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Audit of glycemic control in patients with type 1 diabetes referred to a pediatric clinic in a specialized center in Kuwait

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ABSTRACT

Introduction: Intensive glycemic control reduces the risk of microvascular and macrovascular complications. Furthermore, optimal glycemic control is essential for normal growth and development. Thus, there is a need to monitor and evaluate glycemic control in patients with type 1 diabetes (T1D). Our aim was to audit glycemic control in patients with T1D in a specialized center as per the Society of Pediatric and Adolescent Diabetes (ISPAD) Hemoglobin A1C (HbA1C) target recommendations published in 2014.

Methods: This is a retrospective cross-sectional study reporting on glycemic control (HbA1C) of patients younger than 21 years of age and with T1D treated at Dasman Diabetes Institute (DDI) between January 2013 and December 2015.

Results: A total of 470 patients with T1D (250 males and 220 females) were included. Only 53 (11.3%) patients met the ISPAD target for optimal glycemic control with HbA1C < 7.5% (58 mmol/mol). Older age was positively associated with poor glycemic control ($p = 0.001$) while Continuous Subcutaneous Insulin Infusion (CSII) therapy was negatively associated with poor glycemic control, adjusted Odds Ratio (OR) 0.33 (95% confidence interval (CI): 0.16–0.66) for CSII and adjusted OR 0.42 (95% CI: 0.27–0.64) for shifting to CSII ($p < 0.001$).

Conclusion: Achieving optimal glycemic control is a significant challenge for young patients with T1D. Glycemic control goals should be individualized to achieve such goals safely, realistically and with a better quality of life for patients with T1D.

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1. Introduction

The Diabetes Control and Complications Trial (DCCT) has demonstrated that intensive glycemic control reduces the risk of microvascular and macrovascular complications [1]. In addition to long-term complications, type 1 diabetes (T1D) negatively impacts neurocognitive function, which appears to be more affected by persistent hyperglycemia than by hypoglycemia as previously assumed [2–5]. This is now well recognized with the new term "metabolic memory" introduced by the Epidemiology and Diabetes Interventions and Complications Study (EDIC), which highlights the importance of optimal glycemic control since the onset of diabetes [6,7]. In addition, optimal glycemic control is also essential for normal growth and development [8].

There are large differences in the incidence of T1D between different countries [9] and it is increasing worldwide [10]. Among children $\leq$ 14 years, the incidence of T1D ranged from 0.1 to 0.8/100, 000 per year in Venezuela and China to 36.8–39.9/100, 000 per year in Sardinia and Finland [11]. In Kuwait, the incidence of T1D in Kuwaiti children was reported to be 20.9 per 100,000 per year between 1992 and 1997 [12], while the recent estimate of incidence is 41.7 per 100,000 per year [13], which suggest that the incidence is increasing rapidly.

The need to clearly define optimal glycemic control has led The International Society of Pediatric and Adolescent Diabetes (ISPAD) to review and update criteria for optimal glycemic control in children and adolescences with T1D on a regular basis [14]. Recently, it has been shown that achieving the clinical goals set by ISPAD is associated with cardiorenal protection in youth with T1D [15]. Thus, there is a need to monitor and evaluate glycemic control in patients with T1D. In clinical practice, diabetes care is audited by monitoring indicators such as Hemoglobin A1C (HbA1C) to set priorities for improvement of diabetes care and define patient characteristics associated with better outcome. In the long-term, audits will eventually lead to better resource allocation and care delivery.

In this study, our aim was to audit glycemic control in patients with T1D referred to a pediatric clinic in a specialized center as per the ISPAD HbA1C target recommendations published in 2014 [14].

2. Methods

This paper reports on a retrospective cross-sectional study including patients with T1D treated at the outpatient Pediatric Clinic at Dasman Diabetes Institute (DDI) between January 2013 and December 2015. Dasman Diabetes Institute is a non-profitable organization that was established by the Kuwait Foundation for the Advancement of Sciences (KFAS) in 2006, providing ambulatory care and diverse programs in basic and clinical research in diabetes. Children with diabetes are usually referred from all over Kuwait to the center for optimized clinical care. We included patients with T1D who were under the age of 21 years, had at least two visits per year, with at least two separate analyses of HbA1C within one year.

