Auckland;* [4]*Hamad General Hospital, Hamad Medical Corporation;*

Introduction: Diabetes mellitus (DM) is the leading cause of chronic kidney disease (CKD) and on of its top comorbidities. Its management places significant burden on patients and results in

impairment of their health-related quality of life (HR-QOL). Little is known about diabetes mellitus treatment-related burden in patients with CKD. This study aimed to investigate the impact of diabetes mellitus on treatment-related burden and HR-QOL among CKD patients in Qatar.

Methods: This was a mixed-method, sequential explanatory study conducted at Fahad Bin Jassim Kidney Centre in Qatar on haemodialysis and pre-dialysis (GFR<20 but not on dialysis yet) patients. Treatment-related burden and HR-QOL were assessed quantitatively using the Treatment Burden Questionnaire (TBQ) and the Kidney Disease Quality of Life (KDQOL™) questionnaire, respectively. To gain a deeper insight, qualitative one-to-one semi-structured interviews were conducted among the CKD patients. Quantitative data were analysed descriptively and inferentially using SPSS version 24. Thematic content analysis was performed for the qualitative data.

Results: Two hundred-eighty CKD patients (haemodialysis = 223 and pre-dialysis (GFR <20) = 57) were included. 157 has DM and 66 were non-DM (in haemodialysis) while 32 with DM vs 25 non-DM (in pre-dialysis). In general, 35% of patients reported moderate to high burden with haemodialysis patients experienced significantly higher treatment burden compared to pre-dialysis patients with median (IQR) of 45 (36) versus 25 (33), respectively (p<0.001). DM patients expressed significantly higher TBQ score compared to non-DM (47(40) vs. 36(27) p<0.001). Retinopathy was associated with worsened treatment burden (TBQ 46.5(29) vs. 40(38) p=0.019). Medication burden and lifestyle change burden were the highest perceived treatment-related burden, followed by administrative, social, and financial burden. The presence of antidiabetic medications correlated with worse TBQ score (0.207 p<0.001). There was a strong, negative correlation between TBQ score and KDQOL-36™ score [rs (251) = -0.616, p <0.001]. Presence of DM was associated with worse KDQOL (2110(1055) vs. 2685(1170) p<0.001). Thematic content analysis identified religion and faith in God as well as quality of the care provided as factors that reduce perceived treatment burden and improve patients' HR-QOL. Conversely, medication burden, lifestyle changes, challenges with international travelling, financial burden, and empathy were factors that worsen perceived treatment-related burden and HR-RQOL.

Conclusion: This study suggests that diabetes mellitus negatively impacts treatment-related burden and quality of life in CKD patients. This result should be considered in management strategies when designing healthcare interventions directed to CKD patients.

Corneal Confocal Microscopy Detects Corneal Nerve Loss In Children With Type 1 Diabetes Mellitus (T1DM) in Qatar

Hoda Gad[1], Bara Al-Jarrah[2], Saras Saraswathi[2], Ioannis Petropoulos[1], Georgios Ponirakis[1], Adnan Khan[1], Parul Singh[3], Souhaila Al Khodor[3], Khalid Hussain[4], Mamoun Elawad[2], Wesam Almasri[2], Hatim Abdelrahman[2], Ahmed Elawwa[4], Amel Khalifa[4], Fawziya Al-Khalaf[4], Goran Petrovski[4], Mahmoud Al Zyoud[4], Maryam Al Maadheed[4], Mohamed Hendaus-Rahal[5], *Rayaz A Malik[1, 6], *Anthony Akobeng[2]
*Joint senior authors and PI's

[1] Department Medicine, Weill Cornell Medicine-Qatar, Doha, Qatar

[2] Gastroenterology Department, Sidra Medicine, Doha, Qatar

[3] Research Department, Sidra Medicine, Doha, Qatar

[4] Endocrinology Department, Sidra Medicine, Doha, Qatar

[5] General Pediatrics Department, Sidra Medicine, Doha, Qatar

[6] University of Manchester, Institute of Cardiovascular Medicine, Manchester, United Kingdom

Introduction: Children with type 1 diabetes (T1DM) may rarely develop overt clinical neuropathy. Corneal Confocal Microscopy (CCM) is a simple, rapid, non-invasive ophthalmic technique to identify sub-clinical nerve fibre loss. The main aim of this study was to identify corneal nerve alterations in children with T1DM.

Method: Twenty participants with T1DM and 20 healthy controls were recruited from Sidra Medicine outpatient clinics. CCM was undertaken in all participants. Six images per participant were selected and corneal nerve fibre density (no.mm^2) (CNFD), nerve branch density (no.mm^2) (CNBD) and nerve fibre length (mm.mm^2) (CNFL) were quantified manually (CCMetrics) and automatically (ACCMetrics).

Results: Automated CNFD (18.2 ± 8.5 vs. 28.7 ± 7.3, P=0.008), CNBD (19.2 ± 12.1 vs. 39.1 ± 12.3, P=0.001) and CNFL (11.3 ± 3.8 vs. 16.2 ± 3.3, P=0.001) were significantly lower in children with T1DM compared to healthy controls. Manual CNFD (23.0 ± 9.0 vs. 32.9 ± 8.6, P=0.001), CNBD (26.2 ± 14.7 vs. 47.3 ± 20.0, P=0.001) and CNFL (13.3 ± 4.1 vs. 19.5 ± 4.5, P=0.001) were significantly lower. There was good reliability between ACCMetrics and CCMetrics with the average measure ICC for CNFD of 0.858, 95% CI (0.490-0.944) P<0.001; CNBD of 0.772, 95% CI (0.469-0.892) P<0.001; and CNFL of 0.899, 95% CI (-0.027-0.973), P<0.001.

Conclusion: Corneal confocal microscopy identifies significant sub-clinical corneal nerve loss in children with T1DM.

Managing Chronic Diabetic Foot Ulcers At Primary Care Level : A Paradigm Shift

Hashim Mohamed

Background: Traditionally diabetic foot ulcers are managed at secondary level resulting in delayed referral, increased cost, escalating below jnee amputation and reduced quality of life. According to our knowledge no previous data has assessed management of chronic diabetic foot ulcers at primary care level .

 Aims: This current study assess the efficacy of chronic foot diabetic ulcer   (CDFU) management at primary care level in the state of Qatar .

Methods:: A long-term 5-year retrospective cohort study was conducted subjects with (CDFU) who attended Umgwalinah Health Centre, Doha, Qatar. Average clinic follow-up was 1 year. Ulcers failure to heal was the main outcome measure .Independent predictor variables were selected by logistic regression analysis.

Results: A total of 126 subjects with type II diabetes with chronic diabetic foot ulcers were included in the assessment and managed as follows. Five patients(4%) of 126 underwent immediate amputation. Family physician led management of chronic diabetic foot ulcers was successful for 91(92.86%) of 98 neuropathic ulcers, 3(30%) of 10 neuro-ischemic ulcer, 2(66%) of 3 Charcot foot ulceration ,4(100%) of 4 patients with second degree burns & 6(100%) of 6 traumatic foot ulceration or ($P<.001$,chi2 for trend).Independent factors predictive of failure to heal were presence of osteomyelitis(odds ratio [OR]=1.6, 95% confidence interval [CI], 1.0-1.3),increased Haemoglobin A1C level(OR=1.002; 95% CI, 1.2-1.3),severe peripheral vascular disease(OR=1.0,95% CI,1.0-1.03),prior hospitalization for(CDFU) (OR=1.4; 95%CI, 1.2-1.6)& gangrenous lesion(OR=1.7; 95% CI, 1.3-2.1).No side effects were reported and there was a high level of satisfaction (patients and staff).

 Conclusions: Primary care based management of (CDFU) is efficacious, safe and acceptable. These encouraging preliminary findings may lead to a paradigm shift in the management of (CDFU) away from secondary care thereby empowering primary care physicians , reducing cost, and un necessary amputation.

Prevalence and Predictors of Diabetic Complications among Patients with Type 2 Diabetes: A Cross-Sectional Study

Khaled Baagar, Fahmi Khan, Wajiha Gul, Sara Darwish, Hussein Adly, Ahmed Mohammed, Aaiza Aamer, Ahmed Shady, Amr Salama, Ahmed Hussein, Mahmoud Zirie

Internal Medicine Department - Endocrine division, Hamad Medical Corporation, Doha, Qatar

Objective: Type 2 diabetes (T2D) load and cost are mostly related to its complications. We aimed to assess the prevalence and predictors of diabetes complications among T2D patients.

Methods: We conducted a cross-sectional study involving 638 patients with T2D attending out-patient department at a tertiary centre. We recorded patients' characteristics, and diabetes complications and comorbidities. A statistical analysis was performed using the software SPSS 23.0. A multivariate logistic regression analysis assessed the independent predictors of complications.

Results: The patients' mean age was 55.8±10.3 years, and 42.8% were males. The mean BMI was 32.4±12.4 kg/m^2. The mean duration of T2D was 11.5±7.7 years, and the mean age at diagnosis was 44.0±9.98 years. The mean HbA1C was 8.3±1.6%. Table 1 shows the prevalence of diabetes complications and comorbidities. Retinopathy predictors were age above 40 years , T2D duration > 10 years, HbA1C > 8%, and hypertension. Nephropathy predictors were HbA1C above 10%, and hypertension. Age 61-70 years, T2D duration > 5 years, and obesity predicted neuropathy. Foot infection/ulcer predictors were age > 40, T2D diagnosis at age 41-50, and female gender. Age 31-50, hypertension and female gender predicted CAD.

Conclusion: T2D prevalence in our community is 16.7% with high prevalence of complications. However, it is improving when compared to a previous report from our institution e.g. nephropathy improved from 40.9% to 35.6%. Physicians should control modifiable predictors of T2D complications and ensure regular screening especially for those at risk.

Complications and comorbidities	Prevalence: number of cases (%)
Retinopathy (DR)	223 (35)
Neuropathy	173 (27.1)
Nephropathy (excluding ESRD)	227 (35.6)
Albuminuria	205 (32.2)
Glomerular filtration rate (GFR) < 60	41 (6.4)
End stage renal disease (ESRD)	11 (1.7)
Coronary artery disease (CAD)	117 (18.3)
Stroke	14 (2.2)
Peripheral arterial disease (PAD)	15 (2.4)
Foot infection/ulcer	87 (13.6)
Amputation	5 (0.8)
Hypertension	462 (72.4)
Kidney transplant	4 (0.6)
Malignancy	24 (3.8)
Hyperthyroidism	17 (2.7)
Hypothyroidism	102 (16)
Hyperlipidemia	490 (76.8)

Comparison between hybrid diabetes and type 2 diabetes in children in patient`s characteristics at diagnosis: retrospective observational study.

Noor Hamed; Fawziya Alyafei; Ashraf Soliman

Introduction: The "Hybrid Diabetes (HD)" is a new term that emerged in the last few years to describe diabetes with combined features of type 1 and type 2 diabetes. The aetiology behind hybrid diabetes is not well understood, and clinical characteristics for these unique patients were not described before. Differentiating HD from other forms of diabetes will lead to better understanding of the disease process and course, as well as knowing the most appropriate management plan to prevent the future complications.

Methods: Seven children who were identified as HD were compared to 59 children who were diagnosed as type 2 diabetes (age 7 to 18 years) .Their clinical and biochemical data at presentation were collected and analysed to delineate the difference between the 2 groups.

Results: The age at presentation did not differ between the 2 groups. The mean BMI SD of T2DM was significantly higher than the DD group (p< 0.04). None of T2DM patients presented with DKA, while 28% of children with HD presented with DKA. No significant difference among the two groups was found regarding, family history of DM, presence of AN, presence of polyuria and polydipsia or HbA1C concentration. The mean C peptide level at presentation was significantly higher in T2DM versus HD group. (p 0.01)

	HD	T2DM	p value
	7	59	--
Age (yr)	10.8	11.28	0.50
BMI SD	2.73	4.5	0.04
acanthosis	71%	90%	0.16
+ family history	85.70%	87%	0.29
Polyuria/polydipsia	57.10%	78%	0.22
ketosis no acidosis	14.20%	22%	0.64
DKA	28.60%	0%	< .00001
C-peptide	1.42	3.88	0.01
HbA1c at diagnosis	10.63%	10.05%	0.61

Discussion: Our study showed that children with HD were less obese and has lower C peptide levels and higher risk to present with DKA compared to T2DM.

Conclusion: HD is a newly recognized subtype of diabetes and has special characteristics that differentiate from other types of diabetes. Further studies need to be done for long term course and management plan for this group.

The clinical characteristics of hybrid diabetes in children and their response to treatment.

Noor Hamed, Ashraf Soliman, Amel Sabt , Ahmed ElAwwa, Fawzyeh AlKhalaf.

Division of Pediatric Endocrinology, Hamad General Hospital, Doha, Qatar

Introduction: The term hybrid diabetes (HD) describes a form of diabetes in which hyperglycemia occurs in obese children in the presence of positive autoimmunity against the beta cells. Few data are available about the clinical presentation and the course of disease in children with this form of diabetes.

Aim: We describe the clinical characteristics and response to treatment in 7 children with hybrid diabetes.

Results: Seven children with HD diabetic patients whose mean age 10.8+/-0.98 years) were diagnosed and followed in our institution. At presentation, all patients were obese, with mean BMI SD was =2.73 +/-0.58, and 71 percent had acanthosis nigricans. Six out of seven patients had a family history of at least one type of diabetes (type 1, type 2 or gestational diabetes). The was checked and it was found that 2 patients had 2 autoantibodies against beta cells, 4 patients had 3 positive autoantibodies, and one patient had all the 4 autoantibodies positive. The mean HbA1c at diagnosis was 10.6 % +/-2.1%. Four patients presented with the classical symptoms of polyuria, polydipsia and recent weight loss along with hyperglycemia. Three patients presented with moderate to severe DKA. All patients were started on insulin at diagnosis, and 5 patients received metformin in the first week after diagnosis. During their follow up, 4 patients did not require any insulin therapy and the other 3 patients had marked reduction in the insulin requirement up to less than 0.2 unit/kg/day (2. 36 +/-2.79 months) after diagnosis. This was associated with marked reduction of their HbA1c to 6.3%+/-0.7%. In addition, the mean BMI SD has dropped to 2.39 +/- 0.5 in the first 2 months after diagnosis, with a delta change = -0.34.

The duration of either no insulin requirement or marked reduction in the total daily dose to less than 0.2 unit/kg/day continued for an average of 15 months. After this period 5 patients required initiating insulin or increase in the insulin dose/kg. One child remained insulin independent and one required markedly low dose of 0.06 unit/kg/day to control glycemia.

Discussion: The diagnosis of "Hybrid Diabetes" describes a diabetes state with combined features of type 1 and type 2 diabetes. The etiology behind hybrid diabetes is not well understood. In this study we described the clinical characteristics of hybrid diabetes in 7 children and their response to treatment. All children with HD were obese at presentation and had easier control of their glycemia (long honeymoon period) and many did not require insulin during this period.

Evaluation the predictors for fatty liver disease in Type 2 Diabetes Mellitus (T2DM)

*Amer Alasadi, Rufaidah Abd Atheem, Assraa Hmood, Zomoreed Jasiem, Hawraa Tariq, Zaman Waeel, and Mona-Allah Hassan.
*Department of Medical Basic Science, College of Nursing, University of Thi-Qar, Iraq

Type2 Diabetes Mellitus (T2DM) is a metabolic disorder characterized by hyperglycaemia , insulin resistance (IR), insufficient of insulin secretion and disturbance of liver functions. Recent studies have revealed that liver diseases are main cause for mortality in patients with T2DM. Indeed, liver function tests consider as non-invasive biomarker for Non-Alcoholic Fatty Liver Disease (NAFLD). Few studies showed the correlation between hyperlipaemia and IR and with fatty liver diseases. Thus, our study claims that the hyperlipaemia in diabetic patients is predisposing factor for IR and fatty liver diseases in our population. In this study, a total of 289 subjects were studied and divided into two groups (145) Non-Diabetic subjects and (135) T2DM patients. We measured biochemical and non-biochemical parameters like fasting blood glucose level, HbA1c, Total Cholesterol (TC), Triglycerides (Tg), Low-density lipoprotein cholesterol (LDL-C) High density lipoprotein cholesterol (HDL-C), Alanine Amino Transferase (ALT), Aspartate, Amino Transferase (AST), ALT/AST ratio for all our subjects. In addition, we determined the Triglyceride Glucose index (TyG index) as a biomarker for insulin resistance, and C reactive protein (CRP) and Alkaline Phosphate (ALKP) as risk factors for fatty liver diseases for all our subjects. What's more, Age and body weight were evaluated in both groups. Our data showed that all patients with T2DM were characterized by hyperglycaemia and about (75) patients have a significant increase ($p<0.0001$) in TC, TG, and LDL-C and significant decrease in HDL-C compared to second half of diabetic patients and to non-diabetic subjects. Moreover, blood samples from 75 diabetic patients show a significant elevation ($p<0.0001$) in liver enzymes like ALT, AST, ALT/AST ratio, CRP and ALKP compared to the second half of T2DM patients and non-diabetic subjects. Furthermore, the liver enzymes data showed a positive correlation with hyperglycaemia and lipidemia conditions in those diabetic patients. In essence, hyperglycaemia and dyslipidaemia deter liver enzymes function, raise the insulin resistance and increase the fatty liver accumulation and progression. Routine screening lipid profile parameters and liver enzymes could be non-invasive biomarkers for all fatty liver diseases in T2DM patients to monitor and prevent fatty liver progression.

