ABSTRACT BOOK

Second Arab Society for Pediatric Endocrinology and Diabetes Conference, 6th-8th November 2014, Abu Dhabi, United Arab Emirates

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Abstract

The scientific program of the conference featured 62 oral and 84 poster presentations. Diabetes was the topic most heavily presented due to its widespread prevalence and unique features in our region. Milestones in diabetes care, diabetes education, epidemiology, updates in neonatal diabetes and hyperinsulinemic hypoglycemia as well as insulin resistance and type 2 diabetes mellitus were among the topics discussed by leading world-renown authorities as well as by regional experts. Diabetes technology was a particularly hot topic in the meeting featuring 2 symposia on the recent advances in artificial pancreas and regional experience with insulin pumps and continuous glucose monitoring systems. Experience pertinent to diabetes and fasting was elegantly presented by regional experts. The meeting also featured workshops dedicated to diabetes educators and stimulating discussions with behavioral psychologists. Growth disorders were presented in different formats of plenary, "Meet the Expert", multicenter research study presentation, case presentations. Surveillance of growth hormone use was presented from Tunisia and Kuwait. In addition, pubertal disorders were widely covered. Speakers highlighted regional trends in precocious puberty, updates on PCOS management, adrenal disorders and novel mutations in a variety of puberty-related disorders. Exciting data regarding survivors of childhood cancer as well as updates in Turner syndrome management were brilliantly presented. A session of particular interest tackled disorders of sexual differentiation (DSDs), starting with an overview of medical approach to DSDs, followed by an animated presentation and discussion of religion point of view regarding DSDs as well as a valuable psychological approach to youth with DSDs and their families. Last but not least, a highly informative session was held on bone disorders and vitamin D status in the region.

Key Words: Diabetes technology, DSD, Growth, Bone, Puberty

Introduction

The Arab Society for Pediatric Endocrinology and Diabetes (ASPED)

ASPED was launched in Abu Dhabi, UAE on 8th of September 2012 upon the initiative of a group of Pediatric Endocrinologists from the Middle East and North Africa. The society is a non-profit scientific Society organization and is registered under the Dubai Association Center (DAC) 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:

- Care of children and adolescents with endocrine disorders and diabetes by bringing together professionals in this field from the Gulf and North Africa.
- 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.
- Actively support training and education of specialist nurses, diabetes educators, dieticians and other allied healthcare professionals in the field of endocrinology and diabetes.
- Promoting research and training in the field. One key issue to be encouraged is to establish collaboration with international organization and centres 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.
- Advancing education in pediatric endocrinology and diabetes for patients and their parents by enhancing group education and creation of parents/children support groups.
- Generating evidence-based guidelines that will lead to a consistent management of endocrine disorders and diabetes mellitus throughout the area.
- Unifying protocols throughout endocrine centers to ensure updated practice and creating tools for research.

The Second ASPED Conference

The 2nd Arab Society for Pediatric Endocrinology & Diabetes conference was held at the Beach Rotana Hotel, Abu Dhabi between the 6th and the 8th November, 2014. It delivered latest updates and insights to health care professionals involved in managing children and young people with endocrine disorders and diabetes. The meeting highlighted the interests and the needs of pediatric endocrinologists and diabetologists in the region. In addition it was the ideal setting for networking and brainstorming about research ideas and available resources. With prominent international and regional speakers, the meeting attracted 480 participants from 22 countries making it one of the largest educational platforms for the subspecialty in the region. The conference this year had a special atmosphere as it was the first meeting after the official legal endorsement of ASPED and licensing by the Dubai Association Center. Special feature of the conference was that it witnessed the 1st ASPED-ESPE school, an initiative by ASPED in collaboration with the European Society of Pediatric Endocrinology (ESPE) which was held as a pre-conference event. The conference showed a diverse gathering of pediatric endocrinologists, diabetologists clinical dieticians, psychologists, specialist endocrine nurses and adult endocrinologists. Various formats of presentations and specialised sessions were run during the conference including plenary lectures, symposia, oral and poster presentations and workshops. The conference was a platform to share expertise, research and development in the field of diabetes management and endocrinology. There was a special emphasis on religious and cultural issues unique to the region. Renowned regional and international faculty presented various topics over the three days on growth, puberty, disorders of sexual differentiation, bone and calcium disorders, diabetes education & psychology, hypoglycemia & hyperinsulinism, monogenic diabetes and others.

The conference enabled participants to meet and link up with world-renown researchers and clinical experts, as well as with regional experts and fellow clinicians in a collegial environment encouraging active discussions and exchange of ideas. Inspired by the conference success, ASPED has set various goals among its top priorities for the next five years. These are:

setting high standards of care, ensuring continuous medical education and supporting research in pediatric endocrinology and diabetes in the region. Reaching these goals requires commitment, dedication, group work and networking. The annual meeting in Abu-Dhabi was definitely a major step towards these goals.

Abstracts of Presentations

ASPED Special Lectures

The journey and evolution of childhood diabetes

Stephen Greene
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Over the last three decades, while the fundamental need for insulin replacement in T1D in young people remains, the method of delivery has changed dramatically. "Intensive insulin" therapy offers the best outcome, in terms of glycaemia and long-term health, and a shift to multiple injection therapy and pumps has become the approach promoted from diagnosis. A recent recognition is the sustained effect of near-normal glycaemia from diagnosis ('metabolic memory'), achieved through strict glucose targets and dose adjustment of insulin for carbohydrate. To use the developing technology of T1D requires considerable motivation from patients and their families and there is a need for a parallel support program from a multidisciplinary team. The components of successful adherence to the management regimens are a matching of health beliefs, attuned communication and reciprocity between those with diabetes, the families and their health professionals. Innovative approaches are required to deliver these components within a health service. For many patients across the World the context in which they live markedly affects the treatment offered and the acceptance of the condition. With the increasing incidence in T1D the difficulties encountered in different environments and social settings is considerable, requiring support and direction from an international "Diabetes Family".

Diabetes Education and Management; how to overcome challenges?

Mohamed Abdulla
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The incidence of diabetes among children and adolescents is increasing worldwide including the Arab countries. The goals of long-term management are to prevent the acute and chronic complications, have normal growth and psychosocial life. This is best achieved by multidisciplinary teams through securing treatment and monitoring facilities, education and social support at all easily accessible health care levels and community. However it is difficult to secure all these facilities at all levels. This is mainly due to lack of trained personnel, economic factors as well as long distances and scattered population. Therefore, the quality of available care varies at each of pyramidal care health system. Diabetes care services should be structured in a way to have some form of net-working, communication and shared care. This needs collaboration between the health care professionals, the community, non-govermental organizations and various governmental bodies. In this communication I will discuss our experience in advocating and building up such services in Sudan.

Genetics of growth disorders

Jan Lebl
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The cornerstone 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 *GH1* 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 précised. 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 MPHD. 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.

II. Plenary Lectures

Clinical Assessment of Growth and Puberty Disorders

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Most small/delayed or tall/advanced children and adolescents have normal familial short/tall stature and constitutional delay/advance in puberty. The clinician's challenge is two-fold: not to inflict unnecessary and expensive investigations and treatment on children with normal variant growth and pubertal problems; and not to miss the diagnosis in children who do have genuine growth and pubertal disorders such as Turner's syndrome, hypopituitarism and chronic disease. With good auxology and clinical assessment it is possible to avoid investigation in the majority of cases, and to investigate the minority of cases more effectively. Prerequisites for successful growth assessment include an understanding of normal growth and puberty, including knowledge of Karlberg's Infantile-Childhood-Pubertal (ICP) model and Tanner's system of pubertal staging; the acquisition of robust and accurate measuring equipment; and the training of clinic staff in accurate measurement of supine length, standing height, weight, and pubertal assessment. Correct assessment also depends on the faithful following of a logical sequence – the presenting complaint (what is the problem perceived by the patient and family?); the history itself including a thorough past medical, family and social history; the clinical examination; and the clinical diagnosis +/- differential diagnosis. Only when the physician has formulated a clinical diagnosis or a differential diagnosis should further investigation such as basal and stimulated hormone levels, and diagnostic imaging such as pituitary MRI, be considered. In this lecture we will consider three cases and see how applying the principles of auxology, history-taking and examination can result in a reasonable clinical diagnosis, and inform the need or otherwise for further investigation.

Late Effects of Cancer Treatment

Margaret Zachrin
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Survival after childhood cancer treatment has increased significantly over 25 year, with overall >70% survival now recorded. It is estimated that within 25 years of primary diagnosis 4% of survivors will develop a second tumour with risks from 8 – 380 times expected population risk, thyroid cancer 18 times expected population rate, 50% risk of hypothyroidism and 20% risk of thyroid nodules at 20 years. Endocrine late effects of irradiation and chemotherapy can be direct, resulting in endocrine gland hypofunction or indirect via metaplasia and malignant transformation of normal exposed tissues and via altered bone growth. Increasing recognition of evolution of loss of endocrine function underlines a need for surveillance and planning strategies to anticipate loss and to provide solutions. Recognition of major global effects on learning, short term memory impairment and memory processing is necessary, to understand complex management needs. Beliefs related to survival and need for care may be unusual, along with risk taking behaviours. Hypothalamic pituitary axis deficits occur after radiation exposure in a dose related fashion. Low dose XRT (12Gy) with total body irradiation and chemotherapy alone have also been associated with deficits. Growth hormone deficiency is the most frequent loss, occurring 1-4 years after exposure to XRT, followed by gonadotrophin deficiency, TSH then ACTH deficiency. Evolution of losses may take up to 20+ years. Altered timing and tempo of puberty after CXRT or total body irradiation requires in depth understanding, to provide treatment appropriate to current status. Specific losses of gonadal function vary depending on age at exposure to toxins and type of intervention. Testicular radiation of 4Gy causes loss of germinal epithelium. 20Gy before puberty and 30Gy after puberty causes loss of Leydig cell function. The testis is relatively resistant to chemotherapy prior to puberty, although functional loss can occur. Complete germ cell loss occurs with chemotherapy after puberty, making semen collection imperative prior to treatment. Attempted germ cell salvage before puberty is experimental. Ova are lost with either treatment modality at any time. Recovery of the female ovary after chemotherapy varies, more likely after Cyclophosphamide but possible with other alkylating agents. Puberty can occur in up to 50% of males and females after TBI but ongoing losses ad hypogonadism remain risks long term. Acquisition of optimal peak bone mass and maintenance of bone quality in adulthood is compromised by alterations in pubertal and growth cascades. Thyroid nodularity and differentiated carcinoma is common after scatter or direct radiation, with multifocal papillary lesions and local invasion. Risk continues for 40 years. Surveillance with ultrasound every second year is mandatory for detection. Future planning should involve risk-based screening and surveillance, targeted education for risk reduction and healthcare delivered by clinicians familiar with issues and risks.

The KIDS diabetes program; IDF, ISPAD project

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From the age of 5 to 18 the majority of young people with diabetes have to manage their diabetes in the School environment. This can be for many families a major and difficult challenge. Schools might be prepared to deal with young people with diabetes, but parents also should be part of the process. This usually means gathering the information that the school needs, making sure that it gets to the right people, and meeting with school officials to discuss their plans. The young person also will have to be prepared for managing their diabetes away from home, often for the first time. Recently, the IDF, in collaboration with the International Society for Pediatric and Adolescent Diabetes (ISPAD) launched the Kids and Diabetes in Schools (KIDS) project. This a multi-stakeholder initiative, aimed at fostering a safe and supportive school environment for children with diabetes to manage their diabetes and fight discrimination. The fundamental rights of children living with diabetes include the freedom to access care and support to manage diabetes appropriately and to be fully included and engaged in all school activities to achieve their full potential. KIDS also aims to raise awareness of diabetes and promote healthy diet and exercise habits in the school community.

Diabetes Education Strategies; Consultation skills

John Gregory
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Previous research, largely dominated by US-based studies has demonstrated that psychoeducational interventions may have a small but important benefit on outcomes for young people with Type 1 diabetes. As a result, a significant investment has been made in the UK over the last decade to evaluate a range of psychoeducational interventions in a UK context. The results of 8 of the more important of these studies will be briefly summarized and consideration given to the implications of the results in a UK context.

Engaging young people with diabetes

Alexandra Greene
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"Communication is essential to workplace efficiency and for the delivery of high quality and safe work."
The WHO report on Human Factors in Patient Safety (2009). Diabetes in young people in the UK is regarded by professionals as a self-management disease. The clinic consultation between the young person and health professionals (HPs) is central to the motivation of the young person to take on this challenge. There are many opportunities for HPs to gain training in communication skills, with the opportunity to practice key skills and receive constructive feedback about performance. Yet evidence suggests that successful, 'attuned' communication between the multi-disciplinary team; together with patients, leads to improved self-efficacy, clinical change and high quality care. Several initiatives are underway in the UK aimed at giving young people (YP) with diabetes the skills to manage their own care. These do not, however, train them also, to communicate effectively with HPs in a way that articulates their wishes and needs for managing diabetes. A common scenario in the management strategy of 'poor control' in T1D is to offer frequent clinic consultations, however, there is no attempt to improve the communication effectiveness of these consultations. Ineffective clinic meetings fail to improve clinical outcomes adding to the frustration and demoralisation of both HPs and YP. Video Interaction Guidance (VIG) (http://www.videointeractionguidance.net/) is an intervention used to enhance reflection on 'attuned' communication skills between people and has been used successfully to improve professional and client situations in a variety of complex health and social situations; helping them to negotiate their own goals and manage their circumstances. We hypothesise that if YP, who tend to be poor verbalisers with HPs, are taught to enhance their communication skills; this is likely to influence positive change in diabetes outcome and well-being. This presentation explores cultural factors that influences the poor management of diabetes in the young and reports on a VIG intervention we are piloting in the Pediatric, Out-Patient Clinic in Dundee, Scotland, for young people with diabetes.

III. Oral Presentations

The psychological impact of diabetes on glycaemic control in affected Saudi children

Amir Babiker
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Background: Diabetes is the third commonest chronic disease of childhood. When a child or an adolescent is diagnosed with type1 diabetes (T1D), adaptation to a new life is usually a challenge for the whole family. There are specific challenges posed by T1D on the affected children, and their families, at different developmental age groups. The correlation between HbA1c and age specific psychological challenges, to our knowledge, has not been previously explored in the Middle East. **Objectives:** To assess the correlation between children's HbA1c and the psychological impact of T1D on affected Saudi children and their parents at King Khalid University hospital (KKUH), Saudi Arabia. Also to explore any variation between

children and their parents, and between children at different age groups in the impact scores of variable domains of a quality of life specific questionnaire for T1D. **Methodology:** In this cross sectional study, the psychological impact of T1D on children and their parents was assessed using a standard quality of life diabetes specific questionnaire for children – (PedQoL DM™ V3.0 - Arabic translation). The total and individual impact scores of different domains in the questionnaire were calculated from children's and parents' responses. Data were statistically analyzed using Pearson's correlation, ANOVA and t-2 tests. **Results:** There were significant variations in the mean HbA1c between different age groups. Though statistically not significant, the HbA1c showed more of negative correlations with the psychological impact scores of parents compared to very poor correlations with children's scores. There were variations, but not statistically significant, in the correlations of HbA1c with parents' and children's impact scores of individual domains at different age groups. **Conclusion:** Identifying age specific challenges in children with T1D may help focusing on relevant areas of concern in their management. Larger studies may be required to better address the relationship of these challenges with HbA1c in affected Arab children.

Puberty, HRT and fertility preservation

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Major changes in pediatric and adult medical practice have been seen over recent decades with increased prevalence of and longevity in chronic diseases, a marked increase in organ transplantation, rapid increases in recognition of new genetic disorders associated with altered gonadal function. Along with these changes has come recognition of the pivotal importance of adolescent bone mass accrual, to decrease the impact of adult bone loss for those who have a chronic medical condition. These changes have brought new challenges for management strategies and planning of fertility options for affected young men and women. Novel treatments, such as bisphosphonate use have changed the face of some pediatric bone disorders, but may impact on possible future risks for pregnancies in affected individuals. Ethical issues surrounding harvesting of gonadal tissue from minors without proper informed consent, the possibility of removal of gonadal tissue rendering a functional gonad non-functional, and confronting issues of donation and ownership of chromosomal material, all impinge on current practice management. Normal timing of entry into puberty and progress of puberty is essential to optimize linear growth and appropriate feminization or virilization, as well as having a major effect on bone size and mass, with 40 – 50% of total bone mass for life accumulated during puberty. Insults to the gonadal axis, either primary or secondary, may result in absent, delayed or arrested puberty but hypogonadism is often only one manifestation of a complex disorder. Holistic care will optimise outcome. This presentation will outline management strategies for different types of male and female hypogonadism, with particular attention to optimising timing and type of hormone replacement treatment in specific circumstances of chronic disease, after cranial radiation, organ transplantation, in disability and in specific disorders of hypogonadism such as Turner syndrome and hypogonadotrophic hypogonadism. New treatment options incur potential risks and raise new ethical issues. Risks for aortic dissection in Turner Syndrome during pregnancy and the use of cardiac MRI for evaluation is now mandatory. Use of ICSI provides new hope for fertility in Klinefelter syndrome. Adolescent use of gonadotrophins in hypothalamic hypogonadism improves adult fertility management in males. Management outcomes should aim to strike a balance between the achievement of height and adult appearance, while recognizing limitations imposed by the nature of the underlying condition. Awareness of a window of opportunity for best possible outcome can only be achieved through regular surveillance together with a comprehensive knowledge of conditions affecting patients. We should have the capacity to pass our patients to adult care with adequate advice regarding future risks, fertility prospects together with an understanding of the complexity and evolution of their condition.

Updates on PCOS management in adolescents

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No abstract available

Pattern of puberty in Saudi children

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Background: Puberty is the gradual transition period between childhood and adulthood. The ages of onset of pubertal characteristics are influenced by genetic, geographic, dietary and socioeconomic factors; however, due to lack of country-specific norms, clinicians in Saudi Arabia use western estimates as standards of reference for local children. **Aims:** The aim of the Riyadh Puberty Study was to provide data on pubertal development to determine the average age of onset of pubertal characteristics among Saudi children. **Methods:** Cross-sectional study among school children in Riyadh, Saudi Arabia, in 2006, 1267 children of which 542 were boys, aged 6 to 16 years old, from diverse socioeconomic levels were selected into the sample using a cluster sample design. The height and weight and Tanner stages were ascertained during physical examination by pediatric endocrine consultants, and also trained pediatric residents and fellows. **Results:**
The mean age (standard deviation) at Tanner Stages 2, 3, 4, and 5 for pubic hair development of Saudi boys was 11.4 (1.6), 13.3 (1.3), 14.4 (1.0) and 15.1 (0.8) years old, respectively. For gonadal development, the mean age (standard deviation) at stages 2, 3, 4, and 5 were 11.4 (1.5), 13.3 (1.2), 14.3 (1.1) and 15.0 (0.9) years old, respectively. The median age at Tanner stage 2 for breast in girls and pubic hair development in girls was 10 years. The median age at stage 2 in modified scales for axillary hair development was 12 years. **Conclusion:** The ages of onset of pubertal characteristics, based on gonadal development, among Saudi boys are comparable to those reported in Western populations. However, the median age of the onset of breast development at Tanner stage 2 for Saudi girls in Riyadh is lower than what has been reported in some countries in Europe, South Africa, Turkey and India but similar to girls in Hong Kong, China and white girls in the USA, which may support secular trends of an earlier onset of puberty.

Uterine development in Turner syndrome

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Background: It is not clear whether impaired uterine development in Turner syndrome patients is due to delayed estrogen treatment, treatment at too low dosage, or perhaps the use of progestins with androgenic properties. **Aims:** To assess uterine development in Turner syndrome patients and its relation to dose and type of estrogen therapy; and karyotype. **Methods:** Pelvic ultrasound was used to assess uterine size and shape, and ovarian volume in 40 Turner syndrome patients. Information on hormone replacement therapy was collected from patients' notes. **Results:** Among the 40 patients studied, 57.5 % started estrogen therapy and 30 % were taking progestins. Sixty five per cent had immature uterus, 17.5 % had fully mature uterus and 17.5 % had transitional uterus. Uterine volume was associated with age ($p < 0.001$), height ($p = 0.002$), weight ($p = 0.001$), years of estrogen use ($p < 0.001$), estrogen dose ($p = 0.016$), current estrogen use ($p = 0.001$) and Tanner breast stage ($p < 0.001$). Uterine volume was not affected by the type of estrogen used ($p = 0.40$) and karyotype ($p = 0.40$). **Conclusions:** Patients with Turner syndrome treated with estrogen (of adequate dose and duration) may attain a normal, mature uterine size and configuration, even at a late start of hormone replacement therapy and regardless of karyotype.

Genetic basis and diagnosis of hyperinsulinemic hypoglycemia

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Hyperinsulinaemic hypoglycaemia (HH) is a cause of severe and persistent hypoglycaemia in the newborn and infancy period. It is an extremely heterogeneous disorder with respect to clinical presentation, pancreatic histology and molecular biology. The clinical severity of HH varies with age at onset of hypoglycemia (severe hypoglycemia in neonates) and has major consequences in terms of therapeutic outcome and genetic counseling. The commonest genetic cause of persistent HH are autosomal recessive mutations in the genes *ABCC8* and *KCNJ11* (encoding the two subunits SUR1 and KIR6.2 respectively) of the pancreatic ATP-sensitive potassium channel (K_{ATP}). Histologically there are two major subtypes of the disease, namely focal and diffuse. Both the diffuse and focal forms share a similar clinical presentation, but result from different pathophysiological and molecular mechanisms. In addition, diffuse HH usually presents as an autosomal recessive disorder, whereas focal HH is sporadic. Differentiation of diffuse from focal disease is important in terms of management as focal disease requires a limited pancreatectomy (curing the patient from the hypoglycaemia) whereas diffuse disease will require a near total pancreatectomy. Imaging with 18F-DOPA-PET/CT is now the gold standard for differentiating diffuse from focal disease. Other rare genetic causes of HH include mutations in the *GCK* (glucokinase), *GLUD1* (glutamate dehydrogenase), *HAHD* (Short Chain 3-hydroxyacyl-CoA), *HNF4A* (hepatocyte nuclear factor 4-alpha), and *SLC16A1* (monocarboxylate transporter 1) genes. HH may also be part of an underlying syndrome (such as Beckwith-Wiedemann, Costello and Kabuki) and multisystem disorders such as congenital disorders of glycosylation (CDG). HH following gastric bypass surgery for morbid obesity has been reported in adults with pancreatic histological changes similar to infants with persistent hyperinsulinism. The rapid and accurate diagnosis of HH is very important, as a delay and inappropriate management can lead to brain damage. During the talk I will discuss the clinical presentation and diagnosis of HH and review the underlying molecular mechanisms that lead to dysregulated insulin secretion.

New treatment modalities for hyperinsulinemic hypoglycemia

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Persistent hyperinsulinemic hypoglycemia of infancy (PHHI) is characterized by severe hypoglycemia caused by dysregulated insulin secretion. Worldwide, the incidence of congenital hyperinsulinism is estimated at 1 in 50,000 live births with higher incidence of up to 1 in 2500 in areas of high consanguinity. Most patients with neonatal-onset persistent hyperinsulinemic hypoglycemia of infancy (PHHI) have genetic mutations (in ABCC8 and KCNJ11genes) cause alterations of the ATP dependent K+ channels (SUR1 and Kir6.2subunits) in the b-cells, which play a critical role in the regulation of insulin secretion, and require intensive care either surgically or medically. In diffuse CHI, more extensive near total pancreatectomy is frequently performed, with higher rates of complications and less likelihood of cure. The primary goal of therapy in persistent hyperinsulinemic hypoglycemia of infancy (PHHI) is the prevention of acute neurologic symptoms and long-term sequelae like cognitive deficits, of prolonged and recurrent hypoglycemia. The long-term therapeutic approaches for PHHI are directed toward decreasing insulin secretion. This may be accomplished pharmacologically or surgically. Pharmacologic interventions, although frequently unsuccessful, always should be tried before surgery. The treatment options will be presented here including preliminary published case series in using continuous subcutaneous glucagon infusion, long-acting somatostatin analog, and our experience in using Sirolimus in one patient with diffuse form of PHHI. These new medications may be useful in patients with diffuse form of PHHI but should probably not be used as the first line of medication until further experience and better understanding of its relative

Neonatal diabetes; an international overview

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In recent years there has been significant progress in defining the genetic aetiology of neonatal diabetes (NDM). It is likely that all cases result from single gene disorders since markers of autoimmunity associated with polygenic type 1 diabetes are rare in patients diagnosed before 6 months. Activating mutations in the *KCNJ11* and *ABCC8* genes encoding the Kir6.2 and SUR1 subunits of the beta-cell K_{ATP} channel are the most common cause of neonatal diabetes, accounting for around 40% of cases. The majority (~90%) of patients can achieve improved glycaemic control on high dose sulphonylureas. *INS* (insulin) gene mutations are the second most common cause of NDM; either recessive loss of function mutations or dominantly acting mutations that affect folding of the proinsulin molecule with consequent endoplasmic reticulum stress. Recessive mutations in the *EIF2AK3* gene, causing Wolcott-Rallison syndrome, are the most common cause of neonatal diabetes in consanguineous populations. The development of next generation sequencing technologies provides exciting possibilities for large scale sequencing studies. To date, gene discovery studies using this approach have identified 3 novel genetic etiologies for NDM. The identification of specific genetic subtypes of neonatal diabetes not only provides accurate information regarding inheritance and prognosis, but can inform treatment decisions and improve clinical outcome.

Neonatal diabetes; an overview from the Arab region

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Diabetes diagnosed in the first 6 months of life is referred to as neonatal diabetes mellitus (NDM). It usually has monogenic aetiology and mutations in more than 20 genes have been identified in around 80% of patients. NDM can be transient (TNDM) or permanent (PNDM) and each form can be isolated or part of genetic syndromes (syndromic NDM). In Europe and USA the frequency of NDM is splited equally between TNDM and PNDM and syndromic NDM have been reported in <10% of patients. However in Arab countries the spectrum of NDM appears to be different. Our recent work indicated that the incidence of PNDM in Arab is higher and it has a different genotype and phenotype compared to Europeans. In Arabs, EIF2AK3 mutations are the commonest cause of PNDM whereas K_{ATP} channel (*KCNJ11* and *ABCC8*) mutations are the main cause in Europeans. In addition PNDM is generally isolated but in Arab is more likely to be part of a recessively inherited syndrome of which Wolcott Rallison Syndrome (WRS) was the commonest. This different spectrum is most likely due to the higher rate of consanguinity in Arab countries compared to other areas. However; little is known about TNDM in the Arab region. It is possible that, in this region, TNDM is very infrequent, under-diagnosed or under-reported. The presentation will review the genotype and phenotype of NDM in the Arab region. A new data from a large Arab cohort with WRS will be highlighted.

Diabetes and fasting; the religion point of view

Waseem Fathalla
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No abstract available.

Fasting Ramadan in children and adolescents with type 1 diabetes

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Fasting during Ramadan is a major tenet of the Muslim religion. All adults after the age of puberty are required to do so if health permits. However, there are exemptions to this requirement and having a chronic condition such as diabetes is one. Nevertheless, many adults and adolescents feel obliged to fast during Ramadan even though there is no absolute need to do so. This obligation must be respected. There are few data to support this practice in those whose condition, such as diabetes, potentially makes them vulnerable to developing problems during prolonged fasting. This study was designed to examine the ability and safety of young people with diabetes to be able to fast if they so desire. Two groups of patients were studied, those on a multiple injection, so-called basal-bolus, regimen and those on a 'conventional' twice daily pre-mixed insulin regimen. All patients showed a tendency to high blood glucose at the time of commencing their fast. Those on twice daily insulin continued to have hyperglycaemia during the day whilst those on basal-bolus insulin showed a steady fall in blood glucose towards normal by the time of breaking their fast. Although there was a greater tendency to hypoglycaemia in the basal-bolus group, this could be successfully prevented by reducing the dose of basal insulin by 10–20%.We recommend that it is safe for adolescents with diabetes to fast during Ramadan as long as they reduce their basal insulin by this amount and continue to monitor their blood glucose regularly.