Data were extracted from the patients' medical records at DDI including gender, age, body mass index (BMI), HbA1C, and insulin regimen, which includes Multiple Daily Injections (MDI), Continuous Subcutaneous Insulin Infusion (CSII) and shifting from MDI to CSII (Shifted to CSII). BMI measures were expressed as standard deviation scores (SDS) determined by the World Health Organization (WHO) growth standards [16]. BMI was categorized to into normal, overweight and obese based WHO growth charts. BMI for patients older than 19 years (six patients) was categorized according to the WHO cutoff points for adult BMI (Normal: BMI less than 25 kg/m^2, Overweight: >= 25.0 kg/m^2, and Obese: >=30.0 kg/m^2) [14].

HbA1C was measured using the High Performance Liquid Chromatography (HPLC) method. Optimal glycemic control was defined as mean HbA1C levels of <7.5% (58 mmol/mol), suboptimal control as 7.5–9.0% (58–75 mmol/mol) and high risk as HbA1C levels above 9.0% (75 mmol/mol) for all ages as per the 2014 ISPAD recommendations [14]. Data were analyzed using STATA software version 13.1. Differences with p-value of<0.05 were deemed to be statistically significant. Continuous variables were expressed as mean (SD) when normally distributed or median (interquartile range: IQR) otherwise. Chi-square test and Fisher's exact test were used to test for differences in categorical variables as appropriate. Multivariant logistic regression was used to investigate the factors associated with poor glycemic control (HbA1C > 9.0% (75 mmol/mol)). This study was approved by the Ethical Review Committee at DDI.

3. Results

During the study period, a total of 470 patients with T1D (250 males and 220 females) met the inclusion criteria. Characteristics of these patients are shown in Table 1. Half of the patients had mean HbA1C levels in the high risk range (HbA1C > 9% (75 mmol/mol) and only 53 (11.3%) patients met the ISPAD target for optimal glycemic control with HbA1C < 7.5% (58 mmol/mol). No differences were observed between males and females (p = 0.169)

Table 2 demonstrates glycemic control among different age groups. There was a significant difference in HbA1C levels between different age groups. Most of children 6 years and older had their HbA1C in the high risk range whereas children aged<6 years of age mostly maintained their HbA1C in the suboptimal range (p = 0.002). Across all age groups, small proportions of patients achieved the ISPAD targets for optimal glycemic control (HbA1C < 7.5% (58 mmol/mol)) (p = 0.002).

Table 3 shows the association between age, gender, BMI and insulin regimen with poor glycemic control (HbA1C > 9.0% (75 mmol/mol)) using multivariant logistic regression. Both age and insulin regimen were statistically significantly associated with poor glycemic control in this analysis. Older age was positively associated with poor glycemic control (p = 0.001) while CSII therapy was negatively associated with poor glycemic control, adjusted OR 0.33 (95% CI: 0.16–0.66) for CSII and adjusted OR 0.42 (95% CI: 0.27–0.64) for shifting from MDI to CSII (p < 0.001).

Table 1 – Characteristics of 470 patients with Type 1 Diabetes included in the audit.

Variable	Total (N = 470)	Males (n = 250)	Females (n = 220)	P value
Age, years, median (IQR)	12.5 (8.2, 15.0)	12.8 (9.2, 15.0)	11.9 (7.4, 15.1)	0.209
Age categories (n, %)				
<6 years	65 (13.8%)	28 (11.2%)	37 (16.8%)	0.093
6 to <12 years	150 (31.9%)	76 (30.4%)	74 (33.6%)	
≥12 years	255 (54.3%)	146 (58.4%)	109 (49.6%)	
Mean BMI SDS, SD*	+ 0.9 (1.3)	+ 0.9 (1.4)	+ 0.9 (1.2)	0.661
BMI* categories (n, %)				
Normal	253 (53.8%)	134 (53.6%)	119 (54.1%)	0.010
Overweight	129 (27.5%)	58 (23.2%)	71 (32.3%)	
Obese	88 (18.7%)	58 (23.2%)	30 (13.6%)	
HbA1C%, mean (SD)	9.3 (1.7)	9.4 (1.8)	9.2 (1.7)	0.364
HbA1C per ISPAD targets (n, %)				
<7.5% (58 mmol/mol)	53 (11.3%)	29 (11.6%)	24 (10.9%)	0.169
7.5–9% (58–75 mmol/mol)	182 (38.7%)	87 (34.8%)	95 (43.2%)	
>9% (75 mmol/mol)	235 (50.0%)	134 (53.6%)	101 (45.9%)	
Insulin regimen (n, %)				
MDI	274 (58.3%)	154 (61.6%)	120 (54.6%)	0.302
CSII	47 (10.0%)	23 (9.2%)	24 (10.9%)	
Shifted to CSII	149 (31.7%)	73 (29.2%)	76 (34.5%)	

IQR: Interquartile range; BMI: Body Mass Index; HbA1C: Hemoglobin A1C; ISPAD: International Society for Pediatric and Adolescent Diabetes; MDI: Multiple daily injections; CSII: Continuous subcutaneous insulin infusion.
* Missing for 6 subjects (4 Males, 2 Females).