Vitamin D status in relation to C-peptide levels in healthy young adults in Qatar

Umar Bin Rashid, Noor Khalil Jasim, Aisha Al-Baker, Najlaa Al-Mannai, Bassem Mohamed, Alanoud Alshamarri, Mohammed Luigi Bossa, Susu M. Zughaier

College of Medicine, QU Health Cluster, Qatar University, Doha, Qatar University

Background: Low Vitamin D status is highly prevalent among healthy young adults in Qatar. Vitamin D deficiency is associated with insulin resistance and type 2 diabetes mellitus (T2DM).

Aims: To find whether an association exists between vitamin D status and C peptide levels among young healthy Qatari cohort.

Materials and Methods: A cohort of 874 healthy Qataris aged 18-40 years was obtained from Qatar Biobank (QBB) and data analysis was conducted using STATA16 software. 51 subjects with glucose greater than 6mmol/L were excluded. Subjects were divided into 3 groups based on 25(OH)D concentrations. Multinomial logistic regression model using vitamin D status as the dependent and C peptide as the independent variable was conducted. Additional multinomial logistic regression models using independent variables that affect C peptide such as BMI, glucose level, and free thyroxine were also conducted. All models were adjusted for age and sex and odds ratios were presented. A *p*-value of <0.05 was considered statistically significant.

Results: No statistically significant association was found between vitamin D status and C peptide levels in this cohort. Deficient vitamin D status was found to be associated with increased BMI (OR= 1.056 95% CI=1.018-1.097), increased monocyte percentage (OR= 1.18, 95% CI=1.054-1.331) and monocyte percentage to HDL ratio (MHR) (OR= 1.203, 95% CI=1.073-1.348). Lastly, C peptide was found to be positively correlated with MHR (Spearman's r=0.295 p>0.001)

Conclusion: Vitamin D deficiency was associated with markers of increased subclinical inflammation that may increase the risk of prediabetes in healthy subjects.

The Relation Between Vitamin D Status and Glycemic control Parameters in Qataris and Long-term Residents with Controlled Type 2 Diabetes Mellitus

Mohamed Elgamal, Bara Shraim, Nadeen Khamis, Lana Abu Afifeh, Maryam Almahri, Fatima Al-Jaber, Susu M. Zughaier

College of Medicine, QU Health Cluster, Qatar University, Doha, Qatar, P.O Box 2713

Background: Vitamin D deficiency is highly prevalent in Qatar and worldwide. Type 2 diabetes mellitus (T2DM) is also prevalent among the population in Qatar. However, the effect of vitamin D status has not been thoroughly studied in the controlled diabetic population in Qatar. The aim of this study is to explore the association between vitamin D status and glycaemic status parameters in T2DM in Qataris and long-term residents.

Methods: A cross-sectional study of 903 participants (403 T2DM and 500 non-T2DM) from Qatar Biobank, was used to perform multinomial logistic regression to explore the association between vitamin D status and T2DM, adjusting for age groups, gender and hip-to-waist ratio (HWR). P-value, odds ratios, 95% confidence intervals, and Spearman's correlation were calculated.

Results: Unexpectedly, 41% of T2DM subjects were vitamin D sufficient compared to 14% in non-T2DM. Similarly, 17% of T2DM were vitamin D deficient compared to 49% in non-T2DM. This finding is likely because of vitamin D supplementation in T2DM. Further, we observed associations between glycaemic status and subclinical inflammation biomarkers. C-peptide was associated with ferritin (T2DM r_s= 0.14, non-T2DM r_s= 0.1) and monocyte to HDL ratio (MHR) (T2DM r_s= 0.16, non-T2DM r_s= 0.24). Moreover, HWR was strongly associated with ferritin (T2DM r_s= 0.44, non-T2DM r_s= 0.6) and MHR (T2DM r_s= 0.37, non-T2DM r_s= 0.47) in both T2DM and controls. Healthy subjects with sufficient vitamin D had the lowest level of HWR.

Conclusion: Glycemic control parameters were associated with subclinical inflammation biomarkers ferritin and MHR, regardless of vitamin D status.

Studying The Effect Of Migration On The Development Of Metabolic Syndrome In A Group Of Migrants To Qatar

Rana Moustafa[1], Kiriti Prabhu[1], Derek Stewart[2], Cristin Ryan[3], Hani AbdelAziz[1], Mohsen EL Edrisi[1], Mohamed Izham[4], Shahab Uddin Khan[1], Shilpa Kuttikrishnan[1], Ann O'Connor[1], Monica Skarlius Young[1], Antonella Tonna[5]

[1]Hamad Medical Corporation, Doha, [2]College of Pharmacy, QU Health, Qatar University, Qatar, [3]Trinity College Dublin, Ireland. [4]Qatar University, Doha, Qatar, [5]Robert Gordon University, Aberdeen, UK,

Introduction: Migration to Western countries has been recognized to increase the risk of metabolic syndrome (MetS); however, there are no data of the incidence of MetS amongst those migrating to the Middle-East including Qatar.

Aim: To explore the incidence of MetS components and risk factors amongst a group of migrants also employees of Hamad Medical Corporation.

Methods: A prospective longitudinal observational study. Migrants aged 18–65 years were consented and screened for MetS risk factors. Parameters included glycated haemoglobin (HbA1c), triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), blood pressure (BP) and waist circumference (WC). All migrants with identified metabolic abnormalities at screening were referred to physicians for further management. Migrants with normal metabolic parameters at baseline are being invited to be rescreened 24 months post-residing in Qatar.

Results: Of the 1379 identified migrants, 460 consented to participate, 70% (n=322) males and 82.2% (378) were Asians. To date the initial screening phase has been completed and showed 13.9% (64) with abnormal BP, 6.7% (31) had prediabetes, 21.4% (91) had elevated TG, 25% (115) had low HDL-C and 47% (219) high WC. Sixteen percent (75) were found to have MetS and were referred for follow-up. 199 migrants with normal metabolic parameters will be followed-up 24 months post residency in the ME.

Conclusion: The initial phase if this study led to early detection and management of MetS and the associated components amongst migrant population in Qatar. The following phase it will give the incidence of MetS and will contribute to the evidence about the relation between migration to Qatar and MetS development. Given the cultural similarities and importance of migration in Qatar and other Middle-Eastern countries; it is likely that the findings will be applicable beyond Qatar.

Prevalence of Metabolic disorders in the Qatar Biobank Population

Kawthar Al-Dabhani[1], Spyridon Paparrodopoulos[1], Eleni Fthenou[1], Nahla Afifi[1], Asma AlThani[1]
[1] Qatar Biobank

Background/Aim: Due to the rapid change in lifestyle in Qatar, an update to the prevalence of metabolic disorders including diabetes, obesity, and metabolic syndrome (MetS) amongst the Qatari population is required.

Method: The prevalence of metabolic disorders in the Qatar Biobank (QBB), a national representation of the Qatari population, stratified by gender and three study groups (Qatari and non-Qatari long term residence Arab (LTR-Arab), and non-Qatari long term residence others (LTR-other)) were measured. The metabolic disorders included diabetes; defined as HbA1c >=5.7 and previously diagnosed diabetes, obesity was measured based on body mass index, MetS based on the criteria from the International Diabetes Federation, hypo and hyperthyroidism based on thyroid stimulating hormone levels, and dyslipidaemia based on total cholesterol, low density lipoprotein, and triglyceride levels.

Results: The prevalence of obesity, diabetes, dyslipidaemia, hyperthyroidism, hypothyroidism, and MetS was approximately 42.8%, 19.8%, 15.6%, 5.6%, 2.7% and 25.2% respectively in the QBB population. The prevalence of metabolic disorders were stratified by gender and study groups, and higher prevalence of diabetes, obesity, hyper and hypothyroidism were found in females compared to males (p-value< 0.01). While males had a higher prevalence of dyslipidaemia (20.4% and 11.1% for males and females respectively), and MetS (26.0% and 24.3% for males and females respectively).

The prevalence of diabetes was the highest amongst Qataris, with a prevalence of 20.4%. While LTR-Arabs had the highest prevalence of obesity (44.2%) and MetS (31.1%). And LTR-others had the highest prevalence of dyslipidaemia (21.2%). There was no statistically significant difference between the three study groups in regards to hyper and hypothyroidism (p-value=0.91).

Conclusion: With the availability of a large representative cohort of the Qatari population and increased prevalence of metabolic disorders, studies within this population are necessary to understand the etiology of these diseases.

PreRISQ: A Simple Prediabetes Risk Score For Qatari Nationals And Long-Term Residents In Qatar: A Cross-Sectional Study

M. Abbas, R. Mall, Kh. Errafii, A. Lattab, H. Bensmail,*, and A. Arredouani*
Qatar Computing Research Institute-Hamad Bin Khakifa University

Objective: There is strong evidence that progression from prediabetes to overt type 2 diabetes can be prevented by intensive lifestyle intervention and/or pharmacotherapy. The objective of this study was to develop a non-invasive, simple, and cheap risk score to diagnose prediabetes in the population of Qatar.

Methods: Demographic and anthropometric measurements from 7268 adults (4895 controls and 2373 prediabetics) were obtained from the Qatar biobank cohort. Forward and backward Logistic regression (LR) was used to identify significant diagnostic factors and the receiver operating characteristic was used to calculate area under curve, cut-off point, sensitivity, specificity and diagnostic values. The LR model was compared to other complex machine learning diagnostic models. The score was developed for Qatari citizens and long-term residents.

Results: Age, gender, BMI, waist circumference, and blood pressure were the significant risk factors for the Qatar prediabetes risk score (PreRISQ). The AUC of the training model was 79.5% (95% CI 78.3% to .80.7%) and at the cutoff point 20 the respective sensitivity and specificity were 80.7% (95% CI 78.9% to 82.5%) and 64.7% (95% CI 63.1% to 62.2%). For the validation, AUC, sensitivity, and specificity were respectively 81.2(95% CI 78.9% to 83.4%), 82.5% (95% CI 78.8% to 85.9%) and 66% (95% CI 62.9% to 68.9%). The score has five risk levels: very low, low, moderate, high, and extremely high. Other comparable machine learning-based models showed comparable discrimination capability to the LR model in our cohort.

Conclusions: PreRISQ is a prediabetes risk score model that can be used as a first step in risk assessment. It includes only non-invasively measured risk factors, is simple, cost-effective, and can be easily understood by physicians in primary health care settings. Though the score was developed using a Qatari cohort, it could contribute to curb the T2D pandemic in the Middle East region given the shared genetic background and lifestyle habits between the different populations of this region.

Epidemiology of Liver Abscess Among Diabetic Patients in Qatar

Ahmed Husain, Eman Elmekaty, Mohammad Adam, Abdalrazig Fadl-Elmulla, Mahmoud Mohamed, Abdullatif Al Khal, Muna Almaslamani.

 Hamad Medical Corporation Communicable disease Centre

Background: Diabetes is a known risk factor for developing liver abscess and infected diabetic patients are at a high risk of morbidity and mortality.

Methods: The study was conducted at Hamad General Hospital, a tertiary hospital in Qatar. Data were collected retrospectively. All diabetic patients diagnosed with pyogenic liver abscess between 2013 and 2017 were included. Liver abscess was diagnosed based on clinical presentation and radiological findings with or without microbiological evidence. Descriptive data were presented in median, range, and percentages.

Results: Forty-two diabetic patients with liver abscess have been identified out of ninety-four patients (44.6%). The median age was 45 (29-85). 97% were males. The commonest symptom was fever (table1.). 38% of the patient had documented bacteremia. The most common isolated organism was *Klebsiella pnuemonie* (12 out of 16 patients) followed by *E.coli* (2/16), *Bacteroid Fragilis* (1/12), and *Streptococcus anginosus* (1/16). Amoeba serology was positive in six patients. 14.2% developed septic shock (6/42). In-hospital mortality was 4.7% (2/42). Nineteen patients have post-discharge imaging follow up, Eight of them showed complete abscess resolution while 11 patients showed evidence of residual disease.

TABLE1. SYMPTOMS, SIGNS AND LABORATORY RESULTS

SYMPTOMS AND SIGNS	Number of patient (%)
	N0=4
FEVER	40 (95)
ABDOMINAL PAIN	25 (59.5)
NAUSEA	11 (26)
VOMITING	12 (28.5)
DIARRHEA	1 (2.3)
LABORATORY RESULTS	**Median (Range)**
WHITE BLOOD CELLS	12.9 (2.3-25)
HEMOGLOBIN	12.4 (9-18)
PLATELETS	268 (44-667)
SERUM CREATININE	73 (15-604)
ALT	66 (14-309)
AST	44 (12-534)
ALP	196.5 (24-923)
TOTAL BILIRUBIN	17 (5-129)
ALBUMIN	26.5 (14-38)
HBA1C*	11 (6-20.6)

*TWO MISSING OBSERVATIONS

 Conclusion: *Diabetes remains a risk factor for developing liver abscess. Septic shock is one of the serious complications which was observed. Klebsiella pnuemonie* is the most common pathogen. Although less than 50% of the patient had imaging follow up, a high percentage of residual disease was observed. The enhancement of a close and regular follow is highly recommended.

Prevalence Of Depression And Predictors Of Glycemic Control Among Type 2 Diabetes Mellitus Patients At Family Medicine Clinic, Suez Canal University Hospital Egypt

Mansoura Fawaz Salem Ismail (1) & (4), Madiha M Fares (2) Ahmed G Abd-Alrahman (3)
(1) Professor of Family Medicine, (2) Lecturer of Family Medicine, (3) Lecturer of Family Medicine, Faculty of Medicine, Suez Canal University, Egypt ,(4) Senior consultant family medicine PHCC&, Assistant professor family medicine faculty of medicine .Qatar

Background: Diabetes and depression are recorded as the fourth and eighth reason for disability adjusted life years respectively and the cost, morbidity, and mortality from diabetes is expanded when it is associated with depression . People with diabetes mellitus when contrasted to individuals without diabetes have a 2–4 fold greater risk of depression. Higher glycated haemoglobin (HbA1c), diabetic complications and mortality were conveyed among diabetic patients with depression (1-3).

Methodology: This study aimed to assess the prevalence of depression and predictors of glycemic control among type 2 diabetes mellitus patients .A cross-sectional study was conducted in 2018. Patients with type 2 diabetes mellitus (300 participants) were selected by systematic random sampling technique and assessed for depression using Patient Health Questionnaire 9 (PHQ 9). The relationship between depression, glycemic control, and its predictors was studied using Univariate analysis. Multivariable analysis was used to evaluate the combined effect of several factors associated with glycemic control among type 2 diabetes mellitus patients after adjusting for confounding variables.

Results: The prevalence of depression among type 2 diabetic outpatients was 33.3% fulfilled the criteria for minimal depression, 23.3% for mild depression, 11% for moderate depression, and 1.3% for moderately severe to severe depression .When a cut-off score of PHQ 9 ≥ 10 (mild, moderate to severe depression) was used, the prevalence was 35.7% . However, the prevalence of depression was 69 % when a cut-off score of PHQ 9 ≥ 5 was used.69.0%; three-quarters of the studied population had poor glycemic control (74.3%), and the predictors for glycemic control were depression, the presence of other comorbidities and diabetic complications.

Conclusion and Implication: The prevalence of depression was high among Type 2 DM patients; diabetic complications, co morbidities, and depression were found to be independent predictors of poor glycemic control among type 2 diabetes patients in the current study, so it is highly recommended to screen and manage depression among type 2 diabetic patients with more effort from the Multidisciplinary health care team for the patients with diabetes to achieve good glycemic control

Table 1: Logistic regression analysis to determine the independent predictors of glycemic control among type 2 diabetic patients at family medicine clinic Egypt.

	Coefficient	Wald	P-value.	Adjusted Odds Ratio	95% Confidence Interval	
					Lower	Upper
Duration of DM (5-)	-0.475	1.147	0.284	0.622	0.261	1.484
Duration of DM (5-10-)	0.112	0.041	0.839	1.119	0.378	3.312
Duration of DM (>10)	0.799	2.435	0.119	2.224	0.815	6.067
DM Complications	1.578	15.690	**0.000***	4.844	2.219	10.573
Treatment (Insulin)	0.253	0.555	0.456	1.287	0.662	2.502
Treatment (Combined)	0.710	0.841	0.359	2.033	0.446	9.271
Comorbidities	1.022	12.712	**0.000***	2.780	1.585	4.876
Smoking	0.704	0.782	0.368	2.022	0.437	9.359
Depression	1.566	3.684	**0.000***	3.625	2.113	6.220

* Statistically significant at p<0.05

Fasting Serum C-Peptide As A Potential Surrogate Marker For Abnormal Liver Function

Omar Jamil, Kamel Abou Jabal, Abeer Almasalmeh, Nadin Ibrahim, Saghir Akhtar**

College of Medicine, Qatar University. Doha, Qatar

Background: Liver plays a vital role in maintaining body homeostasis, and hence identification of liver dysfunction in its early stages is crucial to minimize the burden associated with liver pathology. To that effect, current literature has focused on the association between liver function tests and glycemic indices. However, in this novel study we have sought to identify the best glycemic index to correlate with elevated liver function tests and serve as a surrogate marker for identifying patients with asymptomatic liver dysfunction.

