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RESEARCH ARTICLE

Glycemic Control in Youth with Type 1 Diabetes Mellitus in Saudi Arabia

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Abstract

Objective: To determine the glycemic control and cardio-metabolic complications of children and adolescents with type 1 diabetes mellitus (T1DM) attending a tertiary care diabetes clinic in Saudi Arabia.

Methods: We conducted a retrospective cross-sectional study of children and adolescents with T1DM attending King Abdulaziz Medical City-Jeddah from 2010 - 2013. We assessed their glycemic control and diabetes management. Vitamin D status was compared with glycemic control and gender differences.

Results: We identified 301 subjects (53.5% females), mean age was 13.9 ± 3.8 years. The mean duration of diabetes was 7.7±3.7 years, BMI 21.1±4.5 kg/m^2 and HbA1c was 9.6±1.9% in both genders. There were modest gender-specific differences in Saudi patients with T1DM, with males having more symptoms than females. Mean age at diagnosis of T1DM was slightly younger in males (6.01±3.65 years) than females (6.33±3.45 years). In males, the most common reason for admission was education (32.9%) while diabetic ketoacidosis (DKA) was the most common reason for females (38.8%). Frequency of symptomatic hypoglycemic attacks was relatively higher in males (47.1%) than in females (42.9%).

The majority of our patients (83%) were on intensive insulin regimen, having 4 injections or more per day. The remaining (17%) were on conventional insulin therapy.

Only 26.2% had satisfactory HbA1c (≤8%). The mean level of 25 hydroxy vitamin D was 35.15±15.9 nmol/l and cholesterol was 4.75 ±1.1 mmol/l. Vitamin D deficiency (25 hydroxy vitamin D ≤ 37.5 nmol/L) was detected in 63.6% males and 67.7% females. No significant correlation between HbA1c and vitamin D deficiency was observed.

Conclusion: Metabolic control among Saudi children with T1DM is less satisfactory compared to other countries. The high prevalence of vitamin D deficiency in this population supports the recommendation of vitamin D supplementation in T1DM subjects. Further studies in a larger cohort are needed to confirm our findings.

Keywords: Type 1 Diabetes Mellitus; Glycaemic Control; Youth

Introduction

Type 1 diabetes mellitus (T1DM) currently affects an estimated 500,000 youth under the age of 15 years old worldwide, with the highest prevalence found in Europe and North America [1]. Epidemiological data further indicates an increasing incidence of T1DM globally with an average relative increase of around 3-4% per year and with an age of onset younger than previously estimated [2]. These observations were documented in many countries including both developed and developing countries, specifically the US, Europe, Australia, Latin America, China, South-east Asia, and India [2-9]. Diabetes type 1 was found to be most common in Finland (with > 60 cases per 100,000) and Sardinia (with approximately 40 cases per 100, 000) [10].

Over the last three decades, the incidence rate of T1DM has also been rising in Saudi Arabia [11]. The most recent data reports an incidence of 27.5/100 000 and 29/100 000 [12,13]. The prevalence of T1DM in Saudi children and adolescents is 109.5 per 100000 [14].

As demonstrated by the Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications study, the improvement of glycemic and metabolic control in both children and adolescents with type 1 diabetes lead to a decreased risk of diabetic complications [15,16]. In previous studies, poor metabolic control in adolescents has been presumed to their changing physiology (pubertal development and growth) as well as to adherence and behavioral issues [17,18]. Previous studies demonstrated that optimal metabolic control is imperative for the prevention of long- term diabetes complications [19,20].

In the present study, we endeavored to determine the current status of glycaemic control, diabetes management and the impact of different factors such as age, gender, pubertal stage, duration of diabetes and insulin regimen on the metabolic control of children and adolescents with T1DM attending the pediatric endocrine clinic at King Abdulaziz Medical City (KAMC) in Jeddah city, Saudi Arabia.

Methods

The study was approved by the Institutional Review Board of King Abdullah International Medical Research Center. In this retrospective cross-sectional study, we included all children and adolescents between the ages of 1 and 18 years with known T1DM and who had regular follow-up for more than 3 months in the pediatric endocrine clinic at KAMC from January 2010 to January 2013. We collected data on gender, puberty staging, duration of T1DM, symptoms at presentation as well as clinical information such as blood pressure (BP) using the Dinamap automated oscillometric device and body mass index (BMI) using Center for Disease Control and Prevention charts. Data on hemoglobin A1c (HbA1c), 25-hydroxyvitamin D [25(OH)D] levels, lipid profile, and thyroid function were also collected from the medical records. At the time of our study, we followed the American Diabetes Association (ADA) 2014 Guidelines for target HbA1c levels per age group ≤ 8.5% (69.4 mmol/mol) in toddlers(1-3years), ≤ 8% (63.9mmol/mol) in school children (3-12 years) and ≤ 7.5% (58.5mmol/mol) in adolescents and young adults(13-18 years).

