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Growth Disorders in Children with Type 1 Diabetes in Aswan, Egypt

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ABSTRACT

Background: Type 1 diabetes mellitus is the most common chronic metabolic disorder in children. Diabetic children who take proper nutrition and good care attain normal growth status**.** One sign of poorly controlled diabetes is poor growth.

Objective: This study was conducted to assess the growth parameters (weight, height, and body mass index) in diabetic children and to study the impact of age at diagnosis, duration of the disease, and disease control on the growth parameters.

Patients and Methods: This is a cross-sectional study that carried out on diabetic children aged from 6 to 18 years old in 8 months period. History, examination with stress on anthropometric measurement (weight, height, and body mass index) together with HbA1c level was done.

Results: Mean HbA1c was (10.85 ± 2.299) %. Patients with HbA1c of more than 9% were 75.5%. There was an insignificant negative correlation between HbA1c and age and disease duration and a significant negative correlation between HbA1c and tanner staging, but there was no relation between HbA1c and sex or family history. There was a significant negative correlation between HbA1c and weight, HbA1c, and body mass index, while there was an insignificant negative correlation between HbA1c and height. There was an insignificant correlation of weight to disease duration, while there was a significant positive correlation of height to disease duration.

Conclusion: in this study, most of our patients were uncontrolled diabetic patients. Weight, height, and BMI were less in uncontrolled patients than controlled patients.

Keywords: Diabetes, Weight, Height, BMI

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is one of the most common chronic metabolic disorders in children and adolescents and its incidence is increasing worldwide [(1)]. It is characterized by chronic hyperglycemia and body composition is important in disease control [(2)]**.** The etiopathology of hyperglycemia includes a defect in insulin secretion, insulin action, or both with resultant of different complications [(3)].

Diagnostic criteria by the American Diabetes Association (ADA) include the following: A fasting plasma glucose level ≥126 mg/dL (7.0 mmol/L), *or* A 2-hour plasma glucose level ≥ 200 mg/dL (11.1 mmol/L) during a 75-g oral glucose tolerance test, *or* A random plasma glucose ≥2 00 mg/dL (11.1 mmol/L) in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis [(4)]**.**

Many complications affect diabetic patients including impaired growth, represent a major concern despite the advances in treatment [(5)]. Nutrition is the main factor in the management of diabetes [(6)]. The other cornerstone in the management of type 1 diabetes is insulin injection [(7)].

Factors affecting growth in diabetic patients include gender, age at diagnosis, duration of disease, glycemic control, and puberty status [(8)]. Although most diabetic children at the beginning of diagnosis were less in weight comparing to the controlled group, they gain weight after taking insulin especially during puberty [(9)]. Diabetic children who take proper nutrition and good care attain normal growth status [(10)]**.** One sign of poorly controlled diabetes is poor growth [(11)].

So we conducted this study to assess the growth parameters (weight, height, and body mass index (BMI) in diabetic children and to study the impact of age at diagnosis, duration of the disease, and disease control on the growth parameters.

MATERIAL AND METHODS

This is a cross-sectional study carried out on diabetic children who attained Endocrinology Outpatient Clinic at Aswan University Hospital for regular follow up in the duration of study from July 2019 to February 2020.

Inclusion criteria:

- The age of children between 6 and 18 years old.

Exclusion criteria:

- Children < 6 years or above 18 years old.
- Children who have a duration of disease less than 2 years.
- Children have medical syndromes, and /or other chronic diseases.

Complete history taking including child's gender, age, duration of the disease, and presence of

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any chronic disease or medical syndrome. A complete physical examination was performed to evaluate the health status of the children and determine the Tanner stage of each child for sexual maturity.

Anthropometric measurements:

Height: we used a stadiometer (SECA 217, graduation length: 1 cm, range: 20-205 cm), the participants were asked to remove their shoes and heavy clothes, and stand erect on the floorboard of the stadiometer with their back on the side of the vertical board; the weight should be evenly distributed on both feet, the legs closed and stretched, the arms to the sides and the shoulders relaxed; the heels, buttocks, and back should slightly touch the vertical board.