Methods: This cross-sectional study, utilized the NHANES III database to obtain data on 33,994 participants. After the application of our inclusion and exclusion criteria, we ended up with 1,933 samples. Subsequently, during the analysis of the data we classified the subjects into two groups; one with normal ranges of Liver function tests, and the other with abnormalities of these tests. Using ROC curve test, we looked at the tests' cutoff points at 90% specificity, and then determined the sensitivity at the 90% specificity of the glycaemic parameters and compared them to each other.

Results: 1933 participants were included, of whom 347 (18%) had at least one abnormal liver function test and gamma glutamyl transferase was the most frequently elevated liver test. Our results indicated that both HOMA-IR and Fasting Serum C-Peptide had the highest sensitivities, at 90% specificity. The cutoff for serum c-peptide was 1.27 nmol/L and for HOMA-IR was 3, with sensitivities of 21.61% and 21.33% respectively.

Conclusion: In summary, this study has identified a potentially novel surrogate marker (i.e. serum c-peptide & HOMA-IR) for the diagnosis of mild liver dysfunction in the general American population. Therefore, Fasting Serum C peptide levels above 1.27nmol/L & HOMA-IR levels above 3 maybe useful for diagnosing asymptomatic liver dysfunction.

Rising to the Challenge: Preventing and Managing Type 2 Diabetes

Sanaa Alharahsheh,Maha El Akoum, Feras Al Meer , M. Walid Qoronfleh

World Innovation Summit for Health, Qatar Foundation, P.O. Box 5825, Doha, Qatar

Diabetes, especially type 2 is one of the major challenges facing policymakers today. Globally, the rates of diabetes have risen with 424.9 million people now affected by the condition and **predicted to reach around** 628.6 million in 2045. It has also been estimated that as many as half (50.0%) of all people with diabetes are unaware of their disease. **Type 2 diabetes** is more common in adults and accounts ca. 90% of all diabetes cases[1].

This high prevalence and the associated health risks and economic impact are overwhelming. The health consequences of type 2 diabetes are more severe than generally recognized, and include an increased susceptibility to blindness, lower limb amputations, kidney failure, heart attacks and stroke. Diabetes is among the top 10 causes of death globally and it accounts for over 80% of all premature non-communicable diseases (NCDs) deaths together with the other three major NCDs (cardiovascular disease, cancer and respiratory disease). The direct and indirect costs are also a serious drain on healthcare budgets and productivity. In 2017, IDF estimates the total healthcare expenditure on diabetes will reach USD 727 billion. Although there is now a clear consensus on how to manage the disease through drug treatment, screening, self-management and behavior change, the question in diabetes is not what to do, but how to do it[2].

Based on secondary data, literature review, and case studies, this investigation discusses the diabetes challenges, especially type 2 and proposes key policy goals for policymakers based on innovative practices that together will reduce incidence of diabetes .The key challenges addressed include: health service reform; disease *vs.* broader health focus; health ministry *vs.* cross-government; long time frame; tailored approach; and prioritization. In an attempt to tackle these challenges, this study proposes three key policy goals for policymakers based on innovative practices: improve disease management for people with diabetes to reduce complication rates; establish effective surveillance to identify and support those at risk of type 2 diabetes; and introduce a range of interventions that help to create an environment focused on prevention.

---

[1] International Diabetes Federation, *IDF Diabetes Atlas*. Eight edition, International Diabetes Federation, 2017. Available at www.diabetesatlas.org
[2] Colagiuri, S., Kent, J., Kainu, T., Sutherland, S., & Vuik, S. Rising to The Challenge Preventing and Managing Type 2 Diabetes. Report of the WISH Diabetes Forum 2015.

Cabergoline De-escalation Practice- A Retrospective Audit.

Abeer Abdalrubb, Ahmed Saleh, Mostafa Najim, Adeel Khan, Zaina Alamer, Mohammed Bashir

Qatar Metabolic Institute, Department of Medicine Department, Endocrine Department, Hamad Medical Corporation, Doha, Qatar

Background: Cabergoline is the first-line treatment for patients with lactotroph pituitary tumors. It is a long-acting dopamine receptor agonist with a high affinity for D2 receptors. Due to the activation of 5HT2B serotonin receptors, side of effects of Cabergoline includes increased risk of fibrotic cardiac valvulopathy and Impulse Control Disorders e.g. gambling. The former complication is linked to the cumulative dosage of Cabergoline. This audit aims to study the current practice in deescalating Cabergoline dosage in patients who achieved normal prolactin levels.

Patients & Methods: We conducted a retrospective audit at Hamad General Hospital in patients receiving Cabergoline treatment for hyperprolactinemia. We extracted data from the patient's electronic medical records. We categorized the prolactin levels as Normal (≤450 mIU/l) or Elevated (>450 mIU/l)

Results: We included 257 patients; of which 187(65.4%) were females. Pituitary microadenoma was diagnosed in 113(44.8%) while macroadenoma was diagnosed in 60(23.8%). Mean starting dose of Cabergoline was (0.8± 0.4 mg/week) in patients with macroadenoma and (0.6±0.4 mg/week) in patients with microadenoma. Over four years of follow up, 55.6% of the patient achieved normal prolactin levels; 65% in those with microadenoma and 35% in those with macroadenoma. In those who achieved normal prolactin levels, the mean dose of Cabergoline remained unchanged at 0.6 ± 0.4 mg/ week. In those with persistently elevated prolactin levels, the mean dose of Cabergoline increased to 1.0±1.1mg/week. The cumulative discontinuation rate of Cabergoline over this period was 10.0%.

Conclusion: There is a low tendency to deescalate the dosage of Cabergoline in patients with hyperprolactinemia who achieved normal prolactin levels, increasing their exposure to the treatment. As outlined, the fibrotic valvular complications are linked to the cumulative dose of Cabergoline. Hence, we recommend that the dosage of Cabergoline in patients with hyperprolactinemia should be tapered down and stopped in patients who achieve normal prolactin levels- after careful assessment.

Gender differences in clinical, biochemical and radiological presentation of patients with Hyperprolactinemia.

Abeer Abdalrubb, Zaina Alamer, Mostafa Najim, Adeel Khan, Ahmed Saleh, Mohammed Bashir

Qatar Metabolic Institute, Department of Medicine Department, Endocrine Department, Hamad Medical Corporation, Doha, Qatar

Background: Lactotroph adenomas are the most common hormone-secreting pituitary tumor accounting for 30-40% of all pituitary adenomas. It is known that females tend to present earlier than males, but the gender differences in the pathology and response to treatment have not been reported in Qatar.

Patients & Methods: We conducted a retrospective audit at Hamad General Hospital in patients receiving Cabergoline treatment for hyperprolactinemia. We extracted data from the patient's electronic medical records. We categorized the prolactin levels as Normal (≤450 mIU/l) or Elevated (>450 mIU/l)

Results: A total of 257 patients had hyperprolactinemia, 89 patients were males (32.2%), and 187 were females (67.8%). The males were older, mean age 41.7 ± 11.4 years vs 35 ± 10.2 (p<0.001). The Median prolactin level at diagnosis was higher in males than females [5845 mIU/l (IQR-1210-14340) Vs 1628 mIU/l (1029-2671) P <0.001]. Macroadenoma was the common cause of hyperprolactinemia in males 43(55.85); while microadenoma was the most common cause of hyperprolactinemia in females 93(53.1%). The mean weekly starting dose of Cabergoline was significantly higher in males than females (0.8 ± 0.4 vs 0.5 ± 0.4, p<0.001). Over four years of follow up, more males achieved normal prolactin levels than females (64.1% vs 52.2%, p=0.072)

Conclusion: To our knowledge, this is the first report on the gender differences in the clinical and biochemical presentations in patients with hyperprolactinemia. Males tend to present at an older age, with higher levels of prolactin and are more likely to have macroadenomas compared to females. However, despite having a more aggressive disease, the treatment response was numerically higher in males compared to females- albeit not statistically significant. Long term follow- up is needed to examine the difference in remission rates.

Echocardiogram Evaluation In Hyperprolactinemia Patients On Cabergoline – HMC

Abeer Abdalrubb, Adeel Khan, Mostafa Najim, Ahmed Saleh, Zaina Alamer, Mohammed Bashir

Qatar Metabolic Institute, Department of Medicine Department, Endocrine Department, Hamad Medical Corporation, Doha, Qatar

Introduction: Cabergoline is the first-line treatment for patients with lactotroph pituitary tumours. Due to the activation of 5HT2B serotonin receptors, side of effects of Cabergoline includes increased risk of fibrotic cardiac valvulopathy. Although the former complication was mainly reported in patients with Parkinson's disease receiving high doses of cabergoline, a recent meta-analysis of case control studies has reported a 3 folds increased risk of tricuspid regurgitation in hyperprolactinaemic patients treated with cabergoline. Regulatory bodies, including the FDA, recommend regular echocardiography surveillance at baseline and every 6 to 12 months thereafter. This audit aims to review the compliance rates with echocardiography screening in patients with hyperprolactinaemia treated with cabergoline.

Material and Methods: We conducted a retrospective audit at Hamad General Hospital in patients receiving Cabergoline treatment for hyperprolactinaemia. We extracted data from the patient's electronic medical records.

Results: We included 257 patients; of which 187(65.4%) were females. The mean age was 35 ± 10.2 years. Pituitary microadenoma was diagnosed in 113(44.8%) while macroadenoma was diagnosed in 60(23.8%). Cabergoline treatment was started at a mean dose of 0.62 ± 0.4 mg/week and was continued in 89.5% of the patients at the same dose. Baseline echocardiogram was done in 4.3% of the patients. Over the 4 years period, 89.1% of the patients did not have any echocardiography screening. Of those who did have echocardiography (28 patients) there was three cases of fibrotic valvulopathy; One at baseline and two detected during follow up.

Conclusion: This is the first report from Qatar on the rates of echocardiography screening in patients with hyperprolactinaemia treated with cabergoline. There is a quite a low rate of compliance with echocardiography recommendations. Due to the low rate of surveillance, it is hard to draw any conclusion on the rates of fibrotic valvulopathy in Qatar.

The Use of MRI Pituitary in Evaluating Hyperprolactinemia Patients.

Abeer Abdalrubb, Mostafa Najim, Adeel Khan, Ahmed Saleh, Zaina Alamer, Mohammed Bashir

Qatar Metabolic Institute, Department of Medicine Department, Endocrine Department, Hamad Medical Corporation, Doha, Qatar

Introduction: Magnetic resonance imaging (MRI) of the pituitary gland is indicated in all patients with prolactin to establish the underlying aetiology. Annual MRI pituitary is indicated in patients with pituitary macroadenoma, increasing prolactin level, or if new symptoms have developed. This audit aims to evaluate the use of MRI pituitary in managing patients with hyperprolactinemia.

Methods: We conducted a retrospective audit at Hamad General Hospital in patients receiving Cabergoline treatment for hyperprolactinemia. We extracted data from the patient's electronic medical records. We categorized the prolactin levels as Normal (≤450 mIU/l) , Intermediate (450-4000 mIU/l) and Elevated (>4000 mIU/l).

Results: We included 257 patients; of which 187(65.4%) were females. The mean age was 35 ± 10.2 years. Pituitary microadenoma was the most common finding in the baseline MRI 44.8%, macroadenoma in 23.8%, normal scan in 11.1%, empty sella in 2.4%, other findings in 2.4% and it was not done in 15.5%. At baseline, MRI scans were not done in 16.4% and 9.5% of patients with intermediate and elevated prolactin levels, respectively. The rates of annual MRI scans in patients with macroadenoma and persistently elevated prolactin levels ranged between 40-60% while in those with normalized prolactin levels, the rates were 40-55%. In patients with microadenoma, the rates of annual MRI scans in those with persistently elevated prolactin levels was 40-60% and in those with normalized prolactin levels was 40-50%.

Conclusion: Our study showed that there was a high rate of an apparent un-necessary MRI scanning in patients with microadenoma who had normal prolactin levels; and a reduced rate of annual scanning in patients with persistently elevated prolactin levels. Overall, the yearly scanning rates were similar in both normal and high prolactin levels regardless of the tumor size. This data should be a starting point to develop more precise protocols for managing hyperprolactinemia patients.

Implementation of a Virtual Thyroid Clinic for the management of thyroid dysfunction in pregnancy/WWRC – a clinical audit

Gowri Karuppasamy, Moufida Azek, Manjumole leelamani, Hamda Ali, Mohammed Bashir
National Diabetes Centre, Women Wellness and Research Centre

Background : Thyroid disorder in pregnancy is associated with several adverse outcomes, including early miscarriage. The management of these disorders is critical especially in the first trimester. Between 120-200 cases are referred monthly to the endocrine antenatal clinic. However, most of them haven't done a recent thyroid function test (TFT) at physician visit leading to delayed interventions.

Aim: This audit aims to review the referred cases at the endocrine antenatal clinic at WWRC during the month of July 2019.

Materials and Methods: The Virtual Thyroid Clinic (VTC) was established to provide timely review and intervention in pregnant women with thyroid disorders and to reduce inefficient clinic appointments. Once a patient is referred through either electronic or by manual request, the endocrine nurse will contact the patient to record the treatment, the dose and to repeat the TFT and/or thyroid antibodies. On a dedicated day, the endocrinologist, together with the nurse, review the investigations and then draft and phone the patients with the care of plan.

Results: A total of 117 patients included in this study. The mean (±SD) duration between referral to review was 6 days ±4.2, and the mean gestational age at referral (SD) was 20.8± 8.9 weeks. Only 26.5% of women were referred in the first trimester. With regards to diagnosis, 52.1% had pre-existing hypothyroidism, 11.9% were newly detected hypothyroidism, 22.2% had subclinical hypothyroidism, 5.1% had hyperthyroidism, 1.7% had gestational thyrotoxicosis, and 6.8% were diagnosed with a transient thyroidal illness. Medications were adjusted in 29.9% of patients, while no changes were made in 65.8%. Follow up was arranged for 70.9% of the patients, while 29% were reassured and discharged.

Conclusion: Introduction of VTC is providing patients an efficient and cost-effective service. It ensures that thyroid function is reviewed in a timely manner, with appropriate measures. It also reduces unnecessary clinic visits. In this regards we encourage earlier referral of pregnant women with thyroid disorders.

Audit on the anomaly scanning in pregnant women with type-1 diabetes.

Fatema Asheer[1], Ibrahim Al-Abdulla[1], Justin Konje[1], Mohammed Bashir[2]
1-Department of Obstetrics and Gynaecology- WWRC
2- National Diabetes Centre-WWRC

Background: - Pregnancies in women with type 1 diabetes mellitus (DM-1) is associated with increased rates of congenital malformations compared to the general population. Current national guidelines recommend a first trimester scanning for nuchal translucency and a fetal anomaly scan at 18-20 weeks' gestation. There is no data on the frequency of congenital malformation in women with DM-1

Aims :- We aimed to examine the current compliance with ultrasound scanning in women with DM-1 and the frequency of congenital malformation.

Methods:- This is a retrospective audit that included women with DM-1 who were managed in the NDC-WWRC between Jan 2015-June 2019. We excluded all pregnancies that continue beyond the first trimester or lost to follow up

Results:- We studied 216 pregnancies in women with DM-1 and included 193 pregnancies (50.8% were Qatari and 39.9% were non-Qatari Arabs. Mean age was 29.5 ± 5.2 years , mean duration was 13.5± 7.7 years, mean pre-pregnancy BMI was 27.3 ± 5.2 years, mean pre-pregnancy HBA1c was 8.0 ± 1.5 % . Mean gestational age at review in the NDC-clinic was 10.6 ± 6.0 weeks. As shown in table 1, 90.3% of the women had anomaly scanning performed yet only 57.0% of them had a dedicated fetal echocardiograph. Congenital malformation was detected in 9/192 women(4.7%); of which 4 were renal, 3 were cardiac, 1 was anencephaly and 1 was chromosomal.

Table 1 frequency of U/S scans	
First trimester scanning	Yes (83.4%)
	No (16.6%)
Anomaly scanning	Yes (90.7%)
	No (9.3%)
Fetal Echo	Yes (57.0%)
	No (43.0%)
FMU scanning	Yes (85.5%)
	No (14.5%)

Conclusion: - The audit showed a high rate of compliance with the current national guidelines. The rate of congenital malformation was 4.6% similar to rates reported from other cohorts, yet this rate is limited by the number of pregnancies studied.

Admission for blood glucose control in pregnant women with GDM-reasons and outcomes

Noora Al-Thani, Laila Al-Hail, Mohammed Bashir
 National Diabetes Centre-WWRc

Background:- Hospital admission could be considered in women with insulin-treated diabetes in pregnancy to optimise blood glucose control at the peripartum period. Admission for optimisation of diabetes control among women with gestational diabetes (GDM) is still a common practice among obstetrics physician; albeit has been on the decline. This audit aims to examine the indications for admission for blood glucose control among women with diabetes in pregnancy.

Methods:- We included all women who were admitted to the WWRC with the reason being "glucose monitoring" over six months (Feb-August 2019)

Results:- We included 97 women; 30(30.9%) were Qatari, 41(42.3%) were Arab, and 26(26.8%) were Asian. Majority -73(75.3%)-had Gestational diabetes (GDM) , 17 (17.5%) type 2 diabetes ,3 had type 1 diabetes (3.1%) and 4(4.1%) had no clear diagnosis. The indications for admissions were; blood glucose monitoring 59(60.8%), a decision for delivery 18(18.6%) and non-diabetes related 20(20.6%). In the 43 women GDM who were admitted for blood glucose control, the median gestational age at admission was 36 weeks (IQR 35-37), and the median duration of admission was 3 days (IQR 2-4). Most of the women, 27(62.8%), were not on any treatment; no documentations of pre-admission self-monitoring blood glucose in 30(69.8%) and 29(67.4%) women were not seen in the diabetes clinic. Thirteen women (30.2%) delivered during this admission. Among those who were discharged, the treatment plan was not altered in 19(63.3%).

