Glycemic Control in Children and 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 to 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, body mass index (BMI) was 21.1 ± 4.5 kg/m^2, and hemoglobin A_{1c} (HbA_{1c}) 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 in females (6.33 ± 3.45 years). Education was the most common reason for admission in males (32.9%), whereas diabetic ketoacidosis (DKA) was the most common reason in 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 HbA_{1c} (⩽8%). The mean level of 25-hydroxyvitamin D was 35.15 ± 15.9 nmol/L and cholesterol was 4.75 ± 1.1 nmol/L. Vitamin D deficiency (25-hydroxyvitamin D ⩽ 37.5 nmol/L) was detected in 63.6% males and 67.7% females. No significant correlation between HbA_{1c} and vitamin D deficiency was observed.

CONCLUSIONS: Metabolic control among Saudi children with T1DM is less satisfactory compared with 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, glycemic control, youth, children

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Introduction

Type 1 diabetes mellitus (T1DM) currently affects an estimated 500 000 youth under the age of 15 years old worldwide, with the highest demographics found in Europe and North America.[1] Epidemiological data further indicate an increasing incidence of T1DM globally with an average relative increase of around 3% to 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 United States, Europe, Australia, Latin America, China, Southeast 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 3 decades, the incidence rate of T1DM has also been rising in Saudi Arabia.[11] The most recent data report an incidence of 27.5/100 000[12] and 29/100 000.[13] The prevalence of T1DM in Saudi children and adolescents is 109.5 per 100 000.[14] A recent (2017) report from International Diabetes Federation (IDF) showed that Saudi Arabia (35 000) has highest number of people with T1DM (0-19 years) and has highest number of new cases (3900) of T1DM.[15]

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 T1DM leads to a decreased risk of diabetic complications.[16,17] 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.[18,19] Previous studies demonstrated that optimal metabolic control is imperative for the prevention of long-term diabetes complications.[20,21]

In the present study, we endeavored to determine the current status of glycemic 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 Centers for Disease Control and Prevention charts. Data on hemoglobin A_{1c} (HbA_{1c}), 25-hydroxyvitamin D [25(OH)D] levels, lipid profile, and thyroid function were also collected from the medical records. At the time of study, we followed the American Diabetes Association (ADA) 2014 Guidelines for target HbA_{1c} levels per age group: ⩽8.5% (69.4 mmol/mol) in toddlers (0-6 years), ⩽8% (63.9 mmol/mol) in schoolchildren (6-12 years), and ⩽7.5% (58.5 mmol/mol) in adolescents and young adults (13-18 years).

Hemoglobin A_{1c} was measured using ion-exchange high-performance liquid chromatography technique. hemoglobin A_{1c} 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 per 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 1 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 (IBM SPSS Inc, USA, version 14). 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 HbA_{1c} and vitamin D values was undertaken to identify the association between vitamin D status and glycemic control. Significance was set at a P value <.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 years for males and 14.06 ± 3.86 years for females). Mean age at diagnosis of T1DM was slightly younger in males (6.01 ± 3.65 years) than in females (6.33 ± 3.45 years). 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 <.46 (Table 1).

The mean daily insulin dose (unit/kg/day) was 1.01 ± 0.25 for males and 1.04 ± 0.23 for females. Intensive diabetes therapy with multiple daily injections (MDIs) 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 were the most common types of insulin used (61.4% males, 64.6% females; Table 2).

For self-monitoring blood glucose (SMBG), most of our patients did 3 to 4 tests per day (54.3% in males and 49.1% in females).

Anthropometric and Metabolic Data

Table 3 illustrates the anthropometric and metabolic measures of the patients.

Females have a marginally higher BMI than males (P = .07). There was no significant difference in BP readings, lipid profile, and HbA_{1c} between both genders. The average HbA_{1c} was 9.67 ± 1.93 (9.66 ± 1.98 in females and 9.7 ± 1.8 in males); 26% (79 out of 301) had HbA_{1c} (⩽8%). When stratified according to the age, 28.6% of toddlers, 15.6% of children, and 12.8% of adolescents had acceptable HbA_{1c} (Figure 1).

The mean level of 25(OH)D was 35.1 ± 15.9 nmol/L. It was higher among males than females (36.93 ± 14.69 vs 33.37 ± 17.28 nmol/L; P = .02).

There was no association between 25(OH)D level and HbA_{1c} (Figure 2; R = .04, P = .60). For lipid profiles (total cholesterol, LDL, Triglyceride [TG], and HDL), the levels were higher in females than in males with non-statistical significance.

