

# First ASPED/ISPAD Diabetes Postgraduate Course Proceedings and Abstracts

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## Abstract

The first ASPED/ISPAD Diabetes postgraduate course was an initiative by the Arab Society of Pediatric Endocrinology and Diabetes (ASPED) in collaboration with the International Society of Pediatric and Adolescent Diabetes (ISPAD) and is exclusively sponsored by Lilly. It was held in Abu Dhabi and run by an expert group of faculty; four from ISPAD, five from ASPED and nine mentors from nine different countries over three days. Candidates were selected following open competitive applications which was advertised by both ASPED and ISPAD. Strict enrollment criteria were agreed on by the ASPED/ISPAD course committee. Sixty five candidates (out of 135 applicants) from 13 countries were enrolled and attended the course. Course curriculum was delivered in the form of lectures, interactive sessions, case scenarios and research presentation in small group sessions. The themes of the curriculum featured; Diabetes in Children; etiology, epidemiology and classifications, Diabetes in clinical practice and research, Technology applications in Diabetes, Diabetes management in special circumstances (school, sick days and Ramadan fasting), Diabetes complications; acute and chronic, Psychology and patient empowerment in Diabetes. Seven sessions were run by course faculty during which, 18 lectures were delivered. Five parallel small group sessions were run and featured 39 clinical case scenarios and 22 research projects presentations by candidates.

The course ended up with tasks to follow and recommendations. These included initiating ASPED diabetes registry amongst different Arab countries. Also, it was planned that a committee from ASPED will be formed to put together guidelines for fasting Ramadan by young people with diabetes. In addition, various multi-centric studies were proposed from different countries involving common diabetes issues. Neonatal diabetes and type 2 diabetes are particularly common in the ASPED region and collaborative work will be initiated. Feedback reports from candidates and faculty will be analyzed. Plans regarding curriculum, venue and course format for future annual courses will be implemented based on faculty and attendees feedback reports.

2. Be a body for governing the training of doctors in the field of Pediatric Endocrinology and diabetes through support of the existing fellowship programs and creating others. Other educational programs will be arranged to offer the most updated knowledge and experience to trainees in pediatric endocrinology.
3. Actively support training and education of specialist nurses, diabetes educators, dieticians and other allied healthcare professionals in the field of endocrinology and diabetes.
4. Promoting research and training in the field. One key issue to be encouraged is to establish collaboration with international organization and centers of excellence around the world. Considering the unique set up of the population and the genetic characters in this geographical area, research will help uncover specific disease mechanism relevant to this area and to come up with new innovations for treatment.
5. Advancing education in pediatric endocrinology and diabetes for patients and their parents by enhancing group education and creation of parents/children support groups.
6. Generating evidence-based guidelines that will lead to a consistent management of endocrine disorders and diabetes mellitus throughout the area.
7. Unifying protocols throughout Endocrine centers to ensure updated practice and creating tools for research.

## The first ASPED/ISPAD Diabetes Postgraduate Course

The first ASPED/ISPAD Diabetes Postgraduate Course was held at the Sofitel hotel, Abu Dhabi between the 11<sup>th</sup> and the 13<sup>th</sup> June 2015. It was an initiative from ASPED in collaboration with ISPAD. The aim of the course was to empower and update physicians practicing in the Arab countries who are involved in the care of young people with diabetes and is intended to be a platform to share expertise, research and development in the field of diabetes. The course was advertised for open competition at ASPED and ISPAD sites and a strict enrolment criterion was enforced by ASPED/ISPAD course committee. The curriculum covered the main issues related to diabetes management in young people and the latest updates and insights to physicians involved in managing children and young people with diabetes.

The meeting highlighted the interests and the needs of pediatric endocrinologists in the region. In addition it was the ideal setting for networking and brainstorming about research ideas, collaboration with international societies and programs and available resources. With prominent international and regional speakers from ISPAD and ASPED, the course gathered 65 participants from 13 countries, nine mentors and nine faculty members from ISPAD and ASPED.

## Introduction

### The Arab Society for Pediatric Endocrinology and Diabetes (ASPED)

ASPED was launched in Abu Dhabi, UAE on the 8th of September 2012 upon the initiative of a group of Pediatric Endocrinologists from the Middle East and North Africa. The society is a non-profit scientific Society organization and is registered under the Dubai Association Center (DAC), license number DAC-0001. Its aim is to ensure a high standard of care and development in the field of Pediatric Endocrinology and Diabetes in the Arab region extending from the Gulf through the Northern African countries. The main pillars of its mission are:

1. Care of children and adolescents with endocrine disorders and diabetes by bringing together professionals in this field from the Gulf and North Africa.

The course showed diverse gathering of paediatricians and diabetologists who participated heavily in the course curriculum.

Various formats of presentations and specialised sessions were run during the course covering the main topics in Diabetes including:

1. Diabetes in Children; etiology, epidemiology and classifications
2. Diabetes in clinical practice and research
3. Technology applications in Diabetes
4. Diabetes management in special circumstances (school, sick days and Ramadan fasting)
5. Diabetes complications; acute and chronic
6. Psychology and patient empowerment in Diabetes

The small group discussion, aligned in five parallel sessions, featured various interesting issues in diabetes. In addition to the scientific part of the talks, there was a special emphasis on religious and cultural issues unique to the region. Ramadan fasting by young people with diabetes was the main example. In addition, there has been a lot of discussion about diabetes service provision in less developed countries where resources are sparse.

#### **The main topics for the small group discussion were**

1. Diabetes Unusual Presentations
2. Challenges of Diabetes Management
3. Type 1 Diabetes Complications
4. Diabetes & Psychology
5. Diabetes Education
6. Monogenic Diabetes; MODY & Neonatal Diabetes
7. Hyperinsulinemic Hypoglycemia

8. Obesity & Type 2 Diabetes
9. Diabetes & associated syndromes

### **Course special features and highlights**

Amongst all the interesting topics discussed in the course, there was an obvious common interest in presenting topics markedly related to the regional features of diabetes. Neonatal diabetes, metabolic complications of childhood obesity and type 2 diabetes were highly popular topics presented by candidates. Ten abstracts related to neonatal diabetes were presented both as case scenario or research project presentation. Equally commonly-presented are type 2 diabetes-related issues in which 14 abstracts were submitted and presented.

### **Course tasks-to-follow and recommendations**

The conference enabled participants to meet and link up with senior ISPAD and ASPED researchers and clinical experts, as well as with regional experts and fellow clinicians in a collegial environment encouraging active discussions and exchange of ideas. Inspired by the course success, ASPED has set various goals among its top priorities for the near future. Various projects are planned by the ASPED group in collaboration with ISPAD. Amongst those, the following will have the priority:

- ASPED will set a committee to work on providing guidelines for Ramadan fasting in young people with diabetes.
- ASPED will initiate diabetes registry amongst various countries from the region

### **Acknowledgement**

We would like to thank the ISPAD speakers; Andrea Scaramuzza, Anju Vermani, Maartje de Wit and the ASPED speakers; AbdelhadiHabeb, Mona Al Khawari, Ahmed El Awa, Walid Kaplan, Abdelsalam Abu-Libdeh and Pamela Durant for their valuable input during the course.

## Abstracts for Case Presentations

### Type 1 Diabetes Mellitus with Recurrent Severe Hypoglycemia

Mohamed Kasem

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A 12-year-old female, known to have type-1 diabetes mellitus for one year, was admitted. She is under regular follow-up in a pediatric outpatient with sub-optimal diabetes control. Her hemoglobin A1C was 10%. One year after diagnosis, she was admitted with severe symptomatic hypoglycemia. Parents gave history of recurrent similar episodes at home in the last two weeks before admission. Insulin dose was reduced gradually, and then discharged. Readmitted ten days later with a similar episode of severe hypoglycemia. Blood glucose level was reduced to 34mg/dl. She was managed with dextrose; insulin doses were reduced and stopped completely as blood glucose readings were still low. Provisional diagnosis was that she is going through honeymoon period. She continued to have recurrent severe episodes of hypoglycemia even after discontinuation of insulin injections for more than 10 days. Low blood sugar readings were reported up to 19mg/dl. She was transferred to PICU for management and monitoring as she has altered level of consciousness with severe tachycardia. She was on dextrose infusion up to 12.5%. During management, within few hours blood glucose rose up to 500mg/dl with urine ketones +++ and metabolic acidosis (bicarbonate was 5). At that stage, she was treated for DKA and improved. Possibility of receiving extra insulin by the child herself (Munchausen syndrome) was strongly suspected. Other possible associated conditions such as glycogen storage diseases were suspected. Investigations revealed very low C-peptide level ( $< 0.03$ ) with relatively high fasting insulin level (18.8 in spite of stopping insulin injections for more than 10 days). She was referred to tertiary care hospital, same diagnosis of Munchausen syndrome was confirmed, and she managed accordingly by a multi-disciplinary team including pediatric endocrinologist, pediatric psychiatrist and dietitian. No more episodes of hypoglycemia were reported.

### Neonatal Diabetes Mellitus in Three Siblings with Identical INS Gene Mutations and Different Clinical Courses

Noura Al Hasani

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**Introduction:** Neonatal Diabetes Mellitus (NDM) is a rare condition with an incidence of 1 in 300,000 to 500,000 live births. Many genes have been implicated as causes of non-syndromic neonatal diabetes. Molecular diagnosis might have immediate clinical consequences for affected patients. It also helps in genetic counseling of affected families and predicts the clinical course and prognosis.

**Case Presentations:** We present the different clinical course of three Emirati siblings with non-syndromic neonatal diabetes mellitus, born to clinically unaffected consanguineous parents. Family genetic analysis confirmed identical INS mutations in all siblings. Both parents were heterozygotes for the same mutation. In one sibling, the neonatal diabetes was transient while diabetes was permanent in the other two siblings.

**Conclusion:** This is the first report of variable clinical courses

of three siblings carrying the same homogenous mutation (c.-331C>G) of the INS gene in the UAE.

### Challenging Diabetes Control in an Adolescent

Adil Al Amry

*Armed Forces Hospital, Muscat, Oman*

**Background:** There are multiple factors which are important in the control of diabetes in children. Adolescent period can be challenging. There are multiple physiological and psychosocial factors that can complicate diabetes.

**Method:** We describe a girl who was diagnosed with type 1 diabetes at the age of 10 years. Her mother has diabetes and was on insulin. She was initially managed with twice daily insulin. She comes from a large family and did not accept injections. Her course was complicated with multiple admissions with diabetes ketoacidosis as well as with hypoglycemic episodes. She had different insulin regimes including multiple dose injections and twice daily insulin. On annual screening, she was found to be hypothyroid. There are unfortunately no adolescent services. Hence as she got older, her care had to be transferred to adult services. The transition was not easy. Adult physicians had difficulties managing her. She was admitted in adult wards with paracetamol poisoning shortly after the transition.

**Conclusion:** Control of diabetes in adolescent can be difficult. Apart from the physiological changes during this age causing brittle diabetes, adolescent is a time of major psychological changes that greatly affect diabetes control. This is compounded by the absence of adolescent services that facilitate transition to adult care.