Conclusion: - This audit revealed that women with GDM are admitted at an advanced gestational age; the majority of them were not on treatment before admission and had no SMBG records. In the majority of those who did not deliver, there were no changes in the diabetes treatment. These findings do not support the continuation of this practice due to the lack of benefits.

Impact of obstetricians' awareness for the indication of admission of gestational diabetes on hospital admission rate for glycemic control in pregnant women with diabetes in Al Khor hospital.

Riyadh Ali Hammamy, Wissam K Ghadban, Nedaa Khaiyon, Hemalatha Charles HN Obs/Gyn.

Background: Open gestational diabetes clinics are designed to provide the best clinical care and support women patients with diabetes during pregnancy to improve maternal and fetal health outcome. Another goal of these clinics is to reduce the unnecessary hospital admission to optimize glycemic control during pregnancy. Giving regular awareness to obstetricians about the indication of admission of gestational diabetes can reduce further hospital admission.

Aim: To evaluate the impact of delivering more awareness for obstetricians on the rate of hospital admissions for optimizing glycemic control in pregnant women with diabetes.

Methods: Data from January 2013 until December 2019 looking for the total admission rate to the obstetric department, measuring specifically the rate of admission for glycemic control in pregnant women with diabetes before, and after implementation of regular awareness to obstetricians since 2018.

Results: The total admission for glycemic control in 2018 is 58 patients while it was 135 patients in 2017. However, the total admission for glycemic control in 2019 till October is 27 patients.

We have noticed significant reductions in the rate of admission for glycemic control in pregnant women with diabetes/gestational diabetes after implementing the quality project of GDM in Al Khor hospital and after giving regular awareness to obstetricians regarding the gestational diabetes admission since 2018. We have found that majority of pregnant women with diabetes admitted by obstetric physicians for glycemic control they do not have strong indication for admission and can be manage in outpatient according to NICE guideline.

Conclusion: Implication of gestational clinics and regular awareness to obstetricians has significantly reduced the need for hospital admission to optimize glycemic control during pregnancy. Further improvement can be achieved to reduce the rate of admission; by improving the direct communication between obstetric physician and diabetes physician before the decision of admission.

A quality improvement project to reduce the no show rate and improve clinic utilization in Al Wakra National Diabetes Centre.

Bashar Al Ayash, Maha Hasanain, Eman Musleh, Noureddin Al Rabaya, Ceferina Du Nalasa, Wafaa El Zibk, Dona Thomas, Khaled Ashawesh, Khaled Dukhan.
National Diabetes Centre – Al Wakra Hospital

Introduction: No show (NS) in outpatients leads to longer waiting times, patients missing important appointments and improper utilization of resources. In our hospital, a reminder text message system is used to improve this quality of care target. However, our baseline data showed up to 40% NS of new and 21% of follow-up appointments with 20% average clinic overbooking (COB).

Aim: To reduce the NS and COB rates and improve clinic utilization in Al Wakra National Diabetes Centre (AW-NDC).

Methods: Between November 2018 and October 2019, all patients were phoned 3 days before their appointment by AW-NDC patient coordinator and staff nurses to confirm attendance. Those who can't attend were put in a waiting list to be given future appointments. Available slots were utilized to accommodate patients from the waiting list and overbooked patients. The percentage of NS, COB and clinic capacity utilization (CCU) were measured before and after the project.

Results: In 12 months, a total of 7987 patients were contacted. On average, 76.1% confirmed their attendance, 6.2% requested appointment rescheduling and 17.7% were not reachable. Patient response rate dropped during summer holidays to 67.2% with 32.8% were unreachable in July. Data from 4 consecutive months (July, August, September and October) of both years was analysed to allow for seasonal variation. The median NS rate reduced from 38.47% to 25.91% in new appointments and from 18.2% to 13.0% in the follow-ups. Average COB was available from September and October and showed reduction from 21% in 2018 to 10.6% in 2019. Average CCU remained unchanged at 86%.

Conclusion: Patient telephone contact and development of waiting list improved clinic attendance, reduced no show rate and enhanced proper utilization of clinic capacity. Reduction in clinic overbooking improved patient flow in clinics which positively impacts quality of patient care.

Effectiveness of staff health education on Flu vaccination in diabetic patients at NCD (Non-communicable disease) clinic, Mesaimeer Health Centre

Muhammad Naeem Barg, Leena Abdallah, Dianne Candy Rose Figueroa, Abdul Wajid Safi

Background: It is recommended for people with diabetes to get annual influenza vaccine, Multiple studies show a reduction in hospitalization from flu-like illness, pneumonia, influenza, ICU admissions and reduce deaths among those who take Influenza vaccination.

Method and Initial results: We, at Mesaimeer health Centre, carried out an Audit and identified that offering Influenza vaccination to people with Diabetes is alarmingly low in our NCD clinic. All patients with diabetes who attended NCD clinic from 15th August 2017 to 30th August 2017 were included in Audit. Results showed that a total of 142 patients were reviewed. Only 7.7% (11 patients) were offered the vaccine, among these patients only 8 patients (5.6% of the total number of patients) received the influenza vaccine while 3 patients refused to have the vaccine

Intervention: We developed posters and organized presentations and workshops to health care workers covering NCD regarding the importance of flu vaccination in people with diabetes. Posters regarding Flu vaccination were displayed at important locations such as NCD reception, Nurse room and physician room. We aimed to increase the flu vaccination in people with diabetes by 20%.

Results: Repeat audit of our practice from 17th September to 28th September 2017.We managed to increase the influenza vaccination uptake from 7.7% to 78%. A total of 165 patients were reviewed in NCD and among them, 78% (130 patients) were offered flu vaccination. 94 patients (56.9% of the total number of patients) agreed to have an influenza vaccine while 36 patients refused to have the vaccine.

Conclusion: We conclude that simple measures, timely and short presentations and reminders to staff looking after people with diabetes are integral components to improve patient care.

Effectiveness of the Diabetes Education and Self-Management Program (DESMOND) for people with type 2 diabetes: Qatar Version

Ragae Dughmosh, Amani Ajina, Lal Malak, Doha Sabbah, Tomader EL-Abd, Sanaa AL Arabi, Muneera Al-Ali, Manal Musallam

National Diabetes Centre – HMC

Introduction: DESMOND is an internationally recognized evidence based self-management structured group education program for people with type 2 diabetes. The 6 hours program is delivered in the NDC by 2 diabetes educators. It is offered as a one-day or two half-day sessions for a group of 6-10 patients. In collaboration with Leicester diabetes centre at UK, DESMOND program has been adapted for Qatar population to meet their cultural and specific needs.

Aim: To evaluate the effectiveness of DESMOND Qatar program on metabolic parameters in people with type 2 diabetes.

Methods:- We are reporting on metabolic outcomes in 140 consecutive adults with type 2 diabetes.

Results: We included 140 adults , 110 males (78%). The mean age was 49.1 years. At 6 months, the median A1c was reduced by 0.7%(p<0.001), and at 12 months it was maintained at 0.5% (p=0.0648). Both systolic and diastolic blood pressure decreased at 12 months from baseline [- 6.66 mmHg (95% CI -2.35 to -10.97] and [-3.34 mmHg (95% CI -1.28 to -5.39)] , respectively). The LDL and the total cholesterol decreased after 12 months from baseline [-0.232 mmol/l (95% CI -0.065 to -0.399) and [-0.351 mmol/l (95% CI -0.096 to -0.606)], respectively.

Conclusion: Implementing the DESMOND Qatar showed a sustained improvement in the metabolic outcomes in people with type 2 diabetes. Future studies will focus on local barriers for patients to improve their metabolic profile to enhance the program further.

Evaluation of the Effectiveness of a Structured Diabetes Education Program for patients with Type-1 Diabetes

Suzan Albayed, Ragae Dughmosh, Ahmed Al-Omari, Khaled Dukhan, Khaled Ashawesh
National Diabetes Centre, Alwakra Hospital

Introduction: In patients with type 1 diabetes, structured diabetes education has been shown to improve CHO counting skills and psychological outcomes.

We established a structured type 1 diabetes education program (at Alwakra Hospital) that involves three- 5 hours group (an average of 4 patients) education sessions, delivered on weekly basis. Over the 3-week program period, patients monitor their blood sugar using freestyle libre and are provided with an ongoing support via social media (WhatsApp group). The curriculum includes educating patients on CHO counting, insulin adjustment, use of capillary ketone meters and glucagon injections, and management of their diabetes during sickness, exercise and fasting.

Objectives: To determine the effect of this diabetes education program on CHO counting skills, self-efficacy, and depression. Knowledge of use of capillary ketone meter and glucagon kit was also evaluated.

Methods: From April 2019- November 2019, 16 type 1 diabetes patients were enrolled on this program. Participants were given AdultCarbQuiz, Beck Depression scale and Diabetes Self-Efficacy Questionnaires to be completed at the start of the structured diabetes education program and also at the end of the program

Results: At baseline, the mean scores for AdultCarbQuiz, Beck depression scale and Self-Efficacy questionnaires were 22.75/41, 11/27 and 6.64/10 respectively; these scores significantly improved, post educational program, to 35/41, 6.62/27 and 8.3/10 respectively.

Number of patients who had knowledge of capillary ketone meter and glucagon kit use, at baseline, was 0/16 and 1/16 respectively; which improved following the educational program to 16/16 and 16/16 respectively.

Conclusion: Our structured type diabetes education program led to an improvement in CHO counting skills and psychological outcomes. These results are consistent with the current body of evidence regarding the positive impacts of diabetes education programs but may be limited by the small number of the patients included in the study.

Quality Improvement Project to Reduce the No-Show Rate in WWRC-NDC Outpatient Clinic

Hana Abukhadijah[1], Ifrah Hassan[2], Salma Abdel-Rahman[3], Raissa Jacinto Puddao[4], Moufida Azek[5], Dr. Mohammad Bashir[6]

[1] Quality Improvement Reviewer-NDC, [2] Patient Pathway Coordinator-NDC [3], Associate Consultant-NDC; [4] Senior Quality Improvement Reviewer-NDC, [5] Registered Midwife [6] Senior Consultant-NDC

Background:- Failure of patients to attend their clinic appointments has negative impacts on the patients' medical care, especially during pregnancy where time is foe. Besides being a waste of resources, the wasted clinical slots lead to longer waiting time and impact the medical care of other patients. The NDC-WWRC is the largest provider- in Qatar- for diabetes care during pregnancy, with over 20000 patients' visit in 2019. The project aims to identify factors associated with "No-Show", and to develop working plans to achieve a 40% reduction in March 2020. This is an interim report.

Results : Baseline data from November 2018- showed that the rate of No- Show was 27%. Figure 1 shows the identified reasons for "No-Show". The main deficiencies were post-natal visits, lack of reminders and personal reasons. Hence, we have developed a new criterion for post-natal referrals to target women on insulin therapy and main streamed the referral of other women to other appropriate services. We ensured that women are receiving text message reminders and that the clerks always check the correct contact details. Implementing these changes resulted in an 11% reduction in the No-Show rate from 27% to 24%. Reassessment has shown that the current main deficiency is "personal reasons".

CAUSE AND EFFECT DIAGRAM

[Figure 1]
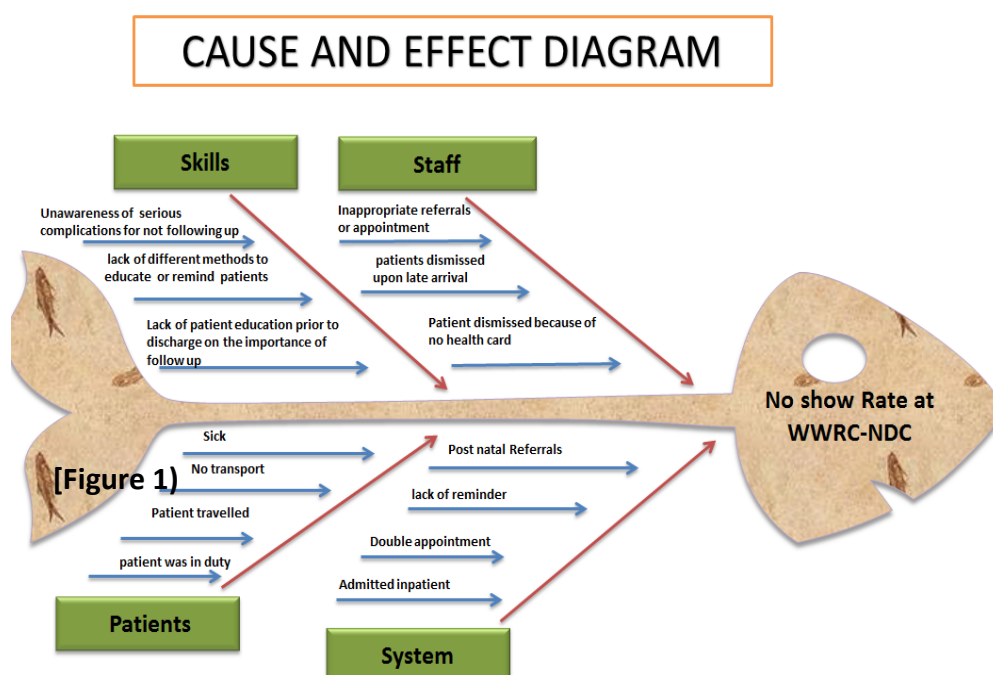
Discussion and Conclusion: - The No Show project in still an ongoing process. The intervention so far has resulted in a modest reduction on the No-Show rates. Currently most of the No-Show reasons are attributed to "personal reasons". To address this issue, patients have to made aware of the impact of "No-Show" on their medical care and on other's. They should be provided with a timely alternative arrangement to facilitate re-scheduling. Hence, an awareness campaign will be undertaken in the NDC-WWRC about the No-Show. We will report future the results in the future.

An audit on improving effectiveness of Dietetic intervention in Gestational Diabetes Mellitus (GDM)

Zainab Miqdad[1], Dana Malik[1], Tarik Elhadd[1], Khaled Ashawesh[1], Siddique Mashhood Ahmed[1], Hiba Satti[2], Osric Navti[2], Stephen Beer[1,] Khaled Dukhan[1].
[1] *National Diabetes Centre, Al Wakra Hospital, Hamad Medical Corporation.*
[2] *Department of Obstetrics and Gynaecology, Al Wakra Hospital, Hamad Medical Corporation*.

Introduction: Regular monitoring of Gestational weight gain (GWG) and adapting appropriate dietary therapy are key measures to reduce adverse outcomes of mothers and babies in pregnancies with Gestational Diabetes Mellitus (GDM). In Al Wakra Hospital and when the joint Obstetric/Endocrinology clinic was established in 2015-16, an initial assessment of dietetic status on 54 women with GMD showed 76% were judged concordant with diet and 50% achieved target self-reported blood glucose. However, GWG was not systematically recorded and was not incorporated in the dietary evaluation and interventions.
Aim: To improve the standards of dietary assessment and intervention in women with GDM integrating GWG as part of the process.
Intervention: Cerner pregnancy summary function was used by multidisciplinary team (MDT) to record pre-pregnancy weight and body mass index (BMI). Weight changes at each visit during pregnancy were also recorded. The MDT was reminded of the maximum expected weight gain according to baseline BMI and appropriate GWG focused dietary advice and intervention were provided. Re-audit against these new standards was performed on a similar cohort in 2019.
Results: 53 ladies were studied, 8 lost follow up (delivered elsewhere). 51.1% were Arab, 40% Asian, 4% Qatari with mean age of 32yrs (±4.67). 58% were judged concordant with diet and 45% achieved target self-reported blood sugars. Average pre-pregnancy BMI was 29.8kg/m^2 (±7.41). All cases had their weight changes recorded with 41/45 (91.1%) had GWG. Average GWG was 8.28kg (±4.72) with 78% achieved the target of 7-11.5kg maximum acceptable GWG for the average baseline BMI. This was demonstrated across all BMI categories with mean GWG of 6.8kg (±3.98) for BMI ≥30, 8.7kg (±5.54) for BMI 25 – 29.9 and 9.9kg (±4.04) for BMI: 18 – 24.9 (Targets: 5 – 9kg, 7 – 11.5kg and 11 – 16.5kg).
 Conclusion: In this high-risk group of patients, implementing the new measures resulted in improvement in the MDT dietary assessment and management.