The participants were then asked to look straight ahead, inhale deeply and stand fully erect while the examiner lowered the horizontal bar to the head crown with hair compressed, and took the measurement to the nearest 0.1 cm.

Weight: We used a calibrated flat beam scale for mobile use (SECA 877, scale division: 100 g, capacity: 200 kg), the participants were asked to remove their shoes and all clothes except underwear, and then step on the center of the scale, remaining in a relaxed position. Weight was recorded to the nearest 0.5 kg; if the participants refused to remove their clothes, 1 kg was subtracted from the measurement reading to account for the garments worn [(12)].

Body mass index was calculated by this equation: weight in kg divide by height square in a meter.

An investigation was done including HbA1c:

A fasting blood sample (5 ml) was collected between 7 am and 9 am by a trained pediatric nurse. HbA1c was measured by High-performance liquid chromatography (HPLC) (BIO-RAD, Germany).

The reference ranges for hemoglobin A1c (HbA1c) levels are as follows: HbA1c (4-5.9 %) is normal in adult or child without diabetes, HbA1c < 7% is good control in the diabetic patient, HbA1c from 8-9% is a fair diabetic control, while HbA1c > 9% considered a poor diabetic control [(13)].

Ethical Consideration:

An approval of the study was obtained from Aswan University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Statistical analysis

Data were analyzed by using SPSS version 22. Summary of measures was reported as mean ± standard deviation (SD) for quantitative variables such as age and weight, while categorical variables such as sex and Tanner stage were represented as percentages. A comparison between 2 quantitative data was analyzed by independent t-test. The correlation between two variables was done by using the Pearson correlation test to identify the degree of correlation of numerical variables. P-value ≤ 0.05 was considered statistical significance.

RESULTS

Our study included 98 diabetic children, socio-demographic data as shown in **Table (1)** showed that the mean age of our patients was (14.17± 3.514) year, 45.9% of them were males and 54.1% were females, family history was positive in 27.6% of cases and disease duration was (6.482 ± 2.8751) years. Tanner stage was 0 in 37.1% of cases, 1 in 2% of cases, 2 in 8.2% of cases, 3 in 5.15% of cases, 4 in 6.18% of cases, and 5 in 41.2% of cases.

Table (1): Socio-demographic data of studied cases

Variable	Cases (N= 98)
Age: (in years)	
Mean ± SD	14.17± 3.514
Range	12 (6 – 18)
Sex:	
M	45 (45.9%)
F	53 (54.1%)
Family history:	
Positive	27 (27.6%)
Negative	71 (72.4%)
Disease duration: (in years)	
Mean ± SD	6.482± 2.8751
Range	13 (2-15)
Tanner stage	
0	36 (37.1%)
1	2 (2%)
2	8 (8.2%)
3	5 (5.15%)
4	6 (6.18%)
5	40 (41.2%)

Regarding anthropometric measurement in diabetic children as shown in **Table (2).** The mean height of diabetic children was (1.48 ± 1.63) m, the mean weight was (47.541 ± 17.257) kg, mean BMI was (21.06 ± 4.5). The investigation done for diabetic children revealed that the mean HbA1c was (10.85 ± 2.299) %. Patients with HbA1c of more than 9% were 75.5%.

Table (2): Anthropometric measurement and investigation of studied children

Variable	Cases (N= 98)
Weight: (in Kg) • Mean ± SD	47.541 ± 17.2568
Height: (in meter) • Mean ± SD	1.48 ± 1.63
BMI: • Mean ± SD	21.062 ±0.5553
HAIC: % • Mean ± SD	10.851± 2.2994
HAIC: % • < 9 • >9	 24 (24.5%) 74 (75.5%)

Table (3) shows a comparison between controlled and uncontrolled cases regarding anthropometric measurement in which weight in controlled patients was (52.1 ± 21.7) vs (46.1 ± 15.5) in uncontrolled patients, height in controlled patients was (1.496 ± 2.09) vs (1.472 ± 1.46) in uncontrolled patients and BMI in controlled patients was (22.3 ± 5.3) vs (20.6 ± 4.2) in controlled patients, with insignificant P-value in comparison of all growth parameters.

