Mean glycosylated hemoglobin in children with type 1 diabetes at King Fahad Medical City, Riyadh, Saudi Arabia

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Abstract:

BACKGROUND: Type 1 diabetes is the third most common chronic disease among teenagers. In Saudi Arabia, there is a gap of knowledge regarding hemoglobin A1C (HbA1c) concentration levels, and adherence to regular follow-up visits by patients. The aim of this study was to determine the mean glycosylated hemoglobin (HbA1c) levels in diabetic children who have been diagnosed with type 1 diabetes and were being followed up at a tertiary care center in Saudi Arabia.

MATERIALS AND METHODS: This cross-sectional study was conducted among all diabetic children treated at King Fahad Medical City (KFMC) in Riyadh, Saudi Arabia. Data were retrieved and analysed during the period from September to December 2018. Diabetic patients of <18 years and who were being followed up at KFMC were included in the study. Data on age, sex, duration of illness, associated comorbidities, antidiabetic regimen, and HbA1c levels were obtained. Student t-test was used to compare quantitative parameters between two groups, and Chi-square employed to test for associations between categorical variables at 5% significance level.

RESULTS: A total of 510 patients of were included in the study; about 53% were females. The mean HbA1c level was 10.6% and females showed higher HbA1c levels. Data showed a strong correlation between age and HbA1c levels ($P < 0.001$), with older patients showing higher HbA1c levels. The HbA1c levels also increased as the duration of disease increased. The median number of patient visits to KFMC was two per year. No statistically significant differences were observeed for type of treatment for diabetes. Celiac disease, the most frequent comorbidity, was seen in 50% of patients.

CONCLUSION: Diabetic children who were followed up at KFMC had high HbA1C level (10.6%), and lower than recommended follow-up visits per year. The treating physicians should educate patients and their legal guardians on the importance of follow-up visits and their role in controlling HbA1C levels, and following healthier lifestyle.

Keywords:

Diabetes duration, glycated hemoglobin a, hypoglycemic agent, pediatrics, Saudi Arabia, type 1 diabetes mellitus

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Introduction

Type 1 diabetes is the third most common chronic disease of teenagers.[1,2] Hence, multiple studies have focused on the prevention and alleviation of the emotional and physical burden of the disease. Consequently, researchers have focused on determining the variation of a biomolecule called glycosylated hemoglobin, denoted as hemoglobin A1C (HbA1c), which is increased in type 1 diabetes patients. The levels of HbA1c have been found to be

affected by factors such as gender and blood glucose levels.[3] Studies have also revealed that girls have higher HbA1c concentrations than boys. In addition, individuals showing increased HbA1c concentrations in the 1st month of the onset of diabetes are at a higher risk of having raised HbA1c levels during the months following diagnosis as well,[3] thus proving that HbA1c concentration is directly related to the progress of type 1 diabetes in teens. These findings, supported by several other studies,[3,4] reveal that HbA1c concentration is also related to metabolic regulation in patients. Another study showed that HbA1c concentrations in adolescents and young adults have seasonal variations.[5] The majority of the patients had higher HbA1c concentrations in September and the lowest concentrations in January.[5] It should be noted that while variations have been observed across diverse studies, these variations are not uniform.[3,5] This is possibly due to the sample size and years in which the samples were obtained and analyzed. The metabolic control methods for patients with type 1 diabetes improved a great deal between the 1970s and 1990s, making a correlation between HbA1c concentration and disease progression more uniform and stable with time.[6] The effect of sample size can be seen in a study where a relatively small sample of 306 children with type 1 diabetes was used.[7] The analysis revealed only a small yet statistically relevant difference between HbA1c concentrations before and after metabolic treatment.[7]

The average concentrations of HbA1c also vary significantly among different ethnic groups, further complicating the diagnosis and analysis of type 1 diabetes and its associated diseases.[8] It was initially thought that glucose concentration in patients' blood was the cause of these variations, but it has been revealed that patients with similar blood glucose levels also display significant variations in HbA1c concentrations. These variations, including those shown in previous studies, are proof that further investigations and data are required to understand how HbA1c concentrations can be used to properly guide the diagnosis and treatment of type 1 diabetes. In Riyadh, Saudi Arabia, there is a gap in the knowledge on HbA1c concentration levels, associated comorbidities, and adherence to regular follow-up visits by patients. To the best of our knowledge, no researcher has tried to explore this area. We thought there was the need to explore it and give a comprehensive image of HbA1c levels as well as patient adherence and compliance to medication.

