PREDICTION AND PREVENTION OF TYPE 1 DIABETES MELLITUS

Abdullah Al Herbish FRCPC, FAAP
Professor and Pediatric Endocrinologist KSU / HMC

Type 1 Diabetes Mellitus (T1DM) is a chronic inflammatory disease caused by a selective destruction of the insulin producing Beta cells in the pancreatic islets of Langerhaus leading to disturbance in Carbohydrate, protein and fat metabolism. Incidence and Prevalence are increasing worldwide. We are perhaps witnessing a 400 fold increase in the last few decades. The aetiology and the exact pathogenesis remain a mystery. The natural history is however well explored in the recent literature. There is a well established genetic susceptibility and protection link. This is clear in the studies done on monozygotic twins and first degree relatives to patients with T1DM. These are also many contributing environmental factors towards development of multiple specific antibodies preceding overt diabetes. Many studies established a predictive association of both genetic as wells as autoimmunity disturbance. The T1DM is of a significant burden for both the individual and the society. Several attempts have therefore been conducted trying to come up with a safe and effective way to prevent T1DM. Studies like Environmental Determinants of Diabetes in the young (TEDDY), Diabetes Autoimmunity study of the young (DAISY) and The prospective assessment of newborns of diabetes Autoimmunity (PANDA) looked at the predictive factors. The European Nicotinamide Diabetes Intervention Trial (ENDIT), Diabetes Prevention Trial - Type 1 (DPT - 1), Trial to Prevent Diabetes in the Genetically at Risk (TRIGR) did not however respectively prove a clear benefit from Nicotinamide, insulin or cow's milk avoidance.

Prevalence of Type 1 Diabetes Mellitus

by:

Al Herbish A., El Mouzan M., Al Salloum A., Al Qureshi M., Al Omar A.

Diabetes Mellitus (DM) is becoming a very common disease in this century. It's incidence and Prevalence are increasing. This is unfortunately true not only for Type 2 but also for Type 1 DM. There are many epidemiological studies in the Arab world showing the frequency, Incidence and Prevalence of Type 1 DM. Some of these studies are hospital based with extrapolated epidemiological figures and some are community based which give a more realistic and accurate figures. These epidemiological studies are important not only as reference for the database but also vital when the aetiology and the clinical presentation are considered.

Through a nationwide project supported by King Abdulaziz City for Science and Technology in Saudi Arabia looking at the health profile of Saudi children and adolescents from birth to 19 years of age, inquiry about some chronic illnesses like Type 1 DM was made. Type 1 DM is a disease with clear symptoms and treatment (injections, etc.) so it was easy to document presence of this disease based on a questionnaire. Random selection of households was done based on the most recent Saudi national census where multi stage probability sampling was conducted all over the Kingdom of Saudi Arabia. 45,682 children and adolescents were surveyed, where households were visited by trained health personnel to record the requested information. The number of children and adolescents with Type 1 DM identified was divided by the denominator of a sample size. 50 were found to have Type 1 DM giving a prevalence of 10.95 per 10,000. The male to female ratio was almost equal (26 males and 24 females). The higher prevalence as per age was among adolescents 13-16 years showing a prevalence figure of 24.3 per 10,000. The region which had the highest prevalence was the central region showing a prevalence of 16.2 per 10,000

Prevalence of Type 1 Diabetes Mellitus in Saudi Children

By: Abdullah Al Herbish FRCPC, FAAP

Diabetes Mellitus (DM) is becoming a common disease worldwide. Its incidence and prevalence is increasing. This increase is also projected to give rize to high number of affected individuals. This is unfortunately true not only for Type 2 but also for Type 1 DM. This country is not immune against this rize of this disease.

There have been several studies indicating prevalence, incidence and frequency of DM in children and adolescents in Saudi Arabia. Some of these studies are hospital based with extrapolated incidence and prevalence and some are community based studies with random sampling reflecting a more realistic figures. In a recent study conducted on a representative sample of Saudi children and adolescents the prevalence was estimated to be 11 per 10,000.

Establishing incidence and or prevalence periodically is essential for every community. This is not only for statistical purpose but also to gain more knowledge in the epidemiological factors which may delinate the aetiology of this chronic disease.

Prevalence of Type 1 Diabetes Mellitus in Saudi Arabia Children and Adolescents

AL HERBISH Abdullah[1], El Mouzan Mohammed[1], Al Salloum Abdullah[1], Al Qureshi Mansour[2], Al Omar Ahmed[2]

1. King Saud University, Riyadh
2. Ministry of Health, Riyadh

Introduction:

Type 1 Diabetes Mellitus is a chronic disease which is becoming more prevalent worldwide. Data from various neighboring countries show different figures. Most of the data from Saudi Arabia and these countries are extra polluted hospital based data.