Diabetes and fasting; Egypt experience

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No abstract

Ramadan Fasting in Adolescents with Type 1 Diabetes, CGM Study

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Introduction: Even though adults with chronic diseases and children are exempted from fasting in Ramadan, the vast majority elect to fast even if it is against the physician's advice. Due to the scantiness of data about the effect of fasting on glucose profile in patients with type 1 diabetes, and especially in children and adolescents, healthcare providers have been giving conflicting advices, based mainly on their personal experiences, about the safety of fasting during Ramadan. **Aim:** This study was done to assess the ability and safety of fasting, and to monitor glucose profile using continuous glucose sensing (CGM). **Method:** Children and adolescents with type 1 diabetes who intended to fast the month of Ramadan, 2013 were asked to wear the CGM for a minimum of 3 days, and to report to us any episodes of severe hypoglycemia (patient needed the help of others), DKA, or ER visits, and the total number of days they could fast. Patients were seen before Ramadan to adjust their insulin pump rate according to the eating pattern during the fasting month. **Results:**
A total of 21 patients were enrolled (15 females), age (mean ± SD) was 15±4 years, duration of diabetes 6±3 years, and HbA1C 8.6±1.1%. 18 patients were on insulin pump therapy (CSII), and 3 on multiple daily injections (MDI). Subjects were able to fast 85% of the days (ranged between 50%-100%), in the remaining 15% of the days fasting was interrupted due to hypoglycemia and/or not feeling well. The average number (±SD) of fasted days was 25±5, and 38% of patient could fast the whole month. There were no reported episodes of severe hypoglycemia, DKA or ER visit throughout the whole month. The 24h average BG was 182 ± 17 mg/dL (171±6, and 197±17 during fasting hours and eating hours, respectively). Hypoglycemia (BG <80 mg/dL) and hyperglycemia (BG>300 mg/dL) were reported in 14% and 10% of the CGM time, respectively. There was no significant difference in HbA1C between pre and post-Ramadan (8.6±1,1% vs. 8.3±1.2%). **Conclusion:** Children and adolescents with type 1 DM were able to fast most of the days during Ramadan. Even though BG fluctuation was evident on the CGM, there were no episodes of DKA or severe hypoglycemia.

Apparent Mineralocorticoid Excess Syndrome

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The syndrome of apparent mineralocorticoid excess (AME) is an autosomal recessive disorder characterized by hypertension, hypokalemia, low renin, and hypoaldosteronism. It is caused by deficiency of 11β-hydroxysteroid dehydrogenase which results in a defect of the peripheral metabolism of cortisol to cortisone. As a consequence, the serum cortisol half-life (T½) is prolonged, ACTH is suppressed, and serum **cortisol concentration** is normal. The **hormonal** diagnosis of the disorder is made by the increased ratio of urine-free cortisol to cortisone. In patients with AME this ratio is 5-18, while in normal individuals it is less than 0.5. These studies suggest that an abnormality in cortisol action or metabolism results in cortisol behaving as a potent mineralocorticoid and causing the syndrome of AME. We report three siblings, two female and one male, with the syndrome of apparent mineralocorticoid excess who presented with hypertension, hypokalemia, low renin, and low aldosterone levels. The ***finding of abnormally high ratio of 24-hour urine-free cortisol to cortisone in our three patients (case 1 = 8.4, case 2 = 25, and case 3 = 7.5) confirmed the diagnosis of*** apparent mineralocorticoid excess syndrome in these children. **In this study, the genetic** testing of those **three siblings** with the typical clinical features of AME has detected missense mutation c.662C < T (p.Arg208Cys) in exon 3 of the HSD11B2 gene in the homozygous state.

Surgical management of obesity

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Introduction: Obese children grow to become obese adults. In addition, obesity in adolescents is very common in the UAE. Bariatric surgery for adolescents is on the rise. **Methods:** Review of the literature of bariatric surgery in adolescents. **Results:** Obesity in children in the UAE is higher than international rates. Obese children grow up to become obese adults. Bariatric surgery is the most effective therapy for morbidly obese adolescents. Laparoscopic adjustable gastric bands are not FDA approved for use in patients less than 18 years of age. In addition, malabsorptive procedures like biliopancreatic diversion have an unacceptable morbidity and mortality in adolescents. The appropriate options for bariatric surgery procedures in adolescents are the laparscopic gastric bypass and the laparoscopic sleeve gastrectomy. Only experience multidisciplinary programs should offer bariatric surgery with evaluation of both the family and the adolescent child both psychologically and the nutritionaly. **Conclusion:** Bariatric surgery is effective in treating morbid obese in adolescents in the setting of a comprehensive multidisciplinary program.

The clinical dilemma of gender assignment

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Differences or disorders of sex development (DSD) describe a biological discrepancy between chromosomal, gonadal, and phenotypical sex, often affecting the morphology of the genitor-reproductive organs. DSD is most often due to genetic abnormalities affecting chromosomal composition or single genes, which in turn control the endocrinology of sexual development. DSD may have profound effects on gender identity and gender role behavior. In the past, affected children were treated according to the optimal gender policy established by John Money. This optimal gender policy was based on the beliefs that humans with high plasticity towards gender assignment and therefore, children with DSD were pressed into an established sex, either male or female, were surgically corrected to the respective phenotype, and were mostly not told about these procedures to save them from uncertainty of sex assignment. This policy has been challenged since the 1990s, and since then patient support groups and professionals have advocated new ways of management for children

with DSD. A recent national network study in Germany has given insights into the problems of previous management in children, adolescents, and adults with DSD and provides the basis for a current European survey funded by the EU. 46,XX DSD is often regarded different from 46,XY or chromosomal DSD. This is due to the fact that most children with 46,XX karyotype and DSD have congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Many professionals and also the CAH advocacy groups are of the opinion that these children should be regarded as unchallenged females and therefore support early surgery towards feminization of genitalia in conjunction with optimal supplementation with hydrocortisone and fludrocortisones if necessary. For children with 46,XY DSD the situation is more complicated. In many children, an exact genetic diagnosis is still missing. Depending on the phenotype, this may be true for more than 80% of children with severe hypospadias, while in contrast in postpubertal patients with clinical evidence of complete androgen insensitivity, in 95% an underlying mutation within the androgen receptor gene is detected. With advancements in modern genetics due to next generation sequencing procedures, new genes involved in sexual development are detected and cases of DSD with similar phenotypes can be distinguished on the basis of different genes being mutated. Also, modern laboratory techniques to measure steroid hormones have led to the elucidation of specific enzyme deficiencies. At this time, however, it remains elusive if this will have profound effects on the management, especially on the sex assignment of these children.
For some specific disorders, recommendations for sex assignment are made on the basis of the genetic diagnosis. This advice is founded mainly on the understanding of how an individual will develop at the time of puberty, but also includes aspects of future fertility. Children with a 46 XY karyotype who have androgen deficiency (resulting from a deficiency of either testosterone 17βhydroxysteroid dehydrogenase 3 or 5αreductase 2) are usually raised as male, even if severe under-androgenization is evident. These decisions reflect the high potential for androgen synthesis via alternative pathways and the possibility that fertility might be preserved. Uncertainty in this decision-making process is evident in case reports that describe siblings with identical mutations in testosterone 17βhydroxysteroid dehydrogenase 3 who were assigned to opposite sexes. Children with a female phenotype and underlying 46XY complete gonadal dysgenesis or complete androgen insensitivity are usually raised as female as only in rare cases a male gender identity has been reported.

At this time, no straight forward recommendations exist for sex assignment in neonates who have a DSD. To reflect this uncertainty, the German personal status law was changed in 2013 to enable sex assignment to be left open for any child with a DSD who has genital ambiguity. However, current advice still favours a 'social' assignment of sex in all children to protect and maintain the integrity of the family, even though this advice is being challenged by support groups and might be changed in future guidelines.

DSD; the religion point of view I

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DSD is a clinical condition where an individual's external genitalia is indistinct of male or female character. It presents in 2 forms: First form is obvious from its appearance and it is called partial/ mild DSD and the second form which is obscure from its appearance and called complete/ severe DSD. The Share' a purpose did not deprive seeking for treatment for patients, but It also encourage helping patients to get treatment. In the partial form, Share recommends returning back to a male or a female by surgery. This is not a change of sex but a return back to its normal real sex by surgical correction of genital malformation. In the condition of complex DSD, after a thorough investigation, could be corrected by surgery to the appropriate sex. This is in contrary of transsexual surgery to the opposite sex, which is prohibited in Islam, because it is changing of sex.
The Muslim World League has certain recommendation regarding sex transformation including:
1. A normal male or a normal female with normal external genitalia, sex transformation is illegal and prohibited.
2. Those with ambiguous genitalia, surgical correction or hormonal replacement are intended to correct the underlying anomaly.
While Islamic Share' prohibits sex it transformation, it has views on sex correction. The views aim at:

- Intention to repair to normal function and appearance.

- Delaying early correction in complex DSD until puberty when individual behavior is well defined.

Overall, the Share' a statement is always consistent with the Medical statement.

DSD; the religion point of view II

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Sexual behavior is based on biological, linguistic and cultural characteristics, that are necessary to develop since childhood; in other words, accepting the partiality of the human being, male or female, away from non-existent totality, for both genders. Humanity takes its interaction and integration from the unit built by the relationship between the male and the female, in the relationship with the Creator. This means that any male would exclude the feminine part of him and the female the masculine part of herself. The sexual differences between the male and the female are not a transient accident, but are substantial from the very beginning. This means that there is no loss of the sexual differences, nor possession of the whole unity (male and female in one entity, as a unit/entirety, male and female in one person). The foundations of Christian education are hence in living the pact with the Creator, through the mutual trust, even if the trust is fragile between two sexually different persons. This is why there is desire for and in relationships. This relationship is built on communicating and language in a path/course, and not only in a transient relationship; it's a commitment relationship beyond the contract, and the Creator is the third witness for this love, and he is its source. He is the source and inspiration of this relationship: any relationship of love and desire to meet with the different other, and not a pure physiological relation (in terms of consumption), nor contempt for the body or misplaced contempt for the sexualized humanity.The above can only be achieved if the human addresses at the very young age, any confusion in sexual identity in both biological and cultural aspects, in a harmonious way, chromosomal, biological, educational and psychological. So the partial sexual identity of the individual will be firmly founded / rooted (Abstract available in French and Arabic).

Psychology of DSD

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The diagnosis of disorders of sex development (DSD) presents exceptional personal and social challenges. The goal of DSD treatment is the long-term physical, psychological, and sexual well-being of the patient. Therefore, the clinical management of individuals with DSD requires the input of many disciplines in a patient-centered approach. Although accurate diagnosis and delivering appropriate medical and surgical treatment are central in the clinical management of DSD, the quality of life also depends on the psychosocial management. Patient feedback and outcome research showed the long-term psychological distress associated with surgery without consent, medical photography, repeated genital examinations, uncontained disclosure or unhelpful phrasing of sensitive information. The new ESPE/LWPESDSD guidelines acknowledge the significance of psychosocial care and the involvement of mental health staff with expertise in DSD. In practice, the psychologist plays an important role in medical management and individual development, including decisions about sex of rearing, surgical intervention, introduction of sex hormones, information about diagnosis and decisions about sex re-assignment, as well as routine support and monitoring of social and emotional well-being. In addition, psychological input should be available for unforeseen issues, including, for example, parental or individual concerns about gender identity development, school-related problems and bullying.

Hypophosphatasia; an overview

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Hypophosphatasia (HPP) is a rare inborn error of metabolism that is characterised by impaired bone and tooth mineralisation. It is caused by deficiency of tissue nonspecific alkaline phosphatase (TNSALP) activity, which leads to accumulation of inorganic pyrophosphate (PPi), a potent inhibitor of hydroxyapatite crystal formation, which ultimately leads to rickets in children and osteomalacia in older adolescents & adults. Other effects include impaired respiratory function, seizures, muscle weakness and nephrocalcinosis. HPP is inherited as either an autosomal dominant or recessive trait; all patients have inactivating mutations of the gene that encodes TNSALP, located on chromosome 1p36.1-34. The disease severity ranges widely from a lethal perinatal form, to a severe infantile form that is characterised by rachitic skeletal changes and pathological fractures, to mild childhood and adult forms. Based on the age of the patient when the diagnosis is made and severity of the disease, five forms of HPP have been described. The **perinatal form of HPP** is characterised by severely demineralised skeleton so that the affected infant is either stillborn, or dies within few days of birth due to respiratory failure without treatment (see below).Those with the **infantile form of HPP** appear healthy at birth but present with failure to thrive, vomiting, hypotonia, craniosynostosis and some infants go on to have pyridoxine (vitamin B_6) dependent seizures. These infants usually die of respiratory failure, which arises secondary to their soft rib-cage. Premature exfoliation of primary teeth with intact roots before the age of five years is the hallmark of the **childhood form of HPP.** These children are often of short stature, have mild swelling of metaphyses of long bones and myopathy. Chronic recurrent multifocal osteomyelitis is also a feature of this form of HPP. The **adult form of HPP** may come to light through osteomalacia causing recurrent and slowly healing metatarsal stress fractures. They may also develop pseudogout and chondrocalcinosis, caused by precipitation of inorganic PPi crystals. **Odontohypophosphatasia** is the form of HPP that is associated with premature loss of fully rooted primary teeth, without skeletal involvement. Biochemical hallmark of HPP is low serum alkaline phosphatase activity for age of the child. Urinary excretion of phosphoethanolamine/creatinine ratio is increaser, although it may be normal in milder cases. Serum and urinary PPi and pyridoxal-5'-phosphate levels are elevated, although these substrates of TNSALP are not measured by many clinical laboratories. Serum inorganic phosphate concentration is often raised or at the upper end of the reference range for age of the child. Infants with severe (perinatal & infantile) forms of HPP can have symptomatic hypercalcaemia, which in turn may lead to hypercalciuria, nephrocalcinosis and renal impairment. Radiographs of long bones show rachitic changes with "tongue like" areas of lucency projecting from growth plates into metaphyses. Attempts to treat the condition with IV infusions of plasma enriched in alkaline phosphatase (ALP) from patients with Paget's disease, or ALP derived from human placentas were unsuccessful. Enzyme replacement using a bone targeted recombinant TNALP in infants with life-threatening forms of forms of HPP resulted in healing of skeletal manifestations of HPP as well as improved respiratory and motor function [*N Engl J Med 2012; 366:904-13*]. This treatment holds great promise in treating the mineralization defect and non-skeletal complications of HPP Supportive treatment includes respiratory support, management of hypercalcaemia, preventative dental care, pyridoxine for infants with the perinatal form of HPP who develop seizures, physiotherapy and analgesics for pain control. Expert orthopaedic treatment of fractures, limb deformities & kyphoscoliosis, and neurosurgery for treatment of craniosynostosis may also be necessary.

Peritoneal Dialysis Used for Treating Acidosis in a Child with Diabetic Ketoacidosis

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Guidelines for managing Diabetic Ketoacidosis are well established. However, there is no reported DKA cases required peritoneal dialysis for clearing the acidosis in stable renal function. Here, we report a child with first presentation as a severe DKA for whom peritoneal dialysis was done for the acidosis. **Objective**: To highlight our unique experience in managing severe resistant acidosis with peritoneal dialysis in case of diabetic ketoacidosis. **Method:** We report a two years old child presented with severe DKA as a first presentation of type 1 diabetes mellitus whose acidosis was managed

with peritoneal dialysis with good recovery at Royal Hospital, Oman. **Result:** A 2 years old Philipino boy admitted to our pediatric intensive care unit (PICU) with severe diabetic ketoacidosis (blood glucose 22 mmol/l, urine ketone: 4+, PH: 6.8, bicarbonate: 4.9 Base Excess: -22). He had history of polyuria, polydipsia, weight loss and lethargy. Examination revealed that he was severely dehydrated, tachyponic, respiratory rate 36/min with kussmual breathing, tachycardiac, heart rate 170/min and drowsy hence he was intubated and ventilated. The patient was resuscitated with intravenous fluid, followed by insulin and potassium chloride. 48 hours post admission his acidosis remained severe (PH: 6.9-7.1) despite multiple doses of sodium bicarbonate. He developed myocardial decompensation as he dropped his blood pressure and required two inotropic support. He also developed cerebral edema by MRI brain. Using peritoneal dialysis for treating acidosis has its own risk as well as invasive procedure but certainly in experienced center can be considered as a modality of treatment for resisting acidosis. To our knowledge this is first case reported. However further studies are needed to confirm its effectiveness and weighing its risk.

Children with Type 1 Diabetes in the Kingdom of Bahrain: an Audit of a Diabetes Registry

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Introduction: The prevalence of diabetes in the Middle East is amongst the highest worldwide with Bahrain ranking amongst the top 10 countries. In particular, growing numbers of children are being diagnosed with Type 1 diabetes mellitus (T1DM) posing a significant public health concern. **Aim:** To undertake an audit of a Diabetes Registry to explore demographic, health, and nutritional factors associated with T1DM using a case-control approach. **Methods:** Routine clinical data from the Diabetes Registry Form was collated for children with diabetes meeting the inclusion criteria. Non-diabetic comparators were recruited from Local Health Centers and completed an adapted registry form. A total of 59 children aged 6-12 years received a confirmed diagnosis of T1DM in the years 2009 and 2010 and were compared with 53 healthy comparators. **Results:** Children with T1DM were more likely than non-diabetic children to have suffered from an illness prior to their diabetes diagnosis such as tonsillitis (54.2% and 5.7% respectively; $p< 0.001$), to have undergone surgery prior to diagnosis (23.7% and 3.8% respectively; $p=0.001$) and to have mothers with Type 2 Diabetes ($p=0.053$) or a family history of Gestational Diabetes ($p=0.003$). No significant difference in infant feeding practices was observed between children with Type 1 diabetes and the non-diabetic counterparts. Children with diabetes had a significantly higher caloric intake ($p< 0.001$) although no differences were observed in macronutrient intakes. **Conclusion:** Whilst unable to fully investigate any potential genetic differences between cases and controls, this study provides support for the theoretical role of infections as a trigger for T1DM.

Genetic analysis of patients with Neonatal Diabetes in Oman

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Background: Neonatal Diabetes Mellitus (NDM) is rare and occurs in 1:300,000–400,000 births. Neonatal diabetes can be permanent (PNDM) or transient (TNDM). In PNDM, the diabetes affects patients for their entire life; while in TNDM, the diabetes may disappear after the first few months of life but may recur later in life. Distinguishing TNDM from PNDM has significant implications for patient management, prognosis and monitoring of diabetes recurrence. Only genetic testing can make this distinction. Testing for mutations in specific genes can also guide therapy and affect clinical outcome. For example, PNDM patients with mutations in *KCNJ11* or *ABCC8* genes can be transferred from insulin therapy to sulfonylureas. Hence, it is important to establish genetic testing for NDM syndromes in Oman. **Objective:** To study the genotypes underlying NDM syndromes within the Omani population **Method:** DNA from 24 patients with NDM who attended the Diabetic clinic at Royal Hospital from 2008-2013 (inclusive) was analysed for mutations in GCK, ABCC8, KCNJ11, INS, SLC2A2, EIF2AK3 and FOXP3 genes using PCR and Sanger sequencing. **Results:** Of the 24 patients analysed, three patients had homozygous mutation in the GCK gene which encodes for Glucokinase, a key enzyme responsible for regulating insulin

secretion in pancreatic beta cells.one patient has a mutation in Kir6.2 subunit. Two patients had mutations in 6q24 locus and were designated as having TNDM. Another three patients were re-diagnosed as having Fanconi-Bickel syndrome due to mutations in the SLC2A2 gene which encodes a protein that mediates bidirectional glucose transport. The rest of the 15 patients did not exhibit any pathogenic mutations in the genes tested. Among these 15 patients, two were later classified as having hereditary autoimmnune diabetes. **Conclusion:** Of the 18 patients with actual NDM in our study, we were able to detect pathogenic mutations in 33% (6/18) of the patients. The lack of genetic test results in 67% of NDM patients supports the relevance of Next generation sequencing in genetic testing of monogenic diabetes syndromes in Omani population.

Clinical and molecular characterization of maturity onset-diabetes of the young caused by HNF4 alpha mutation

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Objective and hypotheses: The present study was undertaken to elucidate the clinical and molecular characteristics of MODY 1 and to highlight the red flags for prediction of MODY**. Method:** Molecular study of MODY 1 was undertaken for 8 subjects of a Saudi family. The proband is a-12- year old female presented with symptoms suggestive of diabetes. Investigations revealed hyperglycemia, glycosuria and ketonuria with no acidosis. Pancreatic antibodies were negative. She responded well to subcutaneous insulin. Her family history revealed that two of her siblings were diagnosed with type 1 diabetes (T1DM) while her father and mother have type 2 diabetes (T2DM). In view of this strong family history, the possibility of monogenic diabetes was raised, namely hepatocyte nuclear factor 1 α and 4 α genes (HNF 4α, HNF α 1). Accordingly, genomic DNA was isolated from peripheral blood lymphocytes of the 8 members of this family, polymerase chain reaction (PCR) was carried out, and sequencing of the whole HNF1 α and HNF4 α gene was done. **Results:** DNA study of the proband revealed heterozygous substitution at position-nt5 in intron 1 of the hepatocyte nuclear factor 4 alpha gene (HNF 4 α). This mutation was identified in other 5 members of the family. **Conclusion:** This study highlights the importance of considering MODY in any individual diagnosed with either T1DM or T2DM, who have atypical features for these polygenic disorders. The red flags for prediction of monogenic diabetes include strong family history of diabetes and early presentation in young age group especially when ketoacidosis, anti-islet antibodies and obesity are not features. Confirming this diagnosis at molecular level facilitates management, improves outcome and provides effective genetic counselling.

Successful Transfer from Insulin to Glibenclamide in a Neonate with Diabetes: First Case from Pakistan

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Background: Neonatal diabetes mellitus is rare with prevalence of approximately 1 in 500,000 infants worldwide. It is a monogenic form of diabetes with onset within 6 months of age. It is caused by several different genetic abnormalities, and may either be transient or permanent. Previously clinical management of most permanent types of neonatal diabetes required lifelong insulin treatment. Recently, it is known that heterozygous activating mutations in the genes forming the ATPsensitive K_ channel *KCNJ11* and *ABCC8*, are a common cause of neonatal diabetes. Sulfonylurea treatment has been found to restore insulin secretion in patients with these mutations and they can be effectively treated orally instead of insulin, with significantly improved glycemic control and quality of life. **Case summary:** We report a term baby who presented at one month with fever, tachypnea and vomiting. The baby was born to consanguinous parents and there was no family history of Diabetes. His birth and past history was unremarkable. In hospital he was found to have a glucose of 1299 mg/dl with acidosis and ketonuria. He was managed as Diabetic Ketoacidosis and once resolved was switched to subcutaneous NPH Insulin. We sent his samples to for genetic testing. He was found to be heterozygous for the KCNJ11 missense mutation, p.R201H. This result confirmed a diagnosis of neonatal diabetes due to a mutation in the Kir6.2 subunit of the K-ATP channel. Glibenclamide was started at seven weeks of age and Insulin was successfully stopped within one week of starting Glibenclamide. **Results:** At 3 months of age he has achieved normoglycemia (HbA1c 5.9%) on Glibenclamide.

Conclusion: Glibenclamide is a useful treatment option in the management of patients with KCNJ11 mutations.

Persistent Hyperinsulinaemic Hypoglycemic Of Infancy (PHHI)

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Introduction: Persistent Hyperinsulinemic Hypoglycemic of Infancy (PHHI) is a clinically and genetically heterogeneous disorder with familial and sporadic forms due to dysregulation of insulin secretion. PHHI is a severe disease that leads to brain damage. A subtotal to near total pancreatectomy has become the mainstay of surgical therapy for patients with PHHI who did not respond to medical therapy.
Patients & Methods: We have reviewed 15 infants (10 male & 5 female) who presented with severe recurrent non-ketotic hypoglycemia in the period between 1996 and 2014. The age ranges from 1 day- 3 months except one patient was diagnosed at 6 years of his age. Patients were referred from different parts of Libya to our center. The diagnosis of primary form of congenital hyerinsulinaemic hypoglycemia was confirmed by laboratory investigations. Analysis of data regarding the time and mode of presentation, birth history, family history and histopathological pattern in addition to management and outcome of the patients were studied. **Results:** All patients showed persistent hypoglycemia in the presence of normal to high insulin levels which was inappropriately high for the blood glucose levels (Insulin: glucose ratio > 0.3). Other causes of hypoglycemia were excluded. Eight patients with birth weight range from (2.9kg -5.7kg). They found to have diffuse type. Two male infants presented with severe form of hypoglycemia earlier age 1-7 days of life with blood sugar 2-4 mg% and had greater birth weight (4.5 kg & 4.1 kg). Their mothers did not have gestational diabetes. The infants did not respond to medical therapy and were found to have multifocal adenomatosis in the pancreases. 5 patients presented at < 7 days with blood sugar < 20 mg% had focal lesions. 12 patients underwent subtotal to near total pancreatectomy. Post pancreatectomy, unfavorable neurological outcome was seen in 4 pats due late intervention. Diabetes mellitus developed in 3 patients post pancreatectomy with a mean age of 6 years. 2 patients died with fulminate infection postoperatively. **Conclusion:** Early recognition, diagnosis and treatment of the condition are necessary to prevent or minimize neurologic damage. Preoperative investigations such as PET scan to identify a focal lesion of the pancreas can lead to a limited pancreatectomy and minimize the post-operative complications such as development of diabetes. Genetic analysis and counseling should be available for all patients.

Efficacy and safety of insulin pump in type I diabetes during fasting

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Insulin pumps has proved to be an effective way to control blood sugar in type I diabetes. However few data are available to assess its efficacy and safety in fasting diabetic patients during Ramadan. The purpose of this study is to evaluate the efficacy and safety of insulin pump in patient with type I diabetes who were fasting during Ramadan. **Method:** this was a single center non randomized study conducted in Tripoli diabetic center. 20 patients with type I diabetes who fasted Ramadan on insulin pump were enrolled. Patients were seen before Ramadan and once after Ramadan. Weight change, episode of hypoglycemia, emergency visit and days of breaking their fast were evaluated. FBS, HbA1c and fasting lipids were also evaluated. Results: most patients on insulin pump were able to complete their fasting during Ramadan (average 2 fast breaking per patients) with minimal episodes of hypoglycemia (2 episodes per patient). One patient had sever episode of hypoglycemia requiring third part assistance. No emergency room visits, no significant difference was found in biochemical profile before and after Ramadan, there is a mild reduction in body weight. **Conclusion**: the insulin pump proved to be effective and safe in patients fasting Ramadan.

CSII versus MDI in children with type 1 diabetes in Kuwait: Glycemic control, insulin requirement and BMI

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Objectives: Continuous subcutaneous insulin infusion (CSII) and multiple daily insulin injections (MDI) are the two methods currently used for the management of type 1 diabetes (T1DM). The aim of our study was to report experience with CSII in a large cohort of children and adolescents in comparison with MDI in Kuwait.
Research design and methods: Patients ≤ 18 years of age started on CSII during the period of July 1st 2007 until December 31st 2012 and followed up in the government hospitals were included. All patients were initially on intensive insulin therapy of 3-4 injection. Data collected included gender, age at diagnosis and at pump insertion, diabetes duration. Body mass index (BMI), hemoglobin A1c (HbA1c), insulin dose and adverse events were measured at baseline and every 3 months during the follow up period. Similar data were collected on patients on MDI followed during the same period. **Results:** Main reason for switching to CSII was to achieve better control (37%), followed by frequent severe hypoglycemia and better quality of life (13.3% each). Although the drop of HbA1c was most significant in first year of pump therapy, it continued to be significantly lower in the CSII group compared to the MDI throughout the study period (CSII 7.94±0.82 vs MDI 8.31±1.03; $P < 0.001$ in the 1st yr, and 8.28±1.22 vs 9.02±1.62; $P < 0.045$ in the 5th yr.). Total daily insulin requirements maintained significantly lower in the CSII group. BMI z scores increased in both groups, more in the CSII, but the difference was not statistically significant (0.76±1.19 vs 0.71±1.21 in 1st yr; $P = 0.69$ and 1.34±0.89 vs 0.92±1.28; $P = 0.15$ in 5th yr). Five patients discontinued CSII therapy, 2 went back within 3 months. There was no significant change in the rate of diabetic ketoacidosis in both groups. CSII group had more severe hypoglycemic episodes at baseline than MDI group (9.7 vs 3.7 event per 100 patient-year; $P < 0.05$). However, the rate of the episodes were decreased significantly in the CSII group (5.7 vs 17.7; $P < 0.05$ in the 1st year and 4.1 vs 19.7; $P < 0.05$ in the 5th yr). **Conclusion:** CSII is a safe form of intensive insulin therapy in children and adolescents with type 1 diabetes mellitus, without significant adverse effects but with a markedly lower rate of severe hypoglycemia and daily insulin requirements. With the available resources (financial and professional) it could be used for all children with type 1 diabetes.

