Second Arab Society for Pediatric Endocrinology and Diabetes (ASPED) European Society of Paediatric Endocrinology and Diabetes (ESPE) School
9-12th Dec. 2015, Abu Dhabi, United Arab Emirates

Rasha Hamza1, Hala Al Shaikh2, Jan Lebl3, and Asma Deeb**

1Department of Pediatric Endocrinology, Ain Shams University, Cairo, Egypt
2Muscat Private Hospital, Muscat, Sultanate of Oman
3Paediatric Endocrinology Department, University of Prague, Czech Republic
4Department of Pediatric Endocrinology, Mafraq Hospital, Abu Dhabi, UAE

*Corresponding author: Asma Deeb, Chief of Paediatric Endocrinology, Mafraq Hospital & Gulf Medical School, Abu Dhabi, United Arab Emirates, Tel: +971-50-835-0568; E-mail: adeeb@mafraqhospital.ae

Abstract

The second ASPED ESPE school was organized by ASPED (Arab Society of Pediatric Endocrinology and Diabetes) in collaboration with the European Society of Pediatric Endocrinology (ESPE) and is sponsored by an educational grant from Novo Nordisc Gulf exclusively. The second school was held in Abu Dhabi and run by an expert group of faculty from ASPED and ESPE. Candidates were selected following open competitive applications through ASPED and ESPE websites. Strict enrollment criteria were agreed on by the ASPED-ESPE school steering committee. The school included 52 candidates (out of 78 applicants) from 13 countries. The themes of the curriculum featured majority of Pediatric Endocrinology subjects, which were delivered in the format of lectures, interactive group discussion, case and research project presentation. In addition, small group discussion was run in four parallel groups in which over 40 cases and research projects were presented. ESPE E-learning program was introduced to school attendees and a number of topics and cases were discussed through its portal.

Evaluation forms were analyzed and showed satisfactory responses by candidates in relation to course organization, scientific discussion and opportunity for future collaboration and linking.

Keywords: DSD; Growth; Bone; Puberty; Diabetes

Introduction

The Arab Society for Pediatric Endocrinology and Diabetes (ASPED)

ASPED was launched in Abu Dhabi, United Arab Emirates in 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 organization and is registered under the Dubai Association Center (DAC) under 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.
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 ASPED ESPE School

The ASPED ESPE school is an initiative by ASPED in collaboration with the ESPE. It is an annual event that delivers revision and update on endocrine disorders and diabetes to physicians involved in managing diabetes in children and young people.

The school is structured in the format of an intensive course of teaching in pediatric endocrinology and diabetes. Its main aim is to provide an update in this field for pediatricians practicing pediatric endocrinology in the Arab countries. The school is a forum for networking and brainstorming about research ideas and available resources and provides an ideal setting for sharing experience and initiating scientific collaboration. ASPED ESPE school rules are set by the ASPED ESPE committee which consists of senior pediatric endocrinologists form ASPED and ESPE. Enrollment in the school is based on selection following open competition. Essential and preferred criteria for eligibility and enrolment are set by the ASPED ESPE school committee.

The Second ASPED ESPE School

The 2nd ASPED ESPE school was held at the Holiday Inn hotel, Abu Dhabi between the 9th and the 12th December, 2015. With highly educational curriculum and prominent international and regional speakers, the school attracted 78 applicants from 16 countries. Fifty two participants attended the school from 13 different Arab countries; United Arab Emirates, Kingdom of Saudi Arabia, Egypt, Kuwait, Iraq, Algeria, Sudan, Palestine, Oman, Qatar, Bahrain, Lebanon and Jordan.
Curriculum and Format

The school covered most of the important Pediatric Endocrinology topics including: growth, puberty, thyroid disorders, calcium and bone disorders, disorders of sex development, pancreatic endocrinology (hyperinsulinemic hypoglycemia, hyperglycemia and diabetes mellitus) and obesity. The curriculum was delivered in various formats including lectures, small group discussion, case presentations and research projects presentation. Twelve plenary lectures were delivered by senior endocrinologists from ESPE and ASPED. Forty one complex/interesting cases were presented by candidates and faculty in addition to seven research projects. Selected cases and research projects were presented to all audience. In addition, attendees were split into four smaller groups for parallel presentation and discussion in a more interactive manner.

Scientific and Social Linking

The school enabled participants to meet and link up with senior researchers, clinical experts and fellow clinicians in a collegial environment encouraging active discussions and exchange of ideas. In addition to the high scientific level, the social interaction between the school faculty and candidates was remarkable.

Second ASPED_ESPE school special lectures

1) ESPE Training & Education Programs
2) E-learning in Paediatric Endocrinology
3) Research Methodology

ESPE Education & Training Programs

Jan Lebl, Paediatric Endocrinology Department, University of Prague, Czech Republic

ESPE offers a diverse and highly efficient range of training programs suitable for pediatricians in training to become pediatric endocrinologists and for pediatric endocrinologists requiring continuing education. Details on ESPE training programs are available at https://www.europes.org/education/index.html. Medical training, courses, grants and fellowship offered by ESPE are presented. A major form of ESPE education programs are ESPE schools. The schools are intensive courses in pediatric endocrinology in various parts of the world under different organizing hosts/countries. They include ESPE Summer and Winter Schools, ESPE Science School, Maghreb School, Diabetes, Obesity and Metabolism school, the Caucasus and Central Asia School and the Advanced Seminars in Developmental Endocrinology courses.

ESPE has various training programs with sister societies. Of those, the Pediatric Endocrine Training Centers in for Africa (PETCA) Program was established in Nairobi with a grant from World Diabetes Foundation (WDF) in 2008. From this program, 46 students from 12-sub Saharan countries had graduated by the end of 2014. Graduates from this program have established the African Society for Pediatric & Adolescent Endocrinology (ASPAE). In 2012, the second PETCA in Lagos was opened to train pediatric endocrinologists from Western Africa.

In addition to the training programs, ESPE offers various fellowships and grant opportunities for both young and senior members who intend on further building up a scientific, research and clinical career in pediatric endocrinology. Available ESPE grants are ESPE Research Fellowship, ESPE Clinical Fellowship, ESPE Sabbatical Leave Program, and ESPE Visiting Scholarship. ESPE offers opportunities for its members to apply for grants for both attendances at the annual congress and for research specific grants. These include Travel Grants, ESPE-RU Collaborative Project Grant Support, and IFCAH-ESPE grant.

E-Learning in Paediatric Endocrinology

Sten Drop, Rotterdam University, Rotterdam, the Netherlands

The ESPE e learning is an initiative that provides an interactive online learning environment with access to up-to-date resources for pediatric endocrinology. ESPE e-learning web portal allows entrance to an interactive learning environment for up to date paediatric endocrinology. Through this webportal medical students, residents, fellows, specialists, consultants and teachers around the world, can gain, share, contribute and develop knowledge in Pediatric Endocrinology in an accessible and flexible way. The E-learning Portal is available in http://www.espe-elearning.org/.

Research Methodology

Khalid Hussain, Institute of Child Health, University College London, London, UK

Modern research is based on many parameters. Well-structured methodology, ethics compliance and proper application of medical statistics are crucial parts. Medical research facilitates understanding pathophysiology and mechanism of disease, which enables progress of development of new treatment modalities. Translational research is fundamental in improving patient care as it leads to uncovering new diseases though to be idiopathic. In this talk, key components of research are discussed including formulating a concise research question and a hypothesis, generating data and establishing a research group.

Acknowledgement

We acknowledge the ESPE faculty; Prof Khalid Hussain (UK), and Prof Sten Drop (Netherlands) who contributed markedly to the delivery of the school curriculum. We are grateful to Prof Zulf Mughal (UK) for his input on lecturing and running various discussions in the school. We would like to thank ESPE for offering one-year free membership to school attendees.

Funding

The ASPED_ESPE School is funded by an educational grant from Novo Nordisk Gulf.

Official Partners

ASPED is a registered non-profit organization under Dubai Association Center, Dubai, United Arab Emirates.
Approach to Children with Growth Disorders

Jan Lebl

Department of Pediatrics, Faculty of Medicine, Charles University, Prague, Czech Republic

Child’s growth is an orchestrated pre-programmed process. According to the concept of Karlberg, the child’s growth consists from three components – infantile (from intrauterine period up to 2nd birthday), childhood (up to onset of puberty) and pubertal (up to final height). Prerequisites of normal growth include sufficient nutrition, good general health status (absence of long-term inflammatory process), optimal oxygenation of tissues and normal hormonal regulations – regarding growth hormone, sexual hormones, thyroid hormones and hormones of adrenal cortex. Abnormalities of skeletal development and metabolism (skeletal dysplasias) may lead to disproportionate short stature.

Besides of the basic recognition of chronic conditions compromising growth, the main interest of pediatric endocrinologists is given to growth hormone secretion and function. Growth hormone deficiency may be either congenital (genetic or idiopathic), of perinatal origin (e.g., breech delivery) or acquired (brain tumor; brain irradiation). The corner stone for understanding the genetic background of pituitary hormone deficiencies was laid by Prof. Illig in 1971. She proposed that some children with severe congenital isolated growth hormone deficiency may suffer from deletion of gene encoding human growth hormone (later named GHI gene). She has observed that these children tend to produce antibodies against growth hormone after initiation of growth hormone replacement due to the lack of immunological tolerance towards the GH molecule. She assigned these patients as having “A-type of isolated growth hormone deficiency”, later known rather as isolated GHD type 1A.

Nearly two decades later in 1988, the first transcriptional factor was identified to regulate differentiation of specialized pituitary cell lines. It was originally assigned as GHF-1, subsequently as PIT1 and recently as POU1F1. POU1F1 governs the final phase of differentiation of pluripotent pituitary cells into somatotrophs, thyreotrophs and lactotrophs.

Within the past 25 years, the understanding of genetic determination of pituitary morphogenesis, differentiation and function precisely. We are now well aware that pituitary development is governed by a pre-programmed activation of a cascade of transcription factors that orchestrate firstly the pituitary morphogenesis in context with development of mid-line brain structures, optic nerves and eyes, and thereafter differentiation of five cell lineages of the anterior pituitary. Therefore, congenital multiple pituitary hormone deficiency (MPhD) may result from mutations of genes encoding a variety of transcription factors. These include mutations in PROP1, POU1F1, HESX1, LHX3, LHX4, OTX2, SOX2, SOX3, and GLI2. Of these, defects in PROP1 and POU1F1 genes encoding for transcription factors PROP1 and POU1F1 were most prevalent in populations studied so far and may account for up to 25% of all congenital cases of MPH.