Aim and Material:

Through a nationwide project supported by King Abdulaziz City for Science and Technology looking at the health profile of Saudi children and adolescents (0-19 years), enquiring about chronic illnesses and Type 1 Diabetes Mellitus was conducted. Type 1 Diabetes Mellitus is a clear disease with clear symptomatology and treatment (Insulin injection ... etc), so it was easy to document presence of this disease. Random selection of households was done based on the most recent Saudi national census. Households were visited by a trained health team to record a vast amount of information in connection to children and adolescent health in particular presence of Type 1 Diabetes Mellitus. Number of children and adolescents identified was divided by a denominator of the sample size. This was expressed per 10,000.

Results:

45,682 children and adolescents were surveyed. 50 were found to have Type 1 Diabetes Mellitus giving a prevalence of 10.95 per 10,000. The male to female ratio was almost equal (26 males and 24 females). The higher prevalence as per age was among adolescents 13-16 years when 23 out of 9465 were affected (prevalence of 24.3 per 10,000). The highest prevalence is needed in the central region (16.2).

Conclusion:

Type 1 Diabetes Mellitus is an important prevalent chronic metabolic disease with an overall prevalence of almost 11 per 10,000. We feel this figure is quite representative one as this is a community based study.

Sex Assignment / Reassignment: Local Experience and Recommendations

by :

Abdullah Sulaiman Al Herbish

Disorders of sex development (DSD), a term recommended by the International consensus of Wilson and Wilkin, Pediatric Endocrinology Society and the European Society for Pediatric Endocrinology in 2006 replacing the old terminology like Intersex, etc. , are not uncommon among Arabs. Hospital based studies and the clinical experience of Pediatric Endocrinologists indicate that DSD constitute a major clinical and social problem. It is therefore essential for clinicians to be aware of the basic contributing factors known up to date for normal sexual differentiation in the human. Once the aetological factors which may lead to genital ambiguity are understood, It then becomes relatively easy for clinicians to manage once confronted with such conditions. It is now clear that the SRY gene located in the short arm of the Y Chromosome is very important segment for normal male sex determination. In its presence the gonadal ridge will differentiate to be testicular. There are however many factors and co-factors which play an important role in this process. Example of these factors include Lhx9, SF1, WT1, GATA4, SOX9, DAX1, SOX3, FOXL2, WNT4, Lhx1, Emx1, Pax2. There maybe also some important factors for the ovarian development. Once the testicle is differentiated it releases local testosterone which enhances the development of the internal male organs and mullarian inhibitory factor (MIF) which inhibits the Mullarian structures from development. In the case of the female fetus as there is no testosterone or MIF the male internal structures will regress and female structures will progress. The external genitalia is affected by the presence of a normal dihydrotestosterone and testosterone released from testicles which eventually leads to the normal penile development and the normal scrotal fusion. The last but also important part of sexual differentiation is the psychological adjustment towards the own gender. The

most common cause of 46XX DSD is congenital adrenal hyperplasia leading to excessive androgens causing the virulization of the external genitalia of the female. The causes of 46XY DSD includes pituitary, testicle and tissue defects. Diagnosis of clinical conditions which may lead to ambiguity is important for the final management. Management of SDS is challenging. It requires a team of a Pediatric Endocrinologists, Pediatric Surgeon, Psychologist or child Psychiatrist in addition to other supportive services. Clear discussion with parents is always advisable. The final decision for sex assignment and reassignment requires a group decision based both on the clinical aspect in addition to the recommendations available. Presently there are clear religious (Islamic) recommendations towards management of children with DSD.

Sex Assignment / Reassignment

by :

Abdullah Sulaiman Al Herbish FAAP, FRCPC
Professor and Pediatric Endocrinologist
King Saud University and Dr. Sulaiman Al Habib Medical Center

Disorders of sex development (DSD), a term currently recommended by the International 2006 consensus of Wilson and Wilkin Pediatric Endocrinology Society and the European Society for Pediatric Endocrinology replacing the old terms like Intersex, etc., are not uncommon. Hospital based studies and the clinical experience of Pediatric Endocrinologists indicate that DSD constitute a major clinical and social problem. It is therefore essential for clinicians to be aware of the basic contributing factors known up to date for normal human sexual differentiation. Once the aetological factors leading to genital ambiguity are understood, it then becomes relatively easy to manage such conditions. It is now clear that the SRY gene located in the short arm of the Y Chromosome is a very important segment for normal male sex determination. In its presence, the gonadal ridge will differentiate to be a testicule. There are however many factors and co-factors e.g. Lhx9, SF1, WT1, GATA4, SOX9, DAX1, SOX3, FOXL2, WNT4, Lhx1, Emx1, Pax2 which play an important role in this process. There may be also some important factors for the ovarian development. Once the testicle is differentiated, it releases local testosterone which enhances the development of the internal male organs and mullarian inhibitory factor (MIF) which inhibits development of the Mullarian structures. In case of the female fetus, as there is no testosterone or MIF, the male internal structures will therefore regress and the female structures will progress. The external genitalia is affected by the presence of a normal dihydrotestosterone and testosterone released from testicles which eventually lead to the normal penile and scrotum development. The last but also important part of sexual differentiation

is the psychological adjustment towards one own's gender. The most common cause of 46XX DSD is congenital adrenal hyperplasia leading to excessive androgens causing virulization of the external genitalia of the female. The causes of 46XY DSD includes pituitary, testiclular and tissue defects. Diagnosis of clinical conditions which may lead to ambiguity is important for the final management. It consists of chromosome studies, imaging and enzyme substrate assays. Management of DSD is challenging. It requires a team consisting of a Pediatric Endocrinologist, Pediatric Surgeon, Psychologist or child Psychiatrist in addition to other supportive services. Clear discussion with parents is always advisable. The final decision for sex assignment and reassignment requires a group decision based on clinical, legal and Islamic recommendations available. This presentation will cover sexual development, possible aetiologies and its management based on these recommendations.