### Impact of Psychology on Diabetes Control: A Case Scenario

Olivia Al Mutasim

*Gaffer Ibn Aouff Pediatric Hospital, Khartoum, Sudan*

**Background:** Young people with diabetes appear to have greater incidence of psychological problems and distress compared to their healthy peers. This case reflects the significance of psychosocial issues as a factor contributing to the worsening metabolic control in the adolescent with diabetes. With the assumption of greater independence by these teens, there is a tendency to decreased compliance with diabetes management. The adolescents tend to present with hyperglycemia, DKA and hypoglycemia.

**Case:** A 13-year-old girl known diabetic for four years on premixed insulin, presented in hypoglycemic coma and convulsion, preceded by frequent episodes of hypoglycemia managed previously by decreasing insulin dose, she had no symptoms suggestive of acute illness. Family history was non-contributory and her school performance was said to be excellent. On admission the patient was comatose; hemodynamically stable, afebrile, systemic examination was unremarkable. Her random blood glucose was 30 mg/dl, treated with IV glucose. Her serum insulin level was 422 MU/ml and C-peptide level  $< 0.01$  ng/ml.

**Conclusion:** Since negative impact of psychosocial disturbance on diabetes control is well documented, psychosocial problems should be identified and addressed in diabetic adolescent presenting with poorly controlled blood glucose.

## Neonatal Diabetes, Hypothyroidism and Glaucoma due to GLIS3 Gene Mutation

Abdul Aziz AlSayed

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Our patient is a 38 week term baby boy who was born to a 21 year old primigravida. During pregnancy, he was proportionately growth retarded, weighing 1.3 Kg, length 42 cm with head circumference of 28 cm. He was admitted to the NICU due to his low birth weight. Neonatal diabetes was diagnosed due to his persistent high blood glucose which reached 27mmol/l on day 7 of life. The patient was started on IV regular insulin infusion with gradual increase in his feeding although his blood glucose remained labile. His cord TSH level was extremely high, so blood taken for TSH and T4 which showed high TSH of more than 100 uIU/, low T4 of 0.4 pmol/L and the patient started on L thyroxine 25 microgram orally daily. On examination: the patient had subtle dysmorphic features in a form of depressed nasal bridge, pointed chin, with no apparent skeletal deformities, his chest and cardiovascular examination was normal. His abdomen was soft with no organomegaly. Patient was seen by Ophthalmology team and diagnosed to have bilateral glaucoma based on high intraocular pressure (IOP). Genetic study sent and came back to be positive for homozygous mutation c.2313 \_2314 dupTC (p.pro772Leufs\*35) in GLIS3 gene.

## Failure of Sirolimus in Three Cases with Diffuse Type of Persistent Hyperinsulinemic Hypoglycemia of Infancy

Rana Al Balwi

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Persistent hyperinsulinemic hypoglycemia of infancy (PHHI) has an incidence of 1/50,000 live births and is considered the most common cause of severe hypoglycemia in infants. PHHI classified into focal and diffuse type based on histological morphology in which the diffuse type is consider being the most severe and commonly not responding to medical treatment. Therefore, the risk of brain damage is high. Recently, Sirolimus (mTOR inhibitor) have been used as a new treatment option in a multiple cases diagnosed with diffuse type of PHHI with a successful glycemic control and obvious promising results. Based on that study, sirolimus have been started on three infants with diffuse type of PHHI, infant No.1 No.2 & No.3 found to have a refractory hypoglycemia which is not responding to high doses of daizoxide (20mg/kg/day) and octerotide (40mcg/kg/day), the gene mutation involve KCNJ11, ABCC8 for infant No.1& No.2 respectively and both mutations are in homozygous state. Infant No.1 & No.3 are 3rd degree relative and we suspect the result of gene test will show the same type of mutation. Each infant have been started on sirolimus for 3-4 weeks duration with poor glycemic response. We are reporting these three cases to rise the possibility that the sirolimus might not be effective in such type of mutation state which is more frequent to be seen due to high consanguinity marriage in our society and in these three infants we have noticed that each one of them having a feeding & swallowing difficulties that could be an association to PPHI disease itself.

## Multiple Disciplines in Dealing with Complicated Diabetes

Reham Shereef

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**Introduction:** Complications of diabetes include retinopathy, nephropathy, neuropathy, macrovascular disease, and associated autoimmune diseases. Clinical manifestations of complications uncommonly present in childhood and adolescence. Screening during the early years can identify subclinical disease and it offers an opportunity for early intervention.

**Case:** Nineteen years old female known diabetic for the last 14 years on insulin premixed, diagnosed with chronic kidney disease (CKD) two years ago on conservative management. She was not on a regular follow up and had a poor glucose monitoring. She presented with septic shock secondary to untreated hand abscess. Past medical history with several admissions with DKA and hand abscess. She is short with high blood pressure, positive prying sign and hand abscess, right Limb is shorter than the left, no goiter, and liver 2 cm with delayed puberty. During her ICU admission she developed DKA. Renal profile was deteriorating and she developed severe abdominal pain. She developed stroke during her stay in the ICU. Laparotomy was decided. ECHO was done and showed pericardial effusion which contraindicated anesthesia, so emergency haemodialysis was done. Celiac screen found to be positive and thyroid function test showed hypothyroidism.

**Conclusion:** Despite marked reduction in prevalence of micro- and macro-vascular complications, there are patients who present with multiple complications that need multiple disciplines which make management a challenge.

## A Case of Donohue Syndrome: New Genetic Mutation and Added Phenotypic Characteristics

Fawziya Al Yafei

Hamad Center, Doha, Qatar

**Background:** Leprechaunism (Donohue syndrome) is an extremely rare AR disease that presents with special phenotypic features including severe type of insulin resistance with high mortality in infancy.

**Case Study:** We present a three and half year old Syrian girl, born at 35 weeks of gestation with asymmetrical IUGR. She developed hyperglycemia from day one of life of more than 150 mg/dl (350 +/- 60 mg/dl) and her serum insulin and c-peptide were very high (772uU/ml and 29.9 ng / ml respectively). Insulin infusion was started with requirement between 0.4 -0.5 unit/kg/day to keep her BG < 200 mg/dl. By the second month, facial dysmorphism became obvious in the form of prominent eyes and maxilla, upturned nose, large and low set ears, thick lips, gum hyperplasia, long narrow face, thick eye brows hypertrichosis of the forehead and the back, long feet and button-like nipples. CGMS recorded average BG = 350 +/- 100 mg/dl while off insulin with fluctuating levels (hypo- and hyperglycemia) and average BG = 300 +/- 50 mg/dl while on insulin infusion. She was started on Metformin (50 mg PO daily), and her CGMS showed a reasonably good response to metformin with average BG of 150 mg/dl compared to BG on insulin. Continuous nasogastric feeding (NGT) with pancreatic enzyme replacement to prevent hypoglycemia was associated with weight gain. Genetic study



revealed a peculiar autosomal recessive of INSR homozygous mutation (c.3583A>T p.Lys1195\*). Both parents were carriers.

**Conclusion:** We describe a case of Donohue syndrome with peculiar genetic homozygous mutation of the INSR gene and some new phenotypic features (pancreatic insufficiency) and reasonable response to metformin therapy.

## Woodhouse Sakati Syndrome: A Multiple Endocrine Syndrome

**Amer ALAli**

*King Khalid University Hospital, Riyadh, KSA*

WSS is rare syndrome with few cases reported worldwide with nine families diagnosed at our Diabetes center. We present a 20 years old female with DM1 (positive antibody). She was diagnosed with hypopituitarism, alopecia areata, primary ovarian failure and primary hypothyroidism. There was a family history of two siblings with impaired glucose tolerance. Genetic study was positive for mutation at DCAF17 in the patient. Both parents were carrier as was one of the siblings.

## Bariatric Surgery in an Adolescent

**Alaa Youssef Ahmed**

*Ain Shams University, Cairo, Egypt*

Pediatric obesity has been markedly highlighted in recent years not only because of it being an epidemic but also because it represents a threat of early death for the next generations owing to its directly related morbidity and mortality. Therefore, more aggressive treatment approaches for obesity should be instituted at an earlier age. The dangers of obesity paved the way for using bariatric surgery procedures in adolescents. We present a case of morbid obesity in an adolescent with family history of metabolic syndrome culminating in type 2 diabetes in both the parents. He had repeated failures of dieting attempts with body mass index (BMI) above 40kg/m<sup>2</sup>. He had impaired fasting glucose and insulin resistance. The decision to do bariatric surgery was made and the patient had a sleeve gastrectomy. He is following up for more than two years now with better control of his voracious appetite, improvement of his BMI, laboratory parameters and social life. This case illustrates the positive role of bariatric surgery, which is still a relatively new treatment modality in adolescents, offering a better quality of life and a rescue pathway to avoid developing type 2 diabetes in high risk obese adolescents with minimal side effects.

## Mauriac Syndrome and Use of Growth Hormone

**Ola Alsayed**

*Al Sabah Hospital, Kuwait*

Growth failure in Type 1 Diabetes Mellitus (T1DM) can occur for several reasons. Mauriac syndrome is a rare cause of severe growth failure in T1DM. The pathogenesis of growth retardation is not clear, but is thought to be multifactorial. A 15-year-old male with 11 year history of T1DM was admitted for evaluation of growth retardation, abdominal distension and diabetes. The patient was on lantus and novorapid multiple insulin injections in a dose of 1u/kg daily. He had poor control of diabetes with no regular follow-ups. There was no history of diabetic ketoacidosis, but multiple episodes of documented hypoglycemia were reported. His HbA1c was 13.5%. There was no history of hypertension or family history of diabetes. Anthropometric data revealed height 137 cm (< 3rd percentile),

weight 33kg (< 3rd percentile), body mass index 17.58kg/m<sup>2</sup>, height age 10.5 years, weight age 11years, bone age 7.3 years, testes both were less than 4ml. Growth hormone injection SC in a daily dose of 0.03mg/kg was started. On his follow up visits, there was no response to the exogenous growth hormone therapy. G.V. was 3 cm during this year.

**Conclusion:** Growth hormone is of doubtful benefit in improving stature in this syndrome.

## An Interesting Case of Severe Insulin Resistance in an 8 Year Old Sudanese Girl

**Asmahan Basheer**

*Gaffer Ibn Aouff Pediatric Hospital, Khartoum, Sudan*

An eight year old Sudanese girl born to consanguineous parents presented with severe hyperglycemia and Ketonuria at the age of 40 days and diagnosed to have Diabetes mellitus. She required large doses of insulin to control her blood sugars reaching 6unit/kg/day. In spite of that, her glucose levels were uncontrolled. She had severe acanthosis nigricans, a feature of severe insulin resistance. There was associated growth retardation, dental dysplasia, excessive body hair and clitoromegaly. Genetic studies revealed a point mutation in Insulin receptor gene (INSR) confirming the diagnosis of Rabson Mendenhall Syndrome. She responded to insulin sensitizers administered along with high doses of insulin.

## Neonatal Diabetes Caused by Wolcott- Rallison Syndrome: A Case Report from Kuwait

**Abeer Al Tararwa**

*Farwania Hospital, Kuwait*

**Introduction:** Wolcott –Rallison Syndrome (WRS) is a rare autosomal recessive disorder characterized by the association of permanent neonatal or early – infancy insulin dependent diabetes.