Whereas the specific phenotype of POU1F1 defect is characterized by a severe combined deficiency of growth hormone (GH), thyrotropin (TSH), and prolactin (PRL), usually recognized within the first years of life due to severely retarded postnatal growth, the endocrine phenotypes of HESX1, LHX3, LHX4, and PROP1 defects overlap and have been reported to include failure of up to all five cell lineages of the anterior pituitary. Moreover, especially in PROP1 defect the pituitary dysfunction may evolve throughout the human lifespan and a new hormonal deficit (especially ACTH deficiency) may appear years after the initial investigation. In addition, some of those with PROP1 defects may pass through a period of pituitary hyperplasia during their first two decades of life. The pituitary mass seen at magnetic resonance is benign, did not require surgery in any case of those observed so far and tends to resolve spontaneously. Unnecessary surgeries were provided in some patients who were diagnosed with a PROP1 defect thereafter, when testing became available.

Multiple additional signaling pathways are involved in regulation of child’s growth, besides of pituitary development and function, and novel genetic mechanisms are being clarified every year. Of those most fascinating, the RAS-MAPK signaling pathway is one of the most complex, opening new insights into genotypes and phenotypes of Noonan syndrome, LEOPARD syndrome, von Recklinghausen disease and some other conditions.

Diabetes in Children; Not Always Type 1!

Asma Deeb

Paediatric Endocrinology Department, Mafraq Hospital, AbuDhabi, UAE

In the recent years, it has been recognized that a child presenting with diabetes is not necessarily a type 1 diabetes mellitus (T1DM) patient. Various forms of monogenic diabetes have now been recognized. This has been due to the advances in molecular genetics which have led to identification of genes associated with many clinically-identified subgroups of diabetes.

The identification of genes has explained clinical heterogeneity of many conditions with special features of diabetes. The main examples experienced in Pediatrics are; neonatal diabetes and maturity onset diabetes of the young (MODY). In addition to monogenic diabetes, type 2 diabetes mellitus (T2DM) in children and adolescent is becoming an increasingly important public health concern throughout the world. Because of the relatively recent recognition of the problems in this age group, many children with new onset T2DM may be misclassified as having T1DM. Conversely, as the population becomes heavier, overweight adolescents with autoimmune diabetes may be misdiagnosed as having T2DM.

The worldwide changing face of diabetes has spread globally with the Gulf area and the nearby Arabic countries not exempted. The main emphasis of the talk is to discuss various types of diabetes in children and adolescents and to highlight the special characters of individual diabetes subtype in this population. Examples of children from the local population with genetically confirmed various types of diabetes will be presented.

Precocious Puberty: Diagnosis and Approach to Management

Rasha Tarif Hamza

Pediatric Endocrinology Department, Ain Shams University, Cairo, Egypt

Precocious puberty is defined as the appearance of any secondary sexual characteristic before the age of eight years.
in a girl and nine years in a boy. It could be either central or peripheral precocious puberty or incomplete variants such as premature thelarche or pubarche or menarche. The workup of a case of precocious puberty involves a full history, thorough clinical examination including accurate anthropometric assessment and laboratory assessment most important of which is the GnRH stimulation test. In addition, radiologic investigations in the form of bone age and MRI brain (in central type) are also needed. The treatment varies according to the type of precocious puberty where long acting LHRH analogue is the first line of treatment in central causes; while in peripheral precocious puberty, treatment varies according to the cause. Following start of treatment, monitoring the response is also important in the form of growth assessment, Tanner pubertal staging, GnRH stimulation test and bone age.

**Disorders of Sex Development; Structured Approach on Diagnosis and Management**

**Rasha Tarif Hamza**  
*Pediatric Endocrinology Department, Ain Shams University, Cairo, Egypt*

Genital ambiguity is defined as difficulty in determining sex. It occurs in 1 in every 10000 live births but about 1 in every 350 is still born. The Knowledge of embryology and differential diagnosis is important. The proposed revised nomenclature for Disorders of Sex Development (DSD) includes: 46, XY DSD, 46, XX DSD, ovotesticular DSD, 46, XX testicular DSD and 46, XY gonadal DS genesis. A systematic approach based on whether the gonads are palpable or not and on laboratory investigations is important for prompt diagnosis. A multidisciplinarity team is needed for proper diagnosis and management but one contact person for the parents is preferred. Physicians must consider the situation as urgent and a proper decision needs to be made. It is important to consider psychosexual outcome and not only fertility.

**Thyroid Disorders in Children**

**Hala ALSheikh**  
*Muscat Private Hospital, Oman*

Congenital hypothyroidism presents with subtle changes at birth and neonatal screening is crucial to make the diagnosis, due to the Thyroxin role on brain maturity in the early years of life. Furthermore, thyroxin plays an important role in the process of body growth and metabolism. In this presentation, the causes, clinical manifestations, investigation and treatment of congenital and acquired hypo and hyperthyroidism will be discussed. Anti-thyroid drugs and their side effects will be explained. Subclinical hypothyroidism and thyroid hormone resistance and their management will be considered. As well as the clinical approach to goiter which is the most common clinical manifestation in children with thyroid disease, with special consideration to nodular goiter due to its association with thyroid cancer.

**Delayed Puberty; How to Approach**

**Hala Al Shaikh**  
*Muscat Private Hospital, Oman*

Puberty is the transitional period between childhood and adulthood when physical, sexual, and physiological maturation occurs. In this presentation the difference in the age of pubertal onset and pubertal manifestations between males and females will be highlighted, as well as the hormonal changes during puberty and its clinical implication. Delayed puberty will be discussed in regards to definition, frequency, causes, investigations, clinical findings, and treatment in both males and females. Constitutional delay of growth and puberty represents the single most common cause of delayed puberty in both sexes and is usually associated with a positive family history; however, underlying conditions have to be ruled out. Kallmann Syndrome, an example of hypogonadotrophic hypogonadism and Turner Syndrome an example of hypergonadotrophic hypogonadism will be discussed in regards to underlying genetic abnormalities, clinical manifestations and treatment.

**Hyperinsulinaemic Hypoglycaemia**

**Khalid Hussain**  
*Institute of Child Health, University College London, London, UK*

Pancreatic beta-cell dysfunction in the newborn period can lead either to hypoglycaemia or hyperglycaemia. Hypoglycaemia occurs due to inappropriate insulin secretion which leads to hyperinsulinaemic hypoglycaemia (HH). Hyperglycaemia occurs due to too little insulin secretion and this lead to neonatal diabetes mellitus (NDM). Genetic defects in nine different genes have been described which lead to HH. On the other NDM can be due to defects in a large number of genes.

Insulin secretion from pancreatic β-cells is tightly regulated to keep fasting blood glucose concentrations within the normal range (3.5–5.5mmol/L). Hyperinsulinaemic hypoglycaemia (HH) is a heterozygous condition in which insulin secretion becomes unregulated and its production persists despite low blood glucose levels. It is the most common cause of severe and persistent hypoglycaemia in neonates and children. The most severe and permanent forms are due to congenital hyperinsulinism (CHI). Recent advances in genetics have linked CHI to mutations in 9 genes that play a key role in regulating insulin secretion (ABCC8, KCNJ11, GLUD1, GCK, HADH, SLC16A1, UCP2, HNF4A and HNF1A). Mutations in genes ABCB (SUR1 subunit) and KCNJ11 (Kir6.2 subunit) are the most common cause of CHI. Both the ABCB/KCNJ11 genes are localized on chromosome 11p15.1. The most severe forms of CHI are due to reactive inactivating (loss of function) mutations in ABCB and KCNJ11 leading to unregulated insulin secretion despite severe hypoglycaemia. Dominant inactivating mutations in ABCB and KCNJ11 usually cause a milder form of CHI which is responsive to diazoxide. However, medically un-responsive forms have also been reported.

Histologically, CHI can be divided into 3 types: diffuse, focal and atypical. Given the biochemical nature of HH (non-ketotic), a delay in the diagnosis and management can result in irreversible brain damage. Therefore its essential to diagnose and treat HH promptly. Advances in molecular genetics, imaging methods (18F-DOPA PET-CT), medical therapy and surgical approach (laparoscopic surgery) have completely changed the management and improved the outcome of these children.

**Neonatal Diabetes Mellitus**

**Khalid Hussain**  
*Institute of Child Health, University College London, London, UK*

Neonatal diabetes mellitus is characterized by insulin-requiring hyperglycaemia within the first 6 months of life and has the opposite phenotype to CHI. The condition can either be permanent (PNDM), requiring lifelong insulin treatment or transient, where the condition can disappear during infancy but reappear in later life.
(TNDM). Genetic disorders in a large number of children have now been described which lead to either PNDM or TNDM. These gene defects can either be due to abnormalities in transcription factors which regulate pancreatic development, in key enzymes which control glucose metabolism in the beta-cell or in the genes (ABCC8/ KCNJ11) which control the function of the pancreatic KATP channels.

Activating/gain of function mutations in KCNJ11 are the most common genetic cause of PNDM reported to date. Only dominantly-acting KCNJ11 mutations have been described in PNDM. The majority (80%) of these mutations have arisen de novo during embryogenesis and in a few cases mosaicism has been reported. A common KCNJ11 mutation (R201H) has also been found, which leads to reduced sensitivity to ATP, preventing closure of KATP channels and reduced insulin secretion. ABCC8 mutations are less common in PNDM and are only found in 27% of patients in whom no KCNJ11 mutation has been found. These activating mutations are either heterozygous, homozygous or compound heterozygous for both activating and inactivating mutations. Although the majority of these mutations are sporadic (50%), mutations in ABCC8 can also be inherited recessively. A correct genetic diagnosis of NDM is very important as it can affect treatment and clinical outcome. Patients with mutations in the ABCC8/KCNJ11 can be transferred onto oral therapy with sulphonyl ureas.