Materials and Methods

This cross-sectional study was conducted among diabetic children treated at King Fahad Medical City (KFMC) in Riyadh, Saudi Arabia. Data were retrieved and analysed from September to December, 2018. Electronic access was provided to the hospital's patient records by the pediatric department head. The selection of patients was based on a formal Microsoft Excel spreadsheet that was constructed, maintained, and updated regularly by the Diabetes Clinic at King Fahad Medical City (KFMC). The final analysis included a total of 1095 patients under the age of 18 years who were followed up at KFMC. Patient file numbers obtained from the Excel spreadsheet were entered into the hospital's electronic database. Age, sex, date of diagnosis, associated chronic diseases and autoimmune disorders, antidiabetic regimen (insulin, metformin, or mixed, i.e., regular + neutral protamine Hagedorn [NPH] or aspartate + glargine), and glycosylated hemoglobin (HbA1c) laboratory results were obtained from the database. For each patient, HbA1c readings were summed up and divided by the number of visits, thus providing the average HbA1c level. Patients were classified according to age and disease duration into three groups. Less than six years of short duration, 6–11 years of intermediate duration, >11 years long duration, an HbA1c reading in 2017 only, age under 18 years, and regular follow-up at KFMC served as the inclusion criteria. Patients referred to the adult clinic or older than 18 years were excluded from the analysis phase. The study protocol was approved by the Institutional Review Board vide Number 18-375E dated 29/07/2018 with a waiver of informed written consent.

Data were analyzed using the Statistical Package for Social Sciences (SPSS ver. 20, Chicago, IL, USA). The distribution of quantitative variables was tested for normality using the Kolmogorov–Smirnov test, which revealed that the data were normally distributed and

Table 1: Distribution of children with type 1 diabetes by gender and age

Characteristic	Frequency N (%)
Gender	
Male	241 (47.3)
Female	269 (52.7)
Age (years)	
<6	77 (15.1)
6-11	233 (45.7)
12-16	191 (37.5)
17-21	9 (1.8)
Mean±SD	4.3±2.9

SD=Standard deviation

Table 2: Glycated hemoglobin level in children with type 1 diabetes disease by duration and gender

	Males Mean±SD	Females Mean±SD	P-value
HbA1c	10.3±1.6	10.9±1.9	<0.001*
Duration of disease (years)	4.3±3	4.5±3.2	0.364

*By independent sample *t*-test (*P*<0.05) statistically significant.
HbA1c=Glycated hemoglobin, SD=Standard deviation

Table 3: Glycated hemoglobin level and duration of disease among children with type 1 diabetes by age groups

	Age group (years)					*P* value
	≤6 Mean±SD	7-11 Mean±SD	12-16 Mean±SD	17-20 Mean+SD	Total Mean±SD	
Duration of illness	2.1±1.65	3.7±2.4	5.7±2.4	7.7±3.4	4.3±2.9	0.001
HbA1c	9.8±1.3	10.4±1.5	10.7±1.7	9.9±1.8	10.4±1.6	0.012

HbA1c=Glycated hemoglobin, SD=Standard deviation

therefore, were described using mean and standard deviation (SD). Qualitative variables were described using frequency and percentage. An independent sample *t*-test was used to compare quantitative parameters between the two groups. Pearson's Chi-squared test was used to test for association between categorical variables, and Monte Carlo significance probability was used for tables with more than 2 × 2 entries. Correlation between quantitative parameters was performed using the Pearson correlation test. Multiple response analysis was used for the variable of "associated diseases," which has more than one response. Data were represented graphically using Boxplot and Pie chart. All statistical tests were performed at 5% level of significance.

Results

The total number of pediatric patients who met the criteria was 510, 52.73% of whom were female [Table 1]. The study showed that the mean HbA1c for both sexes was 10.6%. There was a statistically significant difference in the mean HbA1c level between genders, males at 10.3% (±SD 1.6) and females at 10.88% (±SD 1.9), (*P* < 0.001) [Table 2].

The mean age for males and females in the study were 9.8 ± 3.1 and 10.2± 3.3 years, respectively. However, our results showed a strong correlation between age and HbA1c values (*r* = 0.213, *P* < 0.001); children <6 years of age had the lowest mean HbA1c levels of 9.8% (±SD 1.3) with a median of 9.7%, patients aged 6–11 years had a mean HbA1c of 10.4% (±SD 1.5) and a median 10.3%, and patients aged >11 years had a mean HbA1c of 10.7% (±SD 1.7) and a median 10.5% [Table 3].

There were no statistically significant difference in the disease duration between males (4.3±3.0 years) and females (4.5±3.0 years) [Table 2]. However, there was a significant correlation between the duration of the disease and HbA1c levels, with longer disease duration corresponding to higher HbA1c levels; patients with disease duration <6 years had a mean HbA1c of 10.5% (±SD 1.7), patients with disease duration between 6 and 11 years had a mean HbA1c of 10.9% (±SD 1.7), and patients with disease duration >11 years showed a mean HbA1c of 11.1% (±SD 2) [Table 2]. The median number of patient visits was two visits per year, ranging from one to four visits per year.

We also did not find any statistically significant differences based on the type of antidiabetic medication used. The mean HbA1c level in the group taking regular + NPH (*n* = 105) treatment was 10.45 ± 1.4%, and in those who took aspartate + glargine (*N* = 2) was 11.08 ± 1.3% (*P* = 0.64) [Table 4].