**Aim:** To describe the clinical features of 3.5 months old girl with Wolcott- Rallison.

**Subjects and results:** Three and half months old girl who was born IUGR to non- consanguineous parents presented with diabetic ketoacidosis. Her older sister also had neonatal diabetes. She was autoimmune negative and had an HBA1c of 11.4%. She was treated for DKA and discharged home. Four weeks later she was admitted with hyperglycemia and post vaccination fever. She was noted to have hepatomegaly and raised liver enzymes (ALT 684 U/L, AST 1256 U/L, GGT 97 U/L). Genetic testing was sent and confirmed the diagnosis of Wolcott-Rallison syndrome.

**Conclusion:** We described a three month old girl presenting with features of WRS. Wolcott –Rallison Syndrome now appears as the most frequent cause of permanent neonatal diabetes in consanguineous families. The genetic testing for patient with neonatal diabetes is of great important for definite diagnosis, detecting associated finding, complication and even treatment.

## Wolfram Syndrome

**Ahmed Al Ghamdi**

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Wolfram Syndrome (WFS) is a rare autosomal recessive disease. It is a progressive neurodegenerative disorder in which patients present with diabetes mellitus, optic atrophy, diabetes insipidus,

sensorineural deafness, urologic abnormalities and multiple neurological abnormalities, like cerebellar ataxia, myoclonus, and psychiatric illness early in the fourth decade. This is a case of 10 years old boy diagnosed with type I diabetic mellitus. He presented with a history of progressive visual deterioration for eight months. On fundoscopic examination, bilateral optic atrophy was recognized, and there was no evidence of diabetic retinopathy. He has a history of nocturia, high urine output in spite his control blood glucose level. Diabetes Insipidus is suspected and the patient was referred to a tertiary center to confirm the diagnosis. In view of the whole clinical picture, Wolfram Syndrome is considered the working diagnosis.

### An Interesting Case with MODY

**Bushra Barakat**

*Dubai Hospital, Dubai, UAE*

Fourteen year old girl found incidentally by her mother, who is a family physician, to have fasting hyperglycemia; the mother randomly checked the fasting BG for the patient in December 2010 and was 126 mg/dl. No significant past medical or surgical history. The patient was born at term by spontaneous vaginal delivery, Birth weight 2.6 Kg, no post-natal complications. Mother had gestational diabetes controlled by diet only. Family history of T2DM in two paternal uncles and one aunt was observed. Examination revealed normal adolescent girl. Weight, height & BMI on 50th centile for age & sex. Systemic examination was unremarkable. Tanner stage B5 P5. Intensive investigation work up done in 2011 and 2012 showed mild fasting hyperglycemia (FBG range 126-147mg/dl), HbA1c (5.6-6.5 %), normal insulin and C-peptide level, negative both GAD & antipancreatic cell antibodies. Genetic testing showed a heterozygous c.1121T>A mutation in exon 9 of the GCK gene. This result confirms the clinical diagnosis of MODY 2 (GCK gene mutation). Her father and other two sibling have the same diagnosis as well.

### Wolcott Rallison Syndrome

**Muna Sharaf**

*Al Makassed Hospital, Jerusalem, Palestine*

Neonatal diabetes mellitus is a rare cause of hyperglycemia, with an estimated incidence of 1 in 500,000 births. It is defined as persistent hyperglycemia occurring in the first months, which caused by mutations in a number of genes that encode proteins that play a critical role in the normal function of the pancreatic beta cells or lead to pancreatic agenesis. Our case was 4y 4 m old male child, with DM type I, hypothyroidism, FTT, elevated liver enzymes, short stature & multiple skeletal epiphyseal dysplasia, assessed as Wolcott-Rallison Syndrome that results from mutations in the gene encoding the eukaryotic translation initiation factor 2  $\alpha$ -kinase 3 (EIF2AK3/PERK). This enzyme phosphorylates EIF2A to regulate the synthesis of unfolded proteins in the endoplasmic reticulum & binding of unfolded protein EIF2AK3/PERK results in phosphorylation of eIF2 $\alpha$ , a factor critical for initiation of translation. The loss of PERK activity abolishes feedback, and the increased stress on the ER can initiate apoptosis. Cells with the greatest secretory load are those likely to be at greatest risk, and impaired EIF2AK3/PERK function will affect many tissues. Null mutation of the Perk gene in the mouse recapitulates many of the defects of the human syndrome including diabetes due to degeneration of  $\beta$ -cell mass after birth and failure of the exocrine pancreas.

### Type 2 Diabetes in an Adolescent Girl with Prader-Willi Syndrome

**Sakina Kherra**

*University Hospital, Algeris, Algeria*

Type 2 diabetes mellitus (DM) in children and adolescents is becoming more frequent, in parallel with the rise in childhood obesity. We report a case of a patient with obesity related to the Prader-Willi syndrome (PWS) who developed type 2 diabetes at a relatively young age. PWS was confirmed to be due to paternal 15q11-13 deletion. She was seen in clinic aged 13.8 years and noted to be short at 142.8 cm (-2.45 SD) and obese with weight 71.7 kg (2.17 SD) and BMI 35.16 kg/m<sup>2</sup> (3.27 SD), Tanner stage B3P2A1. When admitted for insulin tolerance test aged 14.1 years, she was noted to be getting up for drinks at night and to have lost weight (66 kg). Urinalysis showed glycosuria with blood glucose 16.8 mmol/l, HbA1c 13.4%, basal insulin 11.2 mu/l; LH < 0.1/< 0.2 and FSH < 0.1/0.8 IU/L after LHRH; IGF1 low at 30  $\mu$ g/l, peak cortisol 450 nmol/l, growth hormone levels < 0.1  $\mu$ g/l throughout. A diagnosis of type 2 DM was made and Metformin 2 g daily was started. The GLP-1 receptor antagonist Liraglutide 1.2  $\mu$ g daily was introduced at 15.8 years which resulted in improved glycemic control. Diabetes mellitus is seen in up to 25% of adults with PWS patients with a mean age of onset at 20 years. Factors involved in the type 2 DM of PWS include morbid obesity and consequent insulin resistance (although levels may be lower than in typical type Screening for diabetes is recommended in all subjects with PWS and severe obesity (BMI > 30 kg/m<sup>2</sup>) irrespective of age, with periodic surveillance in those receiving GH treatment.

### Poor Diabetes Control in a Teenager: A Conundrum of Manifestation

**Ayman Baker**

*King Khalid National Guard Hospital, Jeddah, KSA*

Fourteen years old boy known case of type one Diabetes Mellitus since age of two years. His level of control is poor with a HA1c 17%. The patient was on pre-mixed insulin (30/70) twice a day with total daily dose of 1.7 U/kg/day. He had poor control of diabetes with no regular follow-ups. Furthermore, he is not compliant to diet control or exercise. His growth parameters were below third centile for age and gender. There is a positive Prayer sign. Abdominal exam showed hepatomegaly with liver span of 11 cm. The patient was prepubertal with tanner stage 1 for testicular and pubic hair development. Investigation showed elevated liver Enzymes. This case shows that Marauic syndrome is still seen in the current era of diabetes advancement.

### Obesity, Autoimmunity, and Double Diabetes in a Young Adolescent

**Manal Mustafa**

*Latifa Hospital, Dubai, UAE*

A few obese youth with type 2 diabetes have evidence of islet cell autoimmunity with autoantibodies toward  $\beta$ -cells typical of type 1 diabetes defining what is called "double diabetes" (DD). I present a ten-years-two-month-old boy, with obesity (BMI 22.8 (> 95th centile), Hashimoto thyroiditis and double diabetes mellitus. He was diagnosed in October 2013. He had insulin resistance, acanthosis nigricans, detectable serum insulin and C-Peptide with positive auto immune antibodies of anti GAD and anti islet cells

antibodies. He was initially managed as type 1 DM by insulin using subcutaneous insulin till December 2014 where he presented to emergency department with history of frequent hypoglycemia mainly at 2 hours postprandial despite eating adequate carbohydrates and being on same insulin doses. He was exercising regularly and controlling his diet so he managed to reduce his weight. In view of frequent hypoglycemia, his insulin doses were reduced gradually until stopped and was started on Metformin. One month after stopping subcutaneous insulin, his fasting and 2hrs postprandial serum insulin levels were high. His weight continued to reduce with regular physical activity and diet control and his blood sugar readings continued to be within target without any hypoglycemia. He is under regular follow up in pediatric diabetes clinic; his blood sugar readings were acceptable on Metformin. He also follows up regularly with dietician. Therefore, a rising obesity trend seems to have a role (in association with other environmental factors) in the increasing incidence and the changing phenotype of type 1 diabetes in youth. Lifestyle modifications, including diet and exercise, which are relevant for the prevention of type 2 diabetes, may be important modifiable environmental factors also for type 1 diabetes prevention in subjects with DD.

### A Teenager with MODY

**Wafa Abdul Fadle**

*Royal Hospital, Muscat, Oman*

Our patient is born to first degree cousins and presented at 12 yr of age with hyperglycemia (12 mmol). He has strong family history of diabetes; sister at 18 yr of age, mother had gestational diabetes, paternal grandmother. There are no features of autoimmune diseases. His weight and height were below 3rd centile and he has negative antibodies. He was weaned off insulin and maintained good glycated hemoglobin. Genetic study showed heterozygous for a novel missense. GCK mutation p.V253F. He remained off treatment with no features of acute or chronic complications.

### Type 1 Diabetes and Other Systemic Illness

**Reham Radwan**

*Ain Shams University, Cairo, Egypt*

A fourteen years old patient, of non-consanguineous parents, presented with manifestation of Type 1 DM at the age of 1 year and 6 months and was treated with insulin with poor control. She failed to grow over the subsequent years. Her height was on the 10<sup>th</sup> centile and weight at the 5<sup>th</sup> and has delayed puberty. Later, she developed progressive increase in abdominal girth. Ultrasonography confirmed hepatomegaly & horseshoe kidney and she was diagnosed with celiac disease. The patient developed acute episodes of impaired renal functions with decreased her GFR shown by DTPA, generalized anasarca, hypoalbuminaemia (albumin decreased to 1.7 mg/dl) and developed a papular rash on both her lower limbs. At the same time, there was unilateral right sided ptosis with oculomotor nerve paralysis. Through this attack her BP and random blood glucose were controlled. This rash was attributed to be diabetic vasculitis rash & ptosis improved after vit B12 injection indicating that it was due to neuritis. With further investigations, she was found to have grade 1-2 nephropathy and proteinuria (> 75 mg/m<sup>2</sup>) that improved on ACEI on anti proteinuria dose. Patient is still having microalbuminuria but renal functions improved. According to the fore mentioned manifestations, the patient was diagnosed to have Mauriac syndrome. Now she is on insulin (1.5 IU/kg), captopril (1mg/kg), gluten-free diet and vitamin B12 injections.

### Propionic Acidemia Mimicking Diabetic Ketoacidosis

**AbdulSalam Abu-Libdeh**

*Makassed Islamic Hospital, Jerusalem, Palestine*

Propionic acidemia manifesting with hyperglycemia is rare. Few cases have been reported mainly of the neonatal-onset form associated with high mortality. We report a nine-month-old Palestinian boy who presented with coma, severe hyperglycemia and ketoacidosis mimicking diabetic ketoacidosis. Family history of unexplained infant deaths was helpful in reaching the correct diagnosis. In response to therapy, the patient regained consciousness without neurologic deficits and had normal examination. This is, to our knowledge, the first case report of late-onset propionic acidemia that had this presentation and survived.