### Miscellaneous Disorders of Bone & Mineral Metabolism

Zulf Mughal

Royal Manchester Children’s Hospital, Manchester, UK

Regulation of calcium and magnesium are intimately related. While hypocalcaemic patients may present with tetany or convulsions, those with hypercalcaemia often present with lethargy, hypotonia, anorexia, vomiting, polyuria, polydipsia, constipation or failure to thrive. Bone disorders in children may arise from several different causes. Disorders that cause impaired mineralization of the growth plate and bone matrix (osteoid), gives rise to rickets. Inherited and acquired disorders that result in low bone mass and deterioration in bone architecture result in osteoporosis and fragility fractures. However, certain high bone mass disorders, such as osteopetrosis and osteogenesis imperfect secondary to homozygous mutation in the BMP1, are also associated with skeletal fragility. Various clinical case scenarios will be discussed to improve understanding of the disease, diagnosis & management of selected childhood bone & mineral disorders.

### Evaluation & Management of the Child with Recurrent Fractures

Zulf Mughal

Royal Manchester Children’s Hospital, Manchester, UK

Distal forearm fractures are common in healthy childhood and adolescence; approximately one third of children will sustain at least one fracture by 18 years of age. The majority of such fractures occur around the time of the adolescent growth spurt. Fragility fractures in children can arise either from a primary bone disorder, such as osteogenesis imperfect, or secondary to an underlying medical or a nutritional disorder: The International Society for Clinical Densitometry has defined osteoporosis in children based on the presence of either a vertebral compression fracture(s) or a combination of both a clinically significant fracture history and bone densitometry findings. Thus, in the absence of severe trauma, the presence of at least one vertebral compression fracture, two or more long bone fractures by 10 years of age, or three or more long bone fractures by 19 years is an indication for further bone health evaluation. Evaluation of a child with recurrent fractures is based on obtaining a relevant medical history, undertaking appropriate laboratory & genetic investigations where necessary. As vertebral fractures are often asymptomatic in children, screening by spinal radiographs or vertebral fracture assessment by dual-energy x-ray absorptiometry (DXA) should be undertaken in those at increased risk, e.g. in children with inflammatory disorders who are treated with oral corticosteroids. In children it is important to adjust DXA measured bone mineral content for size (height) and for lean body mass. Where possible, management involves treatment of the underlying conditions, e.g. inflammatory bowel disease. Correction of vitamin D deficiency, provision of calcium supplements, encouraging weight-bearing physical activity and timely induction of puberty (often delayed in children with chronic medical disorders) is important. The use of bisphosphonates in children is limited to those with moderate-to-severe bone fragility and in those with vertebral compression fractures.

### Abstracts for Case Reports

#### Mauriac Syndrome; Use of Growth Hormone and Insulin Pump

Ola AlSayed

Pediatric Department, Sabah Hospital, Kuwait

**Background:** 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. Inadequate glucose delivery to the tissues, decreased insulin-like growth factor-1 (IGF-1) and GH levels, hypercortisolism, and resistant or defective hormone receptor action contribute to stunted growth and delay in puberty.

**Case Report:** A 15-year-old male with an 11 year history of T1DM was seen for evaluation of growth retardation, abdominal distension and poor diabetic control. The patient was on insulin Glargine and Aspart multiple daily injections at a dose of 1unit/kg. He had poor control of diabetes with no regular follow-up. There was no history of diabetic ketoacidosis, but multiple episodes of documented hypoglycemia as well as hyperglycemia were reported. His HbA1C was 11.5 % on several visits over the last one year. Urine albumin to creatinine ratio was high with a BP on the 97th centile for sex and height. He was on captopril (12.5 mg) to improve his proteinuria. Anthropometric data revealed a height below the 3rd percentile, weight below 3rd percentile, body mass index 17.58 kg/m², and a bone age of 7.3 years. Testes both were less than 4ml bilaterally. Growth hormone injection 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. Growth velocity was 3 cm during this year.

**Conclusion:** The use of exogenous growth hormone can be of little benefit on longitudinal growth and puberty. It is essential to improve glycemic control prior to commencing other growth treatment modalities.

#### A Case of Pseudo Precocious Puberty

Adil Al Amry

Armed Forces Hospital, Muscat, Oman

Precocious puberty is the onset of secondary sexual
A Rare Presentation of Hypercalcemia in Two Siblings

Samar Hassan
Gaffer Ibn Aouf Hospital, Khartoum, Sudan

Familial isolated primary hyperparathyroidism is rare in children. We are reporting a case series of two siblings who presented in infancy with failure to thrive, gross motor delay and hypotonia. In addition, the female had a fracture and was incidentally found to have high serum calcium levels. Both siblings had no evidence of other endocrinopathies. They had a cousin who was diagnosed with primary isolated hyperparathyroidism and was treated by parathyroidectomy. No family history of MEN or other endocrinopathies was reported. Workup of both siblings showed very high levels of parathyroid hormone with high serum calcium and low phosphate. They both had high urinary calcium/creatinine ratio. Ultrasound imaging showed enlargement of parathyroid glands. TC 99m scan was normal. They both required parathyroidectomy. Histopathology of both siblings showed parathyroid hyperplasia. Genetic analyses for gene mutations are needed.

What Type of Diabetes is this? A Rare Form of Cushing’s Syndrome in a Five Year Old Child

Bushra Barakat
Pediatric Department, Dubai Hospital, Dubai, UAE

A 10 year old girl was diagnosed since age of 35 days to have neonatal diabetes. She was started on insulin. Then she continued to follow up at our endocrinology clinic. She used to have high blood sugar readings although her HbA1C was between 6-7% and rarely reached 8%. Her insulin requirement was high at 1.2 UI/kg/day. At the age of 9, she presented with nephrotic syndrome. Her renal biopsy was confirmatory of minimal change nephrotic syndrome and she was started on steroids. As she presented at the neonatal period and her autoantibodies were negative, monogenic diabetes was suspected and genetic testing was done. The results showed that she had STAT3 gene mutation. The patient remained on insulin and is on a tapering dose of prednisolone. She is followed up by the endocrinology and nephrology teams.

A Case of Bardet-Biedl Syndrome

Hajer Berrani
Children Hospital, Rabat, Morocco

Bardet-Biedl syndrome (BBS) is a genetically heterogeneous autosomal recessive disorder characterized by progressive retinal dystrophy, polydactyly, obesity, hypogonadism, mental retardation, and renal dysfunction. We report a boy with BBS who first presented to our clinic for obesity. Our patient was born in 2002 to non-consanguineous Moroccan parents. The family history was unremarkable. At term, birth weight was normal. Polydactyly and brachydactyly of both hands was noted at birth and he was operated for an anal imperforation. At the age of 9 years, obesity was noted. Physical examination revealed the patient to be mildly dysmorphic with micrognathia, and short neck. He was 146 cm tall and weighed 70 kg; the BMI was 31.9 kg/m². Ophthalmologic examination revealed characteristic retinopathy pigmentosa with low visual acuity. There was no renal disease in the ultrasonographic investigations. He didn’t start puberty, with microopenis and bilateral cryptorchidism. Basal gonadotrophins and sex steroid were low. His vision started to deteriorate and he had marked night blindness.

BBS has an adverse prognosis, with an early onset of blindness, obesity and renal impairment, which is the major cause of morbimortality in these patients. The management of this syndrome is multi-disciplinary, which focuses on individual features. A lack of medical awareness of this condition contributes to the delay in the diagnosis and an early institution of therapy and surveillance.

An Interesting Case of Precocious Puberty

Olivia Al Mutasim
Gaffer Ibn Aouf Pediatric Hospital, Khartoum, Sudan

We report a six year old Sudanese girl, known to have Down syndrome and a small VSD since age of six months. She lost her follow up with cardiologist but was seen many times at primary health center due to recurrent chest infections, fatigability, poor school performance which were attributed to her condition. She was referred to the endocrine clinic with a complaint of vaginal bleeding that was preceded by breast enlargement. There was no family history of early puberty. The girl was short with height below the 3rd centile and a delayed bone age. On examination, she had a Tanner stage III of breast and an estrogenized vaginal mucosa. Investigations revealed high TSH, low T3, high basal FSH and low LH. Her pelvic ultrasound was normal. A diagnosis of Van WykGrumbach Syndrome was made.

A Rare Form of Cushing’s Syndrome in a Five Year Old Child

Fatima Al Zahra Fadhil
Pediatric Department, Provincial Hospital, Morocco

Adrenocortical neoplasms are rare in the pediatric population. Adrenocortical carcinoma as a cause of Cushing’s syndrome in a child is a rare occurrence. Functioning adrenal carcinomas are detected at an earlier stage even with smaller size while non-

Citation: Hamza R, Al Shaikh H, Lebl J, Deeb A. Second Arab Society for Pediatric Endocrinology and Diabetes (ASPED) European Society of Paediatric Endocrinology (ESPE) School, 9-12th Dec. 2015, Abu Dhabi, United Arab Emirates; J Diab Rel Dis: 2016.
functioning tumors are usually detected incidentally. We report a case of Cushing’s syndrome due to large functioning adrenal carcinoma in a five year old female child who presented with clinical features of Cushing’s syndrome along with virilization. A combination of biochemical laboratory reports along with radiological investigations enabled a proper diagnosis. The child has lung metastasis on presentation and surgical resection was not thought to be suitable. Various forms of presentation and treatment of Cushing syndrome in children will be discussed.

**Estrogen Resistance due to a Novel Estrogen Receptor Gene Mutation in Two Algerian Sisters**

*Sakina Khera*

*University Hospital, Algiers, Algeria*

Estrogen insensitivity syndrome, although described, is extremely rare. To date two cases have been reported: the first in a man aged 24 years with infertility and bone abnormalities and the second is a girl of 17 years with delayed puberty and absence of breast development.

We present two Algerian sisters aged 24 and 17 years who presented with primary amenorrhea and lack of breast development. Both were found to have 46, XY karyotypes. In the index case high estradiol levels were consistently high, ranging between 8500 and 9200 pmol/L, with FSH and LH levels of 15 and 24 u/L. Pelvic ultrasound has shown evidence of bilateral cystic ovaries. Molecular genetic analysis has identified a novel homozygous mutation of the gene ESR. Functional analysis has shown normal expression of the mutated receptor, but confirms a 100-fold decline in the affinity of estradiol for the receptor. Currently no treatment is available to redress the estrogen resistance caused by the mutant receptor.