Effectiveness of Pump Therapy in Libyan Type I diabetic patients; first Libyan experience

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It is well established that the serious microvascular complications of DM are linked to the duration & severity of hyperglycaemia. There have, therefore, been renewed efforts to help patients achieve near-normal glycaemia. The mainstay of current management of Type 1 diabetes is "physiological insulin replacement "by administering multiple daily injections of insulin as glycaemic control improves with intensified insulin regimens the frequency of hypoglycaemia tends to increase. Insulin pump therapy can improve glycaemic control in patients with type I DM because it can reduce the within-day and between day glycaemic variability that is seen with insulin injections. **Aim:** To know different indications for pump wearing among study group, to assess glycaemic control of study group on pump therapy& To know patients & Family attitude towards pump use. **Patients & Methods:** A total of 37 patients wear insulin pump between March & November 2013. Patients selected from waiting list according to certain criteria. Data collected in terms of demographic characters of patients, duration of DM, indication for pump wearing, BMI at the start & completion of observation. HbA1c level: before pump therapy, after 3 months& at completion of observation on March 2014 and occurrences of severe hypoglycaemia that requires hospital management or DKA episodes. Modified patient questionnaire used in two separate visits: (visit 1) & (Visit 2) to compare patient's data prior to & after pump use including knowledge about diabetes care& patient's attitude towards pump therapy. **Outcome Measures**: Change HbA1c from baseline, occurrence of acute complications including: Severe hypoglycaemia &Diabetic ketoacidosis episodes. Change of BMI & Score results of questionnaire of two visits. **Results:** 49% were female with 86.49% between 2 year & 22 years old. 92% had diabetes for one to fourteen years. Indication for pump use was due to high HbA1c in 30%, compromised quality of life using MDI in 28%, wide glucose variation in 11.7%,

severe hypoglycemia in 18\%, hypoglycemia unawareness in 5% and recurrent diabetic ketoacidosis in 7%. HbA1C mean showed reduction from 9.09% to 7.36% (P=value=0.000) after three months which is maintained till last observation at 12 months. BMI result showed increase in mean from 21.16 to 21.96 which is significant (P =0.018). One patient had 2 episodes of DKA with severe contact dermatitis at site of cannula &sensor .One severe hypoglycaemia required hospital management due to unmatched CHO intake to insulin dose. Questionnaire result showed improving of quality of life score with an increase of average from 34.24 to 46.7 (P value=0.000). **Conclusion:** Insulin pump therapy is effective to achieve and maintain good glycaemic control in most patients with diabetes & very good tool for more contact between patient and health provider for management and education regarding diabetes.

Obesity and Cardiovascular Morbidity in Egyptian Children and Adolescents

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Prevalence of obesity in children and adolescents has increased significantly worldwide with an alarming rise of its co-morbidities that elevate the cardiovascular risk of affected people. Obesity has been found to cause changes in cardiac autonomic modulation with decreased heart rate variability (HRV) as well as Left ventricular structural changes in adults. However, the data in obese children is scarce and contradicting. **Aim: (1)** Evaluating abdominal fat in Egyptian obese children by anthropometry as well as by ultrasonography (US). (2) Determining HRV parameters and structural cardiac abnormalities in these obese children. (3) Measuring carotid intima-media thickness and brachial artery flow mediated dilatation (FMD) using high resolution ultrasound. **Methodology:** Two hundred patients and two hundred controls were enrolled in a cross-sectional study. The patients had assessment of abdominal fat was done using anthropometric and ultrasonographic measurements, blood pressure measurement, laboratory testing of serum lipids profile (serum cholesterol, triglycerides, high density lipoprotein and low density lipoproteins), fasting blood glucose and fasting serum insulin. Insulin resistance was estimated by using the Homeostasis Model Assessment (HOMA), echocardiography: LVMI, Systolic function (FS), Diastolic function (E/A ratio and DT) and ultrasonic assessment of carotid intima media thickness (cIMT) and brachial artery flow mediated dilatation (FMD). Results: among the obese children, males, hypertensive children and those with metabolic syndrome were found to have significantly more visceral fat and subcutaneous fat thickness SDS than the other groups. Obese children with elevated HOMA IR, abnormal lipid profile and high anthropometric measures had poor heart rate variability. Obese children and adolescents had significant Left Ventricular Hypertrophy (LVH) and changes in early diastolic filling, even in the absence of other co morbidities. BMI and HDL were significant independent predictors of left ventricular mass index. BMI and WC showed significant correlation with echocardiographic parameters. cIMT was significantly more increased in obese children when compared to controls (p=.000). There were significant direct correlation between cIMT on one side and BMI (p=0.028) and serum LDL (P=0.038) on the other side. Obese female children had impaired FMD%. In multiple regression analysis: serum TG, serum cholesterol and systolic blood pressure were significant predictors of FMD%.
Conclusion: we conclude that waist circumference is an important anthropometric measurement that highly correlates with visceral fat in obese children. Abdominal ultrasound is a noninvasive technique that measures visceral fat thickness. HRV was impaired among obese children with evidence of parasympathetic withdrawal & sympathetic dominance. Among obese children, those with insulin resistance and high lipid profile seem to suffer the most deviation from normal regarding their HRV parameters. Obese children and adolescents have significant LVH and changes in early diastolic filling, even in the absence of other co morbidities. Vascular changes were present in obese children as evidenced by carotid intima- media thickening. Obese female children had impaired FMD%. Both cIMT and FMD% serve as predictors of coronary artery disease which may help risk stratification of these patients. Improving our understanding of cardiac dysfunction related to obesity may provide clues for new preventive and therapeutic strategies.

Characteristics of adolescents and youths with type 2 diabetes at Dasman Diabetes Institute, Kuwait

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Introduction: Until recently, type 2 diabetes was barely diagnosed in children. The worldwide epidemic of childhood obesity has been accompanied by an increase in the incidence of type 2 diabetes in youth. There are substantial limitations in knowledge of treatment paradigms in youth. The known waning effectiveness of oral hypoglycemic agents in adults' overtime is of particular concern for youth with type 2 diabetes, who will have longer duration of diabetes over the course of lifetime. Early onset of type 2 diabetes is associated with increased risk of morbidity and mortality. Because the development of long-term microvascular and macrovascular complications of type 2 diabetes in adults is related to duration of diabetes and control of glycemia, the increase of number of children diagnosed with diabetes becomes a major public health concern. **Aim:** To describe the baseline characteristics of type 2 diabetic children diagnosed before the age of 20 years at Dasman Diabetes Institute (DDI). **Population/method:** Participants were identified from within the clinical population of DDI. A review of charts of all children less than 20 years of age diagnosed with type 2 diabetes, who were attending Dasman clinics between the 1st of January 2011 and 31st December 2013. Data retrieved include demographics, clinical/medical history and biochemical measurements. **Results:** Among a total population of 455 adolescents and youths diagnosed with diabetes, 21 patients had type 2 diabetes giving a prevalence rate of 4.7%. Of them, 62% were males. Mean age was 16.5 years and mean diabetes duration was 30.7 months. The frequency of type 2 diabetes in second- and first-degree relatives was 85.7%. Polyuria and polydypsia were the frequently recorded symptoms in 57.1% of subjects who were symptomatic at diagnosis. Mean body mass index (BMI) was 35.4 kg/m^2. Acanthosis nigricance was detected in more than 75% of patients. Forty three percent (9/21) had their blood pressure at 90th percentile or greater and 33.3 % (7/21) had their blood pressure at 95th percentile or greater. Mean HbA1C was 8.1%. Abnormalities in lipid metabolism was detected in 76.2%. One third of patients were never tested for microalbuminurea, of those who had the test done, 20% had high microalbumin excretion in the urine. Insulin was used as a sole medication in 20% of cases and in the remaining 80%, oral hypoglycemic agents were used either alone or in combination with insulin. Metformin was used in all patients on oral medications (17/21) and sulfonylurea and or glucagon like peptide agonists (GLP-1) or dipeptidyl peptidase-4 inhibitors (DDP-4) were added in five. Bariatric surgery as a therapeutic procedure was carried out in three subjects. **Conclusion:** Type 2 diabetes accounted for 4.7% of the total diabetes population aged less than 20 years at DDI. We described their demographic, clinical and biochemical characteristics. The decline in the age of onset of type 2 diabetes is an important factor influencing further burden of the disease. Type 2 diabetes in children has now become a major new challenge in diabetes.

The acute effects of different exercise intensities on microalbuminuria and insulin sensitivity in obese sedentary females

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Background: The prevalence of obesity has increased worldwide and represents a major public health problem. Severe obesity is often observed with an increase in urinary albumin excretion and impaired insulin sensitivity. Improvement in insulin sensitivity are positively correlated to exercise intensity; emphasizing greater, longer lasting responses to insulin with higher intensity exercises. Additionally, an increase in microalbuminuria after exercise is an accepted phenomenon in normal and diabetic individuals, although the exact pathophysiological mechanism is unknown. **Aim / Purpose:** The purpose of this study was to investigate the acute effects of different exercise intensities (moderate versus vigorous) on insulin sensitivity and microalbuminuria excretion in obese, sedentary females. The time frame for microalbuminuria and insulin sensitivity to revert back to baseline levels after an acute bout of exercise was also investigated. **Method:** Eighteen female participants (24.78±5.17 years; BMI 34.55±6.22) and 10 healthy controls (24±3.74 years; BMI 22.98±1.48) leading sedentary lifestyles without microalbuminuria, diabetes, metabolic syndrome, hypertension, or anti-angiotensin II therapy participated in a single, 30 minute bout of moderate (65% - 75% Heart Rate Reserve [HRR]; 12-13 Rate of Perceived

Exertion [RPE]) and vigorous (75%-85% HRR;14-15 RPE) intensity exercise. Participants provided blood and urine samples prior to each exercise bout and the following 3 days post-exercise. Results and discussion: Moderate and vigorous exercise bouts demonstrated no changes in urinary albumin excretion, however ACR elevated above baseline at 24H and decreased significantly (p=0.026) at 72H (24%) post ex in the obese group. Glucose/insulin ratio peaked at 24H post exercise (p=0.001), which subsequently declined from 48H (6%) to 72H (7%) post exercise. Fasting plasma glucose (p=0.001), HOMA Index (p=0.043) and QUICKI Index (p=0.038) were significantly different between the obese and control groups. No significant differences were detected between U-Microalbumin, U-Creatinine and fasting plasma insulin. **Conclusion:** Obese, sedentary females do not have elevated microalbuminuria or significantly improved insulin sensitivity. Following an acute bout of exercise at both moderate and vigorous intensities. The benefits of chronic exercise are more numerous than acute exercise, emphasizing the need for regular physical activity in obese individuals.

Tight Versus Standard Glycemic Control of Critical Illness Hyperglycemia in the PICU

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Background: Critical illness hyperglycemia (CIH) is prevalent in pediatric intensive care units (PICUs) and is associated with poor outcomes including death, sepsis, and longer length of stay (LOS). The aim of this randomised controlled study was to compare the effects of standard (SGC) versus tight glycemic control (TGC) on mortality. Secondary endpoints involved the LOS, need for mechanical ventilation (MV), cardiovascular support (CVS), morbidity, and number of hypoglycemic attacks. **Methods:** A total of 30 patients at Cairo University Children's Hospital were enrolled in the study, randomly assigned by sealed envelopes into two groups; SGC (n=14) and TGC (n=16). **Results*:*** A higher proportion of those who had TGC died compared with those who had SGC (68.8% vs 50%), however, the difference didn't reach statistical significance. There was no significant difference between the SGC & TGC groups as regards the LOS. Additionally, the need for MV or CVS and frequencies of patients with positive culture didn't differ significantly between both groups. However, there was a significant increase in the number of deaths among those who had MV. It was found that 93.75%, 42.86%, and 33.33% of the deaths among critically ill children are attributed to MV, CVS, and positive culture respectively. Finally, although not significantly different, hypoglycemic events occurred with a higher percentage in patients with TGC compared with those with SGC. **Conclusion:** The SGC is recommended for controlling hyperglycemia in patients with CIH to decrease mortality.

Dyslipidemia in children and adolescents with type 1 diabetes

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Background: Diabetes is associated with a high risk of cardiovascular disease (CVD). The classic «diabetic dyslipidemia» is mostly described as hypertriglyceridemia and low levels of HDL-C. Elevated LDL-C is an established risk factor for CVD, and Apo B is another reliable risk marker. Identifying the pattern of dyslipidemia and the risk factors for its development, including dietary habits and life-style, can allow effective screening, prevention and timely intervention in children and adolescents with T1DM. **Objective:** To identify the pattern of dyslipidemia in children and adolescents with type 1 diabetes mellitus regularly following at the Diabetes Endocrine and Metabolism Pediatric Unit (DEMPU) at Children's Hospital of Cairo University; and to detect its relation to risk factors including family history, duration of diabetes, glycemic control, body habitus, dietary habits and life-style. **Methods:** Sixty children and adolescents with T1DM (34 males and 26 females, mean age 12.5 ± 2.4 years; and mean duration of diabetes 4.3 ± 2.7 years evaluated by full history and clinical examination including family history of dyslipidemia and CVD, and 3 day dietetic history for analysis, BMI and waist circumference. Records were revised for mean fasting and 2hrs-postprandial blood glucose for preceding one month, and mean HbA1c for the past year. Fasting lipid profile (Total cholesterol, LDL, HDL and triglycerides); and lipoprotein risk ratios were calculated. Serum Apo B lipoprotein was measured in patients with dyslipidemia. Thirty-nine healthy age and sex matched children (18 males and 21 females) were included as control for lipid profile. **Results:** Dyslipidemia significantly more

frequent among T1DM children and adolescents compared to control subjects (39/60, 65.0% vs 11/39, 28.2%, p<0.001); and the dyslipidemic (39/60) compared to normolipidemic (21/60) children with DM had significantly higher serum Apo B (71.25 ± 31.69 vs 48.88 ± 11.41 mg/dl, p< 0.01), and significantly higher mean waist circumference. Both groups were comparable regarding age, age at onset and duration of diabetes, family history of diabetes and CVD, degree of glycemic control and dietary analysis. Apo B correlated significantly with duration of diabetes, mean HbA1c, TC and LDL (p= 0.002, 0.012, 0.00, 0.017), while correlation with TG didn't reach significance (p=0.07). **Conclusion:** Dyslipidemia is significantly more frequent in children and adolescents with T1DM compared to their non-diabetic peers. Hypercholesterolemia was more frequent than hypertriglyceridemia and serum Apo B lipoprotein was higher in the dyslipidemic group and correlated significantly with total cholesterol, LDL, HbA1c and duration of diabetes.

Alleviation of high glucose-mediated oxidative damage in HEK293 cells by telmisartan

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Introduction: There is a large body of evidence highlighting that chronic high glucose (HG) condition leads to renal cell oxidative damage. Telmisartan is an angiotensin II type 1 receptor blocker used in cardiovascular diseases. **Aim:** In this study we investigated the protective effect of telmisartan against high glucose (HG)-elicited oxidative damage in in HEK (human embryonic kidney) cells as an in vitro model for diabetic nephropathy. **Methods:** The activity of superoxide dismutase (SOD), catalase (CAT) as well as the levels of malondialdehyde (MDA), glutathione (GSH), intracellular reactive oxygen species (ROS), cell viability and DNA fragmentation were measured in HG-treated HEK293 cells with and without telmisartan co-treatment. **Results:** Pretreatment of HEK293 cells with telmisartan, prior to HG exposure, was associated with a marked diminution in DNA fragmentation, intracellular ROS and MDA levels. Additionally, the cell viability, GSH level, SOD and CAT activity were increased by telmisartan. **Conclusion:** The results suggest that telmisartan has protective effects on HG-induced cytotoxicity in HEK293 cells.

Regulatory T cells with CD62L or TNFR2 expression in young type 1 DM relation to inflammation, glycemic control and micro-vascular complications

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Background: Alteration of regulatory T cells (Tregs) may contribute to ineffective suppression of proinflammatory cytokines in type 1 diabetes**. Aim:** to determine the percentage of Tregs expressing CD62L or tumor necrosis factor receptor type 2 (TNFR2) in 70 young type 1 diabetic patients compared with 30 controls and assessed their relation to inflammation, glycemic control and micro-vascular complications. **Methods:** High-sensitivity C-reactive protein (hs-CRP), hemoglobin A1c (HbA1c), tumor necrosis factor alpha (TNF-α) and interleukin-10 (IL-10) were assessed with flow cytometric analysis of Tregs, Tregs expressing CD62L or TNFR2. **Results:** The percentage of CD4+CD25high T cells and CD4+CD25highCD62Lhigh cells were significantly decreased while CD4+CD25highTNFR2+ T cells were elevated in patients with micro-vascular complications than those without and controls ($p < 0.001$). ROC curve revealed that the cutoff values of Tregs, Tregs expressing CD62L and Tregs expressing TNFR2 (7.46%, 24.2% and 91.9%, respectively) could detect micro-vascular complications. Significant negative correlations were observed between Tregs expressing CD62L and disease duration, FBG, HbA1c, urinary albumin excretion and hs-CRP, whereas, positive correlations were found between Tregs expressing TNFR2 and these variables ($p < 0.05$). TNF-α was significantly increased while IL-10 was decreased among patients with micro-vascular complications than those without ($p < 0.05$). **Conclusions:** Alteration in the frequency of Tregs and Tregs expressing CD62L or TNFR2 in type 1 diabetes is associated with increased inflammation, poor glycemic control and risk of micro-vascular complications.

Carotid Media Intima Thickness and Other Cardiovascular Risk Factors in Children with CAH

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Patients with congenital adrenal hyperplasia (CAH) are at increased risk for cardiovascular disease due to many factors. The aim of this study is to investigate the presence of dyslipidaemia, insulin resistance, and subclinical atherosclerosis as indicated by carotid intima media thickness in children with congenital adrenal hyperplasia. **Methods:** 32 children with congenital adrenal hyperplasia (3-17 years) were compared with 32 healthy controls. All underwent anthropometric evaluation, measurement of fasting lipids, glucose, insulin, oral glucose tolerance test (OGTT), homeostasis model assessment for insulin resistance (HOMA-IR), and carotid intima media thickness (CIMT). **Results:** Fasting glucose, glucose at 30, 60, 90, and 120 minutes during OGTT were significantly higher in patients. HOMA-IR was also significantly higher in patients ($p = 0.036$). Patients had significantly higher CIMT ($p = 0.003$), and higher systolic blood pressure. ($p = 0.04$). No significant difference existed in lipid profile. Both systolic and diastolic blood pressures correlated with treatment duration ($p = 0.002$, $p = 0.043$ respectively). **Conclusion:** Children with CAH are at increased risk of insulin resistance, glucose intolerance, early atherosclerosis and cardiovascular disease. Screening of these patients at an early age is recommended.

Obesity among children and adolescents with Congenital Adrenal Hyperplasia (CAH)

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Children and adolescents with CAH are at high risk of developing obesity. **Aim:** the aim was to examine the prevalence of obesity in a cohort of patients with CAH at the pediatric endocrine department in Tripoli Medical Center. **Patients & methods:** BMI values for Children and Adolescents with CAH were taken, and were compared with population-based references, other contributing factors which may increase BMI were looked at. 55 children and adolescents with CAH were studied, the type of therapy was monitored and doses were adjusted according to clinical presentation & laboratory findings in the follow-up visits every 3 to 6 months. Gender, age at diagnosis, duration of the disease, skeletal maturations, salt losing or non-salt losing type, parental BMI, birth weight and any other contributed factors were taken in consideration. Current weight & height and BMI were calculated. **Results:** 22 Patients (40%) out of 55 were found to be obese and overweight (15 obese, 7 overweight). their mean age is 12.8 (range 5-19) years. There were 16 girls and 6 boys. 6 patients out of 22 were non-salt losing. Average dose of replacement steroid therapy was 15 mg/m2/day, 9 patients got signs of insulin resistance, 4 patients got strong family history of obesity, and 3 were small for gestational age. **Conclusion:** Children and adolescents with CAH are at higher risk of developing obesity. Age at diagnosis, advanced bone maturation and parental obesity were associated with an increased risk of obesity, while glucocorticoid and mineralocorticoid dosage, and birth weight were not associated with increased risk of obesity. Children and adolescents with CAH need careful monitoring and close follow-up, so that obesity can be prevented or managed early.

Mineralo and glucocorticoid deficiency in early infancy caused by a founder novel mutation in the Nicotinamide Nucleotide Transhydrogenase gene

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Background: NNT (Nicotinamide Nucleotide Transhydrogenase) gene mutations have been recently shown to cause familial glucocorticoid deficiency (FGD), by decreasing reactive oxygen species (ROS) detoxification in adrenocortical cells. Affected infants present within the first few months with isolated glucocorticoid deficiency. Objective and hypotheses: to study the genetic etiology of 4 cases presenting uniquely with neonatal addisonian crisis (both mineralo and glucocorticoid deficiency). Clinical presentation and **Method:** Palestinian male infant with normal external genitalia born

to consanguineous parents, presented neonatally with Na: 118, K: 6 mmol/l, decreased basal and ACTH stimulated Cortisol and 17-hydroxyprogesterone, normal infantile Testosterone, and elevated Plasma Renin Activity (>15ng/ml/hr). Two female cousins and another unrelated female neonate presented with similar manifestations. Whole exom next generation sequencing was performed on two affected cousins from the first kindred. Functional assessment of ROS detoxification capacity by was performed on skin biopsy derived cultured fibroblasts using the 2›7›dichlorodihydroflourescein (DCF) method. **Results:** Whole exom sequencing revealed a G200S homozygous mutation in NNT gene. The homozygous variant found segregated with the disease in both unrelated families, and all four pairs of parents were heterozygous. Haplotype analysis revealed a founder effect while the mutation was not found in 100 alleles from ethnically matched controls. Expression studies of the ROS detoxification capacity in fibroblasts revealed an increase in ROS production in the fibroblasts derived from affected patients when compared to controls. **Conclusion:** The founder and novel G200S mutation in the very recently described NNT gene causes uniquely early-infantile-severe mineralo and glucocorticoid deficiency. NNT mutations should be added to the differential diagnosis of neonatal addissonian crisis. ROS detoxification capacity is reduced in patients with the G200S NNT mutation. Given the ubiquitous nature of NNT, further studies of various mutations are required to elucidate the specific target organs prone to develop pathologies in relation to their impaired antioxidant defense. Furthermore we show for the first time that in fibroblasts from affected patients there are indeed morphological mitochondrial defects and increased levels of ROS with reduced detoxification capacity.

Apparent Mineralocorticoid Excess Syndrome: Case Report

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The syndrome of apparent mineralocorticoid excess (AME) is an autosomal recessive disorder characterized by hypertension, hypokalemia, low renin, and hypoaldosteronism. It is caused by deficiency of 11β-hydroxysteroid dehydrogenase which results in a defect of the peripheral metabolism of cortisol to cortisone. As a consequence, the serum cortisol half-life (T½) is prolonged, ACTH is suppressed, and serum **cortisol concentration** is normal. The **hormonal** diagnosis of the disorder is made by the increased ratio of urine-free cortisol to cortisone. In patients with AME this ratio is 5-18, while in normal individuals it is less than 0.5. These studies suggest that an abnormality in cortisol action or metabolism results in cortisol behaving as a potent mineralocorticoid and causing the syndrome of AME.

We report three siblings, two female and one male, with the syndrome of apparent mineralocorticoid excess who presented with hypertension, hypokalemia, low renin, and low aldosterone levels. The finding of abnormally high ratio of 24-hour urine-free cortisol to cortisone in our three patients (case 1 = 8.4, case 2 = 25, and case 3 = 7.5) confirmed the diagnosis of apparent mineralocorticoid excess syndrome in these children. In this study, the genetic testing of those three siblings with the typical clinical features of AME has detected missense mutation c.662C < T (p.Arg208Cys) in exon 3 of the HSD11B2 gene in the homozygous state.

Ambiguous genitalia; use your hearing sense

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Introduction: The diagnosis and management of Ambiguous genitalia are usually a challenge for pediatricians. Our aim is to discuss a case of ambigious genitalia in which the diagnosis was unusual. **Case report:** The child was referred for gender evaluation within 24 hrs of birth. The baby was the first child to non-consanguineous parents and the delivery and birth weight were normal. During consultation, the 25 years old primigravida mother was noticed to have a “male like” voice. She developed acne and facial hair since the first trimester without exposure to androgen during pregnancy. There was no significant family history of note. Physical examination of the child revealed a 3 cm phallus with basal urethral

opening, dark skin, incomplete fusion of labio-scrotum, and no palpable gonads. **Results:** Pelvic ultrasound showed normal looking female internal genitalia and laboratory investigations excluded congenital adrenal hyperplasia (normal ACTH and 17 Hydroxyprogesterone). The testosterone level on day 2 was 8.6 and chromosomal karyotype was 46XX. Because both the mother and the baby were virilised, diagnosis of aromatase deficiency was suspected and the decision to raise the baby as female was made. Endocrine workup for the mother revealed raise testosterone levels which subsided to normal after 6 weeks post-delivery and her pelvic USS and MRI showed no evidence of adrenal or ovarian pathology.

A case of virilizing adrenocortical carcinoma in a child: a sentinel cancer for detecting a family with germline TP53 mutation

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Background: Adrenocortical tumors (ACTs) are rare in children with a worldwide incidence of 0.3-4 cases per million each year in children younger than 15 years of age. Unlike adult ACTs, pediatric ACTs are functional and hormonally-active in about 90% of cases. Most commonly seen at young age, in female gender and with symptoms of virilization. Surgical resection remains the only potentially curative treatment. Li Fraumeni Syndrome is a dominantly inherited familial cancer syndrome where patients tend to be 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 Li Fraumeni syndrome. **Case report:** A 3-year-old girl presented with rapidly progressing virilization, facial acne and deepening of voice for 7 months. Family history was significant for several family members affected with tumors including two brothers who died of brain tumors around the age of 10 years, a paternal cousin who had acute Leukemia and a paternal uncle who died at the age of 45 years of gastric carcinoma. On examination, she was normotensive, her external genital exam revealed enlarged clitoris, prominent unfused labia folds with Tanner II pubic hair. Her breast was at tanner I and she had soft abdomen with no masses palpable. Her systemic exam was otherwise unremarkable with no obvious skeletal anomalies or cutaneous stigmata. Baseline serum androgens revealed elevated Testosterone of 2.8nmol/L (0.07-0.7nmol/lL), DHEAS 11.34 micromol/L(0.90-7.50micromol/L), 17-HOP 11.42nmol/L(0.1-1.5nmol/L) and ACTH 3.8pmol/L(1.6-13.9pmol/L). ACTH stimulation test confirmed ACTH independent androgen production. She had negative serum β-HCG and prepubertal estradiol and gonadotropins levels. Abdominal ultrasonography revealed right adrenal mass, measuring 25 mm x 20 mm that was confirmed by CT and described as a solid homogenous hypoechoic lesion. She had underwent laparoscopic right-sided adrenalectomy with uneventful postoperative period. Histopathology study confirmed localized adrenocortical carcinoma. Postoperatively, serum Testosterone, 17OHP and DHEAS returned to normal. At 3 months follow-up, the child is doing well, prepubertal with no evidences of tumor recurrence or distant metastasis on CT imaging. Genetic testing for TP53 mutation was sent and results is awaiting. **Conclusion:** 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 an appropriate cancer surveillances in order to detect the cancer at earlier stage if occurred.

A Newborn infant with ambiguous genitalia; what dictates the sex of rearing?

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External genitalia at birth is the marker of the newborn gender. However, genital ambiguity makes sex definition at birth difficult which create a lot of family concerns and occasionally medical confusion to make a precise diagnosis and advice on gender choice. **Case Report:** We report a set of twins who were conceived after IUI. Twin 1 had a normal male genitalia while twin 2 had prominent labio-scrotal folds with darkened skin. Goands were palpable bilaterally. Birth weight was 2595

gm and rest of physical exam was unremarkable. Family history: The baby was the first child to first degree consanguineous parents. Mother has history of infertility for 4 years. Family history revealed 5 family members with disorders of sexual differentiation from the maternal side. One of the father's brothers has genital ambiguity and was raised as a male. He had genital reconstruction and was able to father children with IVF. Another affected member had ambiguous genitalia with XY karyotype and was raised as female. **Biochemical/Radiology results:** Ultrasound showed presence of testes at both sides; and absence of Mullerian duct structure. Karyotype revealed 46 XY chromosomes with a positive SRY gene marker. Serum levels for androgens, 17-hydroxyprogesterone and testosterone were normal. hCG test showed a stimulated Testosterone/ Dihydrotestosterone ratio highly suggestive of 5 alpha reductase deficiency. Genetic testing confirmed a deletion of exon 2 of 5 alpha reductase gene (novel). **Conclusion:** There are no specific rules for gender assignments. Each case needs to be taken individually with consideration to available expertise. Issues related to culture, religion and family believes should have a priority on final gender assignment following a specialized medical advice.

Bone Markers in children with Type I DM

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Background: Care of patients with diabetes should include an assessment of bone health. It is now clear that patients with type I DM have lower bone mineral density which may be manifested as osteopenia in growing skeleton and higher risk of fractures. Objective: To assess bone modelling through the measurement of bone formation and resorption indeces in diabetic children and their correlations with metabolic parameters. Methods: We studied 120 patients with Type I DM (F=68, M=52) who follow up in the diabetes clinic at Benghazi children hospital. Patients were divided into two groups according to duration of disease; Group I (diabetic children with < one year duration of disease) and Group II (diabetic children > one year duration). The following information were collected: gender, age, duration of disease, weight and height measurements were taken. Ca, Po4, ALK, PTH, Osteocalcin, B-Crosslaps, Fasting blood glucose were measured follow up visits in all groups and compared them with 99 healthy children (44 female and 55 male) as control (Group III). Results: Fasting blood glucose significantly higher in both diabetic groups. Serum Ca, Po4, and PTH, were normal in diabetic groups. However, ALP levels were high in diabetic groups and Osteocalcin (OC) and B-Crosslaps values decreased in both Diabetic groups. The changes in serum OC levels significantly correlated with changes in B-Crosslaps. There was a negative weak correlation between changes in OC levels, B-Crosslaps levels with FBG. No correlation was found between changes in metabolic bone markers and duration of disease. Conclusion: Poorly controlled Type I Diabetes Mellitus groups have features of low bone formation rate. Metabolic bone markers correlated positively with age but not with the duration of disease. We conclude that lack of the anabolic effect of insulin in diabetes might contribute to abnormalities of bone metabolism.