### Type 2 Diabetes Mellitus in a Young Female

**Fatima Al Husaini**

*Al Adan Hospital, Kuwait*

An 11 year and 7 month old obese girl presented to the emergency room with hyperglycemia. She had symptoms of polydipsia, polyuria, and weight loss. She was admitted to the pediatric ward for evaluation of her condition, starting treatment and education by the diabetic educator and dietitian. She was started on MDI regimen. At the time of diagnosis, the patient was obese and she was worked up for type 2 DM as well as her obesity. Her C-peptide was high. Diabetes autoantibodies were negative. Patient continued on insulin to control her high blood sugar readings, dietitian follow up and life style advice was given. This case report shows the different face of diabetes in young children where type 2 diabetes can be a differential diagnosis in a child presenting with hyperglycemia.

### Merging of Type I Diabetes in Newly Diagnosed Adolescent with SLE: Another Facet of T1DM In Youth

**Ranya AbuHaleeqa**

*Shaikh Khalifa Medical Center, Abu Dhabi, UAE*

An 11 years old female identified to have a vasculitis spot / panniculitis skin lesion in the right cheek. It was biopsied and skin Lupus was confirmed. JSLE proven in view of other systemic features of lethargy, arthralgia and raised autoimmune markers (ANA 1:2820). She was seen first time in endocrine clinic and diagnosed with an autoimmune Hypothyroidism. Her TSH was 15.4 (high) FreeT4: 11.7 (low). She was commenced on levothyroxine 50 mcg PO daily. Rheumatology started her on a course of oral prednisolone 30 mg daily to be reduced by 5 mg every week to reach 10 mg PO daily if her lupus remains controlled. Other medications included Methotrexate 10 mg PO once a week and Hydroxychloroquine 200 mg PO daily. Ten days after starting the prednisolone she started to complain of polydipsia and fatigue. Blood glucose checked by parent at home and it was high 22 mmol/L. In Hospital fasting blood glucose was 7.5 mmol/L, 2 hours post prandial blood glucose was 15.5 mmol/L and HbA1C was 7.5 %. Her initial hyperglycemia workup confirmed the diagnosis of the diabetes and at that point the differential includes T1D, steroids induce Diabetes or both. She was initiated on MDI insulin regimen as insulin Glargine 7 units SC daily and insulin Novorapid T1D SC premeals sliding scale 4 - 6 units. Antibodies for type 1 diabetes mellitus were sent. GAD 65



positive (83), Insulin Antibodies negative (2) and Islet cell Antibody negative < 5. Her diabetes was identified as diabetes mellitus type 1 that have had been superimposed and accelerated by active steroid therapy. She has achieved acceptable glycemic control for age and the stage of the diagnosis. The case illustrates the importance of recognizing the symptoms and signs of diabetes in a patient with complex systemic disease. Further, it emphasizes the need to consider the differential of diabetes in such patient, which might be multifactorial, which will play a role in choosing the appropriate insulin regimen and guide the diabetes team.

## Early Honeymoon Period in Type 1 Diabetes

**Abeer Al Khalafawi**

*Saqr Hospital, Ras Al Khimah, UAE*

A 12 year and 3 months old boy was admitted with nausea, dizziness and palpitation. He had polyuria for few days before. In emergency room, he was found to have hyperglycemia (capillary B glucose was 630 mg/dl). He was admitted to pediatric ward and found to have diabetic ketoacidosis (PH 7.18,  $\text{PCO}_2$  13,  $\text{HCO}_3$  9.4, BE -23). His ketoacidosis was corrected in 36 hours, IV fluids and IV insulin were discontinued and he was shifted to MDI injection (total dose of 1 unit/Kg /day). Proper education was given and he discharged. Family history was negative for diabetes and other endocrine disease. His father had vitiligo. Investigations revealed high Hb A1C of 7.8%. High C peptide 5.47 ng/ml (1.1-4.4 ng/ml). He had a normal thyroid function tests. Endomyseal and tissue transglutaminase IgA IgG were negative. On follow up after 10 days, the insulin dose was decreased, and then stopped. HbA1C normalized back to 6.6% three months from time of diagnosis. His TSH started to rise up to double the normal range and he was started on thyroxine. This case illustrates the early appearance of honeymoon in type 1 diabetes. Specific education about the risk of hypoglycemia during this period is important.

## Severe Localized Lipoatrophies in Type I Diabetes

**Mahmoud Salah**

*Hadassah Medical Center, Jerusalem, Palestine*

The case is of 22-year-old female patient diagnosed with T1DM at 7 years of age. She had been treated with multiple types of insulin analogues. She developed subsequent Lipoatrophies, after ~13 yrs of treatment and under different types of insulin. Abdominal lesions partially resolved after changing the insulin preparations and injecting sites, while the thigh lesions were severe and only regressed with the use of local hydrocortisone injections.

**Conclusion:** In T1DM, Lipoatrophy still occurs with the use of any advanced insulin preparations (analogues). Management of this condition remains unsatisfactory. Local injection of steroids has been partially effective in some cases.

## Prolonged Honey-Moon Phase in DM

**Bushra Al Jaberi**

*Ministry of Health, Muscat, Oman*

**Background:** In newly diagnosed type 1 diabetic patients, the natural course of the disease is often characterized by transient restoration of beta cell function following initiation of insulin therapy. This period, often referred to as the "Honeymoon Period", is characterized by a striking fall in the exogenous insulin requirements while good metabolic control is maintained. Factors

favoring this period include absence of diabetic ketoacidosis (DKA) at initial presentation, short duration of symptoms and older age at presentation. A few cases have been described where patients remain healthy without any insulin for an extended period of time. We report a 12 years old male who has been in remission for 1.5 years while he is maintaining minimal carbohydrate intake and exercise.

**Clinical Course:** A 12 year old male patient presented with a ten days history of fatigue, polyuria and polydipsia. He was found to have hyperglycemia, ketosis but no acidosis and glycated Hb of 17%. Therefore, he was diagnosed as Diabetes mellitus but it is combined DM (Type 1&Type2) based on his weight on 90th centile, presence of acanthosis nigricans, insulin & c-peptide within normal references, and positive glutamic acid decarboxylase antibodies (GAD Ab) along with positive Anti-Islet cell Antibodies. He was started on NPH and regular regimen of insulin in addition to metformin small dose. In less than a month his blood glucose trend was low and doses tapered down & stopped along with metformin and his Hb 1Ac was 6.5%. He continued follow-up with sequential investigations showing normal C-peptide level and Hb 1Ac dropped to 5.5% after one year while on diet and exercise only. However, his blood glucose and Hb 1Ac started to rise again after a total period of 18 month when he had been restarted on metformin & basal insulin initially then required basal/bolus regimen.

**Conclusion:** The pathophysiology of the honeymoon phase is poorly defined. It may occur more frequently with an older age of onset of autoimmune diabetes. Restored beta cell function and C-Peptide secretion have been reported to last up to two years and in few adult cases up to four years. The question here is the presence of insulin resistance a factor in bringing the diabetes phase early before a significant beta cell mass reduction take place and therefore made patient go in prolonged remission period. Further, as type 1 DM is an autoimmune disease, reducing insulin secretion through a low carbohydrate diet and optimizing insulin sensitivity through exercise in this case may reduce antigen exposure to the immune system. This could play a role in maintaining a longer honeymoon period than usual.

## Neonatal Diabetes: An Interesting Case of Roger Syndrome

**Mohamed Al Hassan**

*Gaffer Ibn Aouff Pediatric Hospital, Khartoum, Sudan*

This is a case report of eight year old male, an outcome of consanguineous marriage, who presented first in early infancy with diabetes, failure to thrive, repeated wheezy chest infections, and anemia requiring blood transfusions, and later on heart arrhythmias and failure, sensorineural deafness, and an ischemic cerebrovascular accident. Investigations were remarkable of pancytopenia, negative pancreatic autoantibodies, and low serum thiamine level. The pancytopenia responded to thiamine therapy, with catch up growth and improvement in cardiac symptoms. Genetic study confirmed the diagnosis of Roger syndrome (monogenic/neonatal diabetes). Genetic study for the family, including a hearing-impaired sister, was also done.

## Hyperglycemia, Ketoacidosis and Abdominal Pain: Not Always Diabetes

**Gamal Mashaly**

*Prince Mohamed Bin AbdelAziz Hospital, Madinah, KSA*

**Background:** The typical picture of diabetic ketoacidosis (DKA)



includes hyperglycemia, acidosis and ketonuria. Abdominal pain is reported in some patients with DKA.

**Aim:** to present a child with the above symptoms; but turned out to have no diabetes and discuss the pitfalls in the diagnosis of DKA.

**Case report:** A 10 year old girl attended the hospital with abdominal pain and vomiting for few days. Her serum glucose was 430 mg and pH 7.17. The diagnosis of DKA was suspected and she was referred for admission. On admission she was in shock, serum glucose 480, pH 7.13, glycosuria +++++, ketonuria +. The management for DKA was started and she was admitted to PICU admission for close monitoring. After eight hours in PICU, pH and blood glucose normalized and had no ketonuria. However the abdominal pain and vomiting worsen. She was assessed by surgeons and a laparotomy showed midgut volvulus with gangrenous bowel. Her HbA1c was normal and there was no history of diabetes symptoms before this episode. This indicates that her initial acidosis and hyperglycemia were the result of stress hyperglycemia due to the severe intestinal obstruction. The mild ketonuria in this child is due to starvation. The child has no diabetes but she lost the majority of her large bowel due to the misdiagnosis of DKA.

**Conclusions:** Hyperglycemia, ketoacidosis and abdominal pain not always DKA. Although the child had the typical picture of DKA, the absence of diabetes symptoms, persistent pain after correcting the acidosis and the mild ketonuria should raise the possibility of other pathology.

### Sirilimus in the Treatment of Persistent Hypoglycemia Following Near Total Pancreatectomy in a Child with CHI Due To Novel KCNJ11 Mutation

**Background:** In congenital hyperinsulinaemia (CHI), recurrent hypoglycemia is well recognized post pancreatectomy. Recently, Sirilimus has been shown to relieve hypoglycemia and avoid the need for pancreatectomy in some children with CHI.

**Aim:** To present a child with CHI in whom Sirilimus was used to relieve hypoglycemia post near total pancreatectomy.

**Case Report:** A girl developed recurrent hypoglycemia on day 12 of life. Her insulin level during hypoglycemia was 36 IU/L. Her glucose requirements were 20 mg /kg/ min and needed maximum doses of Diazoxide and Octreotide to which she showed mild response. The diagnosis of diffuse CHI was confirmed with a novel homozygous KCNJ11 mutation. She underwent a near total pancreatectomy at 6 weeks old. Postoperatively, she developed intestinal adhesion for which she required an ileostomy and continued to have intermittent hypoglycemic without good response to frequent feeds, Octreotide and Diazoxide. She required IV glucose of 7mg /kg/min to maintain blood glucose level above 3.5 mmol. Her insulin level was 501mU/l when blood glucose level was 2.1mmol/L, serum ammonia, lactate, growth hormone and cortisol was normal. At eight months old Sirolimus 4mg /m2/ day (given twice daily) started. After that blood glucose level were between 4-7 mmol/L and not had any blood glucose level below 3.5 mmol/L. Few weeks later, she was on demand feeding and started to gain weight. At 12 months her growth and development were appropriate for age with normal blood sugar level and no history of symptomatic hypoglycemia or sirilimus side effects. The plan is to wean her off sirilimus gradually.