HbA1c was measured using ion-exchange high performance liquid chromatography technique. HbA1c values were based on measurement at regular intervals (3 months) and the average of the last 3 results in the last year of follow-up. Other variables (BP, BMI, lipid profile, and thyroid function) were recorded from the last follow-up visit.

Conventional insulin regimen was defined as the administration of 2 injections of insulin/day as a combination of regular short-acting and intermediate-acting insulin before breakfast and dinner. Intensive insulin regimen was defined as basal bolus regimen (receiving 3 rapid or short acting insulin pre-meals plus one long acting basal insulin or intermediate-acting insulin per day. Patients who were on insulin pumps were also included.

Statistical Analysis

The data analysis was conducted using Statistical Package for the Social Sciences version 14 (SPSS Inc., USA). The results are presented as means ± standard deviations for continuous variables and as percentages (%) for frequencies. Independent t-test was done to compare normally distributed variables and Mann-Whitney U-test to compare non-Gaussian variables. Frequencies were compared using Chi-square test. Linear regression using log-transformed HbA1c and vitamin D values was undertaken to identify the association between vitamin D status and glycemic control. Significance was set at a p-value <0.05.

Results

A total of 301 T1DM patients (161 females – 53.5%) were studied. Table 1 illustrates the clinical characteristics of males and females. The mean age for the group was 13.9±3.8 years (13.86±3.88 for males and 14.06±3.86 for females). Mean age at diagnosis of T1DM was slightly younger in males (6.01±3.65) than females (6.33±3.45). Pubertal signs were noted in 50.7% of male and 57.8% of female subjects. Symptoms of hyperglycemia were the most common presentation (57.9% in males; 51.6% in females). Diabetic ketoacidosis (DKA) as a presentation was more common in females (48.4%) In males, the most common reason for admission was education (32.9%) while DKA was the most common reason for females (38.8%). Frequency of symptomatic hypoglycemic attacks was relatively higher in males (47.1%) than in females (42.9%) p-value <0.46.

Parameter	Males	Females	P-Value
N	140	161	
Age (years)	13.86 ± 3.88	14.06 ± 3.86	0.67
Age of Diagnosis (years)	6.01 ± 3.65	6.33 ± 3.45	0.44
Duration of DM (years)	7.83 ± 3.81	7.71 ± 3.6	0.78
Duration of DM symptoms prior to DM diagnosis (weeks)	2.03± 1.14	2.05± 1.13	0.78
Pubertal Stage (%) **Pre-Pubertal** **Pubertal**	 49.3 50.7	 42.2 57.8	0.22
DM Onset of Symptoms **DKA(Diabetes ketoacidosis)** **Hyperglycemia symptoms**	 42.1 57.9	 48.4 51.6	0.27

Parameter	Males	Females	P-Value
Reasons for Admission			
DKA	27.9	38.8	
Education	32.9	27.5	0.22
Others reasons	39.2	33.7	
Number of Missed Clinics/year			
0	42.1	44.1	
1	40.7	37.9	
2	10.7	13.7	0.72
3	6.4	4.3	
Hypoglycemia Attacks (symptomatic)	47.1	42.9	0.46

Table 1: Clinical Characteristics of Subjects

Medications and insulin regimens used Table summarizes the insulin regimens used. The mean daily insulin dose (unit/kg/day) for males was 1.01±0.25 and 1.04±0.23 for females. Intensive diabetes therapy with multiple daily injections (MDI) was the most common therapy regimen for both sexes. The majority of our patients (83%) were on intensive insulin regimen, having 4 injections or more per day, while only 17% were on conventional insulin therapy. Insulin pump was less commonly used. Regular insulin and Lantus insulin was the most common type of insulin used (61.4% males; 64.6% females). For SMBG, most of our patients did 3-4 tests per day (54.3% in male and 49.1% in female).