A novel pathogenic mutation of CYP27B1 gene in a patient with Vitamin D dependent rickets type 1

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Introduction: Rickets can occur due to Vitamin D deficiency or defects in its metabolism. Three rare genetic types of rickets with different alterations of genes have been reported, including: Vitamin D-dependant rickets type 1 (VDDR-1), Vitamin D resistant rickets (VDRR) and 25 hydroxylase deficiency rickets. VDDR-1 is inherited in an autosomal recessive pattern, and is caused by mutations in the CYP27B1 gene encoding the 1α-hydroxylase enzyme. **Case report:** We report a 13 month old Saudi girl with VDDR-1 presented with multiple fractures and classic features of rickets. A whole exome sequencing identified a novel pathogenic missense mutation [CYP27B1: Homozygous c.1510C>T (p.Q504X)] which results in a protein truncating alteration. Both parents are heterozygous carriers. **Discussion:** Based on data search in Human Gene Mutation Database, 63 CYP27B1 alterations were reported: only 28.6% are protein-truncating (5 nonsense, 13 frame-shift insertions/deletions, 0 gross deletions), while 61.9% are non-truncating (38 missense, 1 small in-frame insertions/deletion),

and 9.5% are possible protein-truncating (5 splice, 1 regulatory).**Conclusion**: Given the deleterious effect of this alteration and the autosomal recessive inheritance, both support a pathogenic nature of the mutation as a cause of VDDR-1.

Mutation of the CYP2R1 Vitamin D 25-Hydroxylase in a Saudi Arabian Family with Severe Vitamin D Deficiency

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Background: Vitamin D (Vit D) deficiency rickets remains prevalent in some countries like Saudi Arabia. Inherited mutations causing this disease have been identified in several genes, including those encoding the Vit D receptor and two cytochrome P450s that hydroxylate Vit D. The identity of the Vit D 25-hydroxylase has been controversial; however, recently a homozygous mutation in exon 2 of the CYP2R1 gene on chromosome11p15.2, which specifies a hepatic Vit D 25-hydroxylase, was identified in members of two Nigerian families and shown to cause selective 25-hydroxyVit D_3deficiency**. Aim:** We present two patients from a Saudi family with a clinical picture of severe rickets that started in childhood and improved on Vit D therapy but relapsed when Vit D therapy was stopped. DNA sequencing revealed that both patients were compound heterozygotes for two previously undescribed mutations in the CYP2R1 gene. **Method:** Here the clinical scenario and lab will be presented **Results:** DNA sequencing of the five exons in the CYP2R1 gene revealed two mutations in the affected siblings. One mutation was a G to A transition in the splice donor sequence of intron 2; this change is predicted to disrupt splicing of the mRNA transcribed from the mutant allele. The second mutation was a T insertion in the coding sequence of exon 3; this change disrupts the translational reading frame and is predicted to produce a truncated CYP2R1 protein. Both patients are compound heterozygotes for these mutations. Although we have not reproduced these mutations in an expressible gene, both lesions are predicted to inactivate CYP2R1 causing Vit D 25-hydroxylase deficiency. **Conclusion:** Although we report only the third family in which mutation of the CYP2R1 gene is associated with selective Vit D 25-hydroxylase deficiency, it seems likely that this disorder is under-diagnosed. A similar molecular basis should be considered in patients with a clinical picture of chronic 25-hydroxy Vit D deficiency rickets with a childhood presentation who respond to Vit D treatment but relapse once off treatment. This diagnosis should be given further consideration in Vit D deficiency endemic area.

Effect of severe Vitamin D deficiency on fetal growth and bone in an Arab Cohort

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Objective: to determine the consequences of mothers' vitamin D deficiency on fetal bone and growth. **Methods:** in this prospective cross-sectional study of healthy pregnant mothers, blood venous samples were drawn within six hours in postpartum period for 25 hydroxyvitamin D levels. Cord blood samples were examined for calcium, phosphorus and alkaline phosphatase levels immediately after birth for all babies, as well as all anthropometric variables. Logistic regression models were fitted to examine the association between babies bone profile and growth parameters in relation to mother's vitamin D deficiency status. **Results:** 108/150(72%) of the mothers were Vitamin D deficient. In mothers, in a multivariate logistic regression model, age [Odds Ratio (OR) = 0.94, 95%CI 0.88-0.99, p=0.04) weight (OR=1.03, 95%CI 1.01-1.07, p=0.02) and decrease milk uptake (OR=0.31, 95%CI 0.13-0.74, p=0.009) were significantly associated with Vitamin D deficiency. Alkaline phosphatase level was significantly higher in newborns to mother with Vitamin D deficiency compared with newborns to mothers without Vitamin D deficiency [median(IQR)=176(139-221) and 156(132-182) respectively, p=0.04]. A significant inverse correlation (pearson coefficient= -0.18, p=0.03) was observed between mothers Vitamin D and babies alkaline phosphatase levels. This association persisted in a multivariate logistic regression model (OR=3.46, 95%CI 1.18-10.18, p=0.024). **Conclusion:** Severe Vitamin D deficiency of Arab mothers showed no fetal growth or bone outcome.

Prevalence of short stature in juvenile hypothyroidism and impact of treatment in a tertiary center

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Background: Juvenile hypothyroidism is a very common problem in developing parts of world, and produces various skeletal manifestations. One of them is short stature which is the most common reason for referral to endocrinologist. **Aim and Objectives**: To study the prevalence of short stature in juvenile hypothyroidism, the various radiological manifestations of juvenile hypothyroidism and the impact of treatment on growth velocity and various skeletal manifestations. **Material and Method:** Out of total nine hundred hypothyroid patients, eighty seven patients found to be of juvenile hypothyroidism were enrolled in the study. Age range was 6-18 years with newly diagnosed or on follow in the endocrine clinic over a period of 1 ½ years were evaluated clinically and by laboratory tests. Serial assays of TSH, T4, and skeletal X rays and anthropometry were done at regular interval and clinical and radiological outcome of patients were analyzed. **Statistical Analysis:** Data were analyzed by SPSS version 17, the *P* value of < 0.05 was considered significant. **Result**: The mean age of diagnosis of juvenile hypothyroidism was 11.2 years. Females had twice the incidence than that of males. Mean TSH value was 118$\pm$ 24.3 µIU/ml. Prevalence of short stature was found to be 45% while delayed bone age was found to be 72% in juvenile hypothyroid populations. Height SDS increased from –2.9 $\pm$ 0.9 at the start of thyroxine therapy to –1.8 $\pm$ 0.8 after 12 months later ($p < 0.001$). Bone age SDS increased from 8.9 $\pm$ 2.5 at the start of thyroxine therapy to 10.8 $\pm$ 2.7 after 12 months later. Height velocity increased from 4.9 $\pm$ 0.8 cm/year in the year before treatment to 8.7 $\pm$ 1.3 during treatment ($P < 0.001$). **Conclusion**: The presentations of juvenile hypothyroidism may be varied. Prompt recognition of the findings can lead to early and effective treatment, and improving the skeletal defects.

Early Severe Neonatal Hyperbilirubinemia Associated with Congenital Hypothyroidism

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No abstract available.

Pituitary Gland Size is a Useful Marker in Diagnosing Growth Hormone Deficiency in Short Children

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Introduction: Diagnosis of growth hormone deficiency (GHD) in children necessitates a battery of tests including dynamic GH stimulation. These tests are not always reliable and complimentary diagnostic criteria are required. As short stature is common in children, strict diagnostic criteria are necessary prior to commencing a long-term treatment of GH replacement. It has been suggested that pituitary hypoplasia can be seen in children with isolated GH deficiency. However, confirmatory studies of this correlation are lacking.
Aim: The study aims to test the possible application of pituitary gland size on MRI scan as a marker for GHD utilizing a population-matched normative control data.
Patient & method: Children diagnosed with GHD at the Pediatric endocrinology department, Mafraq hospital were enrolled for the study. Diagnostic criteria used for GHD were:

- Clinical: height below 2 SD for age, height below mid parental target range and growth velocity of less than 2 SD over a minimum of 12 months.
- Radiological: delayed bone age of 2 SD or more for age
- Biochemical (peak GH less than 8 ng/l on standard glucagon stimulation test)

Children with GHD diagnosis had brain MRI scan to assess the size of the pituitary gland. Height and width of pituitary gland were measured at the longest dimension on selected MRI sections by a single observer. A control group of age and sex-

matched children was recruited from records of the MRI department of children who had MRI scans for other indications rather than short stature. Approval for the study was obtained from the hospital Research and Ethics committee. From the data on pituitary height and width, pituitary volume was calculated by using the formula (height x weight)$^{3/2}$.
Statistical analysis: Categorical data were compared between the two groups using the chi-squared test. Dependent variables; pituitary height, weight and size were used in a stepwise linear regression analysis. SPSS vs. 19 was used. **Results:** 60 patients (42 males) and 130 controls (65 males) were enrolled. Median, range age for patients and controls were (11, 3-16 years) and (9, 3-17 years) respectively. Cases had a significantly lower pituitary height and volume compared with controls ($P < 0.001$). The difference was more marked with increasing age. **Conclusion:** Pituitary volume can be a useful marker in the diagnosis of GHD in children. This marker can be used to compliment the diagnosis of GH deficiency in selected patients when the results of GH stimulation tests are non-confirmatory. We highlight the importance of this case control study as it was performed on matched control from the same local population. Accordingly, results can be applied more confidently and its normative data can give indication about abnormal pituitary size in children with GHD.

Results of treatment with growth hormone in growth hormone deficiency: Multicenter study of central and southern Tunisia

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Background: The growth hormone deficiency (GHD) is less than 20% of the causes of short stature in children. However, the diagnosis is important to confirm as treatment with growth hormone (GH) can often result in achieving a normal/near normal stature. This treatment also helps improve or prevent metabolic abnormalities associated with GHD; however there is a large individual variability in response to GH treatment. **Method**: We conducted a retrospective multicenter study of 150 children and adolescents with GHD followed over 27 years, between 1987 and 2013, in 5 departments of pediatrics in Tunisia (Sfax, Farhat Hached, Sahloul, Mahdia, Monastir) and adult endocrinology department of Sfax. The aim was to determine the clinical, hormonal, etiological characteristics of the GHD in our population and seek predictors of good response to GH treatment. **Results:** We report 82 boys and 68 girls (sex ratio = 1.2), the mean age at diagnosis was 8 years (range: 1 month - 17 years). The presentation was dominated by stunting (85.4%) and slower growth rate (44.2%). Manifestations of hypoglycemia was seen in 6% of cases. Diagnosis period averaged 17 months. On admission, the average height was -3.8 SDS; it was less to 3DS in 66.6% of cases. Characteristic dysmorphic features were noted in 9.6% of cases. Analysis of the growth curve noted slower growth rate in 51.4% of cases. Delayed bone age was almost constant (97%). GHD was isolated in 66.4% of cases associated with a thyroid stimulating deficit in 2.6%, adrenocorticotropic deficit in 5.7%, gonadotropin deficiency in 7.1% and multiple deficits in other cases. The hypothalamic-pituitary imaging showed isolated anterior pituitary hypoplasia in 20.8% of cases, a syndrome of pituitary stalk interruption in 16.7% of cases, and empty sella in 4.2%. Craniopharyngioma was diagnosed in 4 children and ectopic signal of posterior pituitary in two children with Langerhans cell histiocytosis. Genetic analysis was performed for one child with GHD associated with a thyroid stimulating deficit and it was negative for the gene Pit-1. 75% of patients were treated by growth hormone (GH) after an average of 15 months after presentation. The mean age at baseline was 8 years 7months and the average duration of treatment was 3 years. The average dose was 0.033 mg GH/kg/day. The average height gain was 1.2 DS. The final height achieved in patients in our series was 154 +/- 10 cm for men and 148 +/- 7cm in women. **Conclusion:** Our study showed that the diagnosis of GHD is late. Earlier diagnosis might result in achieving a better final height.

Growth Hormone Therapy in Kuwait: First Report on Epidemiology and Clinical Characteristics of Treated Children

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Background: Recombinant Growth Hormone therapy (rGH) was first introduced in Kuwait in the 1990s. Since its introduction, there has been no reported data on the clinical profile of treated children. **Objective:** The objective of this

study is to report the clinical profile of children treated with rGH by the Endocrine Division at an academic center at Kuwait. **Methods:** This study is a retrospective chart review of children treated regularly with rGH by the Pediatric Endocrine Clinic at Mubarak Al-Kabeer Hospital in Kuwait between December 2013 and December 2014. **Results:** A total of 75 children were treated with rGH. Mean age at rGH initiation was 8.4 years (± 2.97). There was no significant gender difference between treated children, males were 35 (47.9 %) and females were 38(52.1%). The most common indications for therapy were in order Growth Hormone Deficiency (GHD) and idiopathic short stature (ISS) (37.5%, 15.6% respectively) with no significant gender differences. Turner syndrome (TS) and variants, and small for gestational age (SGA) were the third most common indications (10.9%). The mean height SDS pre-rGH was -2.5 (± 0.73). Mean height SDS pre-rGH for patients with GHD was -2.7 (±0.66), ISS was -2.5 (± 0.68), TS 2.6 (± 0.64), SGA -2.5 (±0.63). Mean height SDS one year post rGH for patients treated for GHD (-1.9 ± 1.3) and ISS (-2.0 ± 0.49) suggest improvement in growth. **Conclusion:** In our center, GHD and ISS are the most common indications for treating children with rGH. Data after 1 year of therapy suggests improvement. Future research should concentrate on identifying factors that affect response to rGH in Kuwait.

Turner Syndrome Genotype and phenotype and their effect on presenting features and timing of Diagnosis

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Background: Turner syndrome (TS) is one of the most common genetic disorders. It is caused by abnormalities of the X chromosome and is associated with characteristic clinical features. **Objectives:** We aimed in this study to describe the phenotypic and genotypic characteristics of TS patients and evaluate their effect on presenting clinical features and time at diagnosis. **Methods:** This study is a retrospective, observational study of females aged from birth to 39 years with karyotype-proven TS diagnosed and managed at King Abdul Aziz Medical City Hospital, Riyadh between 1983 and 2010. Patients were classified based upon their karyotype into females with classical monosomy 45X (group A) and females with other X chromosome abnormalities (mosaic 45,X/46,XX, Xq isochromosomes, Xp or Xq deletion) (group B). Detailed clinical features of the two groups were analyzed .**Results:** Of the 52 patients included in the study, 16 (30.8%) were diagnosed with classical monosomy 45,X and the rest with other X chromosome abnormalities. Only 19 (36.5%) patients were diagnosed in infancy and the remaining during childhood or later (odds ratio (OR) = 4.5, 95% CI 1.27-15.90, (P = 0.02). Short stature was universal in group A versus 77.8% in group B. All patients in group A had primary amenorrhea compared with 63.2% of those in group B (P = 0.04); the rest of group B had secondary amenorrhea. Cardiovascular abnormalities were higher in group A (OR=3.50, 95% CI 0.99-12.29, p-value = 0.05). Renal defects and recurrent otitis media were similar in both groups. **Conclusion**: This study suggests that karyotype variations might affect the phenotype of TS; however, it may not reliably predict the clinical presentation. Therefore, chromosomal analysis for all suspected cases of TS should be promptly done as early as possible during childhood in order to design an appropriate management plan early in life.

Pelvic ultrasonography for differentiation between true precocious puberty and premature thelarche

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Early signs of puberty are frequent motive for consultation in pediatric endocrinology. In most cases, it is a normal variant of puberty (premature thelarche or pubarche), however it is important not to misdiagnose a true precocious puberty. **The aim** of this study was to determine elements allowing differentiating between true precocious puberty and premature thélarche. **Materials and Methods:** This was a retrospective study, including all the girls consulting for "precocious puberty" from January 2007 to December 2012. Pubertal staging was performed according to Tanner-Marshall method on physical examination, Bone age according to Greulich and Pyle. Height and weight data were analysed using WHO Anthro-Plus software. Pelvic ultrasound allowed defining internal genitalia: impuberal (uterus < 37 mm and Ovaries < 25mm) or presenting signs of beginning of puberty (uterus > 37 mm and/or Ovaries > 25 mm). Precocious puberty (PP) was defined as the development of pubertal changes before 8 years of age in girl. We defined True precocious puberty criteria as: early clinical signs of puberty, change in internal genitalia and accelerated bone age) and a peak of LH> 5 mUI after stimulation.

Results During this period of five years, 150 girls presented with early signs of puberty. The mean age of patients was 3,98 ± 3,09 years, 25% of whom were born SGA. The Tanner Stage was B3 in 42% of the cases. Bone age was advanced in 28 patients. Pelvic ultrasounds showed signs of precocious puberty in 22 girls (18.3%). 28 patients had an advanced bone age. Lab exams were performed in 54% of cases.The diagnosis was: Central precocious puberty in 24 patients, early puberty in 13 patients, Peripheral precocious puberty in 5 cases, congenital adrenal hyperplasia in 4 cases, Premature pubarche in 24 cases and Premature thelarche in 80 cases. There was a significant difference ($p < 0,01$) in uterus length between patients presenting CPP and premature thelarche. **Conclusion:** The diagnosis of CPP is obvious when all signs of puberty are presents, however some patients with slowly evolutive, spontaneously resolvent or incomplete forms of puberty need to be thoroughly investigated. Pelvic ultrasound is a simple examination allowing the discrimination between CPP and premature thelarche in most cases.

Insulin Resistance in Patients on Valproic Acid: Relation to Adiponectin

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Objectives: To investigate the presence of insulin resistance in obese children with idiopathic epilepsy on valproic acid (VPA) monotherapy in comparison to obese otherwise healthy subjects. Secondary outcome was to explore the relation between adiponectin and insulin resistance among those patients. **Materials and Methods:** Fifty obese children with generalized idiopathic epilepsy on VPA monotherapy and a control group of 49 obese clinically healthy age and sex matched children with simple obesity were recruited in the study. Anthropometric Assessment, fasting plasma insulin (FI), fasting glucose (FG) and fasting adiponectin levels were measured. Fasting glucose insulin ratio (FGIR) and Homeostasis model assessment for insulin resistance (HOMA-IR) were calculated for both patients and control subjects. Measurement of serum VPA trough level was also performed in patients. **Results:** Patients had significantly higher fasting blood glucose, fasting insulin, lower FGIR, and higher HOMA-IR values, compared to controls. Mean adiponectin level was significantly lower in patients compared to controls. The duration of treatment with valproic acid negatively correlated with adiponectin ($r= -0.285$, $p= 0.045$), but did not correlate with fasting glucose, insulin, FGIR, or HOMA-IR. Total daily VPA dose significantly correlated with fasting insulin ($r= 0.495$, $p < 0.001$), FGIR ($r= -0.525$, $p <0.001$), and with HOMA-IR ($r= 0.404$, $p= 0.004$). **Conclusion**: This study ascertains the relationship between dose and duration of VPA-therapy, insulin resistance, and the adipocytokine axis. We report a proposal that obese VPA-treated children are more insulin-resistant and have lower adiponectin levels than obese and otherwise healthy children.

Poster presentations abstracts

A case of Donohue Syndrome: New Genetic Mutation and added phenotypic Charateristics

Fawzia Al Yafei

Background: Leprechaunism (Donohue syndrome) is an extremely rare AR disease that presents with special phenotypic features including severe type of insulin resistance with high mortality in infancy. **Objective:** We report a 3 months old girl with Donohue syndrome with characteristic facial features, severe insulin resistance, growth retardation, cholestatic jaundice, unexplained abdominal distention, and Bartter-like syndrome. New clinical features included exocrine pancreatic insufficiency, central hypothyroidism and severe lethal obstructive cardiomyopathy. Continues glucose monitoring (CGMS) without treatment, both on insulin and on metformin clarified his glycaemic abnormalities and different response to treatment. **Results:** Partial response to metformin has been demonstrated with weight gain especially after pancreatic enzymes replacement. **Conclusion:** A new genetic homozygous mutation of the INSR gene has been found with added new phenotypic features

IGF 1 therapy via continuous subcutaneous infusion for 1st time in Libya to treat boy with insulin resistance syndrome

Faten Ben Rajab

We report a Libyan infant who presented at 3 months old, born to consanguineous parents by normal delivery at term with birth weight 1.3Kg. Since birth, he had attacks of hypoglycemia before meals & hyperglycemia post meals and was admitted to SCBU for 5 days for adjusting blood sugar level. He had severe growth failure markedly-diminished subcutaneous adipose tissue. He had classical elfin features, excessive hair all over the body and velvety hyper- pigmented skin. Clinical diagnosis of insulin resistance syndrome was confirmed genetically. The child was started on IGF1 therapy by continuous subcutaneous infusion and high calorie formulas with a good effect on growth parameters.

Challenges in managing an infant with Donohue syndrome

Ibtisam Hadeed

We report an 18 months old infant with a diagnosis of Donohue syndrome. He was born at term with a birth weight of 1800 grams. There is no family history of consanguinity. At birth; he had dysmorphic features in consistent with Donohue syndrome, which later was confirmed by molecular genetics. Biochemical analysis demonstrated fasting hypoglycemia, postprandial hyperglycemia, severe hyperinsulinemia (3112pmol/l), and mild conjugated hyperbilirubinemia. A trial of therapy with IGF1 was started on twice daily injections, then, he was put on continuous SC infusion IGF1 via insulin infusion pump trial. Description of the child's presentation and response to treatment will be detailed.

Hypochondroplasia, Acanthosis Nigricans and Insulin Resistance in a Child with FGFR3 mutation

Manal Mustafa

Fibroblast growth factor receptor 3 (FGFR3) gene mutations are well-known causes of skeletal dysplasia syndromes which encompass a wide spectrum of disorders that range from the relatively mild hypochondroplasia to thanatophoric dysplasia. Hypochondroplasia is the most common type of short-limbed dwarfism in children resulting from fibroblast growth factor receptor (FGFR) mutations. Acanthosis nigricans (AN) is associated with severe skeletal dysplasias due to activating mutations in FGFR3, including thanatophoric dysplasia and SADDAN syndrome, however, insulin insensitivity with secondary hyperinsulinemia are uncommonly seen in Hypochondroplasia patients with FGFR3 mutations. **Objectives:** To describe the association of Hypochondroplasia, Acanthosis Nigricans and Insulin Resistance in a Child harboring FGFR3 Mutation. Few case reports described the association of AN, achondroplasia/Hyochondroplasia and insulin resistance. To our knowledge, this is the first case report associating the p.N540 with acanthosis nigricans. **Methods:** We report a Saudi child with short stature due to hypochondroplasia with a heterozygous c.1620C>A mutation in FGFR3 gene, who developed acanthosis nigricans and hyperinsulinemia while he was on growth hormone treatment. Insulin insensitivity with secondary hyperinsulinemia are uncommonly seen in HCH patients with FGFR3 mutations which may represent a new association. **Results**: Our patient had high fasting serum insulin 111 pmol/l (15.8 μU/l) as well as high homeostasis assessment index for insulin resistance (HOMA-IR = 3.69 (0.36–2.41)) indicating insulin resistance. Heterozygous missense c.C1620A (p.N540K) mutation in FGFR3 gene was identified. It is not clear whether hyperinsulinism seen in our patient is associated with the FGFR3 mutation or is a potential long-term side-effect of growth hormone treatment. **Conclusion:** Our findings suggest that the development of acanthosis nigricans in patients with hypochondroplasia might be due to insulin insensitivity either related to skeletal dysplasia itself or secondary to treatment with recombinant human Growth hormone or may represent a new association that should be further established by searching for AN in HCH patients. Given the complexity of FGFR3 downstream signaling, the mechanism involved in the development of AN in these patients is still unclear. Further studies are needed to clarify the mechanism of AN in skeletal dysplasia, association with insulin insensitivity and its long-term metabolic complications.

Persistent Hypoglycemia in 7-year Saudi child
Fayez Al Azmi

We present a successful diagnosis and treatment of nine years old Saudi child who presented for the first time with severe episodes of hypoglycemia at seven years old. With critical samples at the time of hypoglycemia, he was found to have persistence hyperinsulinemia. Initially the disease responded very well to anti-insulin medications at small doses, but with time it became progressive in severity requiring high dose of anti-insulin medications, frequent glucagon injections and hospital admissions for symptomatic hypoglycemia that required intravenous dextrose infusion. We will present his disease course, final diagnostic steps and curative therapy.

Prognostic factors in patients hospitalized with DKA
Manish Gutch

Background: Diabetic ketoacidosis is characterized by a biochemical triad of hyperglycemia, acidosis, and ketonemia. It remains a life threatening condition despite improvement in diabetes care. Timely identification and intervention remain the backbone of treatment. **Aim and Objectives**: 1. To evaluate the clinical and biochemical prognostic markers in diabetic ketoacidosis. 2. To correlate the various prognostic markers with mortality in diabetic ketoacidosis. **Settings and Design:** A prospective multicenteric observational study done at tertiary care center. **Methods and Materials:** Eighty seven patients with type 1 diabetes hospitalized with diabetic ketoacidosis over a period of 1 year were evaluated clinically and by laboratory tests. Serial assays of serum electrolytes, glucose and blood pH, and clinical outcome of either discharge home or death were evaluated. **Statistical Analysis:** Data were analyzed by SPSS version 17 and were presented in the values of mean, median, and percentages. The p value of <0.05 was considered significant. **Results:** The significant predicators of final outcome obtained were further regressed together and subjected with multivariate logistic regression (MLR) analysis. The MLR analysis further revealed that the male sex had 7.93 fold higher favorable outcome as compared to female sex (OR=7.93, 95% CI=3.99-13.51) while decrease in mean APACHE II score (14.83) and S. PO_3^{--} (4.38) at presentation may lead 2.86 (OR=2.86, 95% CI=1.72-7.03) and 2.71 (OR=2.71, 95% CI=1.51-6.99) fold better favorable outcome respectively as compared to higher levels (APACHE II score: 25.00; S. PO_3^{--}: 6.04). **Conclusions:** Sex, baseline biochemical parameters like APACHE II Score, and phosphate level, were important predicator of mortality from DKA.

Managing Fluids in Pediatric DKA: The Two Bag Way

Khadija Humayun

Monitoring of blood beta-hydroxybutyrate as a screening test for diabetic ketoacidosis at the Emergency department

Rasha Elmetwally
Introduction: The purpose of this study was to evaluate if bedside monitoring of blood beta-OHB levels can simplify management of diabetic ketoacidosis (DKA) through elimination of laboratory monitoring and to evaluate its cost effectiveness than other parameters. **Methods:** A prospective observational study was performed on 50 patients presented with DKA with a mean age of 8.24 ± 4.05 years at the Emergency department of Ain Shams University. All patients that were admitted had their blood glucose, pH, pCO2, HCO3, BUN, and consciousness levels serially monitored in relation to (beta-OHB) levels measured using blood β-OHB meter (Optium, Abbott/Medisense Laboratories, Abingdon, UK) from a single five microlitre prick capillary blood sample. **Results:** The percentage of newly-diagnosed cases presented with DKA tended to be higher and more severe than known diabetics (62% vs 38%, P=0.03).Level of (β-OHB) was inversely correlated to the level of consciousness (P=0.04). The correlation between β-OHB and other laboratory parameters at different timings in our study showed that β-OHB was significantly negatively correlated with PH (r= -0.57; P<0.0001), HCO3 (r=-0.85; P<0.0001), PCO2 (r=-0.65; P <0.0001) and positively correlated with blood glucose (r=0.57;P<0.0001) with no significant correlation with BUN (r=-0.01; P=0.94) at all point of measurement during the treatment. More importantly, this test is timely effective more than other laboratory parameters ,as it minimizes the time of hospitalization by

early diagnosis and following up DKA patients (P<0.001). Subsequently, reduces the cost of intensive care unit (p<0.001) by reflecting earlier normalization of metabolic status than other laboratory tests. **Conclusion:** Measuring bedside B-OHB is a useful, safe and non-invasive tool in managing DKA in pediatric patients in the emergency department .In addition, its use reduces hospitalization/emergency assessment and offers potential cost savings.