**Conclusion:** Sirolimus can be useful in the management of persistent hypoglycemia in postoperative patient with diffuse CHI when other treatments are ineffective.

### A Child with DKA Complicated By Kidney Failure

Naseem Fahad

*Salmanya Medical Complex, Manama, Bahrain*

An 11 years old Bahraini female presented to Accident and emergency department with history of Vomiting and abdominal pain. She has history of drowsiness and deep fast breathing with acetone smell. She has osmotic symptoms and a loss of 13 kg. Investigations showed severe metabolic acidosis with leukocytosis and random blood sugar of 46 mmol with ketonuria. She was treated for diabetes ketoacidosis. In view of the drowsiness, CT scan brain was done which ruled brain edema. Oliguria was noted with deteriorated renal function and acute kidney injury was suspected. Presentation of management steps for this complicated child will be discussed.

### Management of Diabetes in Infants

Ayed Al Anezi

*Al Jahra Hospital, Kuwait*

Infants diagnosed with diabetes are a challenge to both families and health care professionals. In this case presentation, I shall discuss the management of two infants diagnosed with diabetes. The different therapeutic options and the various challenges will be highlighted.

### Double Diabetes

Ahmed Naaman

*Paediatric Department, King Saud Hospital, Qassim, KSA*

Seventeen years old Saudi girl presented to emergency department with symptoms of Polyuria and Polydipsia. She also reported weight loss over the preceding weeks but was well otherwise. Her family history was positive for type 2 diabetes mellitus and negative for any auto-immune disease. On the basis of history, the girl was assumed to be a case of type 2 diabetes mellitus. Our patient was also found to have positive antibodies directed against beta cells and thus clearly has auto-immune type 1 diabetes. She has also evidence of insulin resistance which is found in type 2 diabetes mellitus. Therefore, our patient may have the possibility of "double diabetes."

### A Challenging Case of Diabetes

Umaima AbuShofa

*Tripoli Medical Center, Tripoli, Libya*

**Severe Acute Renal Failure in a child with Diabetic Ketoacidosis as her initial presentation of T1DM**

The frequency of DKA at the onset of T1DM varies widely worldwide, with rates of 15-70% inversely correlated with incidence of the disease. Acute renal failure (ARF) is a rare but can be lethal complication of DKA. We present our local experience of treating a 14 year old girl presented with DKA and ARF as initial presentation of T1DM. She presented with severe metabolic acidosis refractory to appropriate fluid therapy and Insulin infusion. Subsequently she developed oliguria, acute renal failure, hypercalcaemia and hypophosphatemia. Continuous VenoVenous Haemodialysis (CVVHD) was started in PICU with good response in term of correction of acidosis and normalization of kidney function. In conclusion: Early recognition of DKA and appropriate fluid therapy

can prevent serious complications of DKA in children. Increase public awareness of diabetes symptoms in children will allow early diagnosis and avoid complications like DKA.

## Abstracts for Research Projects

### Demographic and Clinical Characteristics of Type 1 Diabetes Mellitus in Omani Children - Single Center Experience

Irfan Ullah

*Department of Child Health, College of Medicine, Muscat, Oman*

**Objectives:** To describe the demographic characteristics and clinical presentation of Omani children with type 1 diabetes mellitus at Sultan Qaboos University Hospital, Muscat, Oman.

**Methods:** A retrospective analysis of all children with type 1 diabetes mellitus attending the Pediatric Endocrine Unit at Sultan Qaboos University Hospital, Oman from June 2006 to May 2013.

**Results:** One hundred and forty-four patients were included in the study. The mean  $\pm$ SD of age at diagnosis was  $6.7 \pm 3.7$  years. The median duration of symptoms was 10 days (IQR; 5-14). The most commonly reported presenting symptoms were polyuria (94%), polydipsia (82%), and weight loss (59%). Diabetic ketoacidosis at initial presentation was diagnosed in 31% of the patients. Different insulin regimens were prescribed: multiple daily injections in 109 (76%) patients, twice daily insulin regimen in 23 (16%) patients, and insulin pump therapy in 12 (8%) patients. Family history of type 1 diabetes mellitus was present in 31 (22%) patients. There were no significant differences in presenting complaints (polyuria,  $p = 0.182$ ; polydipsia,  $p = 0.848$ ), duration of symptoms ( $p = 0.331$ ), reported weight loss ( $p = 0.753$ ), or diabetic ketoacidosis at presentation ( $p = 0.608$ ) between patients with and without family history of type 1 diabetes mellitus.

**Conclusion:** Polyuria, polydipsia and weight loss are the most common presenting symptoms. Family history of type 1 diabetes mellitus is highly prevalent among the studied patients. Diabetic ketoacidosis was found to be less common in Oman compared to other diabetes centers in the Middle East.

### Switching to Multiple Daily Insulin Injections in Children and Adolescents with Type 1 Diabetes: Revisiting Benefits from Oman

**Objectives:** Optimal glycemic control is an important goal in the management of type 1 diabetes mellitus (T1DM). Although the use of multiple daily injections (MDI) is a common regimen worldwide, its use is not yet universal in many countries. Our aim was to evaluate the effects of switching from a twice daily (BID) to a MDI insulin regimen in children and adolescents with T1DM in order to revisit its benefits in the Omani population.

**Methods:** We conducted a retrospective cohort study of children and adolescents with T1DM at Sultan Qaboos University Hospital, Muscat, Oman, between January 2007 and June 2013. Patients using the BID regimen for more than six months who were then switched to MDI were included in the analysis. We compared glycated hemoglobin levels (HbA1c) before and after the regimen change.

**Results:** Fifty-three children were eligible for the study. Ten patients were excluded for various reasons. The remaining 43 patients were 58% male and 42% female, with a mean age of  $9.4 \pm 3.7$  years. There was significant decrease in the overall mean HbA1c level from baseline (10.0) compared to three months after switching to MDI (9.5);  $p = 0.023$ . Nevertheless, the improvement was not significant in the subsequent follow-up visits at six and nine months. The reduction in HbA1c values was observed mainly in children five to 11 years.

**Conclusions:** Switching from a BID to MDI insulin regimen has favorable effects on the overall control of T1DM in children and adolescents, as assessed by HbA1c levels. In addition, this regimen has been proved to be safe and well tolerated by patients.

### Contribution of Selective HLA-DRB1/DQB1 Alleles and Haplotypes to the Genetic Susceptibility of Type 1 Diabetes among Lebanese and Bahraini Arabs

Khadija Alola

*Salmanya Medical Center, Bahrain*

**Context:** Human leukocyte antigen (HLA) class II genes contribute to the genetic susceptibility of type 1 diabetes (T1D), and both susceptible and protective alleles were implicated with its pathogenesis, which varies among various ethnic/racial groups.

**Objective:** This study investigated the heterogeneity in HLA class II haplotypes distribution among Bahraini and Lebanese T1D patients.

**Design:** This was a cross-sectional retrospective study.

**Setting:** The study was conducted at primary care private and public health centers.

**Patients:** Subjects comprised 126 T1D patients and 126 healthy controls from Bahrain and 78 Lebanese T1D patients and 111 control subjects.

**Results:** Although Lebanese and Bahraini patients share DRB1\*030101, DQB1\*0201 as susceptible and DRB1\*100101 and DQB1\*030101 as protective alleles, DRB1\*040101 was an additional susceptible allele in Bahraini patients, and DRB1\*130701 and DQB1\*050101 were additional susceptible and protective alleles in Lebanese, respectively. DRB1\*030101-DQB1\*0201 was susceptible, whereas DRB1\*070101-DQB1\*0201 and DRB1\*110101-DQB1\*030101 were protective haplotypes in Bahraini and Lebanese. DRB1\*040101-DQB1\*0302 and DRB1\*040101-DQB1\*050101 displayed different associations: they were protective in Lebanese but susceptible or neutral among Bahrainis. Whereas the frequency of homozygous DRB1\*03011-DQB1\*0201 was higher in Bahraini and to a lesser extent Lebanese patients, homozygous DRB1\*110101-DQB1\*030101 was significantly more frequent in Lebanese but not Bahraini controls, whereas DRB1\*030101-DQB1\*0201/DRB1\*040101-DQB1\*0201 was the major genotype among Bahraini patients but not Lebanese subjects in whom it was present at very low frequencies.

**Conclusion:** In view of these differences between Bahraini and Lebanese, this demonstrates that the contribution of HLA class II to the genetic susceptibility to T1D must be evaluated with regard to specific HLA haplotypes and also ethnic origin and racial background.

## Abnormal Glucose Tolerance in $\beta$ -Thalassemia: Assessment of Risk Factors

Amany Attia

*Diabetes Endocrine Unit, Children University Hospital, Cairo, Egypt*

In  $\beta$ -thalassemia ( $\beta$ -thal) major, the pathogenetic mechanisms leading from siderosis to diabetes are poorly understood. We assessed the glycometabolic status in transfusion-dependent Egyptian  $\beta$ -thal patients and evaluated their possible risk factors for abnormal glucose tolerance (AGT). An oral glucose tolerance test (OGTT) was done on 54 multi-transfused patients and 28 age-matched normal controls, measuring their serum insulin levels at 0 and 120 min. Insulin sensitivity and insulin release indices were calculated. Indicators of iron overload and liver status were recorded. Thirteen patients (24.1%) had AGT. Cases with AGT had significantly higher mean postprandial insulin, fasting insulin resistance index (FIRI) and homeostasis model assessment (HOMA) insulin resistance (IR),  $p = 0.0001$  for all, and significantly lower mean HOMA  $\beta$  cell,  $p = 0.007$ , when compared with normal glucose tolerance (NGT) cases. Abnormal glucose tolerance is common in multi-transfused  $\beta$ -thal major patients and could be attributed to early impaired  $\beta$ -cell function with increasing IR.

## Neonatal Diabetes: First Moroccan Series

Iman Zeinab

*Department of Paediatric Diabetology, Children Hospital, Rabat, Morocco*

**Introduction:** Neonatal Diabetes Mellitus (NDM) is rare monogenic diabetes, with an incidence ranging from 1 in 90000 to 500000 newborns in Europe. It is defined as persistent hyperglycemia occurring in first six months of life, due to an insulin deficiency. Based on the treatment duration, NDM is stratified as transient NDM (TNDM) and permanent NDM (PNDM). Transitional and permanent forms have different genetic bases. TNDM is linked in the majority of cases (~ 70%) to abnormalities in an imprinted region on chromosome 6q24, and in 30% to genetic mutations: KCNJ11, ABCC8, INS and HNF1 $\beta$ . PNDM are genetically heterogeneous and several genes have been linked to this disorder. It may be isolated or associated to other syndromic entities. Its etiology is increasingly elucidated.

**Aim:** This work aims to study epidemiological, clinical, biochemical, genetic, therapeutic aspects and outcome of NDM.