Multidisciplinary Approach for Patients on Insulin Pump

Dr. Dabia Al Mohanadi, Dr. Hamda Ali, Dr. Khalid Baagar, Dr. Salma AbdelRahman, Dr. Zeinab Dabbous, Ms. Ameena Ahmed, Ms. Kawsar Mohamud, Mr. Mohammad Subh, Ms. Raissa Puddao
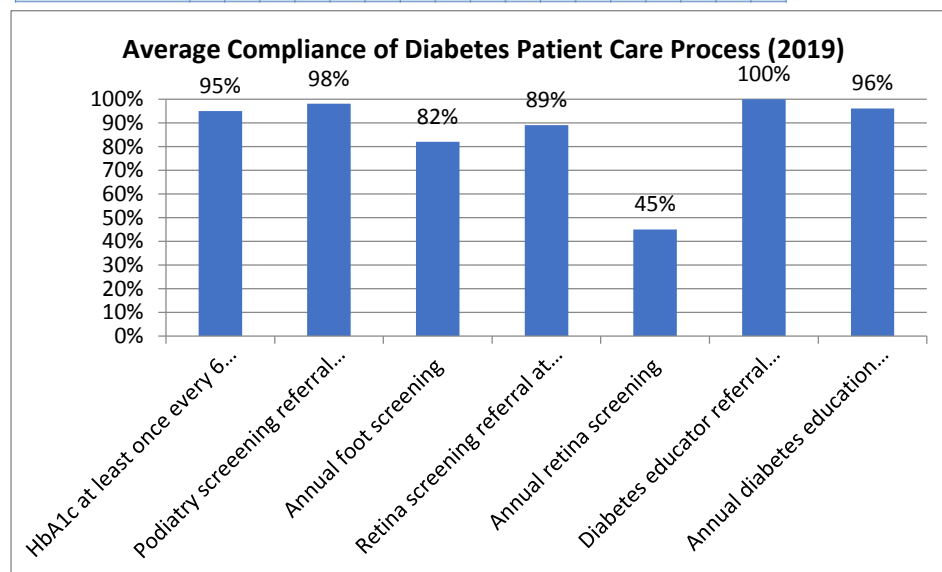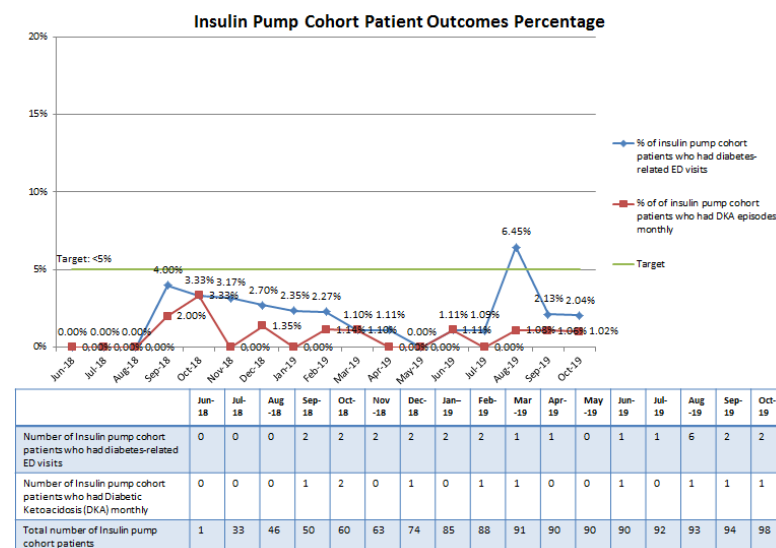
Introduction: Diabetes Mellitus Type 1 patients on insulin pump therapy are complex cohort of patients that need a multidisciplinary approach to optimize their glucose levels, prevent hypoglycemia and prevent Diabetic Ketoacidosis (DKA).The use of this technology mandates a team that empowers patients to take control of their disease including teaching, support, and follow up.

Objective: To improve clinical outcomes (DKA and diabetes-related emergency visits) of insulin pump cohort patients through multidisciplinary team approach.

Aim: To sustain <5% incidence of DKA and diabetes-related emergency visits among insulin pump cohort patients over a period of 1 year.

Methods: A way to identify the patient cohort was established last June 2018. An MDT was formed consisting of diabetologist, diabetes educator, dietitian, podiatry nurse, and patient pathway coordinator. The team meets once monthly for 1 hour to discuss the care of 8 cohort patients. Triage criteria were set to aid in scheduling the patients for MDT discussion.

Results: Presently, there are 98 patients in the cohort and 70 patients went through MDT. Below are graphs of patient outcomes and care processes' compliance.

Insulin Pump Cohort Patient Outcomes Percentage

	Jun-18	Jul-18	Aug-18	Sep-18	Oct-18	Nov-18	Dec-18	Jan-19	Feb-19	Mar-19	Apr-19	May-19	Jun-19	Jul-19	Aug-19	Sep-19	Oct-19
Number of Insulin pump cohort patients who had diabetes-related ED visits	0	0	0	2	2	2	2	2	2	1	1	0	1	1	6	2	2
Number of Insulin pump cohort patients who had Diabetic Ketoacidosis (DKA) monthly	0	0	0	1	2	0	1	0	1	1	0	0	1	0	1	1	1
Total number of Insulin pump cohort patients	1	33	46	50	60	63	74	85	88	91	90	90	90	92	93	94	98

Average Compliance of Diabetes Patient Care Process (2019)

Assessment of the Reporting and Methodological Quality of Systematic Reviews and Meta-analyses With Protocols in Diabetes Mellitus Type II: A Review of Systematic Reviews

Dr. Daniel Rainkie, Nada Nabil Abdelkader and Zeinab Abedini

Objectives: Our research question was to identify the correlation between the reporting of manuscripts and protocols. The second objective was to identify the association between reporting and methodological quality of systematic reviews and meta-analyses using PRISMA-P, PRISMA, and AMSTAR2 in type II diabetic patients using hypoglycaemic agents.

Methods: In this review, we searched PubMed and Embase for only systematic reviews and/or meta-analysis with protocols assessing any drug therapy (hypoglycaemic agents) for type II diabetes. We included articles from (01/01/2015) till (20/03/2019). Guidelines, Cochrane reviews and systematic reviews/meta-analysis without protocols were excluded. For statistical analysis; Kolmogrov-smirnov was used for normality, while Pearson's correlation test was used for the primary objective, and multiple linear regression for the secondary one (p-value <0.05)

Results: 58 studies were found eligible and a randomized sample of 19 articles were included. The reporting of PRISMA (93.2%) was better than PRISMA-P (66.0%), however, the availability of protocols has increased from 2015 (5%) compared to 2019 (38%). Regarding the primary outcomes, there was no correlation between PRISMA-P and PRISMA. The secondary outcome showed no association between PRISMA-P and AMSTAR2 (p-value=0.245) and PRISMA and AMSTAR2 (p-value=0.182) scores.

Conclusion: In systematic reviews assessing type II diabetes management through hypoglycaemic agents, the reporting of the protocol for systematic reviews was not associated with adequate reporting in the published manuscript; as good or bad reporting of protocols doesn't necessarily mean good or bad reporting of manuscripts. There was no association found between complete reporting assessed by PRISMA-P for protocols or PRISMA for manuscript and methodological quality assessed by AMSTAR2.

A Collaborative MDT approach to managing Type 2 Diabetes between Primary and Secondary Care

Samya Ahmad AL – Abdulla[1], Buthaina Ibrahim[2], Dahlia Hassan[1], Abdulazim Modasser[1]

[1] Primary Health Care Corporation, [2] Endocrine Department- HMC

Introduction: Globally Type 2 diabetes is rapidly on the rise with an estimated 463 million adults (between the age of 20-79) currently living with diabetes in 2019. The burden of managing Diabetes remains to be a global challenge and an economic burden with high health care costs. Multidisciplinary care delivered through an MDT is considered one of the best practices in the management and treatment of chronic diseases namely Diabetes, thereby achieving better management outcomes and patient centered care through a team approach.

Objectives: To investigate whether patients with Type 2 Diabetes that were reviewed in a Diabetes Multidisciplinary Team (MDT) case discussion can achieve better outcomes in management and avoid long term complications.

Target population: Type 2 diabetes patients from a primary care clinic list with HbA1c of 9-11%.

Method: Weekly MDT meeting forum was created and conducted by family physicians with special interest in diabetes from the primary care setting (Primary Health Care Corporation/ PHCC) alongside an Endocrinologist/ diabetologist from secondary care to discuss, review and recommend management of identified uncontrolled type 2 diabetics within the community. The MDT also encompassed a dietitian, social worker, diabetic nurse, health educator and care coordinator, all working towards a personalized and individual care plan to help achieve desirable outcomes. The plan was then shared with the patient's primary care physician for further discussion and implementation.

Primary outcome: Patients with an elevated HbA1c levels of (9-11%) were identified as per primary and secondary care criteria for referral into the MDT forum. Results from the initial phase revealed a 1.26% mean reduction in HbA1c amongst those patients discussed.

Conclusion: Diabetes MDT meetings can contribute to achieving better glycemic targets, thereby reducing referrals to secondary care and reducing the progression of long-term complications; while providing personalized and patient centered care with better health outcomes.

Artificial Intelligence (AI) & Gamification In Diabetes Care
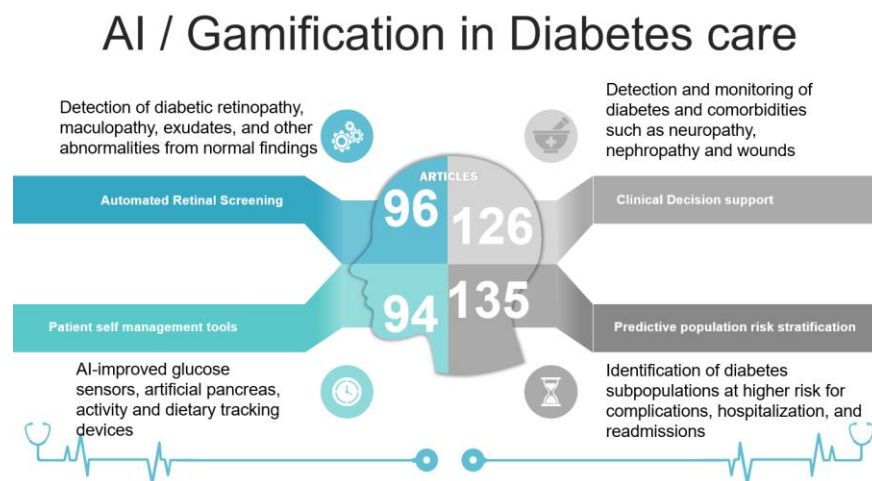
Mr. Raghakrishnan Mahalingam

Health Information Communication & Technology, HMC

Background: With as estimated 440M global diabetes patients & one-in-two still remains undiagnosed and untreated, Artificial intelligence (AI) & Gamification platform expectations are looking for a major shift towards Diabetes care management as indicated by the global trend. There is a vital need for an advanced care management techniques to ensure collaborative health for diabetic patients which can be effectively managed to improve clinical outcome and contain healthcare costs. There are few immediate needs to address which are patient-centric management regarding high incidence diabetic diseases and identification and optimization of at-risk parameters.

Methods: This is an ideation for exploring "Artificial Intelligence (AI) & Gamification" implementation to tackle the diabetes medical care through advanced techniques like employing Virtual coaches, sensor networks, gamification platforms. Hence, a study of 400+ articles were taken as reference under four major areas of specialization that includes Automated retinal screening, Clinical decision support , Predictive population risk stratification, Patient self-management tools(Figure 1).

Results: The expected outcomes and advantages are expected to be delivered for patient's diabetic care management are achieving better blood glucose control, reducing hypoglycaemic episodes, reducing diabetes comorbidities and complications. This will take care of millions of diabetes patients offering greater accuracy on early detection, dietary tracking devices for Person with Diabetes (PWD).

Conclusion: As a promising breakthrough, this idea has yielded that patients can be treated through advanced techniques which will bring down late detection of diabetes by various advanced clinical support systems and self-management tools.

AI / Gamification in Diabetes care

Detection of diabetic retinopathy, maculopathy, exudates, and other abnormalities from normal findings — **Automated Retinal Screening** — ARTICLES 96

Detection and monitoring of diabetes and comorbidities such as neuropathy, nephropathy and wounds — **Clinical Decision support** — 126

AI-improved glucose sensors, artificial pancreas, activity and dietary tracking devices — **Patient self management tools** — 94

Identification of diabetes subpopulations at higher risk for complications, hospitalization, and readmissions — **Predictive population risk stratification** — 135

Acute Pancreatitis Associated With Dual Use Of DPP-4 Inhibitor (Saxagliptin) And GLP-1 Receptor Agonist (Liraglutide)

Sarah Premraj[1], ElameinYousif[1], Mohamed El-Rishi[2]
[1]Specialist, Internal medicine [2]Consultant Endocrinology and diabetes
Al-Ahli Hospital, Doha, Qatar

Patients with diabetes mellitus are at an increased risk of acute pancreatitis in general. Drugs such as DPP-4 inhibitors and GLP-1 agonists are known to be associated with acute pancreatitis, and an unlicensed combination of these two drugs could double the risk.

A 55 year old gentleman with a background of type 2 diabetes, hypertension, dyslipidaemia, coronary artery disease and gout, was admitted in September 2019, with complaints of severe epigastric pain radiating to the back for 3 days. He was on treatment with Kombiglyze (Saxagliptin/ Metformin), Gliclazide, Empagliflozin and Insulin Degludec (Tresiba). He had recently been started elsewhere on Liraglutide (Victoza), but he had commenced himself on higher than recommended dose (1.8mg daily). On admission, he was found to be in severe pain, but with stable vital signs.Examination of the abdomen revealed tenderness in the epigastrium. Investigations revealed a high capillary blood glucose (464 mg/dL), with elevated serum lipase (2343 U/L), raised amylase (146 U/L),mildly raised triglyceride (3.31 mmol/L),high fasting blood sugar (8.3 mmol/L) and HbA1c 11.9%, normal white blood cell counts, CRP, urea and electrolytes, liver function tests, and serum calcium,. Ultrasound scan of the abdomen revealed no evidence of pancreatitis or gall bladder disease but CT scan showed edema and fat stranding around neck of pancreas suggestive of acute pancreatitis.He was diagnosed to have acute pancreatitis based on clinical, biochemical and radiological features, as a result of an irrational and unlicensed combination of DPP-4 inhibitor with high dose GLP-1 agonist.

He was managed conservatively, his offending drugs were discontinued and subsequent blood investigations showed declining pancreatic enzymes. His blood sugars also came under optimal control.

The index of suspicion for acute pancreatitis must be high in any patient with diabetes mellitus on DPP-4 inhibitors and/or GLP-1 agonist who presents with acute abdominal pain. Careful consideration should be given to the potential risk of pancreatitis before initiating these medications, with gradual up-titration of liraglutide. Patient education while initiating any new drug should be emphasized.

The effectiveness of continuous renal replacement therapy (CRRT) in severe hypertriglyceridemia-induced multi organs failure (MOF).

El Madhoun I1, Emam A2
1 Consultant Nephrologist, Al Wakra Hospital, Qatar
2 Nephrology Specialist, Al Wakra Hospital, Qatar

Introduction: Severe hypertriglyceridemia- induced acute pancreatitis & MOF is a rare but fatal condition, Fenofibrates is still the evident treatment. Few case reports addressed the role of CRRT in severe hypertriglyceridemia [1-3]. In this case we used CRRT for severe complicated hypertriglyceridemia which showed excellent response.

Case Presentation: A 29-year-old male with no past medical history presented with severe abdominal pain and vomiting for one day. On examination BP=168/112 mmHg, temp.=38.5^{o}c, respiratory rate= 34/minute, O2 saturation: 90%, abdomen was tender all over. He was put on oxygen 3 L/min. Blood samples were taken (were lipemic) showed triglyceride (TG) 11.3 mmol/l, lipase >800 U/L, WBC= 16000/L, CRP= 160 mg/L & creatinine=140 umol/l. CT abdomen showed acute necrotizing pancreatitis and mesenteric vein thrombosis. Patient desaturated more, so he was intubated. Next day despite medical treatment including fenofibrate 200 mg/day, he became oliguric, TG went up to 14.7 3 mmol/l, CRP=486 mg/L and creatinine=290 umol/l.

We provided CRRT for 24 hours (Continuous veno-venous haemodialysis with 1.5 m^{2} dialyzer, blood flow rate 100 ml/min, dialysate flow rate 35ml/kg/h without heparin or ultrafiltration), after which TG came down to 8.1 mmol/l, patient started to pass urine, inflammatory markers came down. Patient was extubated 1 week after, his symptoms recovered fully. He was discharged after 10 days with TG=2.4 mmol/l and creatinine = 77 umol/l.

Discussion: In this case we used CRRT for severe hypertriglyceridemia especially when complicated by MOF, we believe its rapid lowering of TG contributes to better outcome and reduction of mortality and morbidity in such patients.

Hypophosphatemic Osteomalacia In A Young Adult: Case Report

Firjeeth Paramba [1], Silas Benjamin[1]

1. Department of Internal Medicine, Hamad Medical Corporation, PO Box 3050, Doha, Qatar.

Introduction: Chronic hypophosphatemia caused by excess renal excretion of phosphate can cause inadequate mineralization of bone matrix. Tumour induced osteomalacia is a rare acquired paraneoplastic syndrome causing excessive renal excretion of phosphate and most patients have an over expression of fibroblast growth factor 23(FGF 23).

Case Report: A 34-year-old gentleman presented with severe pain in his left ankle and was found to have a calcaneal fracture. Over 6 months he continued to have bone pain and significant reduction in mobility. MRI showed multiple non traumatic fractures and Bone densitometry showed T score of -3 right femur neck. Fibroblast growth factor 23 was not measured due to unavailability of investigations at the institution. Further investigations showed nasopharyngeal tumour for which he underwent surgical removal. He improved clinically and his biochemical parameters 1 year post-surgery showed Phosphate 1.16mmol/L, Alkaline phosphate 165 u/L, Cal – 2.29 mmol/l.