Epidemiology of type 1 diabetes mellitus in children in Tunisia: a multicenter study

Hajer Aloulou

Introduction: The geographical incidence of type 1 diabetes mellitus in children varies widely worldwide. Both genetic and environmental factors have been implicated. **Objective:** evaluated the incidence of type 1 diabetes in children in Tunisia and identify the epidemiologic characteristics. **Patients and Methods:** We conducted a retrospective study of new cases of type 1 diabetes in children (0 -15) years, discovered during the years 2009 - 2010 - 2011 in 17 pediatric center from Tunisia. We divided our patients into 3 groups: group 1 (0-4 years), Group 2 (5 – 9 years) and group 3 (10 - 15 years). These three groups were compared with regard to their epidemiological characteristics. **Results:** We identified 627 diabetic children. They were 332 boys and 295 girls. The incidence was estimated at 8.5 / 100 000 children under 15 years and 9.6 / 100 000 children (0 – 4years). The incidence was 7.7/100 000 children (0- 15 years) in 2009, it passed to 8.93/100 000 in 2011. The patients were aged 0-4 years in 33% of cases, 5 - 9 years in 34.1 % of cases and 10-15 years in 32.9 % of cases. The discovery of diabetes was in winter in 35 % of cases. Parental consanguinity was noted in 31.2 % of cases. The average duration of breastfeeding was 10,4mois. The average age of introduction of cow's milk was 6 months. The introduction of the gluten is carried out before the age of 4 months in 9.3% and after 7 months of age in 22.5% of cases. Family history of type 1 diabetes was noted in 22% of cases. Family history of type 2 diabetes was noted in 35.6% of cases. 260 patients had an immunological study, 71.2% of them have at least one positive autoantibodies: anti-GAD (59.7%), ICA (31.3%), IA2 (42.5%), anti-insulin (19.2%). The anti-transglutaminase antibodies were checked in 231 cases and were positive in 5.6% of cases. The majority of patients (98%) received 2 daily insulin injections (insulatard® and Actrapid®). The average dose was 0,9U / kg / day (0.5 to 1 U / kg / day). **Conclusion**: Type 1 diabetes is a public health problem in Tunisia, its incidence increased and the age of diagnosis shifts to ages younger. Winter predominance of discovery supports the hypothesis of a triggering viral infection.

Glycemic control, complications and associated autoimmune disease in children and adolescents with type 1 DM in Jeddah, KSA

Maram Al Afif

Introduction: Type1 diabetes mellitus (T1DM) is a common autoimmune disease among children and adolescents. The primary goal in the management of T1DM is to prevent acute and long-term complications by achieving a good glycemic control. Studies have highlighted the relation between glycemic control and other factors including age. Other studies have demonstrated that T1DM patients are at high risk of developing other autoimmune diseases such as autoimmune thyroiditis (AIT) and celiac disease (CD). On the other hand, T1DM can lead to many complications in pediatrics. **Aim:** This study intended to investigate the relation between metabolic control, acute and long-term complications and the co-existing of autoimmune diseases with T1DM among children and adolescents at Jeddah, Saudi Arabia**. Methods:** This is a cross-sectional study, includes 243 T1DM children and adolescents visiting pediatric diabetes clinic at King Abdul-Aziz University Hospital (KAUH), Jeddah, Saudi Arabia. Clinical and laboratory characteristics of the patients were all recorded. Metabolic control, complications and associated autoimmune diseases were evaluated. Ethical approval for this study was obtained from the research ethics committee (REC) of KAU Hospital. **Results:** mean age of patients was 10.5 ±3.8 years and HbA1c level was 8.8%. Acute complications illustrated though out disease duration included ketoacidosis in 61.3% of the patients, and hypoglycemic attacks in 60.5%. Long-term complications includes retinopathy, micro albuminuria, and dyslipidemia, were detected in 6.2%, 16.9%, 19.3% respectively. Vitamin D deficiency was found in 77%. Thyroid dysfunction was noted in 9.1% of the patients and celiac disease in 6.2%. A significant difference was found in pubertal and pre-pubertal age groups in terms of glycemic control (p=0.001). **Conclusion:** The level of HbA1c found to be higher among

pubertal age group. A relation between autoimmune diseases and gender were determined, and vitamin D deficiency was highly detected in our population.

Diabetic Ketoacidosis, Determinants and Mortality Rate in Sudanese Children with Type 1 Diabetes Mellitus

Bashir Elwasila

Background: DKA is common at diagnosis in children with T1DM, and has significant morbidity and mortality. Many risk factors were implicated in its development and degree of severity. **Objectives:** To describe the frequency of DKA at the onset of T1DM, identify the determinants of DKA, assess its severity, and determine its mortality rate in children in Sudan. **Methods:** Hospital records of 466 diabetic children up to 18 year of age, diagnosed during the period 2006-2010 were reviewed (Gaafar Ibn Auf Children's Hospital, Khartoum). DKA was assessed mainly clinically using the severity criteria of Endocrine Clinics of North America 2000. Data were analyzed using the SPSS version 18. The differences in the mean values were calculated using the ANOVA test. Pearson's correlation coefficient was used to evaluate the relationship between variables. For all tests, P value < 0.05 was accepted as significant. **Results:** Of all patients diagnosed with T1DM, 173 (37.1%) presented with DKA in the latest admission. The frequency of DKA in newly diagnosed children was 35.2%. The majority had either mild (50%) or moderate DKA (37.2%). The frequency of DKA was higher in older children ($p < 0.05$). The major precipitating factors were infection (56.0%), omission of insulin dose (25.6%) and low socioeconomic status (21.8%). There was a significant positive relationship between age groups and HbA1c levels ($p <0.0001$). Moreover, girls had significantly higher latest HbA1c levels ($p < 0.003$). Two children died (0.4%). **Conclusion:** Our study provides recent data in East African population, for whom data are sparse. The incidence of DKA at initial presentation of T1DM among children in Sudan is high due unawareness of the population. Older children with T1DM face an increased risk for developing DKA, due to frequent omission of insulin doses and problems of non-compliance. Intensive educational programs about the early symptoms of diabetes will reduce the frequency of DKA in new patients.

Epidemiology of type 1 diabetes under the age of 5 years

Ibtisam Hadid

Introduction: The incidence of type 1 DM in children is increasing worldwide, more so under the age of 5 years. Therefore, this study was conducted between 2000- 2013, and included all children who were diagnosed under the age of 5 years in our region. **Aim:** the aim is to describe epidemiological features, clinical pattern and laboratory characteristics at presentation of type 1 diabetes under the age of 5 years. **Methods:** Data was collected as: Gender, family history of diabetes, breast feeding, initial presentation(preketotic- ketotic), hospital stay, HbA_1c at diagnosis, thyroid function tests, screened for Hepatitis B, C and HIV viruses, celiac disease antibodies, growth parameters were assessed as time went. **Results:** 675 children were diagnosed to have type 1 diabetes (10 were under the age of 6 months), family history of diabetes in 56% of patients, almost equal sex incidence, 352 were males, mean age at diagnosis was 3.2 year, 20% presented in ketotic phase, mean HbA_1c was 10%, and their mean hospital stay at diagnosis was 4 days. **Conclusion**: Type 1 diabetes is on the increase worldwide and more so under the age of 5 years, and it shows some clinical and epidemiological differences from diabetes in older children. More efforts are needed for early recognition of the disease to avoid severe types of presentation.

Prevalence, clinical profile and glycemic variability of celiac disease in patients with type 1 DM in Western, Uttar, India

Manish Gutch

Background: Celiac disease is frequently associated with type 1 diabetes mellitus, but is usually ill-defined and not usually suspected until the disease become advance. **Aim:** To study the prevalence, clinical profile and glycemic variability and the effect of gluten free diet on growth and diabetic control in celiac type 1 diabetes patients in a tertiary care referral centre in

north India. **Materials and Method:** Total of two hundred and fifty six patients were screened (149 males and 107 females) during the study period of two years, patients were evaluated for the clinical signs, biochemical investigations and family history of celiac disease in tertiary care health center in western U.P. **Results:** Twenty four (9.37%) patients were diagnosed to have celiac disease; the mean age at diagnosis of diabetes was 9.34 ± 7.3 years. Only 1/24 patients with celiac disease had been diagnosed before detection of diabetes mellitus. The common manifestations were normocytic normochromic anemia (66.6%) followed by diarrhoea (62.5%), abdominal pain/bloating sensation (58.3%), and short stature (58.3%). Weight SDS increased from –0.12±1.3 at the start of gluten free diet to 0.8±0.9 after 12 months later ($p<0.05$). Height SDS increased from –2.46±1.1 at the start of gluten free diet to –2.14±0.9 after 12 months later ($p =0.087$). Bone age SDS increased from 9.2±6.3 at the start of gluten free diet to 10.3±6.7 after 12 months later. Height velocity increased from 4.7±0.7 cm/year in the year before treatment to 5.1±1.2during treatment ($p= 0.05$). The increased in Hemoglobin, serum calcium, and serum iron is statistically significant ($p<0.05$).

Prevalence of autoimmune disorders in Pediatrics type 1 DM in Meerut, Western Uttar Pradesh, India

Manish Gutch

Background: Various autoimmune disorders are associated with pediatric-type 1 diabetes mellitus, but are usually ill-defined and not usually suspected until the disease becomes advanced. The prevalence of these autoimmune conditions is usually not very well defined in developing part of the world. **Aim:** To find out the prevalence of various autoimmune disorders associated with pediatric- type 1 diabetes mellitus. **Materials and Methods:** Total of one hundred and sixty four patients were screened (90 males and 74 females) during the study period of one year, patients were evaluated for the clinical signs, biochemical investigations and family history of autoimmune disorders in a tertiary health care center in western U.P. **Results:** Autoimmune thyroiditis was found to be most commonly associated with type 1 diabetes, followed by the celiac disease, and graves disease. Others less commonly seen were pernicious anemia, juvenile rheumatoid arthritis and vitiligo. **Conclusion:** Autoimmune hypothyroidism was found to be significantly associated with type 1 diabetes. Timely identification of these disorder are of paramount importance for better glycemic control and to reduce the morbidity and mortality associated with the conditions.

Lack of association of CTLA-4 +49 A/G polymorphism with predisposition to type 1 diabetes in a cohort of Egyptian families

Marwa Farouk

Background: Type 1 diabetes is one of the most common chronic childhood illnesses. Interplay between genetic susceptibility and environmental factors is thought to provide the fundamental element for the disease. Apart from the Major Histocompatibility locus which is the main contributor to risk susceptibility, more than 40 loci are recognized. One among these is the CTLA-4, however data from the literature are controversial. **Objectives**: The aim of our study was to investigate the role of CTLA4 49 A/G as a risk susceptibility factor for the development of type 1 diabetes in a cohort of Egyptian families.**Subjects and methods**: This is a case control study including 88 Egyptian families with one or more index cases (<18 years). The control group comprised 369 healthy unrelated subjects with no family history of diabetes or autoimmune disease. Using PCR-RFLP methodology, CTLA4 49 A/G was analyzed in 738 samples representing 88 families (88 patients, 125 siblings and 156 parents) and 369 control. **Results:** The age of onset was 6 days-12.5 years with a mean of 5.3 ± 3.6 and a median of 5 years. The mode of presentation was classic symptoms in 51 and diabetic ketoacidosis in 37 cases. Twenty-two cases had a history of viral infection or exanthematous disease and four had associated autoimmune diseases. No significant differences were encountered between the different groups with regard to CTLA4 +49 A/G genotype or allele frequencies. Neither was there a relation between the various genotypes and age of ons onset or the mode of presentation. **Conclusions:** CTLA4 49 A/G polymorphism was not recognized as a risk susceptibility factor in our cohort. This may be attributed to the low co-incidence of autoimmune diseases. Up to our best knowledge, this is the first study involving families. We recommend that all studies performed on risk susceptibility to type 1 diabetes should include proper investigation for other

autoimmune diseases to exclude their confounding effect on data analysis.

Identification of a novel mutation in an Egyptian infant with microcephaly, epilepsy and permanent neonatal diabetes

Nancy Elbarbary

We report an Egyptian female infant (deceased) fourth order of birth born to consanguineous healthy parents. The pregnancy was uneventful and she was delivered at term vaginally .At 2 months of age she presented with severe hyperglycemia and was diagnosed as infantile diabetes. On examination, she had microcephaly greater than -2.5 SD below the mean, developmental delay, hypotonia, epilepsy. At 4 months of age, the seizures were a combination of focal seizures with secondary generalization and generalized seizures. Electroencephalographs (EEG) showed polyspikes and slow waves with burst suppression pattern. Brain magnetic resonance imaging revealed microcephaly with simplified gyration, cortical atrophy, hypoplastic corpus callosum, cerebellar vermis hypoplasia, and delayed myelination .The diabetes and epilepsy were difficult to control despite treatment with clonazepam, vigabatrin, and sodium valproate and patient continued to have repeated pneumonias. No neurodevelopmental progress was noticed and she required intervention via nasogastric tube. No skeletal defects, liver or renal dysfunction were reported. Patient died at the age of 10 months of a lower respiratory tract infection complicated by therapy-resistant epilepsy and diabetes. Autopsy was denied by the parents. In the family, one more sibling died reported as having respiratory distress, but neither clinical data nor genetic screening were available. The parents also have a healthy daughter and a healthy son. Genetic analysis identified a homozygous missense mutation of the immediate early response 3 interacting protein 1[IER3IP1] gene (exon 3 p.L78P c.233T>C) and parents are both heterozygous for this mutation . This gene mutation mostly leads to loss of activity resulting in apoptosis of neurons and pancreatic beta cells in patients implicating mechanisms of brain development and on the pathogenesis of infantile epilepsy and early-onset permanent diabetes.

Monogenic Diabetes (MODY) a study from Kuwait. Initial report

Hessa Al Kandari

Introduction: Maturity –onset diabetes of the young (MODY) describes a heterogeneous group of monogenic dominantly inherited disorder of non-insulin dependent diabetes diagnosed before the age 25 years. The exact prevalence of MODY is not known, however it is estimated to affect 2 to 5% of people with diabetes. MODY3 is the most common subtype found in more than 60% of cases and is caused by mutation in the gene for transcription factor *HNF-1 alpha* (hepatocyte nuclear factor -1 alpha) which is essential for regulation of beta-cell function. Mutations in *HNF-1 beta* (hepatocyte nuclear factor -1 beta) is an uncommon cause of MODY accounting for only 6% of the cases. Renal developmental disease is the core phenotype in MODY5 and their diabetes is usually associated with pancreatic atrophy and exocrine insufficiency. In contrast to MODY 3 these patients are not sensitive to sulfonylurea and require early treatment with insulin therapy. **Aim:** To detect the presence and estimate incidence and prevalence of MODY subtypes in Kuwait. **Population/method:** The subjects are diabetic patients who tested negative for pancreatic auto-antibodies and have positive family history of diabetes. Six out of nine patients with suspected MODY were enrolled in the study. Mutations of the known /putative monogenic diabetes genes was tested by targeted next generation sequencing. In the following report we describe the clinical features and the molecular genetics results of two mutation positive subjects. The first is a female diagnosed at the age of 16 years as type 1 diabetes, had positive c. peptide 1.2 ng/ml (0.8-3.2) and strong family history of type 2 diabetes in her mother and sister. She required small insulin dose (0.5 unit/kg) to maintain good glycemic control. After confirming the diagnosis of monogenic diabetes, she was weaned off insulin therapy and her glycemia was well controlled (HbA1C was 6.8%) with sulfonylurea (gliclazide). The second subject is a 13 year old male diagnosed soon after birth with chronic renal failure due to bilateral cystic kidney disease. He had renal transplantation at the age of 3 years. At the age of 9 years, he started to show intermittent symptomatic hyperglycemia with short courses of steroid therapy and with infections. His hyperglycemia became persistent and required insulin therapy at the age of 10 years. **Results:** Sanger Sequencing analysis of exon 4 of the *HNF1A* gene revealed a heterozygous mutation, insertion of cytosine at nucleotide 872 (c.872dupC) confirming the diagnosis of MODY

3 in the first subject and sequencing of exon 4 of *HNF1B* gene revealed a novel mutation p.E138K consistent with a diagnosis of renal cyst and diabetes syndrome (RCAD) in the second subject. **Conclusion:** To our knowledge, this is the first report from Kuwait of monogenic diabetes due to mutations in *HNF1A* and *HNF1B* causing monogenic diabetes type 3 and type 5 respectively. Making a specific diagnosis of MODY can have important implications for the guidance of appropriate treatment, prognosis and genetic counseling.

Variable phenotype in five patients with Wolcott-Rallison syndrome due to the same EIF2AK3 (c.1259delA) mutation

Manal AShawi

Backgrounds/objectives: Wolcott-Rallison syndrome (WRS) is a rare condition characterized by permanent neonatal diabetes (PND), skeletal dysplasia, and recurrent hepatitis. Other features, including central hypothyroidism, have been reported. We aimed to compare the phenotype of five patients from two families with WRS caused by the same EIF2AK3 mutation who have been followed up since diagnosis. **Methods**: detailed phenotype and direct sequencing of the EIF2AK3 gene. Comparison of the phenotype between patients. **Results**: a homozygous frameshift EIF2AK3 mutation (c.1259delA) were identified in all patients. All patients presented with PND and there was a variation in other features. Four children experienced recurrent hepatitis. Two children developed skeletal abnormalities and two had transient central hypothyroidism. Other reported features of WRS were not detected. A 3.5-year-old girl has isolated PND, whereas her younger sister has typical WRS features. **Conclusions:** The EIF2AK3 c.1259delA mutation results in a variable phenotype, ranging from isolated PND to typical WRS. Thyroid dysfunction in WRS is a transient phenomenon reflecting euthyroid sickness.

DEND syndrome

Sabeen Khan

Neonatal Diabetes mellitus requiring insulin in the first month of life is a rare entity with an estimated incidence of 1 in 400,000 neonates. It can be either transient or permanent. The transient form of the disease, in the majority of cases, resolves by a median of 12 weeks and is generally associated with an abnormality of the imprinted region 6q24. Permanent neonatal diabetes mellitus on the other hand needs insulin therapy for life. It may occur as a result of developmental abnormalities of the pancreas (such as pancreatic agenesis or hypoplasia) or defects in the genes encoding the pancreatic β-cell ATP-sensitive potassium channel. DEND syndrome is defined as developmental delay with epilepsy, muscle weakness and neonatal diabetes and is caused by mutations in the K_{ATP} channel subunits Kir6.2 (encoded by *KCNJ11)* or SUR1 (sulfonylurea receptor 1; encoded by *ABCC8*).[1] Intermediate DEND syndrome (iDEND) is a less severe condition in which neonatal diabetes is accompanied by muscle weakness and developmental delay but not epilepsy. The diabetes of these patients is similar to that found for patients without neurological features, but its management is more difficult due to marked communication problems and the risk that hypoglycemia can precipitate seizures in patients with epilepsy. We report a novel case of permanent neonatal diabetes mellitus in association with DEND syndrome. She showed mutation in KCNJ11 gene encoding kir6.2 subunit of K-ATP channel.

Permanent Neonatal DM in Monozygotic Twins with p.C109Y Mutation in INS Gene: First Report from Saudi Arabia

Iman Talaat

Introduction: Permanent neonatal diabetes mellitus (PNDM) is a rare condition associated with genetic defects that play major roles in pancreatic beta cell development and function. Insulin gene mutation (*INS*) is the second most common cause of permanent neonatal diabetes (PNDM). **Methods**: We present female twins with average birth weight and simultaneous onset of hyperglycemia without ketosis at the age of 3 months. Patients started insulin therapy. At the age of 13 years started follow up in our facility, noted that the twins on glargine only, poorly controlled and molecular genetic testing done for them

and their parents. **Results:** p.C109Y (p.Cys109Tyr, c.326G>A) heterozygous missense mutation in exon 3 of the insulin (*INS*) gene was identified. The twin patients had the same mutation while their parents are unaffected with normal genetic testing suggesting that this mutation had raised de novo. **Conclusion:** This p.C109Y mutation affects a highly conserved cysteine residue which is crucial for protein folding. Subjects with this form of diabetes will need lifelong insulin therapy. Our twins are considered the first reported cases of PNDM with insulin gene mutation from Saudi Arabia and to the best of our knowledge; this is the first reported case worldwide monozygotic twins presented with PNDM with *INS* gene mutation.

Permanent neonatal Diabetes secondary to KCN 11 gene mutation, First report from Saudi Arabia. Diarrhea is it a possible side effect of Glibenclamide?

Iman Talaat

Neonatal diabetes is rare 1 in 21.196 live births in Saudi Arabia and 50% of patients have permanent Diabetes. Genetic testing is essential to identify the exact molecular etiology that affects treatment strategies. To date neonatal diabetes due to mutations affecting K channel has not been reported in Saudi Arabia. **Case report:** We identified a 2 month old female presented with diabetic ketoacidosis. He was born small for gestational age and had hypeglycemia of 11.3mmol/L in the second day of life. Molecular genetic testing done and patient was successfully shifted from insulin NPH to Glibenclamide. **Results:** Patient is heterozygous for KCN11 missense mutation. We initiated Sulphonylurea therapy and eventually insulin therapy ceased with improvement of HbA1c from 9.7 to 5.8 in 2 months. However, the patient is noted to have increased number of bowel motions after Glibenclamide treatment. **Conclusion:** This is the first report of permanent neonatal diabetes due to a mutation in the Kir6.2 subunit of the K-ATP channel highlighting its possible role in neonatal diabetes in Saudi Arabia. Sulfonylurea treatment is effective in controlling this type of diabetes making genetic testing is mandatory for all cases of diabetes onset <6 month. Diarrhea reported after Glibenclamide treatment is questionable and may make other new generations of sulphonyl urea better options.

Epidemiological and clinical outcomes of congenital adrenal hyperplasia

Sana Kmiha

Background: Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders resulting from the deficiency of one of the five enzymes required for the synthesis of cortisol in the adrenal cortex. The most frequent is steroid 21-hydroxylase deficiency, accounting for more than 90 percent of cases. **Methods:** We conducted a retrospective study of 26 cases of congenital adrenal hyperplasia collected in the department of pediatrics of the University Hospital Hedi Chaker Sfax for a period of 29 years (1984-2012). **Aim:** The aim of this study was to investigate the epidemiological, etiological, therapeutic and characteristics of congenital adrenal hyperplasia in our region. **Results:** There are 10 boys and 16 girls. Parental consanguinity was found in 21 cases. Similar cases in the family were found in 7 patients. An infant death in siblings was noted in 8 cases. The average age at diagnosis was 9 months. Two cases were diagnosed prenatally. Ambiguous genitalia were found in 16 cases. Vomiting with acute dehydration revealed the diagnosis in 4 cases. Precocious puberty was found in 5 cases. A salt wasting syndrome was found in 13 cases. Genotype was identified in 7 cases. There are 21 cases of 21-hydroxylase deficiency (including 18 cases of classical adrenal hyperplasia and 4 cases of no classical adrenal hyperplasia), 3 cases of 11-beta hydroxylase deficiency and one case of 3 beta deshydrogenase deficiency. All the patients was treated by hydrocortisone at a dose of 30 to 35 mg/kg/m2 in 2 or 3 doses per day; 20 patients had received 9-alpha-fluorohydrocortisone at a dose of 50 micrograms/day and 13 patients had received NaCl. Genitoplasty was performed in 9 cases. The main long-term complications that we identified were the occurrence of obesity in 4 cases, precocious puberty in 2 cases and the appearance of testicular inclusion in 2 boys. **Conclusion:** Congenital adrenal hyperplasia is still common in our country because of the high rate of consanguinity. Newborn screening is not available in our country.

Neonatal diabetes; report of 8 cases

Sana Kmiha

Background: Transient (TNDM) and Permanent (PNDM) Neonatal Diabetes Mellitus are rare conditions occurring in 1:300,000–400,000 live births. TNDM infants develop diabetes in the first few weeks of life but go into remission in a few months, with possible relapse to a permanent diabetes state usually around adolescence or as adults. The pancreatic dysfunction in this condition may be maintained throughout life, with relapse initiated at times of metabolic stress such as puberty or pregnancy. In PNDM, insulin secretory failure occurs in the late fetal or early post-natal period and does not go into remission. **Method:** We conducted a retrospective study of 8 cases of neonatal diabetes (ND) collected in the department of pediatrics of the University Hospital Hedi Chaker Sfax for a period of 32 years (1983-2014). The aim of this study was to investigate the epidemiological, etiological, therapeutic and evolutive characteristics of neonatal diabetes in our region. **Results:** We report 8 patients (4 boys and 4 girls) from 7 families with ND. Parental consanguinity was found in 5 cases. All patients were born at term and 6 patients were small for gestational age. The average age at diagnosis was 40, 25 days. All patients were pancreatic autoantibody negative. For 6 patients, radiological exploration of the pancreas was performed showing a normal pancreas. All patients were on twice daily injections of insulin. Two patients died from sepsis at ages 12 and 52 days. Neonatal diabetes was transient in 2 cases and was permanent in 2 cases. For the other two patients, the decline is still insufficient to judge the transient or permanent neonatal diabetes. Genetic analysis was carried out in 4 cases. Two patients had heterozygous mutations in the KCNJ11 gene, these two brothers had transient neonatal diabetes and their mother was confirmed to be heterozygous carrier. One patient was homozygous to a mutation in insulin gene (substitution 3'UTR C333* 59 A > G), and one child had homozygous mutation stop GLIS3 (C. 1597 C>A/p.S295X). **Conclusion:** Neonatal diabetes is a rare condition. However, it is probably of great relevance to our understanding of monogenic diabetes within the general population. Patients with NDM are often misclassified as having type1 diabetes. Widespread education is essential to encourage appropriate genetic testing and treatment of NDM.

Neonatal diabetes in 3 siblings

Suha Hadi

Objective: Neonatal Diabetes Mellitus is a rare condition with an incidence of 1 in 300,000 to 500,000 live births. Many genes have been implicated as causes of nonsyndromic neonatal diabetes. Molecular diagnosis might have immediate clinical consequences for affected patients. It also helps in genetic counseling of affected families and predicts clinical course and prognosis. **Case presentations:** we present the clinical course of three Emirati siblings with nonsyndromic neonatal diabetes mellitus, born to clinically unaffected consanguineous parents. Family genetic analysis confirmed identical *INS* mutations in all siblings. Both parents were heterozygotes for the same mutation. **Conclusion:** This is the first report of identical INS mutations in 3 siblings who had different NDM clinical courses.

Ramadan fasting in Adolescents and young adults

Talal Osman

Ramadan fast is well watched in nearly 100% in Libyan society. This study was carried out during Ramadan month in the year 2014, to see the effect of Ramadan fasting on adolescents and young adults in our center. **Patients and methods:** 125 diabetic adolescents and young adults were selected randomly before Ramadan, and they were put in Ramadan insulin dose regimen, and were advised on how to manage. Age, duration of diabetes, insulin dose, and associated diseases were looked at. **Results:** Data were completed in 62 patients, 31 males, and 31 girls, mean age 19 years, mean duration of diabetes 10 years. 33 completed their fasting (54%), 29 broke their fasting; 16 for 1 day, 3 for 2 days, 2 for 3 days, 3 for 4 days, and the other 5 broke between 5 and 12 days. The main causes were hypoglycemia, and hyperglycemia. **Conclusion:** Adolescents and young adults can fast Ramadan safely, provided they are given the right supervision, and the right advice.

Fasting the Holy month of Ramadan in older children and adolescence with Type 1 DM in Kuwait

Kholoud Mohamed

Ramadan, the ninth month of the Islamic lunar calendar, is the holy month of fasting. New evolving technology in the treatment of type 1 diabetes (T1D) continues to play a critical role in normalizing daily lives of diabetic children. This had encouraged Muslim diabetic children to pursuit the practice of fasting the holy month. Therefore creating a challenge for them, their families, and their healthcare providers. There are limited data on fasting of T1DM in older children and adolescence and on pump therapy during Ramadan. Aim: We have designed this study to investigate the ability and safety of children with T1D to fast the Holy month of Ramadan 2014. It is also designed to compare between patients on insulin pump and those with conventional insulin therapy as regards improvement in glycemic control and less complications especially hypoglycemia. Material and methods: A total of 50 Patients aged 10-16 years and diagnosed T1DM for at least one year were included in the study. Patients on conventional and insulin pump therapy were included. Patients with the following characteristics were excluded from the study; sustained poor glycemic control, history of DKA within 3 month prior to Ramadan, recurrent hypoglycemia, unwilling to monitor blood glucose, and those with diabetes-related complications. Prior to the start of the Holy month, Children and their families were evaluated and educated about Diabetes management during Ramadan. The following clinical outcome were investigated before, during and after the Holy month: Body weight, glycosylated hemoglobin , number of days fasted, number of hypoglycemia and hyperglycemia episodes, and number of emergency hospital visits.
Results and conclusion: Results and conclusion will be discussed on the presentation.