**Methods:** Descriptive Retrospective study from January 2006 to February 2015. We included all infants diagnosed with diabetes before 6 months of age, and followed at our department for diabetes mellitus.

**Results:** Thirteen infant with NDM were studied. Consanguinity was present in 54%, and a familial story of diabetes in 77%. Thirty eight percent of these children had IUGR. Cardinal symptoms were dehydration, vomiting, diarrhea, osmotic polyuria. Sixty two percent presented with diabetic ketoacidosis (DKA), and only 46% had a provisional diagnosis of diabetes or DKA at first physician contact. Peptide C levels were generally low, and all patients tested were negative for autoimmune markers of diabetes. No case of pancreatic agenesis was found in our study. Recessive genetic disorders were the commonest cause of NDM. Mutations of EIF2AK3 and INS were found to be responsible for 46% of NDM cases. Mutations in ABCC8 gene were found in only two cases (15%), which one is candidate for DEND syndrome. Transfer from insulin to oral sulfonylurea was started in index patient. Hypoglycemia and associated co-morbidities are the major problems in the majority of our patients.

**Conclusion:** In our study, genetic etiology are different compared to Europeans and British patients, and it may due to the higher rate of consanguinity. However KATP mutations (ABCC8, KCNJ11) should be systematically screened due to their impact on the management and prognosis.

## Diabetes Burden on Bone Turnover among Children and Adolescents

Mona K Abdelrahman

*Suez Canal University, Ismailia, Egypt*

**Background:** Diabetes has its burden on bone turnover among children and adolescents. Little is known about the relationship between both.

**Objective:** To determine the relationship between diabetes and bone turnover among children and adolescents.

**Design:** Cross-sectional descriptive study.

**Settings:** Suez Canal University Hospital Pediatrics department.

**Participants:** Thirty nine diabetic cases and 39 matched healthy controls.

**Measurements:** Glycosylated hemoglobin (HbA1c), alkaline phosphatase (ALP), urinary Pyridinoline crosslinks (PYD).

**Results:** One third of the patients had high levels of ALP. The PYD level was significantly higher among all the diabetic patients. Values of PYD/creatinine among type 1 diabetic participants were +3 SD away from the mean of the control group. There was no statistically significant correlation between ALP and HbA1c among diabetic participants. There was no statistically significant correlation between PYD/creatinine and HbA1c among diabetic participants. There was no significant correlation between ALP and PYD/creatinine ratio.

**Conclusion:** Type 1 diabetes is significantly associated with higher bone catabolism indicated by the higher bone markers of PYD levels without coupling bone formation. No correlation or association among glycemic control and bone marker. Diabetes and bone resorption could be co-morbid condition stemming from a common pathological route.

## Diabetes Program in Sudan

Ilham Omer

*Department of Pediatrics, University of Khartoum, Sudan*

Monitoring diseases is critical for understanding their etiology and natural history and for the allocation limited health resources. Thus it is impossible to prevent and control diabetes and its complications unless we know the incidence and prevalence at which they occur. Diabetes registries need definition of cases and collection of very simple data like date of birth, sex, date of birth and residence. Khartoum state represents most of the Sudan, as all the tribes and the different ethnic groups are represented in the capital. There was an overall increase in the prevalence in type 1 diabetes mellitus in the last decade. Some cases of type 2 were seen every now and then with the increase in the incidence of obesity among children. The main diabetes center in Khartoum is Jabirabulaliz, there were more than thousand diabetic children were registered. Eight hundred and sixty of them are originally from Khartoum state, while the rest represent the other states. Five other diabetes clinics scattered in the different areas in the capital. Between 1991 and 1995 the children with diabetes in Khartoum were 534, the highest



rate was in the 10-14 year age group. There were slight more girls than boys. This is an initial attempt to establish a diabetes registry in Sudan which is an important step in improving the health service in this disease.

## Neonatal Diabetes: A Case Series from Oman

Hanan Al Azkawi

*Royal Hospital, Muscat, Oman*

**Background:** Neonatal diabetes mellitus is a rare genetic form of pancreatic  $\beta$ -cell dysfunction. We compared phenotypic features and clinical outcomes according to genetic subtypes in a cohort of patients diagnosed with neonatal diabetes mellitus in Oman.

**Method:** We prospectively investigated 18 Omani children referred for Neonatal Diabetes in a period of seven years (2008-2014). This is being done with collaboration with Department of Molecular Genetics Peninsula Medical and Research Center, Exeter. Patients with hyperglycemia requiring treatment with insulin below age one year were eligible. We assessed changes in the 6q24 locus, KATP channel subunit genes (ABCC8 and KCNJ11), and preproinsulin gene (INS) and investigated associations between genotype and phenotype.

**Results:** We tested 18 index patients of whom 8 (47%) had no detectable genetic mutation. The remaining 10 patients with positive mutation, 2 (20%) had 6q24 abnormalities 3 (30%) had mutation in GCK, 3 (30%) had FBS, 1 (10%) had mutation in KCNJ11 (kir6.1) subunit and 1 (10%) has CD25 mutation. Out of those patients with negative mutation two turned to be type 1 Diabetes Mellitus (T1DM) with strongly positive anti GAD and anti-Islet cell antibodies. Two children with permanent Neonatal Diabetes Mellitus (PNDM) has generalized autoimmunity, one of them has positive mutation of CD25 which is also known as IPEX-Like syndrome, while other child is negative for mutation.

**Conclusion:** Our patients with neonatal diabetes mellitus have heterogeneity in both phenotype as well as genotype clinical presentation. This is the first extensive work done for neonatal diabetes in Oman.

## Evolution of Type 1 Diabetes Mellitus

Fatima Zahra Fadil

*Department of Pediatrics, Provincial Hospital, Morocco*

**Introduction:** Diabetic nephropathy is a serious complication of the type 1 diabetes; it is usually rare in children. We report a case of type 1 diabetes diagnosed at the age of five years that was complicated with diabetic nephropathy four years later after the diagnosis of diabetes.

**Case Report:** A female child, who was born on March 25, 2002 has the history of type 1 diabetes since the age of five years, as well as uncontrolled asthma which is treated with inhaled corticosteroid therapy and  $\beta_2$  mimetic long-acting. She has no family history of type 1 diabetes, autoimmune disease, or renal disease. Patient was started on conventional insulin therapy: The average dose of Insulin was 0.6 UI/Kg/Day for one year, then basal Insulin bolus with an average of 0.90 UI/Kg/Day. The HbA1c at the time of diagnosis was 12% and then the value varied between 6.4% and 10.3% with an average of 8.09%. During the follow-up she had normal growth and development, and never had severe hypoglycemia or diabetic ketoacidosis requiring hospitalization. Autoimmune diseases serology was negative (normal TSH, negative Anti-transglutaminase antibodies (Ig A). At the age of nine i.e. four years

after the diagnosis of diabetes, she had positive micro-albuminuria. The albumin creatinine ratio was 76mg/g. The fundoscopy was normal. The quarterly monitoring showed fluctuating values of micro-albuminuria from 5mg/l to 44mg/l, the patient was started on converting enzyme inhibitor (Enalapril) 5mg daily which led to improvement of the micro albuminuria during the last consultation.

**Discussion:** The probability of development of microalbuminuria is correlated with the duration of evolution of the diabetes and the average of glycemic control. The risk of microalbuminuria increases with the high level of HbA1c. It is recommended to screen children annually for diabetes nephropathy; starting at the age of 11 years and two years after the diagnosis of diabetes or starting at the age of nine years and five years after diagnosis of diabetes. Our case illustrates the possibility of development of a microalbuminuria before the recommended age of screening, which raises the necessity of early screening.

**Conclusion:** The diagnosis for diabetic nephropathy in children has to be a priority for the pediatrician because early screening will assure preservation of kidney function.

## The Frequency of Type 2 Diabetes Mellitus among Diabetic Children in El Minia Governorate, Egypt

Basma Elmoez

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**Objective:** Type 2 diabetes mellitus (T2DM) in children and adolescents is becoming an important public health concern throughout the world. This study aimed to estimate the frequency of T2DM among diabetic young people in El-Minia Governorate, Egypt and to detect its risk factors.

**Method:** A total of 210 diabetic patients below 18 years age in Minia Governorate were included in the study and collected patient history thoroughly, a physical examination and laboratory investigations. **Results:** T2DM was present in 28 patients (13.3%); it was significantly present in 18 females (64.3%) and 20 (71.4%) of them had a positive family history of DM. T2DM patients had significantly higher BMI and waist circumference centiles for age and sex than those with T1DM. Also, haemoglobinA1c %, serum C-peptide and cholesterol levels were significantly higher in T2DM than T1DM patients. Finally, there were weak significant positive correlations between C-peptide level and both BMI and waist circumference. **Conclusion:** T2DM is no longer a disease of adults but can also occur in children and adolescents. The results suggested that obesity, female gender and a positive family history of DM are risk factors for T2DM.

## Bedside Detection of Diabetes Neuropathy in Adolescents with Type 1 Diabetes

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**Objectives:** The aim of this study was to assess the sensitivity and specificity of simple bedside tests for detection of diabetic neuropathy (DN) as compared with standardized electrophysiological tests in the busy diabetes clinic, Endocrine and Metabolism Pediatric Unit (DEMPU), Cairo University. Our aim was to collect and evaluate data concerning the risk factors that may contribute to the development of DN.

**Method:** Sixty children and adolescents with age of eight years

and above with type 1 diabetes mellitus (T1DM), who is consulting at DEMPU from duration of one year or more were evaluated by collecting full history, thorough examination and performing simple bedside screening tests used to detect the presence of diabetic peripheral and autonomic neuropathy (pin prick test, testing for pressure sensation, light touch sensation & vibration sensation in addition to detecting the presence of resting tachycardia and postural hypotension as signs of autonomic neuropathy). Electro physiologic studies were performed and their results were used as our gold standard. In addition, risk factors that may be related to the development of DN were studied as age, gender, age of onset of DM, duration of DM, smoking, mean preprandial and postprandial blood glucose levels, mean HbA1c, glucose variability, and patient's compliance.

**Result:** Pin prick test was found to have a sensitivity of 73.33% and specificity of 91.43% in detection of diabetic peripheral neuropathy (DPN) which did not increase while combining multiple tests. Regarding detection of autonomic neuropathy, presence of resting tachycardia was found to have sensitivity of 72.73% and specificity of 84.62%, while detection of postural hypotension had a low sensitivity of 27.27% and a high specificity of 100%. Age, duration of DM, smoking, BMI, preprandial blood glucose levels, and patient's compliance were found to be significant risk factors for the development of DN in the clinical neuropathy group, while in the group of patients that underwent NCV studies only smoking was found to be of statistical significance.

**Conclusion:** The prevalence of DN in our study group was found to be 36.7% clinically and 30% based on the results of the nerve conduction velocity (NCV) studies. According to our study, the pin prick test was found to be the most reliable simple bedside screening test for detection of DPN. It was also found that the presence of resting tachycardia was a more reliable finding than postural hypotension as an indicator of autonomic nerve affection. There are multiple risk factors that may contribute to the development of DN as Age, duration of DM, smoking, BMI, preprandial blood glucose levels, and patient's compliance

## Emergence of Type 2 Diabetes Mellitus in Adolescents in Constantine, Algeria

Foued Abdel Aziz

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**Background:** Type 2 diabetes mellitus (T2DM) is emerging and increasing all over the world where obesity in adolescents is becoming more common. The aim of this study is to show the occurrence of T2DM in adolescents in Constantine and to identify the diagnosis criteria of T2DM.