**Molecular Detection of a Novel WFS1 Mutation in a Palestinian Family with Wolfram Syndrome**

*Adeeb Naser Eddin*

*Pediatric Department, Hadassah Hospital, Jerusalem, Palestine*

Wolfram syndrome is a rare autosomal recessive neurodegenerative progressive disorder, also known as DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy and deafness). Affected individuals may also show renal tract abnormalities as well as multiple neurological and psychiatric symptoms. We report a novel WFS1 mutation in two female Palestinian sisters. A Palestinian female child, born to consanguineous parents, presented with diabetes mellitus during childhood, developed recurrent attacks of urinary tract infection, renal ultrasound showed hydronephrosis, cystogram confirmed neurogenic bladder requiring frequent catheterization. Ophthalmic exam showed optic atrophy. Her sister also developed type 1 diabetes mellitus and mild hydronephrosis. Wolfram syndrome was suspected and confirmed by molecular testing.

Sequencing of WFS1 gene revealed a CTCT deletion in exon 8, del4115<ins>/ter440</ins>. The deletion was predicted to cause a frame shift at codon 411 with production of truncated protein that has 440 amino acids instead of 890 normal length proteins. This has been found in another affected sister and the mother being heterozygous for the same mutation; also other sisters were heterozygous for the same mutation in addition to the father.

A novel WFS1 mutation has been detected in two Palestinian sisters. To the best of our knowledge, this is the first report of this rare syndrome in a Palestinian family. The coexistence of Wolfram syndrome among patients affected with DM should be considered in the differential diagnosis and ophthalmic exam should be done in any affected patient with DM. Early diagnosis is imperative to enable proper prognosis, anticipate complications and prevent affliction in further pregnancies. The prevalence of this syndrome among Palestinian population remains to be determined.

**Wolfram Syndrome Type II: A Unique Presentation**

*Najwa Abdulhalag*

*Pediatric Department, Hadassah Hospital, Jerusalem, Palestine*

Wolfram syndrome is a rare autosomal recessive neurodegenerative progressive disorder, also known as DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy and deafness). Affected individuals may also show renal tract abnormalities as well as multiple neurological and psychiatric symptoms. Recently other manifestations were reported including gastric ulcers which lead to the decline of Wolfram syndrome Type 2.

We present two separate cases with endocrinological clinical presentations with chronological development in the clinical course over the years allowing the clinical diagnosis of Wolfram Syndrome with molecular confirmation. The coexistence of Wolfram syndrome among patients affected with diabetes mellitus should be considered in the differential diagnosis and ophthalmic exam should be done in any affected patient with DM. Early diagnosis is imperative to enable proper prognosis, anticipate complications and prevent affliction in further pregnancies. The prevalence of this syndrome among the Middle East population is higher than in other regions and the physicians should include Wolfram syndrome in their differential diagnosis.

**Addison Disease**

*Wafa Laimon*

*Mansoura Faculty of Medicine, Mansoura, Egypt*

A 9 years old male patient developed recent onset easy fatigability, drowsiness, abdominal pain, vomiting and darkness of skin. His laboratory investigations confirmed the diagnosis of Addison’s disease. The patient was maintained on oral prednisolone and fludrocortisone with good response on therapy for one year. A year later, the patient developed recurrence of symptoms with exaggerated vomiting and abdominal pain. His new laboratory investigation showed satisfactory adrenal functions. His vomiting did not respond to antiemetics or proton pump inhibitors. Barium meal showed dilated esophagus and manometric studies revealed achalasia of the cardio. The mother reported that he was on artificial tear because of dry eye. A diagnosis of Allgrove syndrome (triple A syndrome) is confirmed. He underwent cardio-myotomy with improvement of his vomiting.

**A Teenager with Oral Ulcers, Hyperpigmentation, and Postural Hypotension**

*Mohamed Talat*

*Pediatric Department, Zagazig University, Cairo, Egypt*

Polyendocrinopathy syndrome is a rare autosomal-recessive disorder that first manifests in early childhood and results in tissue-specific multiorgan autoimmunity, leading to decreased functioning of multiple glands. Endocrine organs such as the adrenal cortex, ovaries, and parathyroid glands are typically affected, which results...
in a variety of clinical presentations, including hypocortisolism, hyperaldosteronism, delayed puberty, premature ovarian failure, and hypoparathyroidism with life-threatening hypocalcemia. PGA-I is clinically defined as the presence of at least two components of the classic triad of hypoparathyroidism, adrenal insufficiency, and mucocutaneous candidiasis.

A 17-year-old girl presented with chronic, recurrent oral fungal infections, chronic diarrhea, recurrent abdominal pain, and vomiting since childhood. She has also been experiencing dizziness (especially on erect posture), darkening of the skin and oral cavity and a low-grade fever for the last 6-8 months. There was also a history of lethargy, easy fatigability, and palpitations on exertion without chest pain, anorexia, weight loss and some hair loss. The patient also reported dysmenorrh, polymenorrhagia but has had amenorrhea for the last year. Family history was positive for two siblings with similar presentations from early childhood. On examination, she was a thin, pale, dehydrated female. Hyperpigmentation of skin was seen, most prominently in the palmar creases, digits of both upper and lower limbs, lips, and oral mucosa. She had a smooth, glossy tongue with white patches consistent with thrush. Laboratory investigations revealed mild hyperkalemia and negative celiac screening. She had a low random cortisol with high concomitant ACTH.

The oral mucosa revealed Candida albicans. The patient was diagnosed with polyglandular failure type 1 (PGA-I).

**Delayed Puberty in an Adolescent with Micropenis**

**Nihed Selim**

Dr Benbadis Hospital, Annaba, Algeria

We report a 14 year old boy referred to the pediatric endocrinology clinic for delayed puberty with a history of micropenis and small testes from birth. Physical examination showed a normal weight and stature. There was a lack of sexual development with small testes and absent virilization (G1P2A1 according to the Tanner scale). Sense of smell was compromised. Hormonal profile showed low FSH, LH and undetectable testosterone levels <0.49 ng / ml. Magnetic resonance imaging (MRI) of the forearm showed the aplasia of the olfactory bulbs and right tract. In view of hypogonadotropic hypogonadism (HH) with anosmia, the patient was diagnosed with Kallman syndrome. A genetic study was requested and results awaited. Treatment was based on hormone replacement therapy, with testosterone 50mg / month for the first year then 100 mg / month (we are at 1 year and a half of treatment).

**5α-Reductase Deficiency**

**Foued AbelAziz**

El Hadjar Association Medical Group, Annaba, Algeria

We report the case of a 14 months old infant referred to the Pediatric endocrinology clinic for a Disorder of sex development (DSD). Examination of external genitalia showed a genital bud of 1 cm, two orifices and a palpable gonad of palpated on the left inguinal area. The karyotype was 46 XY and the abdominal-pelvic ultrasound revealed testes in inguinal position with normal aspect and a lack of internal female genital organs. Hormonal assessment showed a high antimullerian hormone (AMH) 666 pmol/L (< 50 pmol/L), and a low total testosterone 0.18 nmol / L (0.3-3nmol/L) and Dihydrotestosterone (DHT) < 0.15 nmol/L (< 0.17nmol/L). HCG stimulation test showed a dim b- stage of testosterone from 0.04 nmol / L to 37.78 nmol / L. It was difficult to distinguish between complete androgen insensitivity and 5α reductase deficiency. It is the molecular biology that revealed a mutation of the 5α reductase type 2 (SRD5A2) in patients whose parents are heterozygous carriers. Local treatment with DHT cream was started to grow genital bud. Choosing the sex assignment will likely be toward the male if the treatment is effective.

**Neonatal Panhypopituitarism: A Unique Presentation**

**Alaa Shamdan**

Makassed Islamin Hospital, Jerusalem, Palestine

Congenital hypopituitarism is an uncommon cause of neonatal cholestasis, and can present with hypoglycemia. Treatment with glucocorticoid and thyroid hormones, play a significant role in the resolution of cholestasis and hepatosplenomegaly. We aim to report an infant with panhypopituitarism, presenting with cholestatic jaundice, hypoglycemia and high serum ferritin level. Comprehensive clinical and laboratory investigations were performed to establish the etiology of the presenting complaints including genetic, metabolic, infectious, as well as hormonal profile (LH, FSH, PRL, TSH, FT4, ACTH and growth hormone stimulation tests). Hormonal evaluation revealed cortisol and growth hormone deficiency with central hypothyroidism. In addition, there was a high serum ferritin of 2315 ng/ml suggesting neonatal hemochromatosis that was excluded by the absence of hemosidrin deposition in buccal mucosal biopsy. Treatment with cortisol and thyroxin resulted in dramatic improvement of the liver function tests, resolution of cholestatic jaundice and significant reduction of serum ferritin level. These findings support the theory that thyroid hormones and cortisol affect the bile acid independent bile flow and deficiencies of these hormones can cause abnormalities of the biliary structure and function of bile canaliculi essential for bile excretion. To the best of our knowledge this is the first description of an infant with congenital panhypopituitarism, presenting with cholestasis, hypoglycemia and high serum ferritin level. Panhypopituitarism should be considered in any infant who presents with cholestasis, hypoglycemia, and other manifestations of pituitary malfunction. High serum ferritin level most probably suggests acute phase reactant.