CGMS in the diagnosis of early glycemic abnormalities in high risk groups

Ashraf Soliman

Continuous glucose monitoring (CGM) systems are an emerging technology that allows frequent glucose monitoring in real time. **Aim:** To assess the value of using CGM system (Medtronic) versus oral glucose tolerance (OGT) and glycated Hb (HbA1C) in the diagnosis of glycemic abnormalities (Prediabetes) in high risk groups. **Patients and methods:** We performed OGT and monitored glucose for 72h using CGMS combined with 4-5 times/day SGM (before 3 meals and mid-night) and measured HbA1C concentration in 3 groups of children and adolescents with high-risk to develop glycemic abnormalities including: 10 with morbidly obesity, 16 with thalassemia major (on repeated blood transfusion and iron chelation) and 10 with nephrotic syndrome on high dose glucocorticoids for 4 weeks or more as well as 10 normal children (controls). The diagnosis of glycemia status whether normal, impaired fasting glucose (IFG), impaired tolerance IGT (2h after oral glucose load in the OGTT or after a CGMS recording) diabetic (DM), was done according to the American diabetes association criteria. **Results**: Glycemic abnormalities detected in all groups are summarized in table. None of the children and adolescents had elevated HbA1C level > 5.7%. CGMS diagnosed more glycemic abnormalities in the 3 high-risk groups compared to OGTT.

	OGTT-IFG	OGTT-IGT	OGTT-DM	CGM-IFG	CGM-IGT	CGM-DM
Normal	0%	0%	0%	0%	0%	0%
Thalassemia	4/16	2/16	1/16	6/16	9/16	4/16
Obese	0/10	1/10	0/10	1/10	3/10	1/10
Corticosteroid	0/10	0/10	0/10	0/10	3/10	2/10

Conclusion: Our data suggest CGMS is more sensitive method to diagnose glycemic abnormalities (Prediabetes) in high risk patients compared to OGTT and HbA1C. Further studies are required to improve the criteria of early diagnosis of glycemic abnormalities using CGMS.

Continuous glucose monitoring (CGMS) versus oral glucose tolerance test (OGTT) and glycated hemoglobin (HbA1C) in the evaluation of glycemic abnormalities in an obese adolescent before versus after partial gastrectomy

Ashraf Soliman

We compared CGMS (Medtronic) to OGTT and HbA1C in the follow-up of glycemic abnormality in an adolescent girl with morbid obesity and glycemic abnormalities before and after 2 months of partial gastrectomy. This 16 year old adolescent girl presented with obesity (weight 98 kg, height 158 cm, BMI = 39.2 kg/m2), acanthosis nigricans and nocturnal polyuria and polydipsia. Trials to reduce weight through dieting, exercise and use of Metformin were unsuccessful; (Patient lost 3 kg in 4 months). Her fasting BG was 102 mg/dl but 2h BG after oral glucose (75 g) was 225mg/dl. She underwent partial gastrectomy surgery. 2 months after surgery her weight was 70 kg and BMI 28 kg/m2. **Results:** A comparison of her glycemic data using CGMS (for 5 days), OGTT and HbA1C before and 2 months after surgery is shown in table 1.

Table1. Glycemic data before and after surgery.

	Normal values	Pre-Surgery	Post-Surgery (8wk)
Mean blood glucose (MBG) for 24 h	<117	92	78
BG 1 h before breakfast	<108	89	69
BG 1h before lunch	<113	99	70
BG 1 h before dinner	<108	101	84
MBG 3 h after breakfast	<126	105	81
MBG 3 h after lunch	<121	145	69
MBG 3h after dinner	<126	162	130
SD of blood glucose (SDBG)	<25	42	17
Number of high excursions/day	0	2	0
The % of time > 7.8	<9%	19%	0%
Blood Glucose (OGTT - 0h)	<111	121	109
Blood Glucose (OGTT- 2h)	<140	225	140
HbA1C (%)	<6.0%	9.1%	6.7%

Conclusions: Before surgery this obese patient with morbid obesity had normal FBG but abnormal OGTT which was confirmed with CGMS criteria. After surgery CGMS showed correction of her glycemia both during basal and postprandial in real-life settings.

The hypoglycemia effect of moderate to vigorous intensity exercise experienced by active type 1 DM adolescents

Maria Reynolds

Adolescents with Type 1 diabetes are encouraged to exercise regularly as per guidelines. Plasma glucose concentrations are often difficult to manage during prolonged periods of physical activity.The type, duration, and timing of exercise, as well as its temporal relation to meals and premeal insulin doses, may affect the glucose-lowering effects of exercise in children with type 1 diabetes.However, few recent studies have examined the most effective means to prevent hypoglycemia during exercise in children. Physical activity (PA) provides many benefits to adolescents with type 1 diabetes; however, these individuals tend to have lower fitness and PA levels than their disease-free counterparts.The purpose a study for discussion and this Type 1 experience is to examine the acute temporal associations between moderate-to-vigorous intensity PA (MVPA) and hypoglycemia (continuous glucose monitor [CGM] reading ≤70 mg/dL While promoting PA as a healthy behaviour, it is important to educate adolescents with Type 1 diabetes on prevention of hypoglycemia following PA.

Analysis of gait characteristics using dynamic foot scanner in type 2 DM

Shashi Kumar

Background: Diabetes mellitus (DM) is a metabolic disorder with involvement of neurovascular and muscular system. Studies have documented that the gait parameter is altered in type 2 diabetes mellitus with peripheral neuropathy. However, there is a dearth of literature regarding the gait characteristics in type 2 diabetes mellitus (T2DM) without peripheral neuropathy. Therefore, the present study is focused on identifying gait changes in early type 2 diabetes mellitus without peripheral neuropathy. **Objective:** To analyze the gait characteristics in Type 2 diabetes mellitus without peripheral neuropathy. **Methods**: After obtaining ethical clearance from Institutional Ethical Committee (IEC), 36 T2DM without peripheral neuropathy and 32 matched healthy subjects were recruited. Gait characteristics (step duration, gait cycle length, gait cycle duration, stride duration, step length, double stance duration) of all the subjects were analyzed using Windtrack dynamic foot scanner. Data were analyzed using Independent't' test to find the difference between the groups (step duration, gait cycle length, gait cycle duration). Results will be detailed on the presentation.

Troponin I, Lipid profile and Tissue Doppler Imaging in Obese Children and Adolescents

Marwa Farouk

Background: Obesity in children and adolescents increases the risk for various cardiovascular problems. Increase in Body Mass Index BMI is often an independent risk factor for the development of elevated blood pressure and clustering of various cardiovascular risk factors. Objective: To detect early cardiovascular risk factors in obese children and adolescents using cardiac Troponin I and echocardiographic study including Tissue Doppler imaging (TDI). **Subjects and Methods:** In present cross-sectional study we evaluated 32 children and adolescents with obesity and 30 healthy controls. Their ages ranged from 6- 19 years. Studied children were subjected to: anthropometric measurements, lipid profile and serum Troponin I level measurement. Patients had an echocardiographic evaluation to asses left ventricle (LV) dimensions, systolic and global function. TDI to measure Mitral annular S', A` and E' velocities. LV systolic, diastolic and time to peak

systolic velocities were recorded also at lateral and septal walls**. Results:** The mean of serum of Troponin I 0.14± 0.39ng/ml ranged from (0.0- 1.9) and there was a significant positive correlation between Troponin and systolic blood pressure in cases (r = 0.359, p = 0.044). There was highly significant increase in cardiac dimensions LV mass and LV index in obese children (P<0.001, P<0.001 respectively). Tissue Doppler findings in the study groups showed that the Lat. Mitral S, Mitral septum A, in the obese group were higher and statistically-significant than in control group (p= 0.009, p=0.001, p=0.002 respectively) while Lat. Tricuspid E` (cm/s) in the obese group was significantly lower than in control group (p=0.002). Lat. Mitral A` and lat. Tricuspid A in the obese group were significantly higher than in control group (p=0.02, p=0.03 respectively). **Conclusions:** TDI and cardiac Troponin I evaluation proved to be useful tools to detect early cardiovascular disease. Efficient clinical prevention and close follow up programs are essentially needed in obese children and adolescents.

Body mass index in children and adolescent with type 1 DM

Othman Shawesh

Background: Body mass index is often increased in children and adolescents with type 2 diabetes, however, the weight presentation in type 1 diabetes is different with the hyperosmolar symptoms leading often to weight loss. **Aims:** to examine the effect of DM on BMI over 15 years of follow up in children and adolescent treated for Type1 DM. **Methods:** A cohort of 50 children randomly selected with type 1 DM diagnosed in 2000. All were tested for BMI and followed up for 15 years. Variables recorded included insulin dose, annual HbA1c level, parent education, family history of DM and other associated disease. **Results:** 50 children and adolescent with diabetes (28 boy and 22 girl) were studied at diagnosis, 5years, 1o years and 15 years of follow up. Most of the children had normal BMI at diagnosis and throughout the years of follow up. There was an increase in BMI in girls from 7% at diagnosis to 27% at 10years and 15years. Insulin dose, HbA1c level, parent education, family history of DM and associated disease had no effect on BMI. **Conclusion:** Most of affected subjects have normal BMI at diagnosis and throughout the follow up. It seems that in girls BMI increase with DM duration from 7% at diagnosis and 27% at 10years and 15 years. Insulin dose, HbA1c, parent education, family history of DM, and associated disease had no effect of BMI.

Metabolic control of type 1 diabetes in children treated with insulin analogues

Sana Kmiha

Introduction: Glycemic profile is often fluctuant in children with Type 1 diabetes (T1DM), when treated by NPH insulin. Many studies showed that switching to insulin analogues improves glycemic control of the patients. **Aim:** evaluation of the glycemic control in patients with T1DM switched from NPH insulin to insulin analogues. **Methods**: The current study included 37 patients aged 3 to 16 years (12.3±3.4years). Data were obtained from patients and their parents, as well as from medical records. **Results:** transition from NPH insulin to insulin analogues reduces the glycosylated hemoglobin concentration (HbA1C) after one year of treatment (10.1±1.8% vs. 9.1± 1.7, p = 0.06). The mean daily required insulin dose expressed per IU / kg was 1.4±0.3 with conventional insulin versus 0.9±0.2 (p > 0.05) after the use of insulin analogues. Severe hypoglycemia was recorded in 15 children (50.5%) considered before transition to insulin analogues. Contrarily, only 2 children (5.4%) manifested this metabolic complication (p <0.001), under insulin analogues therapy. Ketoacidosis was less frequent (2 children) after the use of insulin analogues than before (12 children (32.4%). **Conclusion:** the use of insulin analogues in children with T1DM provides adequate metabolic control and significantly reduces the risk of complications including acute hypoglycemia.

Turner Syndrome: A Study of 28 Cases

Sana Kmiha

Introduction: Turner syndrome (TS) is one of the most common chromosomal disorders. This condition is typically

characterized by short stature, dysmorphic stigmata, and gonadal dysgenesis. It includes a large phenotypic and genotypic heterogeneity. **Aim:** To study the clinical characteristics of TS in our center. **Patients and methods:** A retrospective study of 28 cases of TS, recorded during a 26-year period (1985-2010). The patients investigated were either followed in the department of Pediatrics and the department of Endocrinology, Hedi Chaker university Hospital, Sfax, Tunisia. **Results:** The average age of girls with TS at enrollment was 11 years. Short stature was the most frequent reason for consultation (75%). The patients had severely short stature (height, 118.5 +/- 16.5 cm; height standard deviation score [SDS], -3.1+/- 0.9). Characteristic dysmorphic stigmata were noted in 18 cases. Other abnormalities were found: nevi (11 cases) and alopecia (2 cases). Biological investigations revealed increased FSH and LH levels in respectively 83% and 60% of cases. The bone age was delayed compared to chronological age in 83% of cases. Pelvic ultrasound showed undetectable ovaries (16cas), atrophic (3 cases) and hypoplastic uterus (13 cases). Conventional karyotyping revealed monosomy in 17 cases and a mosaicism in 9 cases. The thyroid tests revealed a thyroid dysfunction in 3 cases. Echocardiography was abnormal in 2 cases. Therapeutically, 7 patients underwent treatment with GH. The induction of puberty was initiated for 13 patients at a chronological age of 15 years and a bone age of 12 years. Two patients developed during the evolution tumors (ganglioneuroma and nephroblastoms). **Conclusion:** Early diagnosis of turner syndrome leads to adequate management and better outcome.

A case of upper limb pain and edema in a 12 yr old patient with type 1 diabetes

Noha Musa

Introduction: Diabetes may affect the musculoskeletal system in a variety of ways. The metabolic perturbations in diabetes (including glycosylation of proteins; microvascular abnormalities with damage to blood vessels and nerves; and collagen accumulation in skin and periarticular structures) result in changes in the connective tissue. Musculoskeletal complications are most commonly seen in patients with a longstanding history of type 1 diabetes. **Case presentation:** Our patient is known to have T1D since the age of 1 yr, on insulin therapy (basal/bolus regimen). He was poorly controlled, with frequent attacks of hypoglycemia and mean HbA1c 0f 9.4. At the age of 12 yrs, he developed severe pain in his Rt. wrist and forearm extending to the elbow, with oedema, tenderness, limitation of movement. Both LLs showed mild pitting oedema, but with no pain or limitation of movement. Rhematological consultation was done and patient was diagnosed as juvenile idiopathic arthritis (JIA) and started NSAIDs as well as steroids with no improvement. **Result:** Investigations revealed normal CBC and CRP, elevated ESR, positive ANA, negative Anti DNA, heterozygous FMF gene. X-ray wrist and forearm showed mild osteopenic changes. Patient was finally diagnosed as a case of reflex sympathetic dystrophy (RSDS), treated by calcium channel blocker (Epilat), Pregabalin, Gabapentin and Amitryptyline with minimal improvement until he was successfully treated by sympathetic nerve block.

Glycosylated Hemoglobin Level at The time of Diagnosis of Type 1 Diabetes in children and Adolescents
Mysone Abusrewil

Introduction: The signs & symptoms of type 1 diabetes mellitus (T1DM) are overt & often manifest within 2-8 weeks. **Aim**: is to correlate the duration of signs & symptoms as given by the care taker and the level of glycosylated hemoglobin A1C at the time of diagnosis. **Methods** :All the subjects who were diagnosed at Tripoli medical center between (2012-2014) with type I DM were tested for HBA1C level at the time of diagnosis and this was correlated to the family history taken from the care takers. Family education and history of DM was looked at. **Results**: 545 children and adolescents were diagnosed with T1DM. Their mean HbA1c level at diagnosis was 10%, there was no correlation between the duration of signs and symptoms and HbA1c at the time of diagnosis. HbA1c was higher in children with family of limited education and in the adolescent age group. **Conclusion**: There is no correlation between duration of signs and symptoms and HbA1c level at the time of diagnosis. The educated families gave reliable history of duration as reflected by their HbA1c levels when compared with families of limited education. Family history of DM type 1 did not make difference and this may reflect a denial of the disease.

Type 1 diabetes mellitus and precocios puberty

Bessahroui

Precocious puberty is defined as pubertal development that begins at an earlier age than expected; most pediatric endocrinology subspecialists use cutoff ages of 8 years for girls and 9 years for boys. We reported in this case, rare association between type 1 diabetes mellitus and precocios puberty. We present a girl with type 1 diabetes developed at the age of 3 years, with good glycemic control using insulin. She also had a developmental. At the age of 6 years child had breast enlargement, height increase, and an increase in growth velocity. On examination, she was found to have Tanner stage 3 breast development, and her vaginal mucosa was estrogenized. Her height was above the 97th percentile. Biochemically, she was diagnosed as having central precocious puberty, and magnetic resonance imaging of her pituitary gland diagnosed central precocious puberty idiopathic. Treatment with leuprolide resulted in normalization of her growth rate and regression of the breast development; the vaginal mucosa also became unestrogenized. Conclusion: Precocious puberty and type 1 diabetes is a rare association. The relationship has not been determined.

Effect of Insulin Glargine on Glycemic Control in Adolescents with Type 1 DM

Hend Soliman

Background: Hypoglycemia is a common problem in children and adolescents with type 1 diabetes especially nocturnal hypoglycemia with prevalence up to 70%. Severe hypoglycemia is a significant cause for morbidity and occasional mortality in children and adolescents with type diabetes (T1DM). **Aim**: To study the role of long acting insulin analog (insulin glargine) in glycemic control of adolescents with poorly controlled type 1 diabetes who suffer from frequent hypoglycemic attacks and marked glucose variability, and to compare its efficacy and cost versus intermediate acting insulin (NPH) **Methods**: A non-controlled longitudinal study that included 29 adolescents with T1DM (12 males and 15 females, mean age 12.9 ± 2.6 and range 10-18 years), with a mean duration of DM 6.6 ± 2.6 years. All included patients were on MDI regimen. All had unsatisfactory glycemic control with marked glucose variability and/or frequent hypoglycemia. All included patients were shifted from twice daily NPH injections to single bedtime injection of insulin glargine (Lantus), and followed up until target fasting and postprandial blood glucose levels were achieved, and for a minimum period of 6 months.Comparison was done regarding their glycosylated hemoglobin,frequency of hypoglycemic andDKA attacks, body mass index, total insulin and basal insulin requirements, as well as mean monthly costs of insulin therapy before and after switching to insulin glargine**. Results:** The useofinsulin glarginewas associated with significant reduction in hypoglycemic and DKA attacks (p= 0.000 for both), but without significant reduction in mean HbA1c (8.06 vs 8.0, p=0.9).There was a significant increase in mean BMI SDS (P=0.004). Basal insulin requirements decreased significantly (0.52 vs 0.39 IU/kg/d, P = 0.007), without significant reduction in total insulin requirements (1.2 vs 1.12 IU/kg/d, p= 0.098). The mean monthly costs of insulin were approximately doubled (75.67 vs 146.41 Egyptian pounds/month).

Type 1 diabetes-associated cognitive decline; observations and conclusions from a meta-analysis

Nadia Hussain

Introduction: Type 1 diabetes can have a significant impact on the function and structure of the brain. This eventually affects cognition and is termed as T1D-associated cognitive decline (T1DACD). Factors that

contribute to T1DACD include the duration of diabetes, age of onset and the presence of other diabetic complications. Although it affects both adults and children suffering from Type 1 diabetes, the condition has not been compared between the two age groups. **Aim:** The purpose is to investigate the differences between children and adults, pinpoint the issues with cognition, the aspects of brain function affected and to analyse the factors that contribute to T1DACD. The meta-analysis will give a clearer understanding about the rate of occurrence and effects of T1DACD in adults and children Material & Methods: The databases PubMed and ISI Web of Knowledge were utilized. Literature published up until July 2014 was included in the analysis. The standardized differences between the affected and control groups were calculated. **Results:** There was a significant decrease in cognitive performance in T1D patients compared to the non-diabetic controls. Type 1 diabetic children performed poorly, in comparison, in tests of intelligence quotient, motor speed and executive function. However adults performed poorly, in comparisons, in tests for verbal and performance IQ, spatial memory and motor speed. Factors such as age of onset of diabetes, bouts of severe hypoglycaemia, chronic hyperglycaemia can all be important in the observed decline of cognitive function. **Conclusion**: The findings suggest that, comparing adults to children, T1DACD affects adults much more. However the phenomenon affects children of a school going age which adversely affects academic performance and has long lasting implications. Since adults are more affected, it appears that age and duration of diabetes contributes significantly to T1DACD.

Parental Involvement in the care of children with type 1 diabetes

Karima Berkouk

Introduction: Despite education of children with type 1 diabetes designed to gain autonomy from the age of 7-8 years, parents are involved in the daily management of the disease. **Aim:** Evaluation of the degree of parental involvement in the management of diabetes in children over 7 years. **Materials / Methods**: Parents of children with diabetes over 7 years were subjected to a questionnaire assessing their level of involvement in the practice of injections, the selection of dose of the insulin, practice of the glycemic monitoring, and nutritional intake. **Results**: 40 parents responded to questionnaire. The average age of the children was 12.7 years. The mean duration of diabetes was 5.3 years. 92.5% of children (n = 37) are in the multiple injections and 85% (n = 34) have insulin pens. We found that mothers are the parent more involved in the management of the diabetes (86% vs 12% fathers). All children test three to four times a day and no parent participate in the self-controls monitoring that are made by the children alone. 48% of parents (n = 19) inject insulin and decide the dosage to inject. 55% (n = 22) of parents say they worry about their children foods intake. Half of parents admit to being tired out of having to manage their child's illness. **Discussion:** Parental involvement remains important in our population of diabetic children over 7 years. Strengthening our education should develop adequate self-care behaviors in our children and may be way for parents and family members to remain involved and supportive, but not intrusive, in their youngsters' daily care. **Conclusion:** Adolescents should be encouraged to assume an increasing self-care and responsibility for diabetes management tasks but with continuing, mutually agreed parental involvement and support. Routine assessment of the psychosocial functioning of children and their families is important in the overall evaluation of the care of young people with diabetes.

The impact of a health education program on primary school teachers' knowledge and attitudes towards T1DM in Saudi schoolchildren

Buthaina Al Jehani

Introduction: The global prevalence of type 1 diabetes mellitus (T1DM) for children under 15 years is 23/100,000 per year (ADA, 2013). The incidence of T1DM in Saudi Arabia (KSA) is 36.99 per 100,000. The WHO classifies annual T1DM incidence above 20/100,000 as 'high' (Patterson, 2009). Schools are important for the secondary prevention, treatment and management of T1DM (Melton and Henderson 2007). Teachers represent potential first-respondents during diabetic crises in schools. They need to be knowledgeable not only about common health emergencies but also about diabetic emergences (Weingarten *et al*., 2009). **Aim** The aim of this research study was to assess the impacts of a health education program

on primary school teachers' knowledge and attitudes towards T1DM in children attending schools in Jeddah city, KSA. **Methods** The study was conducted in Jeddah City, western KSA. A quantitative, quasi-experimental (repeated measures) non-equivalent groups, pre-test, post-test- follow-up design was adopted, with testing at baseline, and three months and six months post-intervention. Data collection was undertaken between September 2013 and March 2014. A structured, multiple-choice, closed-ended, self-administered questionnaire was employed, based on the literature and provided in Arabic. A total of 540 teachers were recruited (360 experimental and 180 control group) in equal numbers by gender since schooling in KSA is separated by gender for pupils and teachers. The intervention was a standard educational program in the form of a series of lectures and activities. Additional reading materials were provided: "Diabetes & School" a booklet by King Faisal Hospital and Research Centre. The intervention included an overview of T1DM in children; diabetes and school; the importance of cooperation between parents, children, school and health team; diabetic children and stress in school; hyperglycemia and hypoglycemia symptoms and treatments; diet; activity and exercise; management of emergencies (first aid); and storage of the medication. **Results:** SPSS used to analyze the data and results obtained by running ANOVA test. In the pre-test, there were no significant differences in teachers' knowledge of T1DM in children between the control group (Mean=91.18) and the experimental group (Mean=89.62). Also, there were no significant differences in teachers' attitudes towards children with T1DM between the control group (Mean=62.54) and the experimental group (Mean=63.81). In three-month post-test, the level of T1DM knowledge mean was increased significantly in the experimental group (Mean=99.23). Also, attitude towards T1DM in children was improved by the intervention to reach (Mean=64.96). There were no significant differences in the knowledge or attitudes scores for the control group (Mean=63.23). In the follow-up test and over six months, the significant increase in the knowledge scores of the experimental group (F=144.605, df 2, p=0.000) and the significant increase in their attitudes scores (F=5.022, df 2, p=0.007) was not seen in the control group. **Conclusion** This research focused on the provision of health education directly to primary school teachers. The T1DM educational program impacted positively on teachers' knowledge and attitudes. Health education programs should be integrated into the national child health program.

Risk factors related to the development of diabetic neuropathy in type 1 diabetes in children

Marise Abdou

Introduction: Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia due to defective insulin secretion and/or action. Long term sequelae, particularly neuropathy, nephropathy, retinopathy, coronary vascular disease and dyslipidemia can occur. Multiple risk factors may contribute to the development of diabetic neuropathy (DN). **Aim:** to detect the risk factors that may be related to the development of DN. **Methods:** Sixty children and adolescents wit type 1 diabetes (23 Male and 37 Female, age 8.60 to 31.99 years, duration 1.1–23.9 years) were included. After careful history taking and inquiry of symptoms suggestive of peripheral and autonomic neuropathy, each patient was tested by a single observer for peripheral neuropathy (PN) and autonomic neuropathy (AN) using bedside screening tests. Nerve conduction studies were done after explanation and patients' consent. The following risk factors that may be related to the development of diabetic neuropathy were studied: age, gender, age of onset of DM, duration of DM, family history of DM, smoking, mean preprandial and postprandial blood glucose, frequency of DKA and hypoglycemia, mean HbA1c, glucose variability, patient's compliance and lipid profile. **Results:** Neuropathy was detected clinically in 22 patients. Fifty patients agreed to do nerve conduction studies, (19 with PN and/or AN, and 31 with no clinically detectable neuropathy as control). Abnormal nerve conduction velocities were found in 15 out of the 19 cases with clinically detectable PN and/or AN, and in 3 out of the 31 clinically free cases. On comparison of both groups of patients (with and without neuropathy on clinical basis), positive neuropathy group had higher percentage of female sex, older age and longer duration of diabetes (p 0.001, 0.015 and 0.001) respectively) higher weight & BMI, lower height standard deviation score, positive smoking, higher mean preprandial blood glucose, worse compliance and higher cholesterol and triglyceride levels (p 0.025, 0.005, 0.001, 0.009, 0.012, 0.019, 0.026 and 0.01 respectively). However, statistical analysis of the risk factors for the development of diabetic neuropathy detected by nerve conduction studies revealed that smoking was the only statistically significant factor (OR: 4.412, 95% CI: 1.066-18.267). **Conclusion:** Smoking is the strongest risk factor related to the development of diabetic neuropathy. Other risk factors to be considered include older age, female sex, longer duration of diabetes, higher weight, and BMI, and lower height

SDS, higher mean preprandial blood glucose, cholesterol and triglyceride levels and poor compliance.

Prevelence and Predictors for Microalbuminuria

Sahar Taha

Objective: To determine the prevelance and the risk factors for development of microalbuminuria among children with T1DM receiving care in a diabetic centre in Khartoum. **Research Design and Method:** Prospective cross sectional analytic study. A total of 84 patients aged 11-19 years who had been diagnosed as having T1DM and attending a single clinic, with duration of diabetes 2 years or more were included in the present analysis. Data about their age, age at diagnosis, sex, duration of the diabetes, family history of type 1 or 2 diabetes were collected, BMI, BP and SMR were assessed. Collected blood and urine samples were analyzed for glycated hemoglobin (Hb A1c) and urinary albumin. **Results:** Nephropathy was classified as normal in 37 (44.0%), microalbuminuric in 34(40.5%), macroalbuminuric in 13 (15.5%). 33 (39.3%) patients had hypertension and 19 (22.7%) of the total number had prehypertension. Risk factors for microalbuminuria was low BMI. High diastolic BP was associated with the development of macroalbuminuria. The older age, older age at diagnosis, Female sex, positive family history of T2Dm, High BP and high HbA1c were associated with the MA positive group but the relation was not statistically significant. **Conclusions:** prevalence of microalbuminuria was 34(40.5%). Risk factors for microalbuminuria was low BMI and for macroalbuminuria was high diastolic BP. Conclusion: Besides the best possible metabolic control, early diagnosis and prompt treatment of hypertension is mandatory in patients with T1DM.

Left Ventricular Diastolic Dysfunction and P-wave Dispersion in Adolescents with type 1 DM

Amany Ibrahim

Aim: To compare the left ventricular (LV) function in type 1 diabetic adolescents and their healthy peers, and to demonstrate the effect of chronic hyperglycemia on P-wave dispersion (PD) & diastolic function & to correlate the results to diabetes duration and complications. **Methods:** In 50 T1D patients (28 males, 22 females pubertal adolescents, aged 9.5-19 years) and in control group (13 males, 17 females) of same age and sex LV was assessed by M-mode, 2D and Doppler echocardiography, in addition to electrocardiography (ECG) to detect PD. The metabolic control in T1D patients was assessed by glycosylated hemoglobin (HbA1c) (mean HbA1c for the past two pre-study years-HbA1c). This study was conducted in the Diabetes Endocrine and Metabolism Pediatric Unit (DEMPU) at Children's Hospital of Cairo University. **Results:** Diastolic dysfunction of both right and left ventricles and increased PD were found in T1D patients. When correlating PD to echo parameters, a positive correlation was found between PD and LVEED ($r = 0.3$, $p= 0.04$). Significant negative correlation was found between PD and both of A mitral and IVRT ($r = -0.32$, $p=0.03$ and $r =-0.38$, $p= 0.01$, respectively. Significant positive correlation was found between the duration of diabetes and IVRT ($r =0.39$, $p = 0.02$) & significant negative correlation between the duration and E mitral and E/A ratio mitral ($r = -0.38$, $p =0.01$, and $r = -0.29$, $p = 0.04$, respectively). No correlation found to glycemic control, lipid profile, or Alb/ creat. Significant positive correlation between LDL level and Alb/creat ratio ($r =0.32$, $p =0.02$). **Conclusion:** Increased PD in T1D patients make them prone to paroxysmal atrial fibrillation (AF), diastolic dysfunctions are present in T1D patients and should be screened early in order not to progress to diabetic heart failure. Doppler echocardiography is a reliable non-invasive means to assess early impairment of cardiac function in T1D patients.