**Method:** In a pediatric diabetes clinic at the University Hospital of Constantine, between 2002 and 2012, ten cases of overweight or obese adolescents were diagnosed with T2DM. Available data, clinical, history, biology, and autoimmune markers were used in the analysis.

**Results:** The age ranged between 11.3 and 16 yrs. The population included seven girls and three boys. The BMI was between 28.5 and 45. A family history of T2DM was present in all cases. Acanthosis nigricans was present in two cases. HbA1c at the diagnosis was between 7.8 and 12.4, Peptide C was normal and anti-GAD Antibodies were negative when tested. Triglycerides level was elevated in two cases and HDL-C (High Density Lipoprotein Cholesterol) was low in four cases. Four cases were first diagnosed as Type 1 DM and treated with insulin; then the treatment was revised to basal insulin and metformin. Two cases were under

metformin monotherapy and four cases under basal insulin and metformin. The treatment allows a good glycaemic control when diet and physical advices are well followed.

**Conclusion:** Although it is not yet a priority, T2DM in diabetic overweight teenagers having a family history of T2DM needs systematic attention. Discriminative criteria are auto-antibody testing and, in some cases, genetic testing. Screening from the age of 10 yrs in obese youth at risk has to be considered. Prevention is possible by fighting obesity and changing the lifestyle.

## A Series of Wolfram Syndrome

Hajar Berrani

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**Background:** The Wolfram Syndrome is a rare autosomal recessive genetic disease. It is due to mutations in the gene WFS1 which encodes for the wolframin, and which is located at the pancreatic cells. It made diabetes mellitus as a complex syndrome and optic atrophy before the age of 15 years, followed by other attacks during its evolution such as a diabetes insipidus, neurosensorial deafness and urological disorders. The goal of our study is to highlight the epidemiological, clinical and genetic features of this syndrome among children.

**Observations:** We report 10 cases that have been diagnosed and followed at our service. All patients were born from consanguineous marriages and they all presented a diabetes mellitus during their childhood with a median age of 5.8 years. The optic atrophy is present in all patients with an age average of 10.9 years, deafness is present in 70% of patients with an average age of 10.14, 50% of patients suffer from diabetes insipidus with an average age of 10.8 and 60% of patients have urological disorders with a mean age of 11.5 years. The emergence of those symptoms allowed evoking the Wolfram syndrome that has been confirmed by genetic studies.

**Conclusion:** With an average age of death of 30 years old, we highlight the need of a multidisciplinary intervention provided by endocrinologist, pediatrician, ophthalmologist, otorhinolaryngologist, nephrologist, Urologist, geneticist, psychiatric and surgeon in order to support and accompany both the patient and his family in long term follow-up.

## Childhood Obesity: Three Years Experience in Tertiary Care Hospital in Oman

Laila Al Hashimi

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It is a retrospective study done at Royal Hospital which is considered one of tertiary care hospitals from period 2013 - 2015. The main aims were to study the baseline demographic features of children with Obesity and their clinical and laboratory profiles. In addition to this study in pediatric endocrine department, experience in management of obesity in pediatric group was considered. It is a retrospective study included all patients diagnosed to have obesity and seen in pediatric endocrine OPD in national pediatric endocrine and diabetes centre below 15 years of age. Total patients studied were 51, whom either has been referred from peripheral hospitals, health centers or referred from different pediatric OPD in royal hospital. Data extracted from AL Shifa system. The main variables we looked at and collected were including: Gender, age, age of presentation, anthropometric parameters with their centiles during first visit and follow up visits up to one year, BP measurements, presence of nigricans acanthosis,

striae. Investigations which have been done as part of evaluation of obesity and its possible complications including: OGTT, lipid profile, Hb A1C, LFT, TFT, insulin, leptin, C-peptide, microalbuminuria were reviewed. Furthermore imaging like abdominal US to look for presence of fatty liver infiltrates. Complications like dyslipidemia, prediabetes and diabetes, HTN, orthopedic problems and OSA were reviewed and documented. In addition management measures including diet modification and exercise advices based on available resource as well use of pharmacological measures including metformin and use of Victosa. The response for treatment over the period time of follow up of one year illustrated in terms of maintain or reduction in weight or BMI, normalization of abnormal HbA1C, lipid profile or fatty liver. The results showed 34 patients were females and 17 were males with median age of presentation seven years. Median BMI was 31, and all of patients were > 95% centile which is obese category. Around 30 patients were having positive nigricans achanthosis. OGTT was done for two patients only and was normal but 22 patients were considered as prediabetes based on HB A1C readings. Twenty five patients developed fatty liver infiltrates, nine patients showed high level of ALT ranging from 43-273. Two patients showed microalbuminurea and one patient has overt-proteinuria. Other complications were reviewed and documented. TFT were normal in 48 patients. Regarding treatment measures around 38 patient received no pharmacological measures inform of diet advice and exercise advice as first line of therapy and 11 of them metformin as second line of therapy, whereas 13 patients received metformin along with diet modifications and exercise advices as first line of therapy. Around six patient received Victoza as a third line of therapy with Maximum dose 1.8 mg OD. Response of treatment illustrated as maintain weight and BMI or reduction in Both, Normalizations of abnormally lipid profile, HB A1C or fatty liver infiltrations. In conclusion, these results of our pilot study highlighted an observation in which it gives importance of early detection and prompt interventions as most of the patients were already in obese category. In addition, having high number of prediabetes patients giving the importance of doing OGTT right from the beginning. Other observations noted needs more patients to be included and studied.

## Neonatal Diabetes in a Series of Six Patients from Sudan

**Samar AbuSamra**

*Gaffer Ibn Aouff, Hospital, Sudan*

Neonatal diabetes is defined as hyperglycemia in an infant of 37 weeks or more (six months), requiring exogenous insulin. It is rare in 1:100-500000 and it can be transient or permanent. This is the first case series report on neonatal diabetes from Sudan. It shows six patients from different tribes and different ages of presentation collected over one year period. This study shows the importance of international collaboration which enables the genetic studies.

## Ten Cases with Diabetes in First Six Months of Life: Clinical, Molecular and Therapeutic Aspects

**Noha Musa**

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**Background:** Neonatal diabetes mellitus (NDM) is defined as hyperglycemia occurring within the first six months of life; it may be permanent or transient. Diagnosis of NDM is vital for prognosis, genetic counseling and treatment.

**Objectives:** To study clinical, laboratory, molecular and therapeutic aspects of diabetes presenting in the first six months of life.

**Methods:** Ten cases with NDM were studied regarding perinatal based on family history, clinical features and laboratory tests on admission and follow up, HLA typing and molecular studies, and mode of therapy. Molecular studies for the common mutations associated with NDM; KCNJ11, INS, ABCC8 and methylation defects were done.

**Results:** Ten cases developed diabetes in the first six months of life (three in first eight weeks, seven between eight and 24 weeks). All presented with ketoacidosis, one had developmental delay with convulsions. Molecular studies revealed methylation defect in two cases, KCNJ11 in three cases, INS mutations in two cases; and no detectable defect in three cases. Insulin was stopped on follow up in three cases (TND), successfully substituted with glibenclamide in three cases, and continued in four cases (PND). **Conclusion:** Neonatal diabetes can be transient or permanent. Molecular genetic testing is essential in guiding mode of therapy. Glibenclamide was more effective in achieving diabetes control in cases with KCNJ11 mutation.

## Care of DKA in Children's Hospital

**Jamila Lahrach**

*Lalla Mertem Proviacial, Larache Hospital, Morocco*

Diabetic ketoacidosis is a metabolic emergency and a major cause of morbidity and mortality. It is a severe metabolic situation, which represents the extreme manifestation of insulin deficiency, and it can be, either a sign of new presentation or related to rapid decompensation in a known diabetic. The aim of our study is to assess the quality of care for children with DAC intra-hospital, by monitoring the recovery of consciousness, equilibration of diabetes, correction of hydro disorders and establishing short and medium-term prognosis. Diabetic ketoacidosis is a therapeutic emergency. Prevention of complications, particularly Brain Edema, is based on analysis of a pre-treatment protocol which take into account of pathophysiological knowledge, and also, on a very regular clinical and laboratory monitoring. But the best prevention is early diagnosis of diabetes, since 90% of diabetes occurs in the absence of a family history of diabetes. This prevention can be done by raising awareness of the general population and doctors on the warning signs of the disease. Preventing recurrence is summarized in educating parents and children who need to know the signs of ketoacidosis warning, while insisting on the correct home monitoring of capillary blood glucose and ketonuria too. Emphasis is placed on the importance of early diagnosis, awareness of doctors and nursing staff, and improving the management and vigor in the implementation of protocols supported.

## Diabetic Retinopathy in Adolescents Followed at the Pediatric

**Nihad Selim**

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**Background:** Diabetes mellitus (DM) can lead to diabetic retinopathy (DR) and vision loss. While severe retinopathy from DM is very unusual in children, the rates of retinopathy increase over time as adolescents have a higher risk of progression to vision threatening retinopathy. The aim of the study is to obtain epidemiological data on retinopathy in adolescents with DM in Constantine.



**Method:** Of 52 adolescents with DM seen in a pediatric diabetes clinic diagnosed at least eight years prior, fluorescein angiography was performed on 38 of them. Data extracted including DM type, DM duration, treatment, haemoglobin A1C, and presence of microalbuminuria.

**Results:** Fluorescein angiography was performed on 38 patients (21 girls and 17 boys). The mean age was  $17.3 \pm 4.2$  yrs (13 to 22 years). The age at diagnosis of DM was  $6.9 \pm 4.4$  yrs and diabetes duration was  $11.8 \pm 3.6$  yrs (8.3 - 17 yrs). Total 58% of the patients had two injections of insulin per day. HbA1C was between 8 and 9% in 42% of the patients and  $> 9\%$  in 38% of patients. Fourteen DR were diagnosed (37% of patients): five mild to moderate non proliferative, five severe non proliferative, and four proliferative. Patients with DR was aged from 18.5 to 22 yrs with a diabetes duration from 9 to 15 yrs, HbA1C was between 7.9 to 10.2% and micro-albuminuria was positive in four cases of DR.

**Conclusion:** In adolescents with DM, the risk of DR is related to diabetes duration and glycemic control. Improvement in glycemic control will reduce the risk and screening for retinopathy should start at onset of puberty. The most sensitive detection methods available in our region have yet to be determined.

## Primary Dyslipidemia in Children

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**Introduction:** Primary dyslipidemia is a rare condition characterized by abnormal levels of plasma lipids, and premature, severe, accelerated atherosclerosis.

**Objectives:** To study the frequency of occurrence of the different forms of primary dyslipidemia, to display their various clinical presentations and their lipid profile.

**Methods:** Retrospective study conducted in the unity of endocrinology in Casablanca University children's hospital.

**Results:** Six primary dyslipidaemic cases were included: two girls and four boys. Sex ratio: 1/3. One case of hypercholesterolemia and five cases of hypertriglyceridemia. One had xanthoma. Four had milky blood, three cases had pancreatitis: abdominal pain and hyperlipidemia. Pancreatic imaging was normal. One case of hypertriglyceridemia had type 1 diabetes and severe hypothyroidism. One child was treated with hypolipemians. The result was unsatisfactory.