**46XY, DSD: Gonadal Dysgenesis**

**Ahlem Laabed**

Dr Saadane Hospital, Biskra, Algeria

We report a 20 days old newborn, the product of a twin pregnancy with ditalor hypertrophy. There exists a consanguinity of 3rd degree, family antecedents of sterility. Clinical examination revealed a genital bud = 1.3 cm, 2 openings, no palpable gonads but seen on pelvic ultrasound. Testosterone: 1.73 nmol/l at 20 days, and rose from 0.64 to 4.29 nmol/l after HCG, AMH: 303.8pmol/L. The newborn’s twin had normal female external genitalia with uterus seen on pelvic ultrasound. Testosterone: 1.73 nmol/l at 20 days, and rose from 0.64 to 4.29 nmol/l after HCG, AMH: 303.8pmol/L. The newborn’s twin had normal female external genitalia with uterus visualized on pelvic ultrasound showing the presence of a Mullerian remainder. Testosterone and the AMH were low (1.02nmol/l and 17.3 pmol/l), 17hydroxy progesterone: 6.65 nmol for index case and 4.42 nmol/l for the other twin and Karyotype were 46, XY for both twins. Results were in favour of a gonadic dysgenesis. Genetic analysis confirmed a mutation c.938G>A (p.Arg313His) gene SF1 in the 2 sisters and the mother. Thus, the diagnosis of 46, XY DSD related to a mutation of gene SF1 was confirmed. Initially, considering the weak virilization of the 2 young girls it was decided to report an infant with panhypopituitarism, presenting with cholestatic jaundice, hypoglycemia and high serum ferritin level. Comprehensive clinical and laboratory investigations were performed to establish the etiology of the presenting complaints including genetic, metabolic, infectious, as well as hormonal profile (LH, FSH, PRL, TSH, FT4, ACTH and growth hormone stimulation tests). Hormonal evaluation revealed cortisol and growth hormone deficiency with central hypothyroidism. In addition, there was a high serum ferritin of 2315 ng/ml suggesting neonatal hemochromatosis that was excluded by the absence of hemosidrin deposition in buccal mucosal biopsy. Treatment with cortisol and thyroxin resulted in dramatic improvement of the liver function tests, resolution of cholestatic jaundice and significant reduction of serum ferritin level. These findings support the theory that thyroid hormones and cortisol affect the bile acid independent bile flow and deficiencies of these hormones can cause abnormalities of the biliary structure and function of bile canaliculi essential for bile excretion. To the best of our knowledge this is the first description of an infant with congenital panhypopituitarism, presenting with cholestasis, hypoglycemia and high serum ferritin level. Panhypopituitarism should be considered in any infant who presents with cholestasis, hypoglycemia, and other manifestations of pituitary malfunction. High serum ferritin level most probably suggests acute phase reactant.
to leave them in the female sex. At 13 months age, the second twin died from meningitis. The parents decided to leave the other as a boy. The change of sex to the civil status was carried out at 18 months. In front of a clitoromegaly, it is always necessary to search a gonadic mass clinically or with the ultrasonography, which can reveal DSD and must thus lead to meticulous examination for a precise and reliable diagnosis.

An Unusual Presentation of 3β Hydroxysteroid Dehydrogenase Deficiency

Mohamed Al Hassan
Gaffar Ibn Aouf Hospital, Khartoum, Sudan

We report two siblings with unusual presentation of congenital adrenal hyperplasia (CAH). The older, an 8 year old male, was born with ambiguous genitalia (severe proximal hypospadias and small phallus), to consanguineous parents, with negative family history. Testes were in scrotum at birth with no salt losing events thereafter. Hypospadias repair was done during infancy, though no endocrine consultation took place at the time. The first endocrine consultation was at 5 years of age because of isoosmolar precocious puberty, with bilateral testicular and pubic hair development and growth acceleration. He was then already on hydrocortisone for 2 years. After confirming the central nature of puberty with high luteinizing hormone [LH, 59 ng/dl post luteinizing hormone releasing hormone (LHRH) stimulation], the patient was started on long acting LHRH analogue. His blood pressure was normal throughout follow up visits, and he wasn’t hypertensive. His testosterone level at 6 years was 0.79 ng/ml (normal is 0 – 0.2 for 6 – 7 years). Ultrasound reports showed markedly enlarged adrenals during early infancy and at five years. Karyotype was 46 XY. The younger sister, with only slightly enlarged phallus at birth, presented with an adrenal crisis at the age of three months. She was also noted to have darker skin which becomes lighter on hydrocortisone. Karyotype was 46 XX. The change of sex to the civil status was carried out at 18 months.

A Novel Mutation in the AVPR2 Gene in a Palestinian Family with Nephrogenic Diabetes Insipidus

Ghaleb Zughayar
Zughayar Medical Center, Jerusalem, Palestine

Nephrogenic Diabetes Insipidus (NDI) is a urinary concentrating defect resulting from resistance of the collecting duct to the antidiuretic action of vasopressin (AVP). NDI is classified into hereditary and acquired. The X-linked recessive form is the most frequent genetic cause of inherited NDI and is caused by mutations in the gene encoding the V2 vasopressin receptor (AVPR2 gene). We describe a novel mutation in the AVPR2 gene in a Palestinian family with NDI. A Palestinian male infant presented in the neonatal period with failure to thrive, vomiting, irritability, fever, and polyuria of 7 cc/kg/hr. Serum sodium and osmolality were 170 mEq/L and 330 mOsm/kg respectively; while urine osmolality remained low between 45-135 mOsm/kg. The diagnosis of NDI was established based on the clinical picture. A similarly affected older brother suggesting X-linked inheritance of the disease, and absence of response to ddAVP Sequencing the AVPR2 gene for the patient

A Case of Hypercalcemia in an Infant with Subcutaneous Fat Necrosis

Sawsan Ghanem
Pediatric Department, Al Amiri, Hospital, Kuwait

We report a 3 month old baby girl who presented with hypercalcemia due to subcutaneous fatty necrosis. This occurred after a stormy neonatal period including meconium aspiration, for which she was admitted to neonatal intensive care unit (NICU) and kept in incubator for almost a month. She had episodes of excessive crying and cyanosis and was found to have hypercalcemia. She was started on intravenous fluids, intravenous Prednisolone, and furosemide, and special low calcium formula milk was tried for her. Serial serum calcium levels were monitored until calcium was normalized. Subcutaneous fatty necrosis was observed, which was gradually regressing until totally resolved. Serum calcium was normalized after few months of treatment. Furosemide and prednisolone were stopped after 2 months of treatment.

A Case of Craniopharyngioma: Presentation is Not Always Straight Forward

Muneera Al Ghunaim
Bahrain Defense Hospital, Riffa Town, Bahrain

A 10 year old boy was admitted for fever 39°C and cough and vomiting since three days with no history of convulsions. Routine laboratory assessment was normal. On day five of admission, the patient developed diarrhea (yellowish/greenish with mucus) and was vomiting excessively more than 10 times daily. Abdominal U/S reported mesenteric lymphadenitis with rim of free fluid. Reassessment revealed serum sodium of 110, potassium 3.79, chloride 75.3, Calcium 2.06, Magnesium 0.8, Urea 0.6, Creatinine 20. The impression was syndrome of inappropriate antidiuretic hormone secretion (SIADH) which was corrected with NaCl + fluid restriction and KCl. Further assessment revealed sodium: 138.1, potassium: 4.87, Chloride: 99.5, Calcium: 1.23, bicarbonate: 20, INR: 1.2. Magnetic Resonance Imaging of brain reported a rounded mass effacing the suprasellar cisterns extending superiorly with superior bowing of the optic chiasm, no extension to the third ventricle or hydrocephalus impression craniopharyngioma. CT scan revealed a well defined midline rounded mass about 2cm in diameter occupying the sella and the suprasellar regions. The mass shows peripheral rim of calcification, impression craniopharyngioma. Ophthalmology review reported a reactive pupile, normal eye movement, normal fundus, and no visual field defect by confrontation method. Pituitary hormones revealed a thyroid stimulating hormone of: 0.5, Prolactin: 19.85, luteinizing hormone: 0.10, follicle stimulating hormone:0.74. The patient was operated in and currently developed postoperative pituitary deficiencies and he is on thyroxin and hydrocortisone therapy.

Citation: Hamza R, Al Shaikh H, Lebl J, Deeb A. Second Arab Society for Pediatric Endocrinology and Diabetes (ASPED) European Society of Paediatric Endocrinology (ESPE) School, 9-12th Dec. 2015, Abu Dhabi, United Arab Emirates; J Diab Rel Dis: 2016.
Kocher-Debre-Semelaigne Syndrome with Failure to Thrive
Mona Karem
Faculty of Medicine, Suez Canal University, Ismailia, Egypt

We report a 13 months old infant with untreated congenital hypothyroidism and pseudo-hypertrophy of limb muscles (Kocher-Debre-Semelaigne syndrome) with failure to thrive. The infant presented with weight and height below 3rd centile for his age, dull apathetic face, delayed motor and mental development in the form of head lag and absent social smile as well as un-recognition of his mother in addition to hypertrophied both calf and biceps muscles.

There was non-pitting edema of the dorsum of both feet. All the investigations were normal except the thyroid profile that showed a high thyroid stimulating hormone (TSH) and low triiodothyronine (T3) and thyroxine (T4). We started thyroxine replacement therapy as well as nutritional support, and the response was marvelous. Two to three weeks after treatment, weight as well as height increased. Astonishingly, he started to support his head, sit supported and now he sits unsupported. The mental improvement was striking; he started the social smile, responded to the surrounding with recognition of his mother. The syndrome is rare, especially at this age, and the new event is the rapid improvement of mental and motor development.

A Medically Treated Case with Congenital Hyperinsulinism
Taha Darwish
Pediatrics Department, Al Amiri Hospital, Kuwait

We report a 4 year old boy, diagnosed to have congenital hyperinsulinism at two months of age, based upon macrosomia persistent hypoglycemia and increased insulin/glucose ratio (>0.5). Treatment was started in the form of Octreotide. The patient’s hypoglycemia was controlled upon frequent administration of octreotide every four hours. Convulsions occurred once at the age of 18 months upon hypoglycemia. Magnetic resonance imaging of brain and EEG were normal. At two years of age, the frequency spaced to be every six hours. Monitoring the side effects of the drug on this patient, the child experienced mild to moderate persistent abdominal distension and intermittent constipation in the first year of age, and hematemesis occurred once at the age of 3 years and 8 months. Now the child is four years old doing well on octreotide treatment with fair mental and motor development without surgical management.