Discussion

The median age at diagnosis of T1DM in Saudi Arabia, specifically the Western region, was 6 years. It is comparatively younger than that reported at European counterparts, having a median age of 7.2 years.[22] Males with T1DM were displaying more

Table 1. Clinical characteristics of subjects.

PARAMETER	MALES	FEMALES	*P*
N	140	161	
Age (years)	13.86 ± 3.88	14.06 ± 3.86	.67
Age of diagnosis (years)	6.01 ± 3.65	6.33 ± 3.45	.44
Duration of DM (years)	7.83 ± 3.81	7.71 ± 3.6	.78
Duration of DM symptoms prior to DM diagnosis (weeks)	2.03 ± 1.14	2.05 ± 1.13	.78
Pubertal stage (%)			
Pre-pubertal	49.3	42.2	.22
Pubertal	50.7	57.8	
DM onset of symptoms			
DKA	42.1	48.4	.27
Hyperglycemia symptoms	57.9	51.6	
Reasons for admission			
DKA	27.9	38.8	.22
Education	32.9	27.5	
Others reasons	39.2	33.7	
Number of missed clinics per year			
0	42.1	44.1	.72
1	40.7	37.9	
2	10.7	13.7	
3	6.4	4.3	
Hypoglycemia attacks (symptomatic)	47.1	42.9	.46

Abbreviations: DKA, diabetic ketoacidosis; DM, diabetes mellitus.

Table 2. Insulin regimens used by the patients.

PARAMETER	MALES	FEMALES	*P*
N	140	161	
Daily insulin dose (unit/kg/day)	1.01 ± 0.25	1.04 ± 0.23	.25
DM therapy			
Conventional	17.1	14.9	.86
Intensive (MDI)	74.3	75.8	
Insulin pump	8.6	9.3	
SBGM frequency			
0	5.7	6.2	.78
1-2	38.6	42.2	
3-4	54.3	49.1	
>4	1.4	2.5	
Type of insulin used			
Aspart + Lantus	8.6	7.5	.93
Aspart + Levemir	0.7	0.6	
Aspart + NPH	0.7	0.6	
Lispro + NPH	0	3.1	
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 per day			
On insulin pump	7.9	8.1	.98
2 injections	2.9	3.7	
3 injections	5.0	5.0	
4 injections	84.3	83.2	

Abbreviations: DM, diabetes mellitus; MDI, multiple daily injection; NPH, Neutral protamine Hagedorn.

Table 3. Anthropometric and metabolic profile of subjects.

PARAMETER	MALES	FEMALES	*P*
N	140	161	
BMI (kg/m^2)	20.69 ± 4.45	21.63 ± 4.63	.07
BMI *z*-score	−0.11 ± 0.98	0.10 ± 1.01	.07
Systolic blood pressure (mm Hg)	114.19 ± 13.0	112.96 ± 10.80	.44
Diastolic blood pressure (mm Hg)	68.5 ± 8.14	68.29 ± 8.89	.86
HbA_{1c} (%)	9.7 ± 1.8	9.6 ± 1.98	.29
Triglycerides (mmol/L)	1.12 ± 0.7	1.14 ± 0.57	.92
Total cholesterol (mmol/L)	4.68 ± 1.12	4.83 ± 1.1	.53
HDL cholesterol (mmol/L)	1.19 ± 0.31	1.26 ± 0.31	.30
LDL cholesterol (mmol/L)	2.87 ± 1.3	2.99 ± 0.86	.61
25-hydroxyvitamin D (nmol/L)	36.93 ± 14.69	33.37 ± 17.28	.02
TSH (mIU/L)	1.81 ± 1.94	2.0 ± 2.05	.20
Free T4 (pmol/L)	9.49 ± 6.83	11.09 ± 6.02	.11

Abbreviations: BMI, body mass index; HbA_{1c}, hemoglobin A_{1c}; HDL, High-density lipoproten; LDL, low density lipoprotein; TSH, Thyroid stimulating hormone.
Data presented as mean ± standard deviation and as percentages (%).

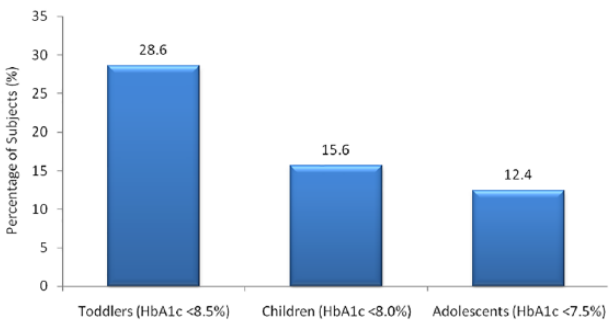

Figure 1. Percentage of subjects with good glycemic control according to the age group. HbA_{1c} indicates hemoglobin A_{1c}.