Table 2 – Glycemic control among different age groups in 470 patients with Type 1 Diabetes included in the audit.

Variable	<6 years (n = 65)	6 to <12 years (n = 150)	≥12 years (n = 255)	P value
HbA1C%, mean (SD)	8.7 (1.3)	9.4 (1.7)	9.4 (1.8)	0.005
HbA1C per ISPAD targets (n, %)				
<7.5% (58 mmol/mol)	9 (13.9%)	12 (8.0%)	32 (12.5%)	0.002
7.5–9% (58–75 mmol/mol)	37 (56.9%)	50 (33.3%)	95 (37.3%)	
>9% (75 mmol/mol)	19 (29.2%)	88 (58.7%)	128 (50.2%)	

HbA1C: Hemoglobin A1C; ISPAD: International Society for Pediatric and Adolescent Diabetes.

Table 3 – Association between age, gender, BMI and insulin regimen with poor glycemic control (HbA1C > 9.0% (>75 mmol/mol)) among 470 patients with Type 1 Diabetes included in the audit.

Variable	N	Poor glycemic control n (%)	Odds Ratio	[95% CI]	P value
Age categories					
<6 years	65	19 (29.2)	1.00	[Ref.]	0.001
6 to <12 years	150	88 (58.7)	3.30	[1.72–6.34]	
≥12 years	255	128 (50.2)	1.97	[1.07–3.62]	
Gender					
Male	250	134 (53.6)	1.00	[Ref.]	0.264
Female	220	101 (45.9)	0.80	[0.55–1.18]	
BMI categories					
Normal	253	123 (48.6)	1.00	[Ref.]	0.599
Overweight	129	64 (49.6)	0.93	[0.59–1.45]	
Obese	88	48 (54.6)	1.25	[0.74–2.10]	
Insulin regimen					
MDI	274	162 (59.1)	1.00	[Ref.]	<0.001
CSII	47	14 (29.8)	0.33	[0.16–0.66]	
Shifted to CSII	149	59 (39.6)	0.42	[0.27–0.64]	

BMI: Body Mass Index; HbA1C: Hemoglobin A1C; MDI: Multiple daily injections; CSII: Continuous subcutaneous insulin infusion: CI: Confidence Interval; Ref: Reference.

4. Discussion

This study aimed to audit glycemic control of patients with T1D treated at the outpatient Pediatric Clinic at DDI by comparison with ISPAD's glycemic control (HbA1C) targets. Of concern is the finding that half of the patients had mean HbA1C levels in the high risk range (>9% (75 mmol/mol)) and only about 11% of patients met the ISPAD target for optimal glycemic control. However, although our findings are of concern, our results are not surprising as similar findings have been reported from the United States and some parts of Europe. Most youth in the T1D Exchange Clinic Registry did not meet the ISPAD clinical targets for optimal glycemic control (57% of patients aged 6 years to < 13 years and 79% aged ≥ 13 years) [17,18]. Furthermore, the National Diabetes Audit 2016–17 in England reported that only about one third of patients with T1D had optimal levels of HbA1C [19]. The majority of patients with T1D in Turkey (HbA1C > 7.5% (58 mmol/mol) in 70.9%) [20], and Kingdom of Saudi Arabia (HbA1C > 7.0% (53 mmol/mol) in 77.2%) [21] also did not achieve optimal glycemic control. Furthermore, several countries had reported means of HbA1C in the high risk range in their study populations (Wales; Mean HbA1C 9.08% (76 mmol/mol)) [22], Asia and the Western Pacific; Mean HbA1C of 9.0% (75 mmol/mol), 10.4% (90 mmol/mol), and 10.5% (91 mmol/mol) in Thailand, Malaysia, and Indonesia respectively) [23]. Nevertheless, there are some differences between our findings and those reported from some other settings. For example, the German and Australian Prospective Diabetes Follow-up Registry (DPV) registries reported that 56% of children<6 years of age met the HbA1C goal of<7.5% (58 mmol/mol) [24] in contrast to only 13.9% of children in the same age range in our study.