Asymmetrical Precocious Puberty
Mustafa Al Qaisi
Zulekha Hospital, Dubai, UAE

Case Report 1: We report a 7 year and 11 months old Indian girl who presented with 1-year history of right sided breast development and 9-month history of pubic and axillary hair; her periods have not started yet. She was preterm (26 weeks gestation and birth weight 980 gm). Neonatal convulsions also occurred, and on day 33 she was oxygen dependent. Chest x-rays showed signs of moderate bronchopulmonary dysplasia. Initial brain ultrasound on day 1 showed bilateral lateral ventricular dilatation right more than left with post hemorraghic ventricular dilatation. Brain CT scan showed no signs of increase intracranial pressure and asymmetrical lateral ventricular dilatation more on the right side. Diffuse hypodensity of the periventricular white matter was also noted with shallow cortical sulcill of the convexity. Since birth, the mother noticed that she had right side of the body bigger than left, with delayed gross and fine motor development. On examination, weight was on 50th centile, height on 25th centile, follow stimulating hormone: 2.74 mIU/ml (1.98-11.6), lutenizing hormone: 0.216 mIU/ml (2.58-12.1), thyroid stimulating hormone: 2.69 uIU/ml (0.60-4.84), 17-Hydroxyprogesterone: 1.12 ng/ml (0.0-0.8). Bone age was advanced (10 years). Ultrasound abdomen revealed an essentially normal study of visualized abdominal organs. The case was diagnosed as symmetrical central precocious puberty. Long acting luteinizing hormone releasing hormone analog (decapetyl) Triptorelin 3.75mg on monthly basis was started.

Case Report 2: A 10 year old boy was referred because of severe backache. He attended the clinic on a wheel chair. His weight was above the 99th centile, height on 50th centile. Initial investigations revealed a serum Calcium: 8.1 mg/dl (range: 8.8-10.8mg/dl), serum phosphorous: 4.10mg/dl (range: 4.5-9.0 mg/dl), alkaline phosphatase: 264 IU/L (normal: 100-300 IU/L), 25-hydroxyvitamin D: 12.4 ng/ml (normal: 20-50 g/ml), parathyroid hormone: 4.2 pmol/l (normal: 0.9-5.5 pmol/l), renal, liver and thyroid functions and tissue transglutaminase were normal. Plain X ray spine demonstrated multiple wedge collapse fractures of several thoracic and lumbar vertebrae and wide space osteopenia. DEXA: z score was -3.2 denoting severe osteoporosis.

Acquired Hypothyroidism in Hepatic Hemangioma
Ahmed Al Ghamdi
King Fahd Hospital, Al Baha University, Al Baha, Saudi Arabia

Case Report 1: We report a case of acquired hypothyroidism in a two month old infant secondary to hepatic hemangiomas. A two month-old infant presented with a huge abdominal mass due to hepatic hemangiomas and was found to have postnatal hypothyroidism. This finding supports a diagnosis of consumptive hypothyroidism as a result of increased type 3 iodothyronine deiodinase activity in the hemangiomas. His hypothyroidism was corrected by L-thyroxine. Coincident with the involution of the hemangiomas, the child’s hypothyroidism improved and L-thyroxin replacement could be stopped at the age of three years. Despite some degree of hypothyroidism for several weeks during infancy, his growth and development were normal.

Is it Growth Hormone to blame?

Case Reports 2: Side effects of growth hormone therapy in two interesting cases: Is that a coincidence?

Case 2a: A 14 year old Saudi girl known case of idiopathic short stature (ISS) started growth hormone (GH) since six months presented to our hospital with history of fatigability and mild polyuria for the last three days. She was discovered to have high random blood sugar (300 mg/dl) (HA1c 11%) and was started on insulin glargine which was discontinued later after stopping the GH and patient cure. All investigations including insulin, c peptide and anti glutamic acid decarboxylase antibodies (GAD) came normal.

Case 2b: A 10 year old Saudi girl known case of idiopathic short stature (ISS) started GH since nine months presented to our hospital with history of diabetic ketoacidosis (DKA). She was admitted and started intensive therapy (insulin glargine and aspart) and GH was stopped. This patient was diagnosed to have type 1 diabetes mellitus in view of positive ant GAD antibodies and increasing in requirement for the insulin therapy.
Hypoglycemia Due to Allgrove Syndrome
Sana Abouzorouk

Department of Pediatrics, Hassan II University Hospital, Morocco

Allgrove Syndrome or triple A syndrome is a rare familial multisystem disorder characterized by achalasia, alacrima and adrenal insufficiency. We describe a 9-year-old boy who was brought to our Emergency Room with deterioration of general health and seizures. He had a history of recurrent vomiting and was found to have deep hypoglycemia, hyperpigmentation of skin with a failure to thrive. Laboratory investigations and imaging studies revealed hypothalamic (glucocorticoid deficiency), confirmed achalasia (barium esophagography, esophageal manometry, and endoscopy) and alacrima (shirmer test). Based on clinical features and investigations, he was diagnosed as a case of 3A syndrome. Glucocorticoid therapy was initiated, and the response was impressive. Allgrove syndrome should be suspected in patients with hypoglycemia and signs of adrenal insufficiency associated with any of the main symptoms of the syndrome (alacrima, achalasia).

A Very Challenging Case of Recurrent Hypoglycemia in a Type 1 Diabetic Child
Kholoud Mohamed

Mubarak Al Kabeer Hospital, Kuwait

A 10 year old girl was diagnosed as type 1 diabetes mellitus (DM) in October 2014. She was admitted with hyperglycemia and ketosis without acidosis. She received full education by diabetic team and dietitian, and started on MDI insulin. She lost follow up and then experienced recurrent hypoglycemia and loss of consciousness. Full workup of hypoglycemia in type 1 DM was done. Critical sample was collected during hypoglycemic attacks and metabolic workup was done. A thorough investigation in the hospital disclosed that with each attack, she had hypoglycemia, high insulin level, and lower normal c-peptide. A diagnosis of exogenous injection of insulin was made. Social workers were involved and psychiatrist also as the mother was very difficult in dealing with and accusing all the medical staff that they wrongly diagnosed type 1 DM and she was refusing to give insulin. The aim of the presenting case is to discuss the challenging and difficult cases of recurrent hypoglycemia in type 1 DM and to alert to the possibility of Munchhausen’s syndrome by proxy. Our conclusion was a high index of suspicion for factitious illness is raised when confronted with history and clinical findings that contradict laboratory findings. Psychological well being of patients with diabetes is a cornerstone in their care.

A Case of Female Virilization in a Child: A Presentation for a Virilizing Adrenocortical Tumor
Ahmed Yousef

Shaikh Khalifa Medical City, Abu Dhabi, UAE

Adrenocortical tumors (ACTs) are rare in children. Unlike adult ACTs, pediatric ACTs are functional and hormonally active in about 90% of cases. Li Fraumeni Syndrome is a dominantly inherited familial cancer syndrome where patients are predisposed to a number of cancers including ACTs. Germline mutation in the gene encoding the tumor suppressor TP53 are found in 70% of affected families. We report a child with ACT presenting with virilization and suspected to have LiFraumeni syndrome. We report a 3-year-old girl presented with rapidly progressing virilization, facial acne and deepening of voice for seven months. She had two brothers who had died of brain tumors at the age of 10 years, a paternal cousin with leukemia and a paternal uncle who died at the age of 45 years of gastric carcinoma. Genital examination revealed enlarged clitoris, prominent unfused labia folds with Tanner II pubic hair and Tanner I breast stage. She had soft abdomen with no masses appreciated. Baseline serum androgens revealed elevated testosterone of 2.8nmol/L (0.07-0.7nmol/L), DHEAS 11.34 micromol/L (0.90-7.50 micromol/L), 17-HOP 11.42nmol/L (0.1-1.5nmol/L) and ACTH 3.8pmol/L (1.6-13.9pmol/L) with prepubertal estradiol and gonadotropins. Abdominal ultrasonography revealed right adrenal mass, measuring 25mm × 20 mm that was confirmed by CT. She underwent laparoscopic right-sided adrenalectomy. Histopathology confirmed adrenocortical carcinoma. Postoperatively, androgens returned to normal. Genetic testing for TP53 mutation was positive.

ACTs are rare in children and should be considered in any child presenting with precocious puberty or virilization. Evaluation of genetic and familial disorders associated with development of adrenocortical proliferative disorders has allowed researchers to identify a number of possible mutations that may be involved in tumor genesis, including mutation in TP53 genes. The clinical implication of confirming such genetic mutations allowed the patient, their first degree relative to be screened and to go through appropriate cancer surveillances in order to detect the cancer at earlier stage if occurred.

Central Precocious Puberty due to Hypothalamic Hamartoma in a Seventeen-Month-Old Infant Girl
Sana Kniha

Department of Pediatrics, University Hospital, Sfax, Tunisia

Precocious puberty is defined as the development of secondary sexual characteristics before the age of 8 years in girls and 9 years in boys. Two types of precocious puberty are recognized, central precocious puberty (CPP) and peripheral precocious puberty (PPP). Hypothalamic hamartoma is the most common imaging finding in central precocious puberty.

We report a seventeen -month-old girl was brought by her parents to the Pediatrics Department with a history of bleeding per vagina since five months of age, with no previous history of genital trauma. She was the first child of the parents, it was a consanguineous marriage. The first episode of bleeding at the age of five months had lasted three days; and since the age of 12 months, she had monthly regular cycles of three to four days; with an increased volume of both breasts and an acceleration of growth velocity. She had a normal psychomotor development. Clinically, her height was at +3 SDS and her weight was at + 4 SDS. Head circumference was 49 cm. She had bilateral breast enlargement, the areolas were bulging and hyperpigmented. There was no axillary hair. In the genitals, vaginal mucosa was rosy and moist, there were some pubic hair. The hormonal analysis revealed pubertal levels of gonadotropins with luteinizing hormone (LH) of 2 mlU / mL (N < 1.1 mlU / mL), follicle-stimulating hormone (FSH) of 6 mlU / mL (N < 1.1 mlU / mL), and estradiol (E2) of 210 pg/mL (N < 6 pg/mL), with normal thyroid functions. X-ray of the left wrist revealed bone age of 24 months. Uterine height on pelvic ultrasonography was 39 mm. The LH-RH test showed a peak of LH of 20 mlU/mL. The brain scan revealed a small hypothalamic mass measuring 8.4 mm, isodense to brain, suggestive of hypothalamic hamartoma. The patient was managed as a case of isosexual (central) precocious puberty, secondary to hypothalamic hamartoma, with monthly GnRH analogs (Triptorelin). There was regression of secondary sexual characters since the first three months of treatment with stabilization of the growth curve. Estradiol and FSH have returned to prepubertal levels. The total duration of treatment was nine years.
An 18 Month Old Infant with Metastatic Insulinoma

Deepti Chaturvedi

Barjeel Hospital, AbuDhabi, UAE

An 18 month old baby girl DK presented in a tertiary care hospital in India with recurrent episodes of transient loss of consciousness, sudden falls, drowsiness and excessive sweating, unaccompanied by abnormal movements. She was found to have low post absorptive blood glucose (40 mg/ dl) with a high serum insulin level (10.8 μU/ml). Magnetic resonance imaging (MRI) of the abdomen revealed a tumor (1.4 × 1.2 cm) at the junction of the head and body of the pancreas which was enucleated. Five months later symptoms of hypoglycemia recurred. A subtotal pancreatectomy was performed. She continued to have hypoglycemia and was put on increasing doses of diazoxide. Seven months later, MRI of the abdomen and a PET scan revealed metastatic deposits in the liver, which were confirmed by histopathology and immunostaining. To the best of our knowledge, this is the youngest child with metastatic insulinoma reported so far.