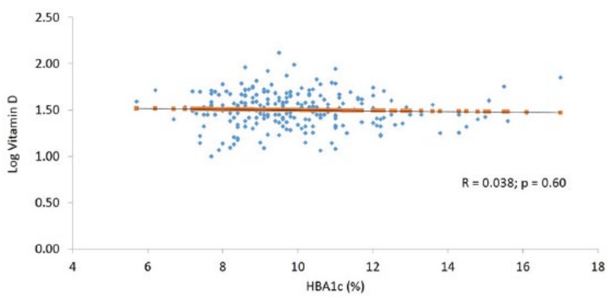

Figure 2. Linear correlation between log vitamin D and HbA_{1c}. HbA_{1c} indicates hemoglobin A_{1c}.

symptomatic (polyuria, polydipsia, and weight loss) as presentation than females. The use of MDI regimens was the most common therapy; findings of the present study confirm the initial observations of Al-Agha and colleagues.[23] Regarding HbA_{1c} control, 28.6% of toddlers achieved HbA_{1c} 8.5% (69.4 mmol/mol), 15.6% of children achieved HbA_{1c} 8% (63.9 mmol/mol), and only 12.4% of adolescents achieved good glycemic control of HbA_{1c} 7.5% (58.5 mmol/mol). Based on the recent ADA recommendations, a target A1C of 7.5% (58.5 mmol/mol) in all children with diabetes mellitus is recommended.[24]

Pubertal growth and development as well as behavioral and adherence issues may play an important role in suboptimal glycemic control. Other studies confirmed such possible attributed factors.[18,19,23] 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.[25] Recent data on the level of glycemic control are shown by the international project SWEET in 2015, gathering data for diabetic children from 48 centers worldwide. In this consortium, the mean HbA_{1c} for all patients is 7.8% (61.7 mmol/mol). The data from this project show that 39.1% of patients have a median HbA_{1c} level under the International Society for Pediatric and Adolescent Diabetes (ISPAD) target of 7.5% (58 mmol/mol), 41.4% are between 7.5% and 9% (58-75 mmol/mol), and 19.5% show HbA_{1c} above 9% (75 mmol/mol). Wide variation still remains between different centers. In total, 14 centers attained a median HbA_{1c} 7.5%.[26] 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 due 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.[23,27] The high prevalence of deficiency of vitamin D in our patients was expected because 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.[28] 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 record 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 T1DM was less satisfactory in comparison with others. A well-structured education program to overcome poor adherence and suboptimal 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.

Author's Note

Author Abdullah M Al Zahrani, is now affiliated with King Abdullah International Medical Research Center, Jeddah, Saudi Arabia.

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Author Contributions

All the authors have made substantive contributions to the article and assume full responsibility for its content.