Genitourinary malformation in congenital adrenal hyperplasia

Nadia Omar

The objective of the study was to determine the incidence, specific abnormalities and clinical significance of genitourinary anomalies in patients with congenital adrenal hyperplasia. **Methods:** Medical charts of children who received a diagnosis of congenital adrenal hyperplasia between 1997 and 2010 were reviewed at pediatric endocrine department Tripoli medical center. **Results:** Of 185 patients with congenital adrenal hyperplasia were identified, 124 (67%) girls, 61 (33%) boys, 69.2 had salt losing while 30 % had non salt losing type of congenital adrenal hyperplasia. 134 children were diagnosed in the first month of life, virlizationand dehydration were the most mode of presentation. 11 children were found to have genitourinary malformation; 5 boys and 6 girls .The anomalies consisted of 7 patients with vesicoureteral reflux, one patient with hydronephrosis, one patient with duplicated collecting system, one had absent Rt kidney, one had uretropelvic junction obstruction. Two patients underwent surgery that consisted of uretral reimplantation and uretral stenting. 123 girls had undergone Feminizing genitoplasty, urinary tract infection was reported in 22 patients and was not correlated with the type of surgery. The reflux eventually resolved in 5 patients and worsened in 2, while renal scaring with impairment of renal function was seen in 2 patients. Hydronephrosis improved in 1 patient. **Conclusion:** The incidence of genitourinary malformation in patient with congenital adrenal hyperplasia is high in our cohort (6 %l), this association represents potentially significant medical issue because some may require surgical intervention and antibiotic prophylaxis to prevent urinary tract infection and impairment of renal function.

Upper genitourinary tract malformations in children with CAH

Roqya Almejrab

Objectives: To determine abnormalities of genitourinary tract in those children with congenital adrenal hyperplasia. **Methods:** All children who were diagnosed with congenital adrenal hyperplasia in our department between 1989 and 2010 were enrolled in the study. **Results:** 185 subjects with congenital adrenal hyperplasia (124 girls, 61 boys). 11 were found to have genitourinary tract malformations consisted of vesicoureteral reflux 7 patients (2 girls ,5 boys) ,1 patient with hydronephrosis (girl), 1 patient with duplicated collecting system (girl), 1 patient with absent right kidney (girl), 1 patient with ureteropelvic junction obstruction and hydronephrosis (girl). Vesicoureteral reflux resolved in 5 patients and got worse in the remaining 2 patients (with renal scarring and impaired renal function) **Conclusion:** This study revealed an increased incidence of upper genitourinary tract malformations in children with congenital adrenal hyperplasia, this necessitates special attention to those patients, because some of them may require surgical and antibiotics prophylaxis to prevent urinary tract infection and impaired renal function.

Is it 21 hydroxylase deficiency?

Manal A Shawi

21 hydroxlyase deficiency results in the commonest form of congenital adrenal hyperplasia. However, other causes of enzyme deficiencies, along the adrenal path of steroid synthesis, is seen particularly in families where consanguinity is common. We report a 2 month old Saudi child who presented with a two days history of sepsis-like picture. She had persistent hyperkalemia, hyponatremia with metabolic acidosis. Random cortisol was 279 nmol/l and ACTH of 3706 pg/l. Blood culture was positive for staphylococcus and her abdominal ultrasound showed absent uterus and suspected bilateral adrenal hemorrhage. A diagnosis of CAH due to 21 hydroxylase deficiency was put and she was started on hyddrocortison and fludrocortison replacement. At the age of 10 years, she was admitted with URTI and was noted to have normal external femaile genitalia. Her random cortisol was 13 nmol, ACTH is 662pg/l, renin 433, adlosteron <138, 17 OH progesterone <0.4. Diagnosis was revised and a more proximal defect of adrenal steroid biosynthesis was confirmed. Although 21 hydroxylase deficiency is the commonest form of CAH, undervirilization of an XY infant should raise the possibility of a proximal adrenal steroid synthesis defect. Abdominal ultrasound scan to show absence of uterus is an easy way of directing

the diagnosis while awaiting for a karyotype confirmation.

11 hydroxylase deficiency in 2 Saudi families: one with a novel mutation

Yasser Alghanmi

11B-hydroxylase deficiency (11B-OHD) is the second most common cause of congenital adrenal hyperplasia. Mutations in the CYP11B1 gene, which encodes steroid 11B-hydroxylase, are responsible for this autosomal recessive disorder, accounting for 5–8% of all cases. Here, we describe four patients from two families in whom diagnosis of 11B-OHD has been established based on their hormonal profiles displaying high levels of 11-deoxycortisol and hyperandrogenism. Virilization and hypertension with or without hypokalemic alkalosis are the main clinical characteristics of this disease. The identical presentation of genital ambiguity (females) and pseudo-precocious puberty (males) can lead to misdiagnosis with 21 α-hydroxylase deficiency. The clinical hallmark of 11B-hydroxylase deficiency is variable, and biochemical identification of elevated precursor metabolites is not usually available. All four patients are of Saudi Arabian origin and there is no self-reported consanguinity in these two families. In order to elucidate the molecular basis for 11B-OHD in the Saudi Arabian population, it is imperative to perform CYP11B1 genetic analysis in more patients from this region.

Genetic susceptibility in autoimmune polyglandular syndrome type 3 variant

Amir Babiker

Background: Autoimmune polyglandular syndrome type 3 (APS3) comprises a wide spectrum of autoimmune endocrine disorders other than adrenal insufficiency. It includes the association of autoimmune thyroid disease (ATD) with type 1 diabetes (T1D), which is known as APS3 variant (APSA3v). Genes linked to possible joint susceptibility for APS3v have been reported in few cases. We report a 10-year-old girl with Graves' disease (GD) who developed T1D after six years of the diagnosis. **Case Report:** A 10-year-old girl was diagnosed with GD at 3-years of age and treated with carbimazole but had frequent relapse when medication was stopped. She was admitted for surgery as definitive treatment rather than radioactive iodine because of an active thyroid eye disease. On admission, she reported classic symptoms of T1D. Investigations revealed a normal cortisol level, HbA1C of 10% and a persistent hyperglycemia, which was well controlled by insulin treatment. Her mother has T1D, and two of her aunts were diagnosed with ATD. **Discussion:** In a cross sectional study, 60% of APS3v patients developed GD before the onset of T1D, and 30% developed GD after the onset of T1D; while only 10% of patients developed both simultaneously. Insidious onset of diabetes was more common in APS3v patients who developed GD first, suggesting an influence of GD on the speed of B-cell destruction. A number of genes were reported in association with APS3v, including: HLA class II, CTLA-4, FOXP3, Insulin VNTR, PTPN22 and IL2Rα/CD25 genes. **Conclusion:** The reported cases of APS3v with genetic association provide potential illustration of genes linked to joint susceptibly of APS3v, and if these genes could be clustered in certain families or ethnic groups. Our patient has a strong first-degree family history of autoimmune endocrine disorders; therefore, genetic testing was planned for the family.

Addrenal Onchocytoma in a 5 year Old Boy

Maryam Al Badi

Oncocytic tumor are very rare in children. Most of cases of oncocytic tumor have been described in kidneys, thyroid, parathyroid and salivary gland.To our knowledge, only four cases of a functioning adrenocortical oncocytoma have been

reported in childhood with age of 6, 12, 14 and 16 years old .We report a case of a functioning adrenocortical oncocytoma in a 5 years old male child who presented with pseudo precocious puberty and cushioning syndrome. He found to have right adrenal mass in which complete laparoscopic resection done. A diagnosis of adrenocortical oncocytoma was made after histology and immunohistochemical studies. **Introduction:** The term "oncocyte," first used by Hamperl in 1950, describes large, highly eosinophilic, granular cells associated with a Hurthle cell tumor of the thyroid gland. Oncocytoma of the adrenal gland is defined as a neoplasm composed exclusively or predominantly of oncocytes. These oncocytes are large polygonal cells with eosinophilic cytoplasm that result from the abnormal accumulation of mitochondria. Adrenocortical oncocytoma is an unusual tumor and mostly nonsecreting adrenal neoplasm. When secretion is noted, the patient produces steroid excess and results in a clinical presentation such as virilization, feminization or Cushing syndrome. Only 11 cases of a functioning adrenal oncocytoma are reported so far in literature and only four cases reported in children manifesting with virilization. We represent a 5 yrs old boy with a functioning adrenal onchocytoma manifested with pseudo precocious puberty and Cushing syndrome**. Case report:** A 5 years old boy was referred to our institution for investigation. He was presented with an eight months history of sexual pubic hair, increase penile length and excessive body hair growth. He also noticed to have body adult odour and weight gain .In addition noted to have puffy face different from before. There was no history of change in voice or acne or abdominal pain or mass. Mental and motor development were appropriate for age. The parents and siblings are healthy .There was no family history of cancer.

Challenging Endocrine cases

Adnan Al Shaikh

Pediatric endocrine field has a lot of difficult cases and challenging diagnosis or treatment. We report three challenging endocrine cases with a theme of Endocrine Hypertension. Endocrine Causes of secondary hypertension in children and adolescents include congenital adrenal hyperplasia, cushing syndrome, primary aldosteronism, hyperthyroidism, primary hyperparathyroidism, diabetes mellitus, pheochromocytoma and hypercalcemia. While renal causes hypertension in children include pyelonephritis, reflux nephropathy, acute glomerulonephritis, henoch-schönlein purpura…etc. Our patients are found to have an endocrine etiology for hypertension. We will go through each case followed by a brief review of the topic and the literature.

Allgrove Syndrome; 8 Cases

Sana Kmiha

Background: Triple A or Allgrove syndrome is a rare autosomal recessive disease with alacrima, achalasia, and ACTH-resistant adrenal insufficiency. **Method:** We conducted a retrospective study at the Department of Pediatric of the CHU Hédi Chaker Sfax, over a period of 24 years from 1990 to 2013 to assess the epidemiologic, clinical, biological, genetic, therapeutic features of the syndrome. **Results:** During the period of study, we have collected 13 cases of triple A syndrome from 9 families. There were 8 boys and 5 girls. The average age was 6 years with ranging from 13 months to 10 years. All our patients had a proven alacrima. Adrenal insufficiency was inaugurated by a seizure related to hypoglycemia in 2 cases however Melanodermia was noted in all patients. Achalasia was noted in 8 cases. The cortisol was low and plasma levels of ACTH were high in all cases. Mineral corticoid deficiency was found in 8 cases. Genetic study identified mutation AAAS in all patients. Our patients have been treated by hydrocortisone. Balloon dilatation was performed in 5 cases and one patient had a surgical treatment. After an average of 5 years 7 months, growth retardation was found in 5 cases, one patient was lost sight and two patients died. **Conclusion:** The Allgrove syndrome is a serious disease, despite the surgical therapeutic, medical treatment of achalasia, treatment of adrenal insufficiency and the alacrima seems to be the best alternative therapy in child.

Corticosteroid Insufficiency Provoking Ventricular Arrhythmia

Amir Babiker

Background: Recurrent syncope may be a presenting feature of a cardiac illness, recurrent hypoglycaemia or both. We report a 13-year-old boy presented with recurrent fainting episodes with corticosteroid insufficiency (CI) and prolonged QT (PQT) interval followed by ventricular arrhythmia (VA). **Case report:** A 13 year old boy of non-consanguineous parents had recurrent Syncope that improved in response to oral or intravenous dextrose despite no documented hypoglycaemia. He has nocturnal enuresis started at the age of 10 years suggesting syncopal episodes during sleep. He was admitted in PICU with one of these episodes and attached to cardiac monitor. His investigations revealed strikingly low 9 am cortisol and a flat response to ACTH stimulation test (Cortisol: 0.5 nmol/l) and ACTH of 0.05 pmol/l. He had, otherwise, normal baseline anterior pituitary functions. Hydrocortisone replacement therapy has been started but he rapidly developed VA, classic ECG features of PQT3 syndrome and progressed to cardiac arrest. He was resuscitated and inserting intra cardiac defibrillator only successfully controlled the arrhythmia. Genetic tests of PQT syndromes have been arranged. **Discussion:** PQT syndromes are caused by mutations of certain sodium or potassium channel genes. It was suggested that hormonal modulation of these ion channels of cardiac cells might mediate this ECG changes and provoke polymorphic ventricular tachycardia. In adults, a unique case (72 years) was reported to develop PQT interval and fatal VA with isolated ACTH deficiency. Though a transient CI is a recognized feature in some patients with acute severe illness, our patient had failed the repeat ACTH stimulation test 3 months later. Simultaneously a very low value of ACTH favoured the diagnosis of isolated ACTH deficiency in the absence of other pituitary hormonal deficiencies. **Conclusions:** CI may provoke QT prolongation responsible for severe VA which may lead to sudden cardiac death.

Mineralocorticoid disorders in pediatric age group in Tripoli children hospital

Faten Ben Rajab

Disorders of mineralocorticoid secretion are common in clinical practice and may be life-threatening if not correctly diagnosed and appropriately treated.In majority of cases; salt wasting with hyperkalemia is the commonest presentation of Aldosterone biosynthetic or receptor defects. Congenital adrenal hyperplasia& hypoplasia are the main differential diagnoses. We report three cases presented with recurrent severe attacks of dehydration &shocks require treatment with normal saline infusion to present again with shock after stopping intravenous fluid. 60 days old boy Presented with diarrhea & failure to thrive. FTND Bt. Wt. 2.7 kg &normal Apgar score. He was admitted to SCBU at 5 days old because of dehydration & metabolic acidosis. There is FH/O consanguinity& FH/O Death of his brother at 4 months of age. Another infant 5 months old girl presented with Recurrent attacks of hypotonic dehydration & failure to thrive (despite good appetite).FT –LSCS /(pre-eclampsia) Bt. Wt 3 kg, She was admitted 10 times because of dehydration & metabolic acidosis. There is FH/O consanguinity. Treated with hydrocortisone as congenital adrenal hyperplasia but no improvement-reassess & investigate to show high level of Aldosterone &Renin. Conclusion: Pseudo hypoaldosteronism; more details will presented regarding therapy &follow up. Third patient 7 months old boy presented with Diarrhea &Vomiting, failure to thrive. FT & LSCS Bt.Wt 3.3kg & normal Apgar score. He was admitted to many hospitals since 2months old because of dehydration & metabolic acidosis treated as acute gastroenteritis about 10 times. There is FH/O consanguinity& FH/O Two deaths at infancy (? CAH) Treated with hydrocortisone but no improvement. Reassess & investigate to show very high level of Renin& low level of Aldosterone.

A case of Transient Pseudohypoaldosteronism Secondary to Urinary Tract Infection in a 6 week old infant

Eman Al Atrash

Background: hyponatremia and hyperkalaemia in infancy is uncommon but life threatening occurrence, most commonly due to salt losing congenital adrenal hyperplasia. Transient pseudohypoaldosternosim (PHA) is a syndrome characterized by a state of renal tubular unresponsiveness to aldosterone and is manifested by hyponatremia, hyperkalemia, and metabolic acidosis. Urinary tract infections (UTI) and / or urinary tract anomalies are the most commonly attributed causes. We report a 6-wek-male infant who presented with severe hyponatremia accompanied by UTI, ultimately leading to the diagnosis

of transient PHA. **Case History:** A 6 week-old full-term male initially seen by his primary physician for poor weight gain and feeding intolerance. His prenatal and immediate postnatal histories were unremarkable. He was born at term for second-degree consanguine parents. He had been breast- feeding and supplemented with Casein based formula milk. Physical examination revealed afebrile, moderately dehydrated but a hemodynamically stable infant. His systemic exam was unremarkable, had well developed male external genitalia with both testes being palpable in the scrotum. Initial laboratory evaluation revealed severe hyponatremia (Na 111mmol/L), hyperkalaemia (K 7mmol/L) with metabolic acidosis (HCO3 17mmol/L) and normal renal function test (urea 6.80mmol/L and Creatinine22 micromole/L). Immediate concern for salt wasting CAH triggered further hormonal workup, though his neonatal screening for CAH was reported as normal. Seum17-OH-progesterone level was mildly elevated at (10.35nmol/L), cortisol of (1047nmol/) (reference range 64-536), mildly elevated aldosterone 1.72nmol/L (reference range 0.19-1.50), and markedly elevated Renin of >128ngm/L(reference range 5.22-56.78). Urinalysis was positive for Nitrite and white blood cells and urine culture subsequently grew *Klebsiella Pneumonia*. The patient was started on intravenous normal saline and antimicrobial therapy. Renal ultrasound and DEMSA scan were normal. His electrolytes abnormalities corrected within 24 hours and remained normal on subsequent follow-up. **Conclusion**: Transient PHA needs to be a considered in any infant presenting with salt wasting after the first few weeks of life. Awareness of this condition is important so that relevant hormonal workup, urine culture and renal tract ultrasonography would be obtained immediately on these infants in whom the diagnosis of CAH was excluded. Appropriate treatment with intravenous saline and antibiotic therapy is sufficient to correct associated electrolyte abnormalities.

Iatrogenic Cushing Syndrome in Children

Zineb Imane

Prolonged use of topical corticosteroids can cause systemic side effects including Cushing's syndrome and an axis suppression hypothalamo-pituitary-adrenal. However, iatrogenic Cushing's syndrome in children is rare and only few cases have been reported to date in the literature. We report a case of iatrogenic Cushing's syndrome in a girl of 5 years and a half hospitalized for overweight associated with psoriasis. **Case report:** 5 ½ years, with Down syndrome presented with psoriasis. She used by twice-daily application of topical corticosteroids in (aceponate hydrocortisone, betamethasone, clobetasol propionate) year. The child is brought to the consultation for significant weight gain lasting for eight months. Physical examination on admission found: Cushingoid facies; weight: 28 kg (> + 3DS) height: 97 cm (- 3DS) BMI = 39; TA = 9 / 6cmHg. We noted the presence of erythematous scaly lesions and horizontal large purple stretch marks on the abdomen and the members. The Laboratory tests showed a cycle of cortisol collapsed, urinary free cortisol to 1, 46 ug / l or 0.58 ug / 24, low ACTH levels, plasma glucose at 0, 79g / l, normal blood electrolytes, total cholesterol = 2,08g / l, triglycerides 1.22 g / L, thyroid tests were normal .The radiological assessment (adrenal CT and MRI) was without abnormalities. The diagnosis of iatrogenic Cushing's syndrome has been mentioned. The therapeutic management was to stop corticosteroids associated with hydrocortisone taken (15mg / m^2 / d). Conclusion: Prolonged use of corticosteroids in children can cause serious side effects with an impact on different metabolisms due to a greater body surface. Awareness of health workers and the general public should be conducted to inform the adverse effects associated with steroid abuse.

Neonatal iodine status in iodine-deficient area of Sudan

Bashir El Naem

Background: Iodine deficiency is a major public health problem throughout Africa. Sudan was classified as a country of moderate iodine deficiency based on last study in 2006. We undertook descriptive cross-sectional hospital based study to assess the adequacy of iodine status in newborns in central Sudan (kosti –locality) using on-site measurement methods of neonatal thyroid stimulating hormone (TSH) levels as recommended by the World Health Organization (WHO) for monitoring the degree of iodine deficiency. **Methods:** The study design consisted of a prevalence study using the percentage of newborns cord blood with TSH >10μIU/mL (serum) measured with a sensitive Automatic Enzyme Immunoassay, as indicator of iodine deficiency. This locality was selected for this study on the basis of a previous study which labeled it as an

iodine deficiency area. Three hundred and nine newborns were enrolled and tested between December 2011 and May 2012. **Results:** The prevalence of TSH levels >10μlU/mL (serum) was 37.5% which indicate moderate iodine deficiency; those with TSH between 30—59μIU/ml were 11 baby (3.6%), the result of their FT4 was normal. The highest TSH was 58.3μlU/mL. No case of hypothyroidism was detected; the mean TSH level was 10.648μlU/mL-std 8.05. **Conclusions:** Based on the percentage of neonates with TSH values >10 μIU/mL(serum), Kosti locality is now an area of moderate iodine deficiency according to WHO criterion, although this result may indicate some improvement as last study done classify it as sever iodine deficiency area.But IDD still constitutes a public health problem in this locality. **Recommendations:** All commercial available salt must be iodized, and affordable to all house hold,Iodine supplementation should be offered to all women of childbearing age and to all pregnant women in Kosti locality, Community base health education about IDD is paramount and the need to establishing neonatal thyroid screening program.

Autoimmune manifestations in a patient with hyperandrogenic virilization

Rana AbdelHakim

Background: We present an 11-year-old girl with complaints of lethargy and poor school performance of 1-year duration with proximal muscle weakness, autoimmune hypothyroidism, hepatitis, and myopathy. On examination the girl showed fair general condition, high blood pressure, hirsutism (score of 19 according to Ferriman Gallwey score) secondary to a hyper androgenic state possibly complicating undiagnosed congenital adrenal hyperplasia (CAH), acne vulgaris over face and back, arthralgia of small and big joints and proximal muscle weakness as shown by the waddling gait and the decreased muscle power in proximal muscles of lower limbs. She had an apical soft blowing murmur, abdominal examination revealed non-tender hepatomegaly 4 cm below costal margin. Height was 144.5 cm (+ 1 SD) and weight was 41 kg. Tanner's sexual maturation score was A3, B3-4 and P5 for axillary, breast and pubic hair, respectively. External genitalia examination revealed clitromegaly and urogenital sinus Prader 3 and by revising the history, the mother said that pubic hair started to appear at age of 2 years and axillary hair at 3 years with hirsutism becoming evident at 5 years age. Laboratory investigations showed a normal ESR, CBC, electrolytes, albumin, serum creatinine and PT, PTT. ALT 115 IU/L (normal 7-31), LDH 747 IU/L (normal 120-300), CPK 7000 IU/L (normal 24-170), positive ANA (speckeled pattern), positive anti-ds DNA antibody, negative rheumatoid factor, lupus anticoagulant 43.9 (normal 31.6-43.6) and positive anticardiolipin antibody. Free testosterone was 1.0 pg/ml (normal <1.7 pg/ml), 17-hydroxyprogesterone 4.8 ng/ml (normal <0.9), dehydroepiandrosterone sulfate (DHEAS) 7.5 ng/ml (normal 0.31-3.4), FSH 5.9 mIU/ml (normal 0.4-6.9), LH 4.7 mIU/ml (normal 0-4), prolactin 7.6 ng/ml (normal 1.6-9.6), CRP 12mg/l (normal <6), ACTH 59 pg/ml (up to 56) and cortisol 2.7 ug/dl (6-16 a.m.). Serum TSH was 13.4 μIU/ml (normal 0.7-6.4), T 3 166ng/dl (normal 75-230), T 4 7.2 μg/dl (normal 7.5-15), anti-TPO antibody level was 1000 IU/ml (normal <8 IU/ml) and anti-thyroglobulin level 306.4 (normal <18 IU/ml). Radiological investigations revealed a bone age of 15 years (Greulich and Pyle). Ultrasonography of the pelvis showed a pre pubertal uterus 2.2 × 1.1 × 0.9 cm with bilaterally normal ovaries. Echocardiography revealed dilated cardiomyopathy with ejection fraction 42%. MRI sella turcica was done to exclude autoimmune hypophysitis as the cause of blunting of the ACTH response to low cortisol. **Conclusion:** The patient presented with multiple autoimmune manifestations including arthritis, fever, oral ulcers, autoimmune hypothyroidism, hepatomegaly, hepatitis, skeletal and cardiac myopathy, and non-salt wasting virilizing CAH with precocious puberty. The non-classic 21-hydroxylase deficiency is known to be associated with HLA B14 and HLA DR1, which are associated with autoimmune myositis and hepatitis respectively.

Endocrine Dilemma: Unusual case of Adrenal insufficiency and Disorder of Sexual Differentiation

Asma Jassim

No abstract available.

A Male Infant with a Unilateral Empty Scrotum: A Case study

Amany Ibrahim

Undescended testis is present in about 1- 4.5% of newborns with a higher incidence in preterms. Undescended testis with ambiguous genitalia mandates immediate systematic work-up. This 1.3 years reared as male, his parents came complaining of an empty scrotum on the right side and an ambiguous genitals. Left testis could be felt in the left scrotal sac and it is of normal size for age (T2), bifid scrotum, penoscrotal hypospadias, hooked phallus, but phallus looked of normal size and girth (about 2.5 cm in length although couldn't be stretched properly due the presence of chordae). The right testis couldn't be felt either in the scrotal sac or in the inguinal canal (empty scrotum). Karyotyping was done and it was 46 XY. Abdomino-pelvic U/S couldn't visualize the right testis, also abdomino-pelvic MRI didn't show the right testicle. Pregnyl test was done and revealed good response. The patient was scheduled for a diagnostic laparoscope. Laparoscopy revealed small dysgentic uterus and fallopian tube on the right side in addition to a small sized gonad which may be an ovary therefore taken as biopsy and was sent for pathological assessment. Biopsy revealed an ovarian strauma with tiny cysts (immature or primordial follicles). This is a case of 46 XY ovo-testicular DSD, and this patient will be reared as male after surgically removing the remnants of the Mullerian structures (hemi-uterus, fallopian tube) and also will undergo corrective surgery for his external genitals (for the hypospedius, bifid scrotum and the chordae). His other testis (left sided) is functioning well as evidenced by the good phallus size and the good testosterone response in the pregnil test.

Neonatal Graves Disease with Unusual Metabolic Associations from Presentation till Resolution

Manal Mustafa

Introduction: Neonatal Graves 'disease is a rare disorder seen in 1 in 25,000 births, and in 1-3% of the offspring of mothers with either an active or a previously treated Graves' disease. The disease is usually due to transplacental passage of TSH receptor-stimulating antibody (TRSAb) from a mother with active or inactive Graves' disease**.** In spite of its rarity, the serious nature of this condition (if not treated) and its association with multisystem abnormalities justifies careful clinical screening and management. **Objectives:** The aim of this report was to describe the rare association of neonatal Graves'disease with unusual metabolic derangements and to evaluate the clinical course, thyroid function, thyrotropin receptor stimulating antibody level (TRSAb) and response to anti thyroid drugs (ATD) during the first six postnatal months. **Method:** We report a neonate with neonatal thyrotoxicosis secondary to untreated maternal Graves' disease, who had in addition to the typical hyperthyroidism symptoms, unusual metabolic associations of direct hyperbilirubinemia (neonatal cholestasis) and hyperammonemia. We followed her from birth till age of six months. **Results**: Our patient had typical symptoms of neonatal thyrotoxicosis , her thyroid function test after birth showed Cord TSH < 0.01 mIU/L (0.35-30), serum TSH < 0.01 mIU/l (0.35-4.9), FT4: 70.6 pmol/l (9.0-19.0), FT3: 13.58 pmol/l (2.6-5.7), elevated serum ammonia 129 µmol/L (18-72), high GTP 831 U/L (9-36), total serum bilirubin peak 123.5 µmol/L (3.4-20.5) and direct serum bilirubin peak 41.4 µmol/L (1.7-8.6), normal metabolic workup. She had high TSH receptor stimulating antibodies (> 36.0 +++ IU/L (< 1.8)). She was started on Lugol's solution, Propranolol in addition to Methimazol and showed good response. Her clinical condition as well as her thyroid functions, Serum Ammonia and Bilirubin all normalized. At age of 6 months, her TRSAb level returned back to normal, Methimazol was stopped and she continued to be euthyroid clinically and biochemically. **Conclusion:** Our case report supports previous reports of direct hyperbilirubinemia (cholestasis) in neonatal Graves' disease, and represents another case report of unusual association of hyperammonemia, cholestatic jaundice with neonatal Graves' disease. Further studies are required to delineate the exact mechanism of these unusual associations.

Twins with hypothyroidism and Papillon - Lefevre syndrome

Amir Babiker

Background: Papillon-Lefevre syndrome (PLS), first described in 1924, is a very rare syndrome characterized by palmoplanter hyperkeratosis and precocious, rapidly progressive exfoliation of primary and permanent

dentition. Hypothyroidism has not been previously reported as a feature of PLS. We report twins with PLS and hypothyroidism suggesting genetic and/or immunological relationship. **Case report:** The twin sisters are 8 years old. Both initially presented with erythaematous palmoplanter rash which later changed into hyperkeratosis. Twin 1 was incidentally diagnosed with hypothyroidism at the age of 6 months when investigated for a small stature while twin 2 was eventually diagnosed with hypothyroidism on further screening. By 5 years of age, both of the twins only had 2 premolar teeth left. They required full dentures because they lost all of their teeth by the age of 8 years. They are on thyroxin treatment and fortunately both are developmentally normal. **Discussion:** The cause of PLS is not fully understood. Genetic, immunologic and microbiologic causes have been proposed. Loss of function mutations in the Cathepsin-C gene located in chromosome 11q14.1-q14.3 has been described. Autoimmune hypothyroidism was reported in an adult with palmoplanter keratoderma and the skin manifestations have improved with thyroxin treatment. However, hypothyroidism is not a known association with or previously reported as a feature of PLS. These twins have both of the conditions. Dyshormonogenesis is the likely cause of hypothyroidism in the twins because the thyroid glands were detected in the normal place in both by USS and tests for anti-thyroid antibodies were negative. We postulate a genetic relationship, though we could not confidently rule out immunological triggers, between PLS and hypothyroidism. **Conclusion:** Further genetic studies of the cause of hypothyroidism in these children are arranged and it may unveil a hidden relationship between PLS and hypothyroidism.