In our patients, children younger than 6 years of age were less likely to have poor glycemic control compared to children older than 6 years (table 2). Our findings are consistent with reports from other settings such as the T1D Exchange Clinic Registry [17], the Hvidoere study [25], Wales [22], Asia and the Western Pacific [23], and the Kingdom of Saudi Arabia [21,26]. However, most of the younger children (<6 years) in our study were not in optimal glycemic control, based on HbA1C analyses. Such findings might reflect the practice of physicians in setting the target HbA1C higher for glycemic control in younger children with T1D as per previous guidelines published by the American Diabetes Association (ADA). ADA recommended maintaining HbA1C levels of<8.5% (69 mmol/mol) for children 6 years and younger [27]. In our setting, it is possible that poor glycemic control in older patients as compared to younger children is attributed to less parental influence on adherence to diet and insulin regimen as the child grows older. Furthermore, it can be attributed to decreased insulin sensitivity as children go through puberty [28]. Also, children's life style can be expected to change substantially as they grow older and transition from childhood to adolescence and into early adulthood.

Treatment regimen was a strong predictor for poor glycemic control in our study, with those on CSII therapy were less likely to have poor glycemic control (table 3). The T1D Exchange Clinic Registry data reported significantly better glycemic control in patients treated with CSII compared to MDI among children older than 13 years [17]. This is consistent with several reports that CSII therapy has a significant positive effect on glycemic control [18,23,29–32]. Such effect might be secondary to eligibility criteria on which the patient is assessed as highly motivated and compliant patients are chosen for CSII therapy. Furthermore, it might also reflect the close monitoring of patients on CSII therapy.

It should be noted that during the final drafting of this manuscript, ISPAD issued updated guidelines on glycemic control targets in children and adolescents with T1D based on expert opinion [33]. In this revised document, a lower target HbA1C of < 7.0% (53 mmol/mol) is recommended for patients with access to comprehensive care and thus applicable to patients cared for in our institute [33]. Furthermore, a lower target of HbA1C (<6.5% (48 mmol/mol)) is suggested to be appropriate in patients if achievable without hypoglycemia, impairment of quality of care, and undue burden of care [33]. After applying the recent guideline for HbA1C targets to our patients, only 40 patients (8.5%) of the study population achieved this goal. In this context, it is important to note that intensively treated adolescents in the DCCT achieved a mean HbA1C of 8.1% (1) and an average HbA1C of 7.8–8.2% was reported in the EDIC study [34]. Clearly, the recently revised targets for glycemic control are intended to be aspirational to motivate patients to aim at better control over the disease. Nevertheless, these goals are very ambitious and might be perceived as virtually impossible to achieve for many patients. Setting the glycemic targets very low could potentially have a discouraging effect as institutions will be considered as failing in their goals to provide optimal diabetes care when evaluated against these targets for optimal glycemic control. As discussed previously, the majority of studies report that children and adolescents with T1D were not achieving optimal glycemic control even when evaluated against higher recommended targets [17–23].

This is the first study auditing glycemic control of patients with T1D referred to a pediatric clinic in a specialized center in Kuwait, a country in which the incidence of T1D in children and adolescents has doubled in the past two decades [13]. One of the limitations of this study is that it was conducted in a single specialized diabetes center that acts as a referral center for challenging cases and therefore probably not representative of pediatric patients with T1D in the country. Furthermore, important information such as detailed information on diabetes history, including the duration of the disease and the presences of acute and chronic diabetes-related complications could not be obtained accurately in the study population. This lack of information clearly limits the overall evaluation of the impact of many important factors on glycemic control and need to be addressed in future studies.

In our study, the majority of patients did not achieve the optimal target for glycemic control as defined by ISPAD. Given the short-term and long-term consequences of poor glycemic control in T1D patients our results are of concern, in particular with the high incidence of T1D in Kuwait and the increasing burden on the health care system. Like in other settings, CSII therapy was associated with better glycemic control in

our patients, indicating the importance of making CSII available as widely as possible to patients with T1D. Finally, it should be recognized that achieving optimal glycemic control is a significant challenge for young patients with T1D. Glycemic control goals should be individualized to achieve such goals safely, realistically and with a better quality of life for patients with T1D.

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Declaration of Competing Interest

No conflict of interest to declare.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.107827.

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