Update in Management of Diabetes Mellitus

by:

Abdullah Al Herbish FRCPC, FAAP

Professor and Pediatric Endocrinologist

King Saud University and Dr. Sulaiman Al Habib Medical Center

Diabetes Mellitus (DM) is a chronic metabolic disorder which affect carbohydrate, fat and protein metabolism leading to serious long term complications and sequalae. DM is classified into 4 major types (Type 1, Type 2, other specific types and gestational diabetes. DM has unfortunately become an epidemic in many countries reaching a prevalence figure of 23% for Type 2 DM in the Saudi Arabian population older than 30 years and 109.5 per 100,000 for Type 1 DM in the Saudi Arabian children and adolescents 0 to 20 years of years of age. Lifestyle changes which the community has witnessed in the recent years may have contributed to the increasing incidence and prevalence of Type 2 DM. Type 1 DM is also increasing with no clear-cut aetiological factors. Prediction of Type 1 DM is therefore difficult and clinical trials studies have failed to reach to a clear preventive nutritional, environmental or pharmacological agents.

Frequency of severe Diabetic Ketoacidosis (DKA) is becoming less frequent due perhaps to the increased level of education and health awareness in the community. Priorities in DKA management include resuscitation, correction of acidosis, ketosis and hyperglycemia in this order. This is usually achieved by fluid and insulin administration with continuous monitoring to avoid the rare but serious complication namely cerebral edema.

A challenging cornerstone of DM management is the child and the family education. This is usually done during the initial few days of the diagnosis which unfortunately is characterized by the shock, denial and depression, the usual psychological stages in response to any bad event namely DM. Most families regardless of their educational and professional background adjust very well and learn all the skills of DM management. Long term management is offered through physical activity, diet and insulin. Insulin administration include many methods (1) The traditional twice a day method (2) The modified insulin regiemen (3) The intensified insulin regiemen (4) Insulin pump (5) Inhaled insulin (approved but .....). Future carries many promising treatment plans (1) Islet cell transplantation (2) stem cells (3) Development of reliable and realistic prediction and prevention methods.

Complications of DM are rare in children but it is important to have good preventive measures.

Growth Charts for Saudi Arabian Children and Adolescents

by:

Al Herbish A., El Mouzan M., Al Salloum A., Al Qureshi M., Al Omar A.

Normal Growth is the ultimate goal for children and adolescents both in health and disease. Growth charts have been established as early as the nineteenth century. Most clinics use growth charts which have its roots from Tanner et al and Hamil et al work in England and USA respectively. WHO approved the NCHS charts which have been recently updated by the CDC. Several studies have been performed in the Arab world. In Saudi Arabia, Many attempts were performed towards establishing normal growth parameters for children and adolescents. Many of these attempts were age, sex, or region limited and therefore did not spread for national use. Al Amoud et al studies established an excellent growth charts for the 0-5 years age group and gained the Saudi Ministry of Health support for clinical use. These charts however remained age limited. In 2001-2007 a national study conducted by El Mouzan et al and supported by King Abdulaziz City for Science and Technology, Ministry of Health and King Saud University, Saudi Arabia studied multi stage probability randomly selected children and adolescents (0-19 years). The Waterlow criteria were applied in the study. 14,000 households were selected and visited by a team with anthropometric measurement tools. Questionnaire was used for each family to inquire about important related matters like exact date of birth, parent's health status, peri-natal history, evidence of chronic illnesses etc. Accuracy was observed as the tools was calibrated and tested. Intra and Inter observer variation was done. Data was subjected to all the statistical recommended ways of checking accuracy, cleaning... etc. Statistical analysis of growth data was performed using LMS (Lambda, Mu, Sigma) methodology proposed by Cole and Green and widely regarded as an effective means for estimation of population percentiles. Only eligible children and adolescents were considered for anthropometric

measurements. The format used in NCHS and CDC growth charts was adopted. Two groups of growth charts were produced. One for birth-36 months of age, and another for 2-19 years age. In each group, ten Charts (5 charts for each gender group) were produced. These included weight for age, length/height for age, head circumference for age, weight for length, and Body Mass index (BMI) for age. 9 percentiles were produced namely 3rd, 5th, 10th, 25th, 50th, 75th, 90th, 95th, and 97th percentile. An additional 85th percentile was produced for BMI charts.

We conclude that these growth charts are the first of their kind which cover all age group birth-19 years of age for both boys and girls in a sample which we feel is very much representative of the Saudi population. We feel that these charts are better used when assessment of children and adolescent growth is considered.