Parameter	Males	Females	P-Value
N	140	161	
Daily insulin dose (unit/kg/day)	1.01 ± 0.25	1.04 ± 0.23	0.25
DM Therapy			
Conventional	17.1	14.9	
Intensive (MDI)	74.3	75.8	0.86
Insulin Pump	8.6	9.3	
SBGM Frequency			
0	5.7	6.2	
1-2	38.6	42.2	0.78
3-4	54.3	49.1	
>4	1.4	2.5	
Type of Insulin Used			
Aspart + Lantus	8.6	7.5	
Aspart + Levemir	0.7	0.6	
Aspart + NPH	0.7	0.6	
Lispro + NPH	0	3.1	0.93
Lispro + Lantus	3.6	8.1	
On pump	7.9	8.1	
Regular + Lantus	61.4	64.6	
Regular + NPH	17.1	15.5	
Number of injections/day			
On insulin pump	7.9	8.1	
2 injections	2.9	3.7	0.98
3 injections	5.0	5.0	
4 injections	84.3	83.2	

Table 2: Insulin regimens used by the patients

Anthropometric and Metabolic Data

Table 3 illustrates the anthropometric and metabolic measures of the patients. Females have a marginally higher body mass index (BMI) than males (p=0.07). There was no significant difference in blood pressure readings, lipid profile and HbA1c between both genders. The average HbA1c was 9.67±1.93 (9.66±1.98 in females and 9.7±1.8 in males). (79 out of 301) 26 % had HbA1c (≤8%). When stratified according to the age, 28.6% of toddlers, 15.6% of children and 12.8% of adolescents had acceptable HbA1c (Figure 1).

Parameter	Males	Females	P-Value
N	140	161	
BMI (kg/m²)	20.69 ± 4.45	21.63 ± 4.63	0.07
BMI Z-score	-0.11 ± 0.98	0.10 ± 1.01	0.07
Systolic Blood Pressure (mmHg)	114.19 ± 13.0	112.96 ± 10.80	0.44
Diastolic Blood Pressure (mmHg)	68.5 ± 8.14	68.29 ± 8.89	0.86
HbA1c (%)	9.7 ± 1.8	9.6± 1.98	0.29

Parameter	Males	Females	P-Value
Triglycerides (mmol/l)	1.12 ± 0.7	1.14 ± 0.57	0.92
Total Cholesterol (mmol/l)	4.68 ± 1.12	4.83 ± 1.1	0.53
HDL-Cholesterol (mmol/l)	1.19 ± 0.31	1.26 ± 0.31	0.30
LDL-Cholesterol (mmol/l)	2.87 ± 1.3	2.99 ± 0.86	0.61
25-hydroxyvitamin D (nmol/l)	36.93 ± 14.69	33.37 ± 17.28	0.02
TSH (mIU/l)	1.81 ± 1.94	2.0 ± 2.05	0.20
Free T4 (pmol/l)	9.49 ± 6.83	11.09 ± 6.02	0.11

Note: Data presented as mean ± standard deviation and as percentages (%);

# denotes Non-Gaussian variable significant at p<0.05

Table 3: Anthropometrics and Metabolic Profile of Subjects

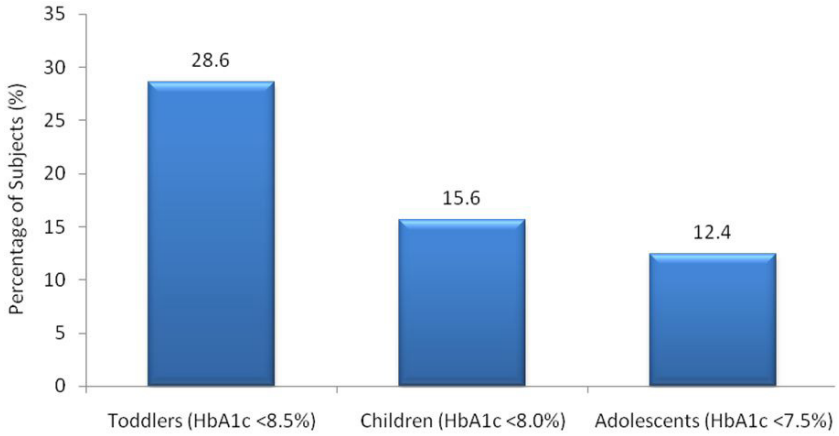

Figure 1: Percentage of subjects with good glycemic control according to the age group

The mean level of (25 hydroxy vitamin D) was 35.1±15.9 nmol/l. It was higher among males than females (36.93±14.69 versus 33.37±17.28 nmol/l; p=0.02).

There was no association between 25(OH) vitamin D level and HbA1c (Figure 2) (R=0.04; p=0.60). The total cholesterol, LDL, TG and HDL levels were higher in females than males with non-statistical significance.