Cheiroarthropathy in an Adolescent with Type 1 Diabetes Mellitus

Nabras Al Qahtani

Pediatric Endocrinology Department, Mafraq Hospital, AbuDhabi, UAE

Diabetic Cheiroarthropathy (DCA) is a recognized complication of diabetes and can be seen in up to 30% of patients. It is a known complication in patients with long-term disease whose glycemic control is suboptimal. The etiology of the arthropathy may be due to glycosylation of collagen at the joints. Stiffness, limited movement and sclerosis of small joints are characteristic features. We report an 18 year old girl who presented with DKA at 10 years. She was diagnosed with type 1 diabetes at the age of two years. She had poorly-controlled diabetes which showed some improvement recently on insulin pump therapy. Clinical examination showed hand contractures, inability to fully flex all fingers bilaterally but her thumbs were spared. Skin over proximal, distal inter-phalangeal joints was sclerotic. Peri-angual skin and skin over her knuckles was hardened and rough. She displayed positive “Prayer sign”. She had no features of inflammation but complained of morning stiffness. Similar findings were noted in both feet involving mainly the 4th and the little toe. She had no diabetic nephropathy or retinopathy. She had a raised ESR but normal CRP and no leukocytosis. She was started on a course of prednisolone and methotrexate and showed some improvement within six weeks.

DCA can be seen in adolescents with type 1 diabetes and can mimic other inflammatory conditions. It can be seen in the absence of retinopathy or nephropathy. Optimizing diabetes control is essential to prevent this disabling complication. Prednisolone and methotrexate treatment might result in some improvement.

Precocious Puberty in a Patient with William’s Syndrome

Laila Al Hashmi

Sultan Qaboos University, Muscat, Oman

A 7 year old female was referred for evaluation of bilateral breast enlargement with no history of pubic or axillary hair and no adult body odour. There was no vaginal bleeding or discharge. She did not attain her menarche. There was no history of vision abnormalities, headache or vomiting. She was born at 36 weeks of gestation by lower segment caesarean section due to breech presentation with birth weight of 2.34 kg. She was having gross motor delay as she walked a 2 years and 6 months of age. She has speech delay as she started to say words at age of 20 months and she had problems with articulation. She joined regular school. Currently she is at grade 3 with average school performance. She has been evaluated during her father’s study at Australia after which she was found to have William’s syndrome which was confirmed genetically. She was not on any medications other than vitamin D supplements. Her parents are not consanguineous. She has three siblings who are otherwise healthy with no family history of a similar problem. On her clinical examination, she is very cooperative, happy child, smiling throughout the examination. She had features of William’s syndrome. Her anthropometry was as follows; weight at 10th centile and height between 10-25th centile. There was no abnormal pigmentation or obvious midline defects. There was no goitre. Tanner stage: breast stage 2, Pubic stage 2, no axillary hair. Her line of investigations was directed to rule out central or peripheral causes of her precocious puberty. GnRH stimulation test done for her which showed LH: 0.2 -15.1-13.7 (IU/L) at (0-30min-60min). FSH: 3.0-18.20.7 (IU/L) at (0-30min-60mins). At baseline, Estradiol was 38 pmol/L and testosterone was 0.4 nmol/L which remained same level after the test. Her thyroid functions were normal. Her bone age was corresponding to her biological age. Abdominal and pelvic US showed a normal prepertubal uterus around 3.8cm × 1cm with no abnormal masses seen in adrenal gland region. MRI showed chiari malformation type 1 and possibility for craniosynostosis. However, she underwent another MRI brain and spine which revealed cervicothoracic syringohydromyelia with background of chiari 1 malformation. She was reviewed by Neurosurgeon and had surgery. She has been started on GnRH analog monthly to suppress her puberty. She is on regular follow up with paediatric endocrine clinic.

Pollyuria, Polydepsia and Polyphagia is Not Always Diabetes Mellitus

Fawziya Al Yafei

Hamad Medical Center, Doha, Qatar

Central Diabetes Insipidus (CDI) is the most common manifestation of central nervous system involvement in Langerhans cell histiocytosis (LCH) with incidence ranging between 25-50%. Moreover, CDI may be the presenting feature of LCH.

We report a six year old female who presented with polyuria and polydipsia for two months. She was drinking about 10 L / day and she had an increased urine frequency and volume (10-15 times during the day and 5-7 times at night). She had significant polyphagia and gained 5 kg in those 2 months. There was no history of fever, meningitis, head trauma, brain tumour, seizures, chronic cough, bone pain, use of drugs (chemotherapy, radiotherapy or nephrotic drugs) or surgery prior to onset of symptoms. She had six healthy siblings. Her examination showed normal blood pressure for age and sex (100/75) and heart rate (100/min). Her height SD = 0.08 and BMI = 17 kg/m2 (BMI SD = 1). Neurological examination showed hyperreflexia with normal power, tone and gait. There was no organomegaly or skin rash. Urinalysis showed low specific of < 1.005 without glycosuria or proteinuria. Her random blood sugar was 5.4mmol/L. An initial diagnosis of diabetes insipidus was suspected. Laboratory workup showed normal serum Na (138mmol/L) and electrolytes (K, Ca, PO4 and HCO3). She had normal hemogram...
and renal functions. Serum osmolality was 281 mOsm/kg. She had raised liver enzymes ALT of 129U/L, AST of 76U/L, ALP 139U/L, GGT of 45mg/L, and Bilirubin of 78mg/L. Thyroid function and 08:00 AM cortisol level were normal. A water deprivation test was done over four hours followed by desmopressin challenge test. The diagnosis of CDI was made based on the symptoms (polyuria and polydipsia) despite the lack of oral intake during the water deprivation test (table), absence of urine concentration on water deprivation followed by an increase in urine and serum osmolality following the administration of desmopressin. MRI brain showed thickening of the infundibulum stalk of the pituitary gland and loss of pituitary bright spot most likely differential was langerhans cell histocytosis. No other abnormalities were detected in her brain and whole body MRI. We are reporting a six year old girl with proven CDI and typical MRI brain finding of LCH. Although tissue diagnosis of LCH is still lacking, this child needs close monitoring and follow-up to confirm this likely diagnosis. Isolated CDI is reported to be the presenting symptom of LCH in 15% of patients. Approximately 50% of them are diagnosed with LCH within one year and more than 80% by second year after the occurrence of CDI. In conclusion, CDI might be the presenting feature of LCH and many patients who were previously diagnosed as “idiopathic” CDI subsequently develop the disease. Therefore, diagnostic evaluation of CDI at diagnosis and during follow-up is essential to detect extra cranial LCH lesions for a tissue diagnosis of LCH and early proper management of the disease.

A Novel Mutation (E767Q) in the Second Extracellular Loop of the Calcium Sensing Receptor (CASR) Gene in a Palestinian Family with Autosomal Dominant Hypoparathyroidism

Muna Sharaf
Makassed Hospital, Jerusalem, Palestine

Autosomal Dominant Hypoparathyroidism (ADH) is a rare familial disorder, caused by activating mutation of the calcium sensing receptor (CASR), or mutations in the PTH gene that impair intracellular processing of the nascent protein. Patients with this inherited form of hypoparathyroidism are commonly asymptomatic and present at any age. Patients generally exhibit mild to moderate hypocalcemia, with serum PTH levels that are inappropriately low given the hypocalcemia. We describe a novel mutation in the CASR gene in a Palestinian family with ADH. A Palestinian infant, born to non consanguineous parents, presented at one week of age with hypocalcemic seizures, hypercalcuria, hyperphosphatemia and inappropriately low PTH response. Screening of the parents, who are asymptomatic, revealed hypocalcemia in the father with inappropriately low PTH. DNA sequencing of the CASR gene for the patient revealed a novel missense mutation in the second extracellular loop with replacement of G by C in codon 767 of exon 6 (GAG → CAG), predicting Glutamic acid to Glutamine substitution (E767Q) in the protein. The mutation was present in one allele and co-segregated with hypocalcemia. The father had the same mutation on one allele while the mother was negative. To the best of our knowledge, this is the first description of such a disease in a Palestinian family with molecular confirmation, allowing accurate genetic counseling, early diagnosis of affected kindreds, early therapeutic interventions and avoiding complications.

A Puzzling Case of Hypoglycemia

Salima Attia
Pediatric Endocrine Department, Mafraq Hospital, UAE

We report a five year old boy, known to have repeated hypoglycemia attacks. He was well until 3 years of age when he was having acute respiratory tract infection with fever and poor appetite and developed hypoglycemia documented in PHC to be 30 mg/dl. So, diagnosed as ketotic hypoglycemia. He continued to have attacks of hypoglycemia so, fasting test done and he didn’t develop hypoglycemia.

Mother reported many hypoglycemia attacks precipitated by eating. So, prolonged OGTT was done for him which showed delay and exaggerated insulin response but, without hypoglycemia.

Few months later, mixed meal test done which showed normal insulin response without hypoglycemia also. He has normal growth and development. Not on any medications. No family history of diabetes or hypoglycemia. His twin brother has many random BG readings on the low side (around 50mg/dl) but, never been symptomatic.

An Interesting Case of XY Female; 46 XY Gonadal Dysgenesis

Hana Al Suwaidi
Pediatric Endocrine Department, Mafraq Hospital, UAE

A 16 years old girl previously healthy, and currently suffering with primary amenorrhea. On examination there was no obvious dysmorphic features, height was 164 cm (50th - 75th %), weight 62 cm (at 75th %), no hirsutism or acne, breast Tanner 1-2, mild pubic hair (examined initially by the gynaecologist), no masses on abdominal examination, genitalia is normal female with normal ditoral size.