Lab findings:

serum calcium	2.21mmol/L (2.10-2.55)
Phosphate	0.49 mmol/L (0.74-1.52)
Alkaline Phosphate	338 u/L (40-150)
Vitamin D	35 ng/mL
PTH	28 pg/ml (8.0-74)

Renal Tubular reabsorption of phosphate (TMP –GFR) - 1.9 mg/ 100ml (Age based normal TmP/GFR in males (2.5-3.5 mg/dl). Tumor induced osteomalacia is characterized by low TmP/GFR levels.
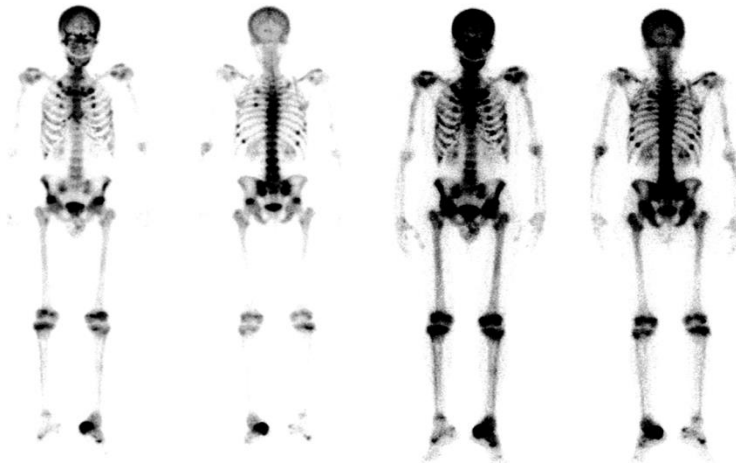
Images:

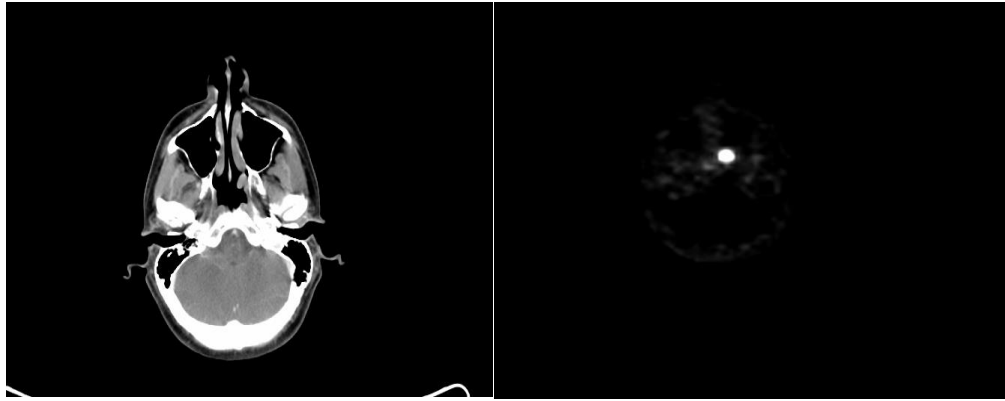**Fig 1:** Bone scan showing increased radiotracer uptake at various sites

Fig 2: DOTATE PET CT shows vascular enhancing lesion from lateral wall of left nasal cavity

Discussion: A secondary cause of hypophosphatemia causing metabolic bone disease is a diagnostic challenge. Tumour induced osteomalacia is a rare condition, usually caused by tumours arising from mesenchymal or mixed connective tissue. Biochemical abnormalities may show a high FGF 23 level, Low serum phosphate, high urinary phosphate. Ga-DOTATATE PET/ CT is reported to be sensitive in localizing these rare tumours. Definitive treatment involves complete removal of tumour which leads to clinical and biochemical improvement.

Challenges in managing hypertriglyceridemia induced acute pancreatitis during pregnancy

Dr Mustafa Seidahmed Mustafa , Dr Abdul Majeed Maliyakkal

Internal medicine Department, Al Wakra Hospital

Introduction: Acute pancreatitis is a rare condition in pregnancy. Hypertriglyceridemia is responsible for 56% of pancreatitis in pregnancy*. Hopefully this report will raise awareness of the difficulties in managing such condition

Case Report: A 35 years old lady 30 weeks pregnant (gravida 5, para 4), presented with severe abdominal pain radiating to the back and associated with persistent nausea and vomiting. She has history of gestational diabetes, well controlled on insulin and metformin. She has strong family history of hyperlipaemia. Upon admission she was diagnosed as acute pancreatitis secondary to hypertriglyceridemia based on typical pain, high amylase and lipase (471 U/L, 280 U/L) and triglyceride >11.3mmol/l.   Ultrasound showed evidence of pancreatitis, with gall stones but no signs of cholecystitis. Serum was lipemic with pseudohyponatremia, Na 123 mmol/l and hypocalcaemia. She was very sick initially. Patient was assessed by multidisciplinary team including physician, intensivist, obstetrician, neonatologist, anaesthesiologist and dietitian. The team decision was to manage her conservatively as far as she remains stable. Plasmapheresis was considered, but wasn't available, so was started on insulin and dextrose infusion along with fenofibrate 200mg and omega3 ethyl ester 1000 mg daily. Genetic testing was considered. She responded, pain gradually subsided and triglycerides dropped significantly, however upon discontinuing the infusion, triglycerides started to rise, hence she required the infusion repeatedly. She remained hospitalized for one month until she delivered a male baby of 2.075 kg without anomalies at 34 weeks following labour induction.

Conclusion: We encountered these challenges:

-Rarity of the condition and lack of experience among clinicians.

- Lack of clear guidelines for screening and managing such cases

-Triglycerides tend to rise after stopping insulin dextrose infusion. It fluctuated between 22 - 8.2. mmol

-Laborious infusion requiring close monitoring for hypoglycaemia.

-The need for multidisciplinary team

Pseudohypoparathyroidism Presented with Seizure: A Case Report and Literature Review

Mostafa Najim[1], Riyadh Hammamy[1], Mohammed Ashour[1], Asaad Imameldin[1]
[1]Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar

Background: Symptomatic hypocalcaemia is frequently encountered in the emergency department necessitating hospital admissions. It has a variety of underlying aetiologies with hypoparathyroidism and vitamin D deficiency being the commonest. However, rarer aetiologies such as Pseudohypoparathyroidism (PHP) in our case should not be overlooked.

Case report: We report a case of a young female patient presented with generalized tonic clonic seizure. ECG showed prolonged QT interval which pointed towards a metabolic cause and this was confirmed by the laboratory results which showed a low calcium level. A parathyroid pathology was obvious as the phosphate level was elevated. Pseudohypoparathyroidism was diagnosed, rather than hypoparathyroidism, as the parathyroid hormone (PTH) level was elevated. Other relevant differential diagnoses were excluded. The patient was treated with intravenous calcium in the acute settings and kept on regular oral calcium, calcitriol and Sevelamer.

Conclusion: Pseudohypoparathyroidism is a rare disease causing hypocalcaemia that should be kept in the list of differential diagnosis.

Table 1: Laboratory tests

Laboratory test	Patient's values	Normal reference range
White blood cells (10^3/µL)	16.4	4-10
Hemoglobin (g/dL)	11.6	12-15
Platelet (10^3/µL)	273	150-400
Urea (mmol/L)	3.5	2.76-8.07
Creatinine (µmol/L)	48	53-97
Sodium (mmol/L)	137	135-145
Potassium (mmol/L)	3.1	3.6-5.1
Chloride (mmol/L)	92	96-110
Magnesium (mmol/L)	0.72	0.66-1.07
Glucose (mmol/L)	6.4	3.3-5.5
C-reactive protein (mg/L)	< 5	0-5
Bicarbonate (mmol/L)	17.5	24-30
Albumin (g/L)	47	35-50
Corrected Calcium (mmol/L)	1.2 **Low**	2.1-2.6
Phosphorus (mmol/L)	1.86 **High**	0.87-1.45
Creatine kinase (U/L)	426	26-192
Myoglobin (ng/mL)	48	25-58
24-hour Calcium (mmol/24 hours)	2.2	2.5-7.5
Parathyroid hormone (pg/mL)	108 **High**	15-65
Vitamin D (ng/mL)	15 **Low**	30-80
Thyroid stimulating hormone (mIU/L)	2.51	0.27-4.20
Thyroxine (pmol/L)	12.1	12-22

Figure 1. Plain CT head showing extensive bilateral symmetrical calcifications of basal ganglia, cerebellar dentate nuclei and subcortical white matter.
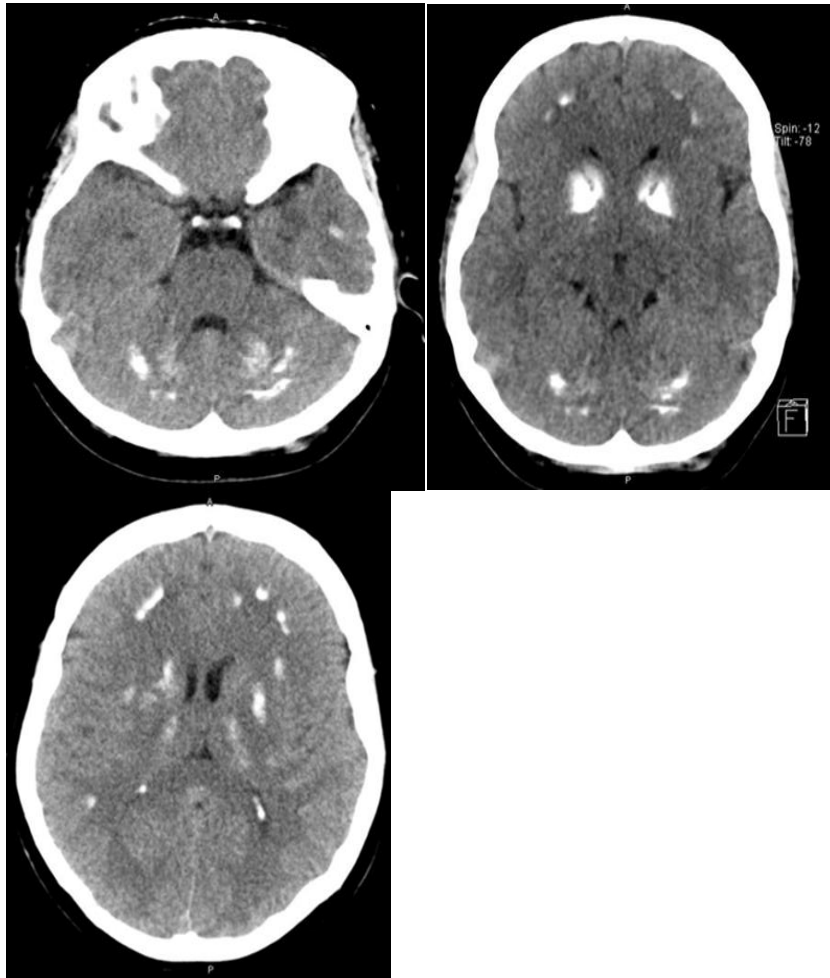
A case of ovarian hyperthecosis in a postmenopausal female with incidental findings of unilateral renal cell carcinoma and bilateral adrenal adenomas

Zaina Alamer[1], Khaled Baagar[1], Samir Al Hyassat[2]

[1]Endocrine department, Qatar Metabolic Institute, Hamad Medical Corporation, Doha, Qatar.
[2]Department of Laboratory Medicine and Pathology, Hamad Medical Corporation, Doha, Qatar.

Introduction: Ovarian Hyperthecosis (OH) is associated with slowly progressive virilization, and affects mainly postmenopausal females.

Case description: A 54-year-old postmenopausal woman presented with hirsutism, frontal balding, and deepening of voice for a year. On examination, she looked masculine with hirsutism over her face, chest and shoulders. Laboratory revealed testosterone 10.32 nmol/L, repeated 9.41 (0.69 - 2.78), and DHEAS 1.8 umol/L (1.5 – 7.7). CT scan showed bilateral adrenal adenomas and a suspicious left renal pelvic mass. Trans-vaginal ultrasound and MRI pelvis showed enlarged ovaries (7 ml) with no lesions. The 1 mg dexamethasone suppression test excluded Cushing syndrome, and DHEAS was suppressed to 1.1. Also, primary aldosteronism and pheochromocytoma were excluded. This work-up denoted an ovarian origin of her hyperandrogenism, mostly due to OH. She underwent left radical nephrectomy and histopathology showed clear cell renal cell carcinoma.

Later, she had abdominal hysterectomy with bilateral Salpingo-oophorectomy. Histopathology confirmed bilateral OH with inactive endometrium. Thereafter, testosterone was normal with improvement of the patient's virilization.

Discussion: Testosterone levels in OH overlap with that seen in malignant adrenal and ovarian tumors. Thus, rigorous assessment of the source of hyperandrogenism is required. Our patient had bilateral adrenal adenomas, which increased the diagnostic complexity. However, the work-up was indicative of OH. Bilateral oophorectomy is the definitive treatment of OH, alternatively a long-term GnRH agonist with careful follow-up can be used if surgery is not desired or risky. Hysterectomy can be done for OH cases, as there is a risk of endometrial atypia secondary to estrogen produced by aromatization of the high testosterone. Up to our knowledge, this is the first reported case of OH with incidental findings of renal cell carcinoma and bilateral adrenal adenomas.

Non-ST Segment Elevation myocardial infarction shortly after starting steroid replacement therapy in patient with adrenal failure

Mustafa Siedeahmed
Internal Medicine Department, Al-Wakra Hospital, HMC

Introduction: Adrenal failure is uncommon disease (1-4). Little is known about cardiovascular disease in adrenal failure, particularly after steroid replacement. Recent reports have linked adrenal failure treatment with cardiovascular disease (5-7). We report 71 years old female who developed non-ST-segment myocardial infarction following steroid replacement.

Case Report: A lady with history of thyroidectomy and parathyroidectomy in 2008. Subsequent biopsy showed Hashimoto thyroiditis. She is diabetic, hypertensive, hypothyroid and morbidly obese. She was admitted with extensive lower limb oedema, found to have hyponatremia (125-129 mmol/l), subsequent tests revealed adrenal insufficiency (19.22 mmol/l), ACTH was 51 pg/ml. MRI showed partially empty sella, CT adrenal showed bilateral adrenal atrophy, she improved on treatment with resolution of hyponatremia. Pituitary hormones were within normal. Tests to evaluate oedema revealed normal ejection fraction 68%, normal troponin T 14.58 mg/l, normal protein creatinine ratio, normal renal and liver function. Her thyroid function test repeatedly normal, HA1C 7.3%. She was discharged on hydrocortisone15 & 5 mg plus her regular medications. She was readmitted 3 day after discharge with severe shortness of breath and chest discomfort. She was admitted to intensive care unit with pulmonary oedema and non-ST segment elevation myocardial infarction. Labs showed raised troponin T (492, 377.2 mg/l), raised proBNP 2705 pg/ml. Chest X ray revealed pulmonary oedema. Ejection fraction was 34% with regional wall motion abnormality, she remained under cardiologist's management for 10 days, with improvement finally. This case is unique being presenting so shortly after starting 20mg/day of steroid replacement.

Conclusion: Physicians should know about increased cardiovascular risk in adrenal failure, educate and treat patients at high risks. Risk is increased with steroid replacement. Dose > 20mg associated with more risk, probably due to endothelial dysfunction and inflammatory involvement.

A Case of Multiple Endocrine Neoplasia Type 1 and Papillary Thyroid Cancer

Zaina Alamer, Khaled Baagar, Zaina Rohani, Mahmoud Zirie

Endocrine Department, Qatar Metabolic Institute, Hamad Medical Corporation, Doha, Qatar

Introduction: Multiple endocrine neoplasia type 1 (MEN1) is rare and characterized by 3 main endocrine tumours (parathyroid, enteropancreatic, and pituitary).

Case presentation: A 30-year-old man presented with abdominal pain. He was vitally stable, dehydrated with coarse facial features, nodular goitre, and trunk neurofibroma-like lesions. Laboratory showed calcium 3.2 (2.20-2.55 mmol/L), low phosphorous, and PTH 400 (15-65 ng/L). He received intravenous saline, calcitonin, and zoledronate. During hospitalization, he developed hypoglycaemia 1.6 mmol/L with C-peptide 5.48 (1.10-4.4 ng/mL), and insulin 22.8 (2.6-24.9 mcunit/mL). Sestamibi scan revealed parathyroid glands hyperplasia. MRI abdomen showed pancreatic lesion suggestive of insulinoma. He had prolactin > 100000 (85-323 mIU/L), IGF-1 456 (96-228 ug/L), secondary hypogonadism and hypothyroidism, and a normal synacthen test. Growth hormone suppression test confirmed acromegaly. Pituitary MRI showed pituitary macroadenoma. Perimetry was normal. MEN1 was clinically confirmed with primary hyperparathyroidism, insulinoma, and pituitary macroadenoma with hyperprolactinemia and acromegaly. Thyroid nodules FNA showed follicular neoplasm. The multidisciplinary team recommended thyroxine, cabergoline, insulinoma surgery, and total thyroidectomy plus total parathyroidectomy with auto-implantation of parathyroid. Histopathology confirmed a well differentiated pancreatic neuroendocrine tumor, and a 9 mm papillary thyroid cancer (PTC) (pT1aN0). Thereafter, He had hypoparathyroidism and no hypoglycaemia. We kept him on thyroxine and monitored his response to cabergoline.