Mutations of TSH receptor

Hajar Berrani

Objective: A case report of a genetic thyroïd dysgenesy by mutation of TSH receptor. Observation: A female infant presented in our hospital at age 10 months. She had a cousin followed for congenital hypothyroidism. The parents observed icterus and constipation at birth. The physical exam showed a hypotonic infant, an icterus, a weak suction, an umbilical hernia and a failure to thrive. The thyroid gland was non palpable. The thyroid function tests revealed a TSH 353 microUI / ml and FT4 <1 pmol / l. Thyroid ultrasound showed hypoplasia of the thyroid gland. Scintigraphy Tc 99 revealed absence of capture in thyroid gland. We diagnosed the genetic thyroïd dysgenesy late at 10 months. The research of the receptor mutation gene TSH was positive. L throxine supplementation was started. **Conclusion:** When cretinism becomes clinically detectable, it is too late for the brain development. Systematic screening is essential in our countries. In the absence of routine screening, all physicians have to know how to detect subtle clinical signs of congenital hypothyroidism.

Rare Manifestation Of thyroid disease in Chidren

Abdullah Aljasser

Introduction: Acquired autoimmune hypothyroidism is the most common endocrine disease in children. There is no specific single sign and symptoms is peculiar to thyroid disease in children. Most of the cases are discovered incidentally by blood test done for thyroid function test. The most majority of symptoms are non-specific but the most common abnormalities frequently associated in the pediatric population are: mild weight gain, Increased cholesterol levels, impaired growth velocity, anemia, Sleepiness weakness, and impaired psychomotor and cognitive development. **Case Report** We present a rare presentation of thyroid disease in a 10 years girl who presented with limping and pain in the leg. This pain is so severe that increased by walking. Initial investigation for her shows moderate vitamin D deficiency and severe hypothyroidism. Her laboratory investigation: Serum FT4: 2.2 (N:12.0-22.0 pmol/L); TSH: 500.000 (0.270 - 4.200 mIU/L); 25OH-Vitamin D: 21.0 nmol/L. She was treated for this and her laboratory investigation normalized in 2 and ½ months. But her limping and pain the leg persist. Orthopedic consultation done and x rays for hips performed which shows: Bilateral symmetrical slipped capital proximal femoral epiphyses are noted with metaphyseal sclerosis and irregularity. She was treated by the

orthopedic internal fixation both sides. the capital femoral heads are covered by the acetabular roofs and they maintained their density, height with no focal abnormal density to suggest avascular necrosis at this stage and by this x-ray. **Conclusion** There are several rare presentation and manifestation of hypothyroidism such as Sexual precocity & severe hypothyroidism (The Van Wyk-Grumbach Syndrome) and the combination of severe hypothyroidism and muscular hypertrophy which gives the child a "Herculean" appearance is known as the Kocher-Debre-Semelaign e syndrome. We think the slipped capital proximal femoral epiphyses is one of the rare presentation of thyroid illness in children which is endocrine disease is one of its etiology. We recommend to screen for thyroid diseases in any patients who present with limping and evaluate for slipped capital proximal femoral epiphysis.

Prevalence of Malignancy in Thyroid Nodules in Children and Adolescents

Nasser Fageeh & Suliman Al Fifi

Aim of the study: This study aims to look at the prevalence of thyroid malignancy in previously healthy children and adolescents presented with multinodular goiter (MNG) and or solitary nodules for which they underwent thyroid surgery. **Patients and Methods:** Twenty one children and adolescents (13 males and 8 females) underwent partial or total thyroidectomy over a 10-year period. **Results:** Papillary thyroid carcinoma was found in 4 (19%) patients. Three of them had metastasis to the cervical lymph nodes. Five year survival for all diagnosed cases having malignancy was 100%. **Conclusion:** Multinodular goiter as well as solitary nodules in children and adolescents may have a higher incidence of malignancy and should always be taken seriously.In absence of known environmental hazards and previously healthy individuals, a prevalence of malignancy (19%) in 21 cases is considered alarming.

Genetics of Growth Hormone Disorders: Who Should get mutation study performed?

Sarar Mohamed
King Saud University Medical City, King Saud University,Riyadh, Saudi Arabia.

The incidence of congenital idiopathic Growth hormone deficiency (IGHD) varies between 1 in 4000 to 1 in 10 000 live births, mainly sporadic. Depending on the cohort studied, between 3% and 30% of cases are familial, implicating genetic factors. Mutations are identified in almost 11% with a higher prevalence in familial compared with sporadic IGHD (34% vs 4%, respectively). Muatation can be identified at the level of hypothalamus (GHRH defect), Pituitary (GHRHR, GH gene defect, Transcription factors defect), GH receptors, GH signaling defect (STAT5b), *SHP-2,* IGF1, ALS, or at IG1 receptors level. Mutation screening for growth hormone disorders should be guided by careful assessment of family history, clinical features and the biochemical profile. This review highlights clinical features that predict mutations in the growth hormone IGF axis and correlates phenotype with genotype that would direct physician to request the right mutation for the right patient.

Implementation of Clinical Practice guidelines for Diabetic oacidosis in a University Center in Riyadh: A quality improvement project decreased length of hospital stay

Sarar Mohamed

Background: Clinical Practice guidelines (CPGs) have emerged as a potentially effective intervention in delivering a high quality, consistent, safe and evidence-based health care. Diabetic Ketoacidosis (DKA) is an acute and life threatening complication of T1D. Proper management of DKA decreases disease related morbidity and mortality. DKA is an ideal candidate for implementation of CPG aiming at reducing associated morbidity and mortality. **Objective and hypotheses:** We aim to review our experience in implementation of CPG for patients with Diabetic ketoacidosis and to determine the impact of CPG on the length of hospital stay
Method: National Institute for Clinical Excellence (NICE) guidelines for management of DKA were appraised and adopted

for use in King Khalid University Hospital, Riyadh, Saudi Arabia. All patients admitted with DKA from November 2010 to April 2013 were prospectively recruited and managed according to these guidelines. Data from patients with DKA admitted between October 2008 and October 2010 before the implementation of CPG were used as control. **Results:** Sixty patients were treated using CPG compared to 40 patients treated before implementation of CPG. The total length of hospital stay was 2.8 days after implementation of CPG compared with 4.5 days before ($P < 0.001$). The length of stay in emergency room was also significantly reduced ($P < 0.01$) as well as the length of stay on wards ($P < 0.001$). **Conclusion:** Implementation of clinical practice guidelines for DKA has decreased length of hospital stay in a busy tertiary center

Does congenital heart disease affect intrauterine growth; cyanotic versus CHD

Ashraf Soliman

Introduction: Embryogenesis, fetal growth, and survival at the peri-natal period all depend on optimal maternal health and normal placental development. The heart-placental axis is associated with parallel development of the placenta and heart that utilizes many common molecules and genes and reflects intimate and synergistic growth of both organs. Abnormal cardiac development leading to CHD can be associated with abnormal placental development with abnormal trophoblast invasion and remodeling resulting in abnormal transfer of nutrients and oxygen. **Objectives:** We measured the anthropometric parameters (length, weight and head circumference) and the placental weight of 49 FT newborns (gestation period > 36 weeks) infants with CHD {(cyanotic (n = 8) and acyanotic (n= 41)} diagnosed clinically and by echocardiography and compared these data with those for randomly selected normal FT newborns (n= 104). **Results:** Newborn infants with CHD were significantly shorter and had lower birth weight and smaller head size compared to normal newborns. Their placental weights were significantly decreased compared to those for normal newborns. However, there was no statistically significant difference in the anthropometric parameters of infants with cyanotic versus acyanotic heart disease. **Discussion:** The intrauterine growth restriction in newborn infants with CHD may represent an adaptive mechanism to cope with the compromised perfusion caused by the congenital cardiac anomaly. However, this restricted growth can pose a risk for postnatal development in these infants. **Conclusion:** In this study CHD was associated with significant affection of birth weight, length and head circumference and lower placental weight compared to normal newborns.

Ellis-van Creveld Syndrome – A case report

Baker Ayyash

Introduction: Ellis-van Creveld syndrome or chondroectodermal dysplasia is a rare, autosomal recessive disorder. It was first described in 1940 by Richard W.B. Ellis and Simon van Creveld now known as Ellis van Creveld syndrome. It is characterized by a tetrad of clinical manifestations of chondrodystrophy, polydactyly, ectodermal dysplasia, and cardiac defects. Mutations of the EVC1 and EVC2 genes, located in a head to head configuration on chromosome 4p16, have been identified as causative. Diagnosis is usually made clinically by observing the signs and symptoms and supported by skeletal survey. **Patient:** We report a 2 years old male who presented to our endocrine clinic for short stature. The child showed the typical features of Ellis-van Creveld syndrome. He was born full term by LSCS with normal Apgar score and birth weight of 2.82 kg. He has polydactyly of both hands and right foot, and syndactyly of the right foot. He also manifested hypoplastic nails, low set ears, and small mandible. The oral examination revealed multiple labial frenula in relation to upper lip. Immediately after birth, the child developed cyanosis which was not responded to Oxygen therapy. Echo done and showed TAPVD which was repaired. Skeletal survey showed marked congenital dysplasia. There is history of parental consanguinity. **Discussion:** The syndrome is characterized by high mortality in infancy and early life because of severe restriction imposed by short ribs and narrow thorax. Presence of congenital heart diseases like common atrium, AV canal defect and VSD also contribute to early morality. 33% can die in infancy or at an early age because of cardiorespiratory problems. EVC needs to be distinguished from a number of closely related entities. Weyer's acrofacial dystosis is an autosomal dominant condition with many clinical features similar to EVC. However, the patients are often of normal stature and cardiac defects and thoracic dysplasia are absent. Jeune syndrome, another related disorder, is an autosomal recessive condition characterized

by small chest, renal anomalies and retinal degeneration. Cardiac defects are seldom present. **Conclusion:** Ellis-van Creveld syndrome should be considered in children with short stature, cardiac defect and polydactyly. Consanguinty is an important association with the disease. This is the first case of confirmed Ellis-van Creveld to be reported from our region.

Variable phenotype of 3-M syndrome in 4 siblings and the impact of growth hormone treatment on height velocity

Omar Afandi

Introduction: 3-M syndrome is a rare autosomal recessive disorder caused by mutations in the CUL7, OBSL1 and CCDC8 genes. It is characterized by dwarfism, dysmorphic features and skeletal abnormalities. Data in the literature showed moderate efficacy of growth hormone in the treatment of dwarfism in 3-M syndrome. **Patients:** We report 2 Emirati siblings- 22 years old and 10 years old, with characteristic features of 3 M syndrome, including a triangle-shaped face with a pointed chin, long philtrum, and a prominent mouth with full lips. Genetic testing confirmed the deletion of an exon in the CUL-7 gene. In view of the dwarfism, rhGH therapy was started for the younger sibling. **Discussion:** The parents are healthy 1st degree cousins with 9 children, of whom two died in the first year of life with thoracic dysplasia. Both our cases had low birth weight and growth retardation. The older sibling reached an adult height of 117 cm (-6.71 SD). She was never treated for short stature. The younger sibling is currently 111 cm (-4.27 SD for age). We started treating him with rhGH at 7 years of age when his height was 94 cm (-5.05 SD for age). His growth velocity is noted to be 5.68 cm/year. **Conclusion:** 3 M syndrome should be considered in children with short stature who have associated skeletal abnormalities. The diagnosis is more likely in family with history of consanguinity and with more than one affected siblings. Presence of death in early infancy due to thoracic dysplasia is another major clue to diagnosis. Genetic testing is important for confirming the diagnosis and for genetic counselling. Growth hormone treatment might be beneficial in improving stature in affected children.

A boy with decelerated linear growth, normal growth hormone (GH) insulin -like growth factor (IGF-I) axis with an exceptional response to GH therapy

Ashraf Soliman

Y M is a boy who presented at the age of 5.5 years with slow growth He was the outcome of normal pregnancy with a birth weight = 3.1 kg and length = 49.5 cm. Infantile and early neonatal periods are uneventful. He had normal development and appropriate nutritional history. No family history of endocrinopathy and/ or short stature was reported. On examination his weight = 16.9kg, height = 104 height = 104 (HtSDS = -1.84) and BMI = 16. His mid-parental height (MPHt) = 172cm (SDS = -0.6). He had no dysmorphic features, skeletal anomalies, goiter or pigmentation. The rest of the examination of the heart, chest, abdomen and genitalia is unrevealing. A year later, he comes for follow-up. His measurements are: weight= 16.9 kg, Height = 104 cm (HtSDS = -1.8), growth velocity (GV = 1 cm/y) and BMI= 16. Physical examination did not show abnormalities. Investigations showed normal CBC, liver and renal functions, ESR and thyroid function. Sweat chloride test, and tissue trans-glutaminase concentrations were normal. His IGF-I level = 70 (IGF-I SDS = -1) and his bone age = 3 years. The peak growth hormone (GH) response to a standard clonidine stimulation test = 10 ng/dl. Brain MRI showed normal pituitary gland. Because of the decelerated growth and marginally low IGF-I a trial of GH therapy was started (0.035 mg/ kg/day S/C HS) with a follow-up every 6 month. The results of therapy (table 1) showed a rapid catch-up of growth during the first 3 years of treatment which was maintained at a slower pace during the following 5 years. Testicular enlargement started at the age of 11 years with normal progress of puberty. At 12 years of age his HtSDS = 0.8 and bone age = 12.5 years. His predicted adult height = 181 cm. Conclusion: Prolonged GH treatment of this boy (with normal GH-IGF-I axis) with GH unexpectedly resulted in a HTSDS which surpassed his MPHtSDS by 1.4 SD.

A rare variant of turner syndrome: first clinical report from Kuwait

Kholoud Mohamed

Introduction: Turner Syndrome (TS) is characterized cytogenetically by X chromosome monosomy, the presence of an abnormal X chromosome, or mosaicism of a 45X or have an abnormal sex chromosome rearrangement. Girls with variant TS show no features, fewer or milder features of TS. We present the first clinical report of a girl with a rare variant of TS (46, X, i(X) (q10)) from Kuwait. Material and methods: A 12 year old Kuwaiti girl was referred to Endocrine clinic for short stature for which she has been started on growth hormone .Moreover, she was diagnosed of hypothyroidism and was started on thyroid replacement therapy. Full assessment and completion of the workup for short stature and hypothyroidism was started at the Endocrine clinic. Results: On assessment at the Endocrine clinic, her height was at -4 SD. She had no physical features of Turner syndrome. Chromosomal analysis of her peripheral blood using G-banding technique revealed 46, X, i(X) (q10). Thyroid function test was normal on treatment with negative anti-TPO antibodies. Ultrasound of the abdomen and pelvis showed small uterus for her age and non-visualized ovaries with no renal anomalies. Echocardiography was normal. ENT examination showed secretory otitis media.

Treatment of precocious puberty with LHRH Agonist Experience of the department of Sfax

Sana Kmiha

Introduction: The treatment of central precocious puberty (CPP) can control the development of secondary sex characteristics and improve the final height limited by the accelerated bone maturation. The long-acting LHRH agonists represent a therapeutic progress in the treatment of CPP. **Aim:** to report our experience on the treatment of (CPP). **Patients and methods:** Were included nine patients with CPP treated with LHRH agonist in the pediatrics department in Hedi Chaker hospital in Sfax over a period of 26 years (1983-2008). **Results:** During the period of the study we collected 15 cases of CPP. Only nine children were treated with LHRH agonist. The treatment was started at a mean age of 4 years (from 11 months to 8 years). All the girls have Tanner 2 to 4 Breast development and pubic or underarm hair development in 5 cases. The two boys have pubic or underarm hair development and an enlarged testicles and penis. Eight children have a short stature. Accelerated bone maturation and biologic signs of hyper function of the hypothalamic-pituitary axis were found in all cases. The causes of CPP were hypothalamic hamartomas in 2 cases, hydrocephaly in 1 case and CPP was idiopathic in 6 cases. All children were treated with triptorelin (Decapeptyl) at a dose of 60μg/kg/month. The duration of the treatment varied from 4 months to 3 years. After a mean retreat of 3 years, secondary sexual characteristics regressed in 5 cases and were stabilized in the other cases. After 6 months of treatment, height velocity and bone maturation decreased and biology was normal. Pelvic ultrasonography showed a decrease of the volume of the uterus of all the girls. After treatment was stopped, outcome was favorable in one girl, while three other girls showed an increase in height velocity with reappearance of pubertal signs. Treatment is still prescribed for 4 children. One patient was loss of sight after 6 months of the beginning of the treatment. **Conclusion:** The LHRH agonist is a well-established therapy for clinical and biological signs of CPP. It also increases the final height, without antifertility effects.

Precocious puberty caused by VWGS: case report from Kuwait

Abeer Altararwa

Introduction:Hypothyroidism is among the most common endocrine disorders in children. Generally hypothyroisidm is associated with delayed sexual maturation and delayed puberty, however, rarely, it is associated with paradoxical precocious puberty especially in long standing untreated acquired hypothyroidism. The syndrome consisting of primary hypothyroidism and precocious puberty was first described in 1905, but later on the term Vk-Grumback (VWGS) was known to describe a condition involving incomplete isosexual precocity (premature menarche, premature thelarche, absence of pubic hair and abnormal milk production), primary hypothyroidism, bilateral ovarian cysts, and pituitary adenoma. The exact pathophysiology is not clear. It involves complex interaction between hypothalamic-pituitary hormonal axis. However, many theories have been put forwarded which proposed an overlap of the negative feed-back regulation with overproduction of gonadotrophins as well as thyrotropin releasing hormone in response to thyroid deficiency. Thyroid replacement plays a

vital role in normalizing all hormone abnormalities and shrinking the pituitary adenoma. Aim: to describe the clinical and the pathological features of 7 yr and 11 month old girls with VWGS.

Is a single pelvic ultrasound enough to diagnose peripheral precocious puberty etiology?

Ouarezki Yasmine

Peripheral precocious puberty is relatively rare; the most common etiologies are Mac Cun Albright syndrome and ovarian tumor. Pelvic ultrasound is a simple examination that leads to diagnosis in most cases, but this did not apply for our three patients.
The aim of our study is to highlight the importance of repeating pelvic ultrasound in PPP and completing the investigations by MRI in some patients. **Methods:** retrospective and observational case report of three patients. Growth spur and pubertal staging according to Tanner-Marshall method were evaluated on physical examination. Bone age was estimated according to Greulich and Pyle, LH-RH test confirmed true precocious puberty if peak of LH < 5 mUI/ml after stimulation, dosage of estradiol, α foetoproteine and βHCG was done. Pelvic ultrasound examined the shape and size of the uterus and ovaries and MRI allowed the exact diagnosis.PPP was diagnosed in patients showing early signs of puberty with abnormal pelvic ultrasound and normal LH levels after LH-RH stimulation. **Results:** 3 cases of PPP are reported; age at onset of puberty was 3, 4 and 6 years old. The first sign was premature thelarche in two patients and premature pubarche in the third. First pelvic ultrasound was normal in the first patient, the other two showed signs of puberty but normal ovaries. Repeated ultrasound showed ovarian tumor in one patient, and ovarian cysts in the others. Pelvic MRI was then performed and revealed an ovarian teratoma LH-RH test was carried out for two patients and was normal. Estradiol level was very high in all cases. All patients underwent surgical treatment with good results **Conclusion:** we can underline the importance of a long follow up in PPP, this can lead to diagnose the etiology years after the onset of puberty.

Testotoxicosis or Familial male precocious puberty: treatment approaches

Zineb Imane

The testotoxicose or male precocious puberty or family is uncommon early puberty resulting from activating mutation LH receptor expressed in testicular Leydig cells. Several therapeutic approaches have been reported but few studies on the effectiveness of treatment in the long term. We report the case of a 3 year old boy sent by the surgeon for signs of precocious puberty found during a circumcision. Examination revealed a weight and size> 3 + DS,penis size over 2DS right and left testis measuring 2.5 / 1.5cm.. Bone age in our patient is 7 years (AC: 3 years). And hormonal laboratory reveals a high level of testosterone to 4 ng / ml and a base rate of FSH and LH low. The test of hypothalamic LHRH and MRI are for the peripheric cause. Other causes of peripheral precocious puberty were eliminated. The genetic study in our patient shows a pathogenic heterozygous mutation M398T in exon 11 of the gene with the LH receptor polymorphism in exon 1, L16Q. Both mutations were found in the father while the mother was unharmed.Treatment with ketoconazole is started at a dose of 20 mg / Kg / day with good therapeutic response in the medium term. Relating with this new observation, we will discuss treatment options and their effectiveness in the short and long term.

Micropenis: prevalence and etiological profile in Morroco

Hajer Berrani

Objective: Determine prevalence and etiological profile of micropenis. Patients and methods: A descriptive and retrospective study from January 2004 to December 2012 at endocrinology unit of Rabat children's hospital. Results: One hundred and thirteen child were collected during the study. The incidence of micropenis was de 7 new cases in 2003, de 17 in 2006, 22 in 2011 and 30 in 2012. The mean of age of our patients was 6.8 ± 2.5 years. The mean length of penile was 2.2 ± 0.5 cm in our series. Concerning the etiological profile of micropenis; central abnormalities of testosterone secretion was

responsible of 14,2%, abnormalities of testosterone action (androgen insensibility or deficit of 5 α reductase) of 30,1%, genetic causes of 16,81% and the micropenis was idiopathic in 39%. **Conclusion:** Prevalence of micropenis is increasing in our service. Etiology are multiples but idiopathic causes stay majoritarian in our series, which suppose hypothesis on parental contamination by endocrine perturbation.

Vitamin D Deficiency Preventable, Reversible Cause of infant heart failure

Fawziya Al khalaf

Hypocalcemia reduce myocardial contractility but incidence of congestive heart failure due to hypocalcemia is quite rare. We report five months old breast feed infant with clinical evidence of nutritional ricket with dilated cardiomyopathy.she responded very well to calcium supplement and vitamin D.The calcium level normalized within 5 days along with gradual improvement of signs and symptoms of heart failure. Left ventricular function and QTc were normalized within 3 months. Pediatrician should be aware that hypocalcemia secondary to vitamin D deficiency is possible reversible cause of heart failure.

A 6 month old female patient with primary hyperparathyroidism

Marise Abdou

Introduction: Hyperparathyroidism is characterized by proliferation of the parathormone (PTH) secreting cells in one or more of the 4 parathyroid glands. It may be primary due adenoma or hyperplasia caused by genetic mutations or due to various underlying conditions causing hypocalcemia as in cases of secondary hyperparathyroidism. Tertiary hyperparathyroidism occurs in cases of prolonged severe uncontrolled secondary hyperparathyroidism when PTH secretion becomes autonomous. This case is remarkable as primary hyperparathyroidism is a rare disease of childhood. The condition is even rarer during infancy and is often fatal. **Case Description**: A 6 month old female presented to the hospital with medical history of recurrent chest infection, purpuric rash on the abdomen and pallor for which she was admitted. Physical examination was remarkable for failure to thrive and hepatospleenomegaly. Laboratory findings demonstrated anemia, thrombocytopenia, hypercalcemia, hypophosphatemia, hypercalcuria and elevated parathormone levels. Bone marrow aspirate was done revealing hypocellularity. Skeletal survey was performed showing osteopenic bone texture, extensive subperiosteal bone resorption of the metacarpal bones, phalanges, distal ulnar border as well as the right femoral head causing total vanishing with residual ill-defined proximal shaft. Abdominal ultrasound revealed the presence of hepatospleenomegaly. Chest CT examination showed ground glass mosaic attenuation of both lung fields. MRI of the brain, neck, chest and abdomen demonstrated no abnormality. Tc^{99} parathyroid scintigraphy was negative for parathyroid adenoma. The patient was diagnosed to have primary hyperparathyroidism and was treated by IV fluids, diuretics (frusemide) and a trial of steroids was given. Successful parathyroidectomy was done and the calcium blood levels decreased postoperatively. Pathological examination of the removed parathyroid gland revealed hyperplasia. However, the patient's condition deteriorated because of nephrocalcinosis which led to renal shutdown and the patient died.

Incidental Diagnosis of 46XXX Karyotype during Admission for Bronchilits

Dr Abdulmagid Bin Nasrat

The external physical features in a child can be sign of the ailments the child is suffering from. However, sometimes there are subtle features, which may be overlooked due to the by the acute trivial problem, and an underlying condition of more long term sequels and implications can be missed. **Case report:** We report 9 month old female born to 46 years old mother at time of birth. Baby born 38 weeks gestation, induced delivery due to maternal diabetes. She was admitted with history of coryzal symptoms and reduced feeding for three days before admission. On examination, the child had signs and symptoms of bronchiolitis. She had slightly up slanting / Mongoloid eyes with mild hypotonia but no other features of Trisomy

21. Mother and brother had phenotypical characteristics similar to the child's. As mum was 46 years and the baby has some features of Trisomy 21. Chromosomal analysis was undertaken which was found to be 47XXX. **Conclusion:** proper physical examination of children admitted for common pediatric disease might reveal other associated abnormalities that might have long term implications.

Keep Sugars on Sheets to Allow for Play and Treats; the Diabetes Automated Manager

Ahmad AbulAinine

Introduction: Day-to-day management of diabetes in children is a continuous challenge not only for the child and his family but also for the health care professionals offering diabetes service. Besides the human factor, there is a multitude of unravelled "biological" territories; which makes a difficult job even harder. Methods: We explored the interconnections between various biological factors influencing glycaemic control. Various methods were tried to develop equations that correlate these factors in children. **Methods**: extrapolating adult diabetes practices and methods specifically developed for children were examined. The latter are tailored to children at various ages based on pharmaco-kinetic principles, considering food, insulin and exercise. Utilising what could be described as gluco-kinetics and insulino-dynamics. **Results:** Over several years, adult methods were found unreliable in growing children, particularly amongst the younger ages. It was found that "Pediatric Clinical Diabeto-Kinetics" approach suits children better. The methodology was so detailed that it had to be transformed into a "Diabetes Automated Manager". The computer utilises lots of variables to enable the professionals provide a detailed care plan in few minutes, print it on just one sheet to be used by parents to guide their child's diabetes care. Conclusion: This effort could lay the foundations of an innovative approach to understand, teach and manage diabetes, insulin, food and exercise; amongst other variables. It needs to be tried on a wide scale to define its place in science and practice.

An Innovative Computer Program for Lifestyle and Weight Control

Ahmad AbulAinine

Introduction: Obesity is a rapidly growing threat to children's health worldwide. It does not only pose challenges for the child, his/her family and various health professionals, but also drains resources into what is largely an avoidable problem. However, patients may not see the problem and may feel "offended" on counselling. Frequently, mis- understanding fuels frustration that bars attending or listening to health professionals. The traditional methods to explain the factors leading to obesity and the relative roles of "lifestyle remedies" such as: daily activity, sleep, exercise or dieting are not always rewarding. **Methods:** We developed a computer programme that helps children and carers' test the effect of various lifestyles before their own. Additionally, children could try out the effects of "healthy & doable" lifestyle combinations over their chosen times. **Results:** The program was un-confrontational and efficient in making children and their parents realise the roles of lifestyle elements in obesity in general. Additionally, it allowed them to engage in designing their own lifestyle modifications, and reaching an agreed therapeutic goal over durations and time scales of their own choice. **Conclusion:** This combination of interactive tools built in LAWAD, was not only helpful in clinics to help treat obesity, but also we could roll it out for educating children in schools in an effort to halt the rising obesity pandemic.

Unexplained Hypothermia; A Case Report

Ahmad AbulAinine

Introduction: We have always thought of humans as warm-blooded beings. However, we report a 9 year old girl who is comfortable while her core temperature was irrecordable (<33^{o}C) and gets uncomfortable when warmed her up to 35^{o}C.

Methods: We reviewed the literature for reported similar cases, investigated the mechanism of thermal control structurally from the gross anatomy to genetic and molecular levels. We have investigated her from the electro-physiology and the metabolic aspects by running an electromyogram and dynamic hormonal testing. **Results:** Her resting metabolic rate was found to be low. She did not respond to arginine or insulin growth hormone stimulation tests. She showed myasthenia gravis pattern on electromyography but not on immunologic studies. Treatment with GH or pyridostigmine did not result in any improvement of her core temperature in spite of being subjectively feeling better energy levels. **Conclusion:** The exact etiology of the hypothermia in this girl remained unexplained.