Investigations showed normal thyroid function, prolactin level, androgens, high LH, high FSH and low estradiol level. Ultrasound abdomen showed small presence of uterus and ovaries could not be visualized. MRI pelvis showed the same finding of ultrasound, her karyotype showed 46XY in all cells. She was started on drospirenone-ethinyloestradiol (Yasmin) tablets, breast reached Tanner 4 but small, pubic hair T5 and she had regular menstrual period.

Abstracts for Research Projects

Complementary and Alternative Medicine Therapy on Diabetes: Aberrant Angiogenesis and Cytokines in Diabetic Complications

Ahmed Al Ghamdi
King Fahd Hospital, Al Baha University, Al Baha, Saudi Arabia

Diabetes mellitus (DM) is a chronic metabolic disorder that is characterized by hyperglycemia due to lack of or resistance to insulin. Patients with DM are frequently affected with ischemic vascular disease or impaired wound healing. Type 2 DM is well known to accelerate the atherosclerotic process, endothelial cell dysfunction, glycosylation of extracellular matrix proteins, and vascular derangement. Herbal medicines and naturally occurring products play an essential role in treating and managing diabetes, especially in developing countries, due to healthcare costs. Therefore, for a long time, natural treatments have been used worldwide to treat DM. Among many medications and alternative medicines, several herbs and natural medicinal plants have been recognized to help in controlling diabetes with no side effects. The present review shows the perplexing features of aberrant angiogenesis, abnormalities in growth factors, cytokines, oxidative stress and metabolic derangements relevant to diabetes. Moreover,
the review exhibits some of these herbal plants and their active chemical constituents which have a role in the management of DM. Additional details and impact of cytokine and nitric oxide in diabetes are compiled here and discussed in this review.

**Plasma Osteoprotegerin Concentrations in Type 1 Diabetic Patients with Albuminuria**

Yasmine Henawi  
*Ain Shams University, Cairo, Egypt*

Osteoprotegerin (OPG) is a recently identified inhibitor of bone resorption. Recent studies indicate that OPG is also associated with endothelial dysfunction in diabetes. We aim to investigate the relationship between plasma OPG levels and urinary albumin excretion (UAE) in Type 1 diabetes.

A total of 80 Type 1 diabetic subjects and 40 control subjects were enrolled. Diabetic subjects were divided into a normoalbuminuric group and a microalbuminuric group according to urinary albumin excretion rate (UAER). Plasma OPG level was measured by enzyme-linked immunoassay. The plasma OPG levels were significantly elevated in patients with microalbuminuria (176.39 ± 25.05 pg/ml) than patients with normal albuminuria (154.73 ± 16.66 pg/ml) and control subjects (44.76 ± 8.7 pg/ml). The plasma OPG level correlated positively with patients’ age, duration of disease, HbA1C and UAER. We conclude that Plasma OPG levels are significantly associated with UAE in patients with Type 1 diabetes. These findings may support the concept that elevated plasma OPG may be associated with diabetic angiopathy.

**Assessment of Environmental Factors and the Risk of Type 1 Diabetes in Children in Minia Governorate**

Basma Abdel Moez  
*Pediatric Endocrinology Department, Minia University, Egypt*

Type 1 diabetes results from an interaction of genetic and environmental factors that triggers the autoimmune destruction of insulin-producing pancreatic beta-cells. Discovering those genetic and environmental risk factors and determining how they interact to cause disease are key steps toward being able to identify individuals who are at risk for T1DM and accurately assess their specific level of risk.

To determine the environmental risk factors of type 1 diabetes mellitus among children in Minia governorate, our study was carried out on 220 child aged from 2-16 years old who were classified into 110 diabetic patients and 110 age- and sex-matched controls. A special questionnaire was designed for the purpose of the study. It included: through history taking (present history, family history, perinatal, natal and postnatal history, feeding history, vaccination history and history of early childhood illness) in addition to full clinical examination. There were many environmental factors which play a very important role in precipitation of T1DM among children, those factors are maternal age, maternal consumption of tea-coffee during pregnancy, gestational diabetes, pre-edamsia, maternal infection during pregnancy, maternal drug intake during pregnancy, (antihypertensive, antacids, and antibiotics), early neonatal illness (RDS and prematurity), short duration of breast feeding, early introduction of cow milk and gluten, lack of vitamin D supplementation, early childhood viral infection especially mumps. We conclude that exposure to environmental risk factors in genetically predisposed persons during pregnancy; neonatal period and early childhood are thought to play an important role in triggering the immune process leading to the development of T1DM.

**Childhood Obesity: An Exploratory Study to Assess Effectiveness of Structured Intervention to Reduce Obese Children BMI**

Nadia Shaukat  
*Dubai Hospital, Dubai, UAE*

The study aims to help children with simple childhood obesity reduce their BMI to normal levels and sustain them for a minimum of 12 months. This will be self-regulated using a structured diary, and will be monitored at regulated intervals of three months for a period of one year followed by a period of 12 months sustenance, also monitored as before. The reason for this time period is that the relatively large expat, mobile population, makes it difficult to observe them over a longer period of time, even though that is desirable.

Research Statement: An exploratory study to assess the effectiveness of structured intervention to reduce and sustain the achieved BMI in children with simple childhood obesity attending the outpatient department in Dubai hospital. The research design is Quasi-experimental. The dyad of mother & child will be observed continuously over a period of two years. The structured intervention consists of engaging the child in active play for a minimum of one hour daily, it will be self-directed to make it enjoyable, thereby increasing motivation. The parent will be advised on a diet with the required number of calories for each child. Baseline and follow up assessments will be done in every three months, in three areas viz. physical, dietary & psychological and will be uploaded, for trends, on a mobile/tablet app.

**Factors Associated with Development of Polycystic Ovarian Syndrome in Girls with Premature Adrenarche**

Shadi Tabba  
*Health Plus Hospital, AbuDhabi, UAE*

It is known that the development of benign premature adrenarche in a girl may indicate risk for PCOS. But it is not very clear yet which girls with premature adrenarche will progress to PCOS and which will not. If we are able to recognize risk factors indicating who is at higher risk within that group, this would allow introducing measures to prevent progression at an early age. Studies have pointed to the early use of Metformin in girls with premature adrenarche to prevent PCOS, however, targeting this medication towards higher risk girls will show a more clear beneficial effect. Our study is a retrospective chart review which looked at different possible risk factors associated with progression into PCOS. Variables studied included rate of change of BMI, birth weight percentile, family history of PCOS or type 2 Diabetes Mellitus, age at presentation with benign premature adrenarche, presence of acanthosis nigricans. Baseline and 30 minute levels of several adrenal hormones after ACTH stimulation testing.
Clinical and Cytogenetic Studies of Patients with Sex Chromosome

Aya Aleidy

National Research Center, Cairo, Egypt

Sex chromosome disorders of sex development (DSD) constitute an important category of DSD. Patients collected from Clinical Genetics and Endocrinology Clinics at National Research Centre over one year, were subjected to pubertal staging, genital examination and chromosomal analysis. FISH analysis was done to characterize unidentified sex chromosome marker or ring chromosomes. Sex chromosome DSD represented 44% of patients. Numerical abnormalities constituted 77 %. X chromosomal abnormalities were encountered in 56.3%; 88.9% of them had monosomy 45,X. Klinefelter syndrome was encountered in 43.8%. By phenotype-genotype correspondence, 47,XXX karyotype presented with hypogonadism and primary infertility while the diagnosis of 47,XXY in the prepubertal period was mostly accidental due to dysmorphic features. Short stature was a cardinal feature in most of patients having complete or partial X chromosome monosomy. Patients with 45,X, in mosaicism with X chromosome, were reared as females and presented with primary amenorrhea. Patients with 45,X, in mosaicism with Y chromosome, three patients, all had SRY +ve signal by FISH; one reared as a female, presented with short stature and delayed puberty, and underwent laparoscopy to exclude gonadoblastoma and the other two patients reared as males presented with genital ambiguity and cryptorchidism; pathology reports confirmed diagnosis of mixed gonadal dysgenesis in one patient and ovotesticular DSD in the other. One patient had trisomy X and dysmorphic features. Our study reported a higher frequency of sex chromosome DSD, with a higher incidence of 56.3%, compared to previous studies. The study also highlighted the importance of phenotype-genotype correspondence in the diagnosis and management of sex chromosome DSD.

CAH Due to Steroid 11β Hydroxylase Deficiency

Sara Abdulla

AbuAlReeshi Hospital, Cairo, Egypt

Congenital adrenal hyperplasia (CAH) is one of the most common inherited endocrine disorders of which steroid 11β hydroxylase deficiency is the 2nd most common form. It is a rare autosomal recessive disorder caused by CYP11B1 mutations with an incidence of 100,000–200,000 in overall population. We aim to study the percentage of CAH due to 11βHydroxylase deficiency in patients presenting with clinical and biochemical manifestations suggestive of CAH. The study is a cross sectional. It included 20 patients (16 females and 4 males) with CAH, who were divided into two groups (11β hydroxylase deficiency and 21 hydroxylase deficiencies) according to 11 deoxycortisol/cortisol ratio. Clinical data collected included demography, family history, age at presentation and clinical presentations. Examination variables included blood pressure measurement, auxology, genital and pubertal staging. All patients had investigations of: adrenal precursors, plasma rennin activity, sodium, potassium and pelvic ultrasound. Both groups showed no statistically significant difference regarding age at presentation, sex, consanguinity and clinical presentations. There was no difference in blood pressure assessment, auxology, Prader scoring in females. There was a highly statistically-significant difference in the 11 deoxycortisol level and 11 deoxycortisol/cortisol ratio between the 2 groups ($P < 0.001$). Differentiation between 21OHD and 11βOHD is difficult to confirm on clinical basis. In order to confirm the diagnosis of 11βOHD, measurement of 11 deoxycortisol is mandatory. Differentiation between the 2 types of enzyme defect is important to avoid the unnecessary use of mineralocorticoids in 11βOHD patients who are prone to hypertension. Furthermore, the need for genetic studies is increasing especially for those patients with atypical presentation (salt wasting 11βOHD).