Discussion: MEN1 can be diagnosed genetically, or clinically by having 2 of the main 3 tumours or 1 tumor in a first-degree relative of a diagnosed case. Our patient had the 3 tumours. MEN1 pituitary adenomas are usually multi-hormonal. Genetic testing is essential for index cases and unaffected at-risk relatives to decide further screening. The MEN1 individual lesions management is similar to sporadic cases; however, patients require life-long surveillance. The PTC in MEN1 patients is usually clinically insignificant but association between both needs further studies.

Anabolic Steroids Induced Delirium-A Case Report

Mohamed Adil , Shah Khoodoruth

Department of Psychiatry, Hamad Medical Corporation, Doha, Qatar.

Introduction: Anabolic steroids are commonly used by athletes, body builders and young adults to improve muscle strength. Deleterious effects of anabolic steroids on physical health are well-established. Psychiatric aspects are of particular importance and include psychosis, delirium, mania, depression and aggression.

Materials and Methods: We describe the case of a young gentleman who was managed as a case of androgenic steroid induced delirium.

Case Report: A 33 years old gentleman presented with increased aggression, hostility, and destructive impulses. He was a regular user of testosterone propionate, testosterone cyprionate and trenbolone acetate up to 200 mg daily in injectable form. Laboratory results showed decreased plasma testosterone level of 9.59 nmol/l (10.4-37.4 nmol/l). Sex Hormone Binding Globulin was 23.8 nmol/l (18.3-54.1 nmol/l) and bioavailable testosterone was 5.110 nmol/l (4.36-14.30 nmol/l)(Table 1). He was managed as a case of anabolic steroids induced delirium. After addition of regular haloperidol and quetiapine, his sensorium, speech and behaviour improved (Figure 1). He was discharged on haloperidol 7.5 mg and quetiapine 700 mg daily.

Conclusion: The purpose of this case report is to emphasize on the neuropsychiatric effects and management of anabolic steroids manifested by delirium, increased aggression, hostility, and destructive impulses.

Table 1

Cortisol AM	548 nmol/l
Testosterone	9.59 nmol/l (10.4-37.4 nmol/l)
Bioavailable testosterone	5.110 nmol/l (4.36-14.30 nmol/l)
Sex Hormone Binding Globulin	23.8 nmol/l (18.3-54.1 nmol/l)
Luteinizing hormone	4.2 IU/L(1.7-8.6 IU/L)
Follicle Stimulating Hormone (FSH)	3.0 IU/L(1.5-12.4 IU/L)
Prolactin	498 mIU/L (85-323 mIU/L)
TSH	0.32 mIU/L (0.30-4.2 mIU/L)
Free T4	20.4 mIU/L (11.6-21.9 mIU/L)
Androstenedioine	4.32 pmol/L (1.60 - 14.70 pmol/L)
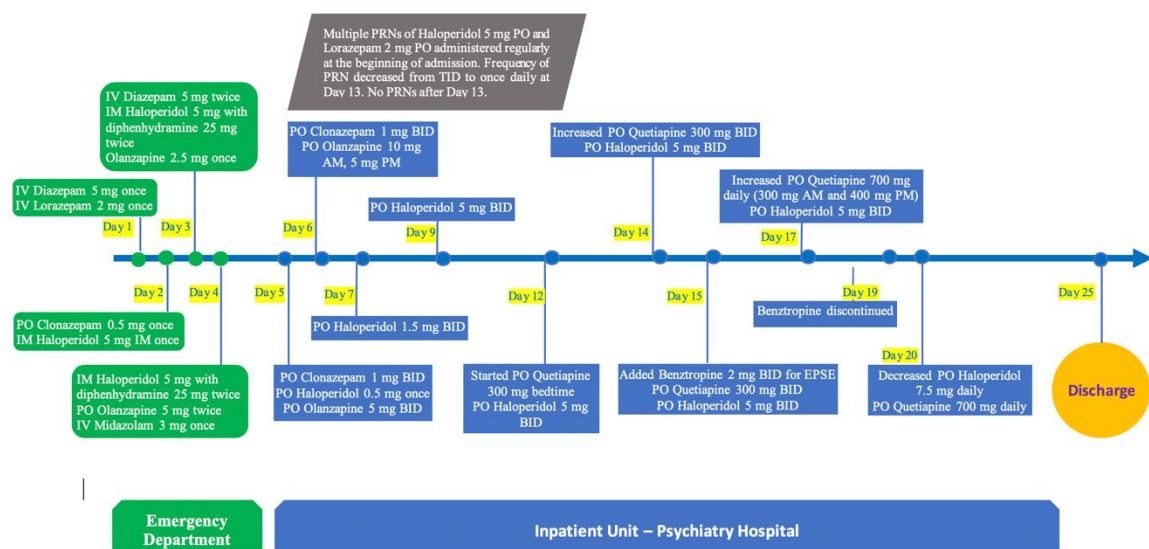
Plasmapheresis as a bridging to total thyroidectomy for a life-threatening thyroid storm

Mohammad Khair Hamad[1], Khaled Baagar[1], Ibrahim Hassan[2], Tasleem Raza[2], Abdel Rauof Akkari[2] Wajiha Gul[1].

[1]Department of Medicine, Endocrinology Division, Hamad Medical Corporation, Doha, Qatar.
[2]Department of Medicine, MICU Division, Hamad Medical Corporation, Doha, Qatar.

Introduction: Patients with thyroid storm and resistance or contraindications to conventional medications may receive plasmapheresis until they have the definitive therapy.

Case presentation: A 46-year-old female presented with palpitations, nausea, and abdominal pain. She was anxious, afebrile with heart rate 204/minute, blood pressure 100/65 mmHg, and respiratory rate 24/minute. She had exophthalmos, goitre and bilateral basal lung crepitations. ECG revealed rapid atrial fibrillation. Laboratory showed FT4 90 (11.6-21.9 pmol/L), FT3 16 (3.7-6.4 pmol/L), and TSH 0.01 (0.3-4.2 mIU/L). Burch-Wartofsky score was 55/140. Her presentation was suggestive of Graves' disease with thyroid storm.

She was started on propylthiouracil (PTU), propranolol, Lugol's solution, cholestyramine, and intravenous hydrocortisone. However, she developed cardiogenic shock with multiorgan dysfunction and she was intubated. PTU was held because of liver injury; ALT 296 (0-33 U/L) and AST 827 (0-32 U/L). Extracorporeal membrane oxygenation (ECMO) was initiated for cardiopulmonary support and continued for 4 days until the improvement of organs' function including liver enzymes. Therefore, carbimazole was tried, then it was stopped shortly as direct bilirubin reached 68 (0-3 umol/L).

As thyroid hormones remained high, plasmapheresis was started. Liver enzymes improved and PTU was tried again; however, it was discontinued due to increasing liver transaminases. After 6 plasmapheresis sessions with FT3 6 and FT4 27, she underwent thyroidectomy. Her thyroid hormones increased after surgery, mostly secondary to thyroid manipulation, requiring 2 plasmapheresis sessions. After the normalization of thyroid hormones, thyroxine replacement was started.

Discussion : The raised liver enzymes were a barrier to thionamaides. With resistance to other medications, plasmapheresis was a rapid and safe option before thyroidectomy.

The mechanism of plasmapheresis is to eliminate thyroid hormones, TSH-receptor antibodies, and cytokines. The guidelines lack clear indications, timing of initiation, and patient selection for plasmapheresis.

Healing Of Foot Ulcer With Type 2 Diabetes Mellitus Treated With Vrana Ropana Chikitsa And Ayurvedic Precision Medicines - A Case Report

Saleena Ummer V*^, Ann Mariya Jose^, Shripathi Adiga^, Ciraj A M^, Kavitha S Shettigar^, L Ramachandra^

*Manipal College of Health Professions, ^Manipal Academy of Higher Education, Manipal

Abstract: Diabetic foot ulcer (DFU) is an intractable complication of diabetes mellitus (DM) with increasing hospitalization, morbidity, and mortality. Management of DFU is still challenging even with advanced treatments. Use of alternative therapies may be effective for the management of DFU. This case report was done after obtaining informed consent from the subject.

A 72 year male with Type 2 DM for 25 years was admitted with painful lesion on right foot since 5 years with loss of sensation and purulent discharge of Grade IV ulcer. The patient was on allopathic medication, Glycomet and Insulin therapy. Though surgery and skin grafting was performed, wound turned out into a non-healing ulcer colonized with Methicillin-Resistant Staphylococcus aureus (MRSA).

On admission the patient was instituted on Ayurvedic treatment of *Vrana ropana chikitsa* with *Triphala guggulu, Jatyadi Ghrita* and *Amrita guggulu,* given every day for 30 days and thereafter on every alternate day for three months. Percentage reduction in ulcer area during the treatment was recorded. Pre and post bacterial load also was determined.

There was a significant improvement in wound healing and a decrease in bacterial load after three months. *Vrana ropana chikitsa* with ayurvedic precision medications can be an effective adjunct in improving wound healing in DFU. Nerve regeneration along with antibacterial activity of Ayurvedic formulations may be a possible explanation.

Fig. 1. Before(a.) and After(b.) therapy

A Syndrome of Early Onset Obesity, Type 2 Diabetes, Insulin Resistance, Hypoactivity and Developmental Delay Caused by AMPKβ1 Mutation

Faiyaz Ahmad[1], Melissa Riachi[2], Senthil Selvaraj[1], Reem Hasnah[1], Navaneethakrishnan Krishnamoorthy[1], Kausik Banerjee[3], Maitrayee T. Kumarasamy[3], Reena Perchard[3], Christine Hughes[1], Jithesh Puthen[1], Detlef Bockenhauer[4], Raphael J. Courjaret[5], Anna M Halama[5], Xavier Estivil[1], Khaled Machaca[5], Khalid Hussain[1]

1. Sidra Medicine, Doha, Qatar; 2. UCL GOS Institute of Child Health, London, UK; 3. Queens Hospital, Romford Essex, UK; 4. Great Ormond Street Hospital for Children, London, UK; 5. Weill Cornell Medicine Qatar, Doha, Qatar

Background: Childhood obesity leads to insulin resistance and type 2 diabetes mellitus (T2DM). AMP activated protein kinase (AMPK) functions as an energy sensor, mostly by regulating fatty acid oxidation, glucose uptake, modulation of insulin secretion and inhibition of lipogenesis. AMPKβ1 is a regulatory subunit of AMPK. The dysfunctional AMPK has been linked to the development of T2DM, obesity, mitochondrial dysfunction, neurodegenerative and cardiovascular diseases, etc.

Patients: We report 2 siblings from a consanguineous family who presented with hyperphagia, severe early onset obesity, T2DM with insulin resistance and developmental delay, and increased energy uptake. Despite extensive investigations no known cause was found for their symptoms.

Method: Whole exome sequencing (WES) was performed on all family members. Primary fibroblast cell lines were established from patients and controls to study AMPK signalling, protein expression, and mitochondrial function. Human AMPK 3D-protein structure was used for the molecular modelling of the mutant protein.

Result: A novel homozygous missense mutation in AMPKβ1 in two siblings leads to multiple defects in AMPK signalling pathway with reduced basal and AICAR (AMPK agonist)-mediated AMPK activation and reduced AMPKβ1 protein expression. Reduced AMPK activation leads to increased acetylation of PGC1 (PPARγ coactivator1-alpha) and reduced cell growth in cultured skin fibroblasts.

Conclusion: We report a novel syndrome of hyperphagia, early onset obesity, T2DM with insulin resistance and global developmental delay associated with AMPKβ1 mutation, causing reduced AMPKβ1 protein expression and AMPK activity, due to defective AMPK signalling pathway. These observations provide further insights into the complex interactions between mitochondrial biogenesis, obesity, insulin resistance and T2DM.

A Case of Insulin Autoimmune Syndrome causing Hypoglycaemia

Marwa Mokhtar, Wajiha Gul, and Monica Skarulis

Department of Endocrinology, Qatar Metabolic Institute, HMC

Background: Insulin Autoimmune Syndrome (IAS) or Hirata disease is reported more in Asians. We report the case of a patient with acute onset hypoglycaemia secondary to IAS.

Case Presentation: A 64-year-old Arab male presented with 2 weeks history of episodic hypoglycaemia with blood glucose (BG) 40-60 mg/dl, unrelated to food and occurring throughout the day. His attacks were associated with sweating, dizziness and palpitations, relieved by intake of juice. He reported 3 kg weight gain.

Past medical history revealed hypertension and past HCV infection with negative PCR. His medications included bisoprolol 2.5 mg daily.

Physical examination was unremarkable. Laboratory investigations: Normal hepatic, renal and thyroid functions. 72 Hours fasting test was performed. At hour 3, the BG was 2.27 mmol (40.86 mg/dl), insulin > 1000 mU/ml (N: 2.6-24.9), c- peptide 15 ng/ml (N: 1.1-4.4), negative beta-hydroxybutyrate, with good glycemia response to glucagon 1mg. Urine sulfonylurea (SU) screen was negative. Insulin antibodies titre: 8.9 nmol/L (N: 0-0.02) and Proinsulin >700 pmol/L (N: 3.6-22). MRI Abdomen showed only 3 mm lesion in the pancreatic head, likely a cyst.

During hospitalization, the patient received dextrose 10% and octreotide injection. Episodes of hypoglycaemia improved with octreotide but did not resolve completely. Prednisolone 30 mg daily was started with improvement and was tapered slowly after 16 weeks. Repeat work up showed reduction in insulin 67.4 mcunit/ml, C- peptide 2.66 ng/ml and insulin antibody titres to 0.24 nmol/L and remission of hypoglycaemia.

Discussion: IAS can be triggered by drugs or viruses including hepatitis C and is associated with autoimmune diseases and hematologic malignancies. Short-term treatment with steroids was effective in treating hypoglycaemia. If the patient recurs, rituximab will be employed.

Conclusion: Physicians need to bear in mind the rare causes of hypoglycaemia while encountering such patients even in the absence of risk factors.

Cardiac tamponade combined with pleural and peritoneal effusions, as the presenting manifestation of primary hypothyroidism.

Muhammad Zahid[a], Gowri Karuppasamy[b]
[a]Senior consultant, Internal Medicine, HMC, Qatar.
[b]Clinical fellow, Endocrinology, HMC, Qatar

Case presentation:- A 38 year old woman presented with shortness of breath and fatigue since 2 months. She also had history of loss of appetite and menstrual irregularities.

On admission, physical examination was significant for muffled heart sounds, bilateral basal crackles jugular vein distension and bilateral ankle edema. Abdomen was distended and shifting dullness was positive. Her skin was dry and rough. Conjunctival pallor and macroglossia were also noted.

She underwent a two-dimensional echocardiogram that showed a large circumferential pericardial effusion, 50 - 60 mm anterior and posterior to the heart, with heart swinging within the effusion, indicating impending cardiac tamponade. Urgent pericardiocentesis was performed and pericardial drain was placed, with drainage of 1400ml of serous fluid. On analysis the pericardial fluid was exudative with negative cultures and cytology. Post pericardiocentesis, two-dimensional echocardiogram revealed minimal fibrinous pericardial effusion with no evidence of tamponade. Laboratory tests revealed severe hypothyroidism, hyperlipaemia and high creatine kinase level. She was also found to have bilateral pleural effusions and ascites. Pleural fluid chemistry was borderline between exudate and transudate with mixed cellularity. Both pericardial and pleural fluid were negative for acid-fast bacilli. Other investigations were negative, including autoimmune workup, investigations for tuberculosis and malignancy. CT chest, abdomen and pelvis did not show any features of malignancy or infection.

The cardiac tamponade was attributed to overt primary hypothyroidism, as all other aetiologies of tamponade had been excluded. Thyroxine replacement therapy was started. Her symptoms improved over the next two weeks.

Discussion: Pericardial effusion is one of the well-known manifestations of hypothyroidism, however cardiac tamponade is rare due to slow accumulation of fluid and marked distensibility of the pericardium. The case demonstrates that patients with hypothyroidism may not have the typical signs of cardiac tamponade, such as pulsus paradoxus, tachycardia or hypotension. Our patient is unique in having a combination of ascites, pleural effusion and pericardial effusion. The pathogenesis of multiple effusions in hypothyroidism is due to the generalized polyserositis, as well as increased leak of plasma proteins because of abnormal capillary permeability. Thyroxine replacement alone is sufficient for resolution of these effusions, however resolution may take about 2 to 12 months.

A Type 1 diabetes patient using interoperable Tandem t:slim X2 insulin pump with Dexcom G6 as a game changer in diabetes control

Khaled Baagar, Dabia Al Mohanadi, Hamda Ali, Salama Bashir, Kawsar Mohamud, Ameena Ahmed, Doha Sabbah, Samah Sobuh, Mohammed Bashir.
Technology And Diabetes Unit (TADU), Hamad Medical Corporation, Doha Qatar

Introduction: Management of type 1 diabetes (DM-1) is challenging due to the high degree of glucose fluctuation. Data from the DCCT showed that, as HbA1C approaches targets, the risk of severe hypoglycaemia increased remarkably. Semi-closed-loop Continues Subcutaneous Insulin Infusion (CSII) systems are promising technology that reduces glucose variability and allows patients with DM-1 to achieve glycemic targets while minimizing the risk of hypoglycaemia.