REFERENCES

1. Patterson C, Guariguata L, Dahlquist G, Soltesz G, Ogle G, Silink M. Diabetes in the young—a global view and worldwide estimates of numbers of children with type 1 diabetes. *Diabetes Res Clin Pract*. 2014;103:161–175.
2. Tuomilehto J. The emerging global epidemic of type 1 diabetes. *Curr Diab Rep*. 2013;13:795–804.
3. Lawrence JM, Imperatore G, Dabelea D, et al. Trends in incidence of type 1 diabetes among non-Hispanic white youth in the United States, 2002-2009. *Diabetes*. 2014;63:3938–3945.
4. Gomez-Diaz RA, Garibay-Nieto N, Wacher-Rodarte N, Aguilar-Salinas CA. Epidemiology of type 1 diabetes in Latin America. *Curr Diabetes Rev*. 2014;10:75–85.
5. Barat P, Levy-Marchal C. Epidemiology of diabetes mellitus in childhood. *Arch Pediatr*. 2013;20:110–116.
6. Tran F, Stone M, Huang CY, et al. Population-based incidence of diabetes in Australian youth aged 10-18 yr: increase in type 1 diabetes but not type 2 diabetes. *Pediatr Diabetes*. 2014;15:585–590.
7. Ghosal S, Batin M. The diabetes epidemic in India: where we stand and future projections. *J Indian Med Assoc*. 2013;111:751–754.
8. Ramachandran A, Snehalatha C, Ma RC. Diabetes in South-East Asia: an update. *Diabetes Res Clin Pract*. 2014;103:231–237.
9. Gong C, Meng X, Saenger P, et al. Trends in the incidence of childhood type 1 diabetes mellitus in Beijing based on hospitalization data from 1995 to 2010. *Horm Res Paediatr*. 2013;80:328–334.
10. Patterson CC, Dahlquist GG, Gyürüs E, Green A, Soltész G; EURODIAB Study Group. Incidence trends for childhood type 1 diabetes in Europe during 1989-2003 and predicted new cases 2005-20: a multicentre prospective registration study. *Lancet*. 2009;373:2027–2033.
11. Cherian MP, Al-Kanani KA, Al Qahtani SS, et al. The rising incidence of type 1 diabetes mellitus and the role of environmental factors—three decade experience in a primary care health center in Saudi Arabia. *J Pediatr Endocrinol Metab*. 2010;23:685–695.
12. Abduljabbar MA, Aljubeh JM, Amalraj A, Cherian MP. Incidence trends of childhood type 1 diabetes in eastern Saudi Arabia. *Saudi Med J*. 2010;31:413–418.
13. Habeb AM, Al-Magamsi MS, Halabi S, Eid IM, Shalaby S, Bakoush O. High incidence of childhood type 1 diabetes in Al-Madinah, North West Saudi Arabia (2004-2009). *Pediatr Diabetes*. 2011;12:676–681.
14. Al-Herbish AS, El-Mouzan MI, Al-Salloum AA, Al-Qurachi MM, Al-Omar AA. Prevalence of type 1 diabetes mellitus in Saudi Arabian children and adolescents. *Saudi Med J*. 2008;29:1285–1288.
15. Robert AA, Al-Dawish A, Mujammami M, Al Dawish MA. Type 1 diabetes mellitus in Saudi Arabia: a soaring epidemic. *Int J Pediatr*. 2018;2018:9408370.
16. The Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977–986.
17. Diabetes Control and Complications Trial Research Group. Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: diabetes control and complications trial. *J Pediatr*. 1994;125:177–188.
18. Amiel SA, Sherwin RS, Simonson DC, Lauritano AA, Tamborlane WV. Impaired insulin action in puberty. A contributing factor to poor glycemic control in adolescents with diabetes. *N Engl J Med*. 1986;315:215–219.
19. Rydall AC, Robin GM, Olmsted MP, Devenyi RG, Daneman D. Disordered eating behavior and microvascular complications in young women with insulin-dependent diabetes mellitus. *N Engl J Med*. 1997;336:1849–1854.
20. Nordwall M, Arnqvist HJ, Bojestig M, Ludvigsson J. Good glycemic control remains crucial in prevention of late diabetic complications—the Linkoping Diabetes Complications Study. *Pediatr Diabetes*. 2009;10:168–176.
21. Al-Daghri NM, Al-Attas OS, Alokail MS, et al. Increased vitamin D supplementation recommended during summer season in the gulf region: a counterintuitive seasonal effect in vitamin D levels in adult, overweight and obese Middle Eastern residents. *Clin Endocrinol (Oxf)*. 2012;76:346–350.
22. Al-Daghri NM, Al-Attas OS, Johnston HE, et al. Whole serum 3D LC-nESI-FTMS quantitative proteomics reveals sexual dimorphism in the milieu interieur of overweight and obese adults. *J Proteome Res*. 2014;1:5094–5105.
23. Al-Agha A, Ocheltree A, Hakeem A. Metabolic control in children and adolescents with insulin-dependent diabetes mellitus at King Abdulaziz University Hospital. *J Clin Pediatr Endocrinol*. 2011;3:202–207.
24. American Diabetes Association. Children and adolescents. *Diabetes Care*. 2017;40:S105–S113.
25. Goran MI, Gower BA. Longitudinal study on pubertal insulin resistance. *Diabetes*. 2001;50:2444–2450.
26. Witsch M, Kosteria I, Kordonouri O, et al. Possibilities and challenges of a large international benchmarking in pediatric diabetology: the SWEET experience. *Pediatr Diabetes*. 2016;17:7–15.
27. Alsaeid M, Qabazard M, Shaltout A, Sharma PN. Impact of glycemic control on serum lipoprotein (a) in Arab children with type 1 diabetes. *Pediatr Int*. 2001;43:246–250.
28. Al-Hayek AA, Robert AA, Abbas HM, et al. Assessment of health-related quality of life among adolescents with type 1 diabetes mellitus in Saudi Arabia. *Saudi Med J*. 2014;35:712–717.