This study also provides information on the frequencies of diseases associated with diabetes in the analyzed patients. We found that 86 out of 510 (16.86%) patients had other diseases associated with diabetes. Celiac disease, the most frequent was present in 50% of cases, followed by hypothyroidism (20.9%) [Table 5].

Discussion

HbA1c is considered to be the gold standard for glycemic control in diabetic patients and is one of the predictors of disease complications. In this study, our aim was to measure the mean HbA1c levels in diabetic pediatric patients followed up at KFMC.

We found that the mean HbA1c in our study population was 10.6%, which appears to be very high compared to the values of HbA1c recommended for maintenance. It is also higher than values reported in previous studies; the mean HbA1c was 7.8% in Germany and Austria, 7.6% (± SD 1.5) for Polish children and adolescents with long-term type 1 diabetes, and >9.3% in more than half (53%) of the patients in a study conducted in Sweden.[3,5,9]

Our study found a significant correlation between the mean HbA1c value and patient age; the older the patient, the higher the mean HbA1c value in both genders. This result is supported by numerous previous publications.[3,5,6,9,10] The general nature of this trend might be explained by factors such as hormonal changes during puberty, since the growth hormone can decrease insulin sensitivity and increase its clearance.[5,11] Furthermore, as the patient gets older, many caregivers cease their supervision of the management of the disease.[5,11] In addition, during puberty, patients undergo emotional and social changes such as the fervent desire in teenagers to be very independent, undertake risky behaviors, and display a lack of acceptance of their disease.[9,12] Aside

Table 4: Comparison of glycated hemoglobin level of children with type 1 diabetes by drug used for treatment of diabetes

	Drugs used for treatment		P-value
	Regular+NPH (*n*=105) Mean+SD	Aspartate+Glargine (n=2) Mean±SD	
HbA1c	10.45±1.4	11.08±1.3	0.64

P value based on independent *t*-test. HbA1c=Glycated hemoglobin, SD=Standard deviation, NPH=Neutral protamine Hagedorn

Table 5: Frequency distribution of associated diseases among children with type 1 diabetes

	Number (%)
West syndrome	1 (1.2)
Vitamin D deficiency	4 (4.7)
Type 2 diabetes mellitus	3 (3.5)
Thyroid Ab+ve	5 (5.8)
Sickle cell disease	1 (1.2)
Short stature	3 (3.5)
Grave's disease	2 (2.3)
Neonatal diabetes	2 (2.3)
Down syndrome	2 (2.3)
Celiac disease	43 (50.0)
Hypothyroidism	18 (20.9)
Mody diabetes	2 (2.3)
Total	86 (100.0)

from this, we observed a significant correlation between HbA1c and disease duration. The levels of HbA1c rose as the disease duration increased, a result that has also been reported.[5]

The results from our study indicate a gender difference in HbA1c values, with females having higher HbA1c values than males. This observation is confirmed by previous studies in Sweden, Germany, and Austria, respectively.[3,5] This could be explained by the fact that females generally experience greater metabolic imbalance than males.[3] Healthy women are known to have lower insulin sensitivity than healthy men, but this is physiologically compensated for by higher insulin secretion.[5,13] Hormonal changes may also have a role as girls reach puberty earlier than boys.[3]

The median number of patient visits to the clinic was two visits per year, which is lower than the number of visits recommended by the American Diabetes Association guidelines (every 3–4 months).[14] This might be one of the contributing factors resulting in the high mean HbA1c levels seen in our study population. Kaufman *et al.* also found that patients with frequent visits to diabetes clinics had lower HbA1C values, suggesting that strategies must be developed to encourage adherence to the recommended quarterly visits.[15,16]

Our data showed no differences in glycemic control in patients who received NPH and regular insulin and those who received aspartate and glargine. This was also demonstrated by Parastoo *et al.*, who showed that there was no significant difference in glycemic control and the lipid profile between patients following either regimen.[17-19]

There is an established link between autoimmunity and type 1 diabetes mellitus.[20,21] We found that celiac disease was the disease most frequently associated with diabetes in our study population, followed by hypothyroidism.

Conclusion

HbA1c levels in diabetic children who were followed up at KFMC appeared to be high and showed a mean HbA1C level of 10.6% for both genders, with higher levels in females. Older children had higher levels than younger children. The median number of follow-up visits per year was lower than recommended. Celiac disease was the most common comorbidity associated with diabetes. We recommend that all treating physicians should educate their patients and their legal guardians on the importance of follow-up visits and their role in controlling HbA1c levels. Patients should follow a healthier lifestyle that includes a balanced diet and regular exercise. Since our study has several limitations, we encourage future investigators to conduct more elaborate studies to determine the cause of high mean HbA1c levels.

Conflicts of interest
There are no conflicts of interest.

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