Table (3): Comparison between controlled and uncontrolled cases regarding anthropometric measurement

	Controlled	Uncontrolled	
WT (Kg)	52.109 ± 21.7318	46.140 ± 15.5395	0.148
HT (M)	1.5 ± 0.1	1.47 ± 0.47	0.530
BMI	22.343 ± 5.3414	20.669 ± 4.2487	0.124

Independent t-test

Regarding the effect of glycemic control as detected by HbA1c level on socio-demographic and physical development as shown in **Table 4.** There was an insignificant negative correlation between HbA1c and age and disease duration and a significant negative correlation between HbA1c and tanner staging, but there was no relation between HbA1c and sex or family history. Concerning anthropometric measurement: there was a significant negative correlation between HbA1c and weight, and between HbA1c and BMI, while there was an insignificant negative correlation between HbA1c and height.

Table (4): Correlation of HBA1Cto anthropometric measurement and investigations

	HAIC	
	Pearson Correlation	Sig. (2-tailed)
Sex	.093	.363
Age	-.007-	.947
Disease duration	-.085-	.404
Tanner stage	-.256*	.011
Family history	.042	.681
Weight	-.242*	.016
Height	-.127-	.212
BMI	-.242*	.016

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Table 5 showed that there was an insignificant correlation of weight to disease duration, while there was a significant positive correlation of height to disease duration.

Table (5): Correlation of weight and height to diabetes control

	Disease duration	
	Pearson Correlation	Sig. (2-tailed)
Weight	.193	.057
Height	.203*	.045

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

T1DM is a chronic disease that needs proper management to avoid short- and long-term complications [14]. The growth of diabetic children depends on the metabolic control, age of onset, and duration of the disease [15]. Moreover, when it is diagnosed in prepubertal stages, and patients have a persistent poor glycemic control [16], the latter will be associated with a decrease in growth and, consequently, a loss in final adult height [17].

Our study included 98 diabetic children, most of our patients were in the adolescent age group with a wide range of disease duration from 2 to 15 years.

More than half of our patients were female (54%), in agreement with our results, **Zurita-Cruz *et al.*** [18] and **Lee *et al.*** [19] reported that 54% and 51.5% of their patients were female. In contrast to our results, **Hassan *et al.*** [20] and **Aljuhani *et al.*** [21] reported a slight male predominance (50.1%) and (56.8%) found among diabetic children. Family history was positive in 27.6% of cases. In agreement with **Lee *et al.*** [19], family history was positive in 28.8 % of their cases.

Most of our patients had poor glycemic control as more than 75 % of our patients had HbA1c more than 9%. **Zurita-Cruz *et al.*** [18] reported that HbA1c levels of 8% presented in 56% of their cases in the first year, increasing to 64% in the second year and **Aljuhani *et al.*** [21] reported that HbA1c levels were 9.15% in their patients and 43.2% of participants had poor metabolic control.

Most of our patients had Tanner stage of 5 (full mature sexual development), but more than one-third of our patients had immature sexual development (Tanner stage was zero), this may be due to most of our patients were in the adolescent age category. In contrast to our results, **Zurita-Cruz *et al.*** [18] reported that 50% of their patients were in the prepubertal stage, and only 5% had reached a Tanner stage IV.

Anthropometric measurement in diabetic children: the mean height of diabetic children was (1.48 ± 1.63) m, the mean weight was (47.541 ± 17.257) kg, mean body mass index was (21.06 ± 4.5). In comparison between controlled and uncontrolled cases: weight, height, and BMI were less in uncontrolled patients than controlled patients with an insignificant p-value.