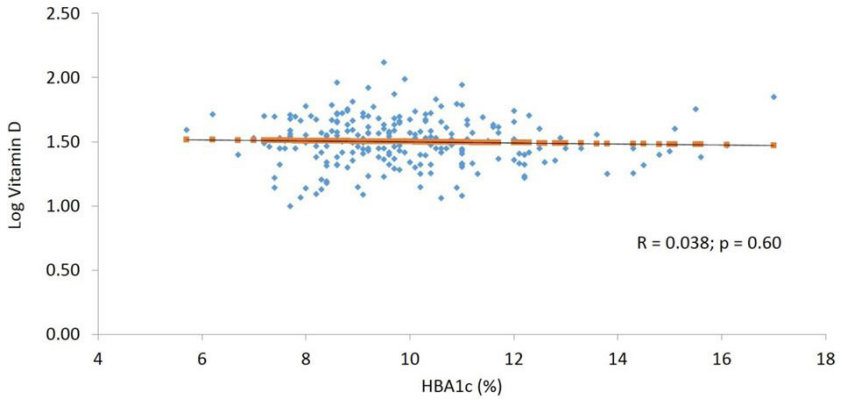

Figure 2: Linear Correlation between log vitamin D and HbA1c

The mean age at diagnosis of T1DM in Saudi Arabia, specifically the western region is comparatively younger than its European counterparts, having a median age of 7.2 years versus 6.0 [21]. Males with T1DM were displaying more symptomatic as presentation than females. The use of multiple daily insulin (MDI) regimens was the most common therapy; findings of the present study confirm the initial observations of Al-Agha and colleagues [22]. Regarding HbA1c control, 28.6% of toddlers achieved HbA1c 8.5% (69.4 mmol/mol), 15.6% of children achieved HbA1c 8% (63.9 mmol/mol) and only 12.4% of adolescents achieved good glycemic control of HbA1c 7.5 % (58.5mmol/mol).Based on the recent ADA recommendations, a target A1C of 7.5% (58.5mmol/mol) in all children with diabetes mellitus is recommended [26].

Pubertal growth and development as well as to behavioral and adherence issues may play an important role in suboptimum glycemic control. Other studies confirmed such possible attributed factors [17,18,22]. A lack of well-structured diabetes education programs for children and their families can be considered as a factor for having poor control. Physiological and hormonal changes that occur during puberty like increase in adiposity and insulin resistance can be considered as another factor [27].

Recent data on the level of glycemic control are showed by the international project SWEET in 2015, gathering data for diabetic children from 48 centers worldwide. In this consortium, the mean HbA1c for all patients is 7.8% (61.7 mmol/mol). The data from this project show that 39.1% of patients have a median HbA1c level under the ISPAD target of 7.5% (58 mmol/mol), 41.4% are between 7.5%–9% (58–75 mmol/mol) and 19.5% show HbA1c above 9% (75 mmol/mol). Wide variation still remains between different centers. Fourteen centers attained a median HbA1c 7.5% [28]. There was a relatively low use of insulin pumps among our patients. It relates to the rigidity of criteria for initiating treatment like awareness of carbohydrate counting and frequent blood glucose monitoring which is lacking duo to poor compliance. Another important reason was the parents' fears of complications like hypoglycemia, hyperglycemia and infections. Diabetic patients with poor glycemic control have high risk for complications including cardiovascular disorders even at an early age and a lower health related quality of life than their non-diabetic counterparts [22,23]. The high prevalence of deficiency of vitamin D in our patients was expected since there is already an abundance of local literature pointing to an increased prevalence of vitamin D deficiency in Saudi children and in the Saudi general population [24]. In the present study, vitamin D status does not seem to exert any effect on glycemic control.

It should be noted that our study has some limitations. The retrospective design limits the findings because it was based on medical records data. Furthermore, the single center approach limits the generalizability of the study. Nevertheless, the sample size was acceptable as one of the largest cohorts assembled for a T1DM study in Saudi Arabia. In conclusion, Glycemic control among Saudi children with Type 1 diabetes was less satisfactory in comparison to others. A well-structured education program to overcome poor adherence and suboptimum glycemic control is highly needed. The care for a child and adolescent with diabetes must be provided to the entire family unit. Management of diabetes requires multidisciplinary approach by highly specialized team members. Being updated about the recent recommendations of diabetes care can help in improving glycemic control by providing appropriate care. The prevalence of vitamin D deficiency was high .It supports the recommendation of vitamin D treatment in T1DM subjects. Additional studies that include larger cohorts are required to confirm our findings.

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Conflict of Interest

The authors have no conflict of interest to declare.

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