**Conclusion:** Primary dyslipidaemia may present early. These children should be put on early strict lipid reduction protocols to prevent complications.

## Proteinuria and Diabetic Nephropathy in Children and Adolescents Type 1 Diabetes

Hend Mohamed

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**Background:** Diabetic nephropathy is a major cause of morbidity and mortality among patients with type 1 diabetes. Many risk factors may influence its onset or progression

**Objective:** To assess the existence of early renal involvement identified by microalbuminuria in patients with type 1 DM at Diabetic Endocrine Metabolic Pediatric Unit (DEMPU), assessment

of the compliance with the screening protocol and the association of microalbuminuria with potential risk factors.

**Methodology:** The current retrospective case-control study was conducted on 284 patients with type 1 DM (T1DM), regularly coming for management and follow up at Diabetic Endocrine Metabolic Pediatric Unit (DEMPU), Cairo University during year 2009 and eligible for screening for microalbuminuria according to ISPAD (2009) guidelines. They were divided into two groups according to the urinary albumin excretion (UAE): microalbuminuric group (cases): included 42 patients with type 1 DM (T1DM) and microalbuminuria, and normoalbuminuric group (control): included 242 patients with type 1 DM (T1DM) without microalbuminuria. They were fully evaluated clinically by both history and examination in addition to reviewing their records for all the available results of follow up laboratory investigations.

**Results:** We studied 284 patients (112 males and 172 females) with T1DM; mean ages were  $17.1 \pm 5.4$  yrs. and mean duration of diabetes of  $10.1 \pm 4.8$  yrs. Of these, 42 patients (14.8 %) had microalbuminuria, 31 % of them at five years duration increasing to 76.2 % at 10 years duration. There was 57% female sex in the normoalbuminuric group, compared to 78.6% in the microalbuminuric group ( $P = 0.004$ ). There was higher percent of patients with family history of diabetes ( $P = 0.13$ ), hypertension ( $P = 0.02$ ), CVD ( $P = 0.02$ ) and renal disease ( $P = 0.008$ ) in the microalbuminuric group. Diabetes duration, HbA1c, limited joint mobility, hypertension and short stature were significantly higher in the microalbuminuric group ( $P < 0.0001$ ,  $P < 0.0001$ ,  $P = 0.03$ ,  $P < 0.0001$ ,  $P < 0.0001$  respectively). Moreover, there was statistically insignificant higher percent of dyslipidemia ( $P = 0.08$ ) in the microalbuminuric group. The compliance of the patients to the screening tests was represented as the ratio of the albumin/creatinine tests already done to the recommended number of tests and it ranged from 5.5 to 300% with median of 50%.

**Conclusion:** Microalbuminuria was present in 14.8% of patients with type 1 DM after a mean follow up of 10 yrs at DEMPU. Microalbuminuria was associated with female sex, longer duration of diabetes, hypertension, poor glycemic control, short stature and limited joint mobility but not significantly associated with dyslipidemia and age of onset of diabetes. Angiotensin converting enzyme inhibitors were the treatment of choice in this study.

## Incidence of DKA Presentation in Sudan

Bashir El Wasila

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**Background:** DKA is common at diagnosis in children with T1DM, and has significant morbidity and mortality. Many risk factors were implicated in its development and degree of severity.

**Objectives:** To describe the frequency of DKA at the onset of T1DM, identify the determinants of DKA, assess its severity, and determine its mortality rate in children in Sudan.

**Methods:** Hospital records of 466 diabetic children up to 18 years of age, diagnosed during the period 2006-2010 were reviewed (Gaafar Ibn Auf Children's Hospital, Khartoum). DKA was assessed clinically using the severity criteria of Endocrine Clinics of North America 2000. Data was analyzed using the SPSS version 18. The differences in the mean values were calculated using the ANOVA test. Pearson's correlation coefficient was used to evaluate the relationship between variables. For all tests,  $p < 0.05$  was accepted as significant.

**Results:** Of all the patients diagnosed with T1DM, 173 (37.1%)

presented with DKA in the latest admission. The frequency of DKA in newly diagnosed children was 35.2%. The majority had either mild (50%) or moderate DKA (37.2%). The frequency of DKA was higher in older children ( $p < 0.05$ ). The major precipitating factors were infection (56.0%), omission of insulin dose (25.6%) and low socioeconomic status (21.8%). There was a significant positive relationship between age groups and HbA1c levels ( $p < 0.0001$ ). Moreover, girls had significantly higher latest HbA1c levels ( $p < 0.003$ ). Two children died (0.4%). **Conclusion:** Our study provides recent data in East African population for whom data are sparse. The incidence of DKA at initial presentation of T1DM among children in Sudan is high due to unawareness of the population. Older children with T1DM face an increased risk for developing DKA, due to frequent omission of insulin doses and problems of non-compliance. Intensive educational programs about the early symptoms of diabetes will reduce the frequency of DKA in new patients.

## Education Program in Diabetes

Ahlem Laabed

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**Aim:** The therapeutic education aims at helping the patients to acquire or maintain competencies which they need for better management of life with a chronic disease. It is the key to successful management of diabetes.

**Objectives:** Diabetes education aims to have a better glycemic control to maintain an optimal HbA1c, to avoid the acute complications, to prevent chronic complications and to improve the quality of life of the child and his family.

**Methods:** Our diabetic children and adolescents coming from Biskra (southern Algerian) for these two last years, have been educated initially in the hospital, either at the time of the discovery of the diabetes or at the time of an incident (hypoglycemia, ketoacidosis). During the evolution the education is programmed within the specialized consultations. Then, an educational program is established with in a multidisciplinary team which composes our educational group (pediatrist, psychologist, a nurse, biologist and dietician), all sensitized or formed with education. During interactive meetings of individual or collective education, we fixed knowledge to reinforce them (educational file), while using posters, videos, meetings of theater within a program of outputs. Evaluations are carried out at the beginning and last of the meetings (by questionnaire). The medical supervision is personalized and the HbA1c is carried out each three months.

**Results:** Our evaluation is always in hand, we showed a reduction in the rate of HbA1C, as well as a reduction in the frequency of hospitalization for acute incident.

**Conclusion:** The evaluation of the effectiveness of diabetes education is complex, it takes into account the evolution of the behavior of the patient and is interested in the impact on quality of life.

## A Novel IGF-1 Receptor Mutation Causing Intrauterine and Postnatal Growth Failure through Kinase-Deficient IGF-1 Receptor

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**Background:** IGF-I receptor (IGF1R) plays an essential role in human intrauterine and postnatal development. Few heterozygous mutations in IGF1R leading to IGF-I resistance and intrauterine and postnatal growth retardation have been described to date. The

clinical and functional relevance of a novel heterozygous IGF1R mutation identified in a girl with short stature and six relatives was evaluated. **Patients:** Affected individuals showed birth lengths between -1.40 and -1.82 sd score (SDS) and birth weights between -1.84 and -2.19 SDS. Postnatal growth retardation ranged between -1.51 and -3.93 height SDS. Additional phenotypic findings were variable including microcephaly, clinodactyly, delayed menarche, and diabetes mellitus type 2. Genetic analyses were initiated due to elevated IGF-I levels of the girl.

**Results:** Denaturing HPLC screening and direct DNA sequencing revealed a heterozygous G3464C IGF1R mutation in exon 19 located within a phylogenetically conserved motif of the kinase domain. The resultant mutation of glycine 1125 to alanine (G1125A) did not affect IGF1R protein expression in transfection of COS-7 cells and Igf1R deficient mouse fibroblasts but abrogated IGF-I induced receptor autophosphorylation and phosphorylation of downstream kinases protein kinase B/Akt and MAPK/Erk. Cotransfection of wild-type and mutant IGF1R resulted in reduced autophosphorylation of  $36 \pm 10\%$  of wild-type levels, suggesting a partial dominant-negative effect.

**Conclusion:** The identified G1125A mutation results in a kinase-deficient IGF1R, which is likely to cause the phenotype of intrauterine and postnatal growth retardation.

## Role of Continuous Glucose Monitoring System in Optimizing Glucose Level in Patient with Type 1 Diabetes Mellitus

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**Objectives:** The aim of this study is to assess the value of (CGMS) in detection of hypoglycemia, hyperglycemia and the possible role of (CGMS) in optimizing glucose control in children with type 1 diabetes mellitus.

**Patients and Methods:** A total of 37 compliant children with type 1 diabetes for more than one year on intensive insulin therapy (age range 4 - 22 years) were included in a non-randomized, non-controlled interventional study for six months. The CGMS the Mini MedMeditronic CGMS gold system was used, the first model approved by FDA (Food and Drug Administration) and it was not real time CGMS. The CGMS reading were compared to that of SMBG (self monitoring of blood glucose) of at least six times a day during the period of study

**Results:** The average number of hyperglycemic attacks detected by CGMS during the whole monitoring period was  $11.7 \pm 3$ , while the average number of hyperglycemic attacks detected by SMBG was  $7 \pm 2.4$ . CGMS based adjustment showed a reduction in the average number of hypoglycemic and hyperglycemic attacks with the P value 0.016 and 0.005 respectively. The average HbA1c was reduced significantly from  $9.2 \pm 1.2\%$  before insulin dose adjustment to  $7.8 \pm 1.2$  and  $7.7 \pm 1.3\%$  at three months and six months, respectively, after adjustment.

**Conclusion:** CGMS improved the rate of detection of hypoglycemic and hyperglycemic events. CGMS based adjustment showed marked improvement in glycemic control.

## Growth in Type 1 Diabetes Mellitus

Chorouk Mansour

*Children University Hospital, Casablanca, Morocco*

**Background:** Type 1 diabetes mellitus is the most common endocrine disease in children.

**Objective:** To assess the height and weight growth of children with diabetes, and look for the factors that influence it.

**Materials and Methods:** Data was collected during the campaign of Diabetes day in 2013. All children with other endocrine, metabolic or visceral disease may affect their growth are excluded. Height and weight were measured compared to the target size according to WHO curves.

**Results:** The number of children was 108 with the age of below 18 years. Age at discovery of diabetes was  $6.25 \pm 3.2$  years [five months to 16 years], and diabetes was known since  $3.1 \pm 2.1$  years [one month to 10 years]. In those patients 33% of cases having a family history of type 2 diabetes, 81% were followed regularly. The HbA1c was  $8.98 \pm 1.8$  %. The measured Height was  $146 \pm 16$  [68-

176] cm for age at the time of the review of  $9.3 \pm 3.08$  [1-18] years. Short stature, average - Three DS was found in 3%. The weight was  $32 \pm 9.5$  [12-87] kg and BMI of  $14 \pm 2.2$  [11.4 to 25.5] kg/m<sup>2</sup>. Underweight was present in 3% of children, 47% were normal weight and 16% overweight.

**Conclusion:** The aim of diabetes management is to avoid medium and long-term complications hence the importance of careful monitoring and adequate education, to minimize the impact on growth and puberty. Our results therefore deserve expansion of prospective data from all clinical and laboratory parameters during all periods of growth including puberty.

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