Case Presentation: We report of a 24-year-old female with DM-1 on multiple daily insulin injections (MDI), with HbA1C 6.4% on the expense of recurrent episodes of severe and non-severe hypoglycaemia. She also had an episode of DKA 6 months before her review. She has then started the education and training on CSII before flying back to her University in the USA. She has thence commenced on a Tandem t:slim X2 insulin pump and Dexcom G6 glucose sensor. Both devices are interoperable through Bluetooth allowing the CSII to suspend insulin delivery if hypoglycaemia is predicted - based on the sensor data. During her last visit, her HbA1C was 5.5% . The 2-months sensor data (fig-1) showed a lower degree of glucose variability with 81-84% of the time within the target range (70-180mg/dL), and only 6-7% of the time was below the targets (mostly modest hypoglycaemia).

Discussion: Tandem t:slim X2 pump can interoperate with other diabetes care devices by different manufacturers. No finger-sticks required for Dexcom G6 sensor calibration. This technology enabled the patient to achieve excellent control with negligible hypoglycaemia in a short time with much less hassle.
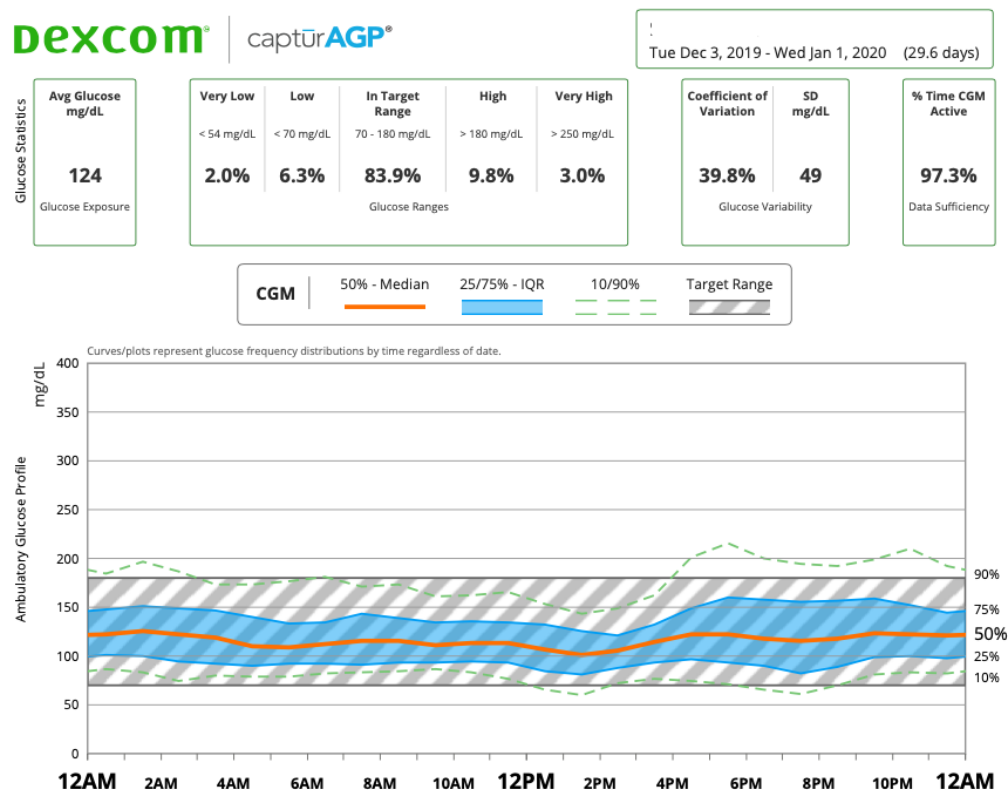
# Ectopic Parathyroid Adenoma; A Rare Cause of Primary Hyperparathyroidism

Obada Khalil, Khalid Baagar, Hind Yousif

Endocrine Department, Hamad General Hospital

Background: Parathyroid glands develop from the third and fourth pharyngeal pouches, descend with the thymus, and are located in the neck. An ectopic parathyroid gland can occur in 2% of the population. The ectopic gland can be one of the four parathyroid gland or could be a supernumerary one. Hyperparathyroidism due to an ectopic parathyroid adenoma is a rare condition which could be difficult to diagnose. It should be suspected in cases with persistent hyperparathyroidism despite surgical treatment. We present a case hyperparathyroidism due to ectopic parathyroid adenoma.

Case Presentation: This is a case of a 52 years old female patient who was undergoing blood investigations in Qatar Biobank . She was noted to have elevated corrected calcium levels (2.73 mmol/l) albeit she was asymptomatic . She was referred to the endocrine team where further testing confirmed the elevated corrected calcium levels, elevated parathyroid hormone (PTH) 365 pgl/ml, elevated 24 hours urinary calcium (6.4 mmol/ 24 hours) , normal renal U/S scan and osteopenia on the DXA scan. A Sestamibi scan showed an increased uptake in the mediastinum (fig-1) and the right inferior parathyroid region. U/S scan of the neck revealed a 3.3 cm right thyroid nodule. CT thorax showed a 2.8x2.6 cm mass, arising from the thyroid gland and abutting the trachea. Fine needle aspiration showed a colloid nodule. The patient underwent right hemithyroidectomy and mediastinoscopy with resection of the mediastinal ectopic parathyroid adenoma. Afterwards, the patient's serum PTH and Ca were normal.

Conclusion: To our knowledge, this is the first case report of ectopic parathyroid adenoma from Qatar. Ectopic parathyroid adenoma is a rare cause of hyperparathyroidism. Systematic approach for localizing parathyroid adenomas is critical to avoid missing this rare condition.
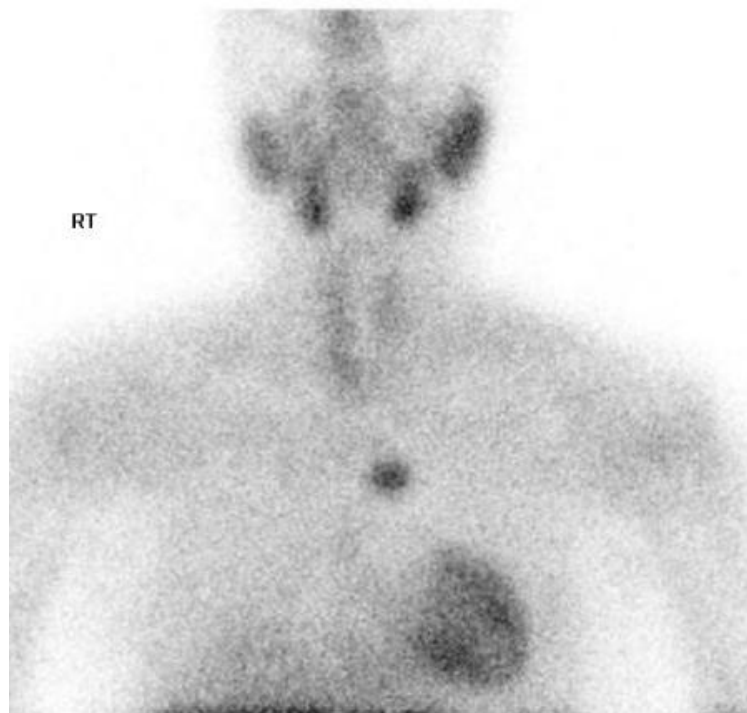
Thyroiditis-Induced Perimyocarditis

Rohit Sharma[1], Sundus Sardar[1], Yaser AlAhmad[2], Khaled Baagar[3]
1: Internal Medicine Department, Hamad Medical Corporation, Doha, Qatar
2: Cardiology Department, Hamad Medical Corporation, Doha, Qatar
3: Endocrinology Department, Hamad Medical Corporation, Doha, Qatar

Introduction: The association of thyroid disorders with heart diseases has been described. We report a rare case of hyperthyroidism secondary to thyroiditis leading to peri-myocarditis.

Case Presentation: A 38-year-old man, previously healthy, presented with severe chest pain radiating to left arm. He was afebrile with respiratory rate 18/minute, BP 149/88mmHg, and regular pulse 119/minute. Physical examination was unremarkable. ECG revealed infero-posterior STEMI with elevated troponin T (1196ng/L). Remaining labs and coronary angiography were normal. Echocardiogram was unremarkable with ejection fraction of 57%. Based on these findings with widespread ST-elevation and PR-depression on subsequent ECG, peri-myocarditis was suspected. High-dose aspirin and colchicine were administered. Tachycardia (115/minute) persisted despite metoprolol 25 mg twice/day. Further questioning revealed 1-month history of diarrhoea and 5-kg weight loss. He denied symptoms of preceding viral illness. He had no exophthalmos, lid retraction/lag, thyromegaly or tremors. TSH was 0.01 (0.30- 4.20mIU/L), FT3 32.8 (3.7-6.4pmol/L), and FT4 >100 (11.6-21.9pmol/L). Anti-TPO and TSH-receptor antibodies were normal. Thyroglobulin antibodies were elevated (813 IU/ml). Thyroid ultrasound was unremarkable. Cardiac MRI revealed subepicardial to mid-wall diffuse enhancement, suggestive of myocarditis. These supported our diagnosis of peri-myocarditis secondary to thyroiditis. He was discharged on aspirin 600 mg/day, colchicine 0.5 mg twice/day, and metoprolol 100 mg twice/day. After 2 months, thyroid uptake scan confirmed thyroiditis with low uptake. TSH was <0.01mIU/L, FT3 5.3pmol/L, and FT4 19.9pmol/L. He is on regular follow up to observe for TFTs.

Discussion: Acute peri-myocarditis often imitates acute coronary syndrome and should be considered in young patients with no cardiac risk factors and normal angiography. Thyroid evaluation may be useful especially in presence of non-cardiac symptoms e.g. diarrhoea and weight loss. Early intervention helps to protect the heart from deleterious effects of uncontrolled hyperthyroidism. Pathophysiology of thyroiditis and acute peri-myocarditis may be autoimmune or unnoticed viral infection.

Olanzapine induced Severe Hypertriglyceridemia and Acute Pancreatitis

Ashraf Ahmed, Hana Qasim, Mouhand Mohamed, Mohammed Danjuma
Internal Medicine department, Hamad General Hospital, Hamad Medical Corporation

Background: Severe hypertriglyceridemia (SHTG), >1000 mg/dl), is a common cause of acute pancreatitis (AP). SHTG can be due to primary or secondary lipid metabolism disorder. Olanzapine is an antipsychotic medication linked to developing obesity and dyslipidaemia. Few case studies linked Olanzapine to developing SHTG, causing AP. Here we report a case of possible olanzapine-induced AP due to SHTG with literature review.

Case Presentation: A 43-year-old gentleman with a history of psychotic disorder on Olanzapine 15 mg and Fluoxetine 20 mg for ten years, presented complaining of upper abdominal pain for two days. His Triglyceride level was 4250mg/dl, with high serum lipase> 400 U/L and HbA1c of 10%. Ultrasound abdomen ruled out gall bladder stones. He had no history of alcohol ingestion, had a normal thyroid profile. He was labelled as a case of SHTG induced pancreatitis and was managed with intravenous insulin. His TG improved after four days, reaching 470 mg/dl. Family history was negative for dyslipidaemia and sudden cardiac death. We are assuming that long term use of Olanzapine along with obesity and newly diagnosed diabetes contributed to his high triglycerides' levels, which induced pancreatitis. However, concomitant familial lipoproteinemia cannot be ruled out as genetic testing was not performed, given its limited added value at this stage.

Discussion and conclusion: Olanzapine is known to cause dyslipidaemia. However, causing SHTG leading to pancreatitis is rare. On reviewing the literature, we found 21 case reports and one case series reporting a total of around 60 patients developing olanzapine SHTG with AP. Clinicians should monitor the lipid profile and screen for metabolic syndromes when dealing with patients on olanzapine. Prevention is by proper counselling, encouraging healthy lifestyle changes, weight loss, avoiding concentrated sugars, exercising, and timely detection.

Myxoedema Madness: Neuropsychiatric Manifestations Unmasking Hypothyroidism

Sundus Sardar[1], Mouhand Mohamed[2], Abdelrahman Alzubier[3]
[1,2,3]Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar.

Background: Hypothyroidism is a common endocrine disorder and may be associated with neuropsychiatric disorders. We report a case of hypothyroidism-induced myxoedema psychosis in a patient post-total thyroidectomy.

Case Presentation: A 36-year-old lady, with no previous psychiatric history, presented with abnormal behaviour and aggressiveness. She had 1-week history of paranoid delusions, persecutory visual and auditory hallucinations, and claimed her roommates were planning to kill her. Previous medical history was significant for papillary thyroid carcinoma, post-total thyroidectomy three years ago, followed by liothyronine sodium 20mg twice daily and fractionated doses of radioiodine ablation therapy, after which she lost to follow up. Upon her current presentation, she was agitated and violent with hospital staff. Physical exam was unremarkable. She had no apparent signs of myxoedema. Initial workup showed normocytic anaemia, hypokalaemia, and elevated creatinine. Further investigations revealed thyroid stimulation hormone of 56.6mIU/L, low free T4 <0.5pmol/L, and elevated creatine kinase of 3601 U/L. MRI of the head was unremarkable. She was diagnosed as a case of hypothyroidism-induced psychosis and thyroxine 100mcg/day was initiated along with fluoxetine 20mg daily and haloperidol as needed. She was closely followed by psychiatry team and was transferred to Psychiatry Hospital for further management. Within 1 week, her symptoms improved and she was discharged with further scheduled follow-ups to monitor TFTs and further response to treatment.

Discussion: Hypothyroidism may be associated with neuropsychiatric manifestations; however, thyroid disorders may be overlooked as an aetiology in patients admitted with psychosis. This case emphasizes the importance of thyroid status evaluation in patients presenting with psychotic symptoms. In such cases, thyroid replacement therapy in conjunction with short-term antipsychotic medications results in successful recovery in hypothyroidism-induced psychosis.

Pheochromocytoma in Pregnancy: Report of a case

Wajiha Gul, Khaled Baagar, Hind Yousef, Mohammed Bashir.
Qatar Metabolic Institute, Hamad Medical Corporation, Doha, Qatar.

Introduction: Pheochromocytoma during pregnancy has serious-potentially fatal- consequences on both the mother and the fetus. It is often confused with severe pre-eclampsia resulting in delay in management.

Case Presentation: A 27-year-old female gravida 4, para 3, was admitted at 18 weeks of gestation because of high blood pressure 210/100 mmHg. She was known to have hypertension for four years. The patient reported intermittent episodes of palpitations, sweating and headaches. The work-up for secondary hypertension revealed an elevated 24-hour urine testing for vinyl mandelic acid (VMA) 108.310 (0 - 33 umol), normal normetanephrines 25.052 (0- 2.13umol), normal dopamine 3655 (0 - 3240 nmol), but elevated noradrenaline 10,719 (0 - 570 nmol). Both plasma normetanephrines and metanephrines were elevated; 8.22 (<0.94 nmol/l) and 0.24 (<0.37 noml/l), respectively. Screening for vasculitis, lupus, Cushing's disease, and primary aldosteronism was negative. MRI abdomen showed left adrenal mass of 6 x 5.5 x 5 cm with features suggestive of pheochromocytoma. RET proto-oncogene mutation testing was negative. Calcitonin level was normal. She was started on nifedipine, methyldopa and prazosin 1.5 mg twice daily, followed by a beta-blocker. Later in the second trimester, she underwent laparoscopic resection of the adrenal mass. Histopathology confirmed pheochromocytoma. Her blood pressure improved and she came off the anti-hypertensive medications. She delivered a healthy baby at term.

Discussion and conclusion : Pheochromocytoma presentation during pregnancy closely resembles pregnancy-induced hypertension and pre-eclampsia. Physicians need to keep a high index of suspicion to have timely diagnosis and management of pheochromocytoma during pregnancy Multidisciplinary planning of tumor resection by endocrinologist, adrenal surgeon, anesthesiologist and obstetrician, is critical in reducing the rates of complications during pregnancy.

A case of unilateral exophthalmos due to thyroid orbitopathy in a patient with subclinical hyperthyroidism.

Adeel Khan, Ahmad Muammar, Ijaz Kamal

Adeel Ahmad Khan, Ahmad Radwan Mahmoud , Ijaz Kamal Medical Resident,
Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar.

Abstract:

Introduction: Graves' disease (GD) is a disorder of autoimmune aetiology and Graves' ophthalmopathy (GO) is its most common extra-thyroidal manifestation. Most cases of GO are bilateral whereas unilateral ophthalmopathy is less common. Unilateral exophthalmos presents a diagnostic dilemma especially in a clinically euthyroid patient and exposes patients to unnecessary testing to rule out sinister causes.

Materials and Methods: We report a case of unilateral exophthalmos in a patient with subclinical hyperthyroidism who was extensively worked up for orbital tumour but later on found to have thyroid associated orbitopathy.

Case report: A 24 years old male patient presented with right sided exophthalmos for 6 months. He did not have any other visual or thyroid related symptoms. Laboratory results revealed low TSH, normal free T3 and free T4, elevated serum creatinine (418 umol/L) and positive TSH receptor antibodies. US KUB showed features of chronic kidney disease (CKD). MRI Head showed unilateral thyroid associated orbitopathy. Patient received 2 weeks course of oral steroid in his home country and his exophthalmos improved significantly.

Conclusion:
Graves' ophthalmopathy is the most common cause of unilateral exophthalmos even in patients who have subclinical hyperthyroidism.
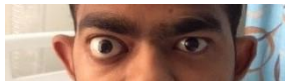
Fig.1   Right eye Exophthalmos

Fig. 2 Thickening of rectus muscles