In agreement with the results of **Khadilkar *et al.*** [22] as they reported that diabetic children were shorter and lighter than control. **Zurita-Cruz *et al.*** [18] observed that about 50% of their patients showed impaired growth at some point in their evolution. **Hassan *et al.*** [20] in their study found that diabetic controlled children were taller and heavier with higher BMI than those of the diabetic uncontrolled children**. Gaete *et al.*** [23] reported that height, weight, and BMI values were lower in the T1DM group than in the control group.

In our study, there was a significant negative correlation between HbA1c and weight, and also between HbA1c and BMI, while there was an insignificant negative correlation between HbA1c and height, this means that our patient had acute not chronic under-nutrition and this may be explained by the effect of insulin they receive as all of our patients were on basal insulin and receive short-acting insulin with meals. In agreement with **Zurita-Cruz *et al.*** [18], they reported in their study that HbA1c and poor glycemic control were lower in the group of patients with normal growth parameters compared with those with growth alterations (median 7.4%vs. 8% and 45.65% vs. 71.43%, respectively). **Aljuhani *et al.*** [21] reported that there was a significant difference in height score as they found lower height z-score in the intermediate control group than those in the good metabolic control group although this correlation was insignificant in the case of poor metabolic control. On the other hand, there was a negative significant relationship between HbA1c level and the weight z-score and BMI z-score.

On the other side, **Salerno *et al.*** [24] concluded that the decrease in height gain was independent of the duration of IDDM or the degree of metabolic control. As in another study, **Clarson *et al.*** [25] studied the growth and pubertal development in 122 children, they found no correlation between mean HbA1c levels and mean height or weight percentiles, nor height or weight velocity percentiles. Therefore, diabetic control, as reflected by HbA1c levels, was not a major determinant of growth in this group of children with TIDM **(11)**. **Kanumakala *et al.*** [26] found that there was no significant correlation between metabolic control and linear growth in diabetic boys or girls.

Linear growth depends on type I and II insulin-like growth factor (IGF), their receptors, and high-affinity binding proteins (IGFBP-1 to IGFBP-6). IGFs and IGFBPs can be observed at their lower levels in children with uncontrolled TIDM [27]. With the improvement of glycemic control the levels of IGF-I increase, producing a compensatory acceleration of growth [28]. Though children with T1DM are often tall at the time of diagnosis, they may experience growth retardation, pubertal delay, or both later, whether due to poor glycemic control, chronic complications, or associated diseases. Children with the prepubertal onset of T1DM are taller than those with onset at puberty [8].

Data from AIIMS Diabetes of the Young clinic (1988–1995) revealed that the frequency of growth retardation in diabetics was 11–14% [29]. In (2006), data from the ICMR registry author's clinic revealed that 16% of the T1DMs had growth retardation. A cohort of 22,651 German and Austrian T1DM achieve a mean adult height of −0.16 ± 1.0 SDS, which is a normal adult height [30]. On the other hand, a group of 72 Sudanese children was found to have a significant reduction in a pubertal growth spurt and final adult height, with an average age at menarche was15.1 years, and the average age of full sexual maturation in boys was 17.2 years [9].

The main causes of poor height and weight gain are poor glycemic control, autoimmune disorders, improper renal function, and psychosocial factors. Poor glycemic control may be due to low socio-economic status, inadequate insulin dosage, poor family support, emotional issues, and other factors causing compliance issues [31]. Eventually, these lead to short stature, delayed puberty, poor bone health, and other problems.

Some studies found that the serum concentrations of HbA1c under 8% were related to an appropriate longitudinal growth [32]. In a German population study, it was observed that patients with HbA1c < 7% had a normal final height, unlike those with HbA1c > 8% lost up to 0.34 SD of the population mean [30]. **Brown *et al.*** [32] analyzed the growth of 184 patients with T1DM and compared it with the growth of healthy children of the same age, they found the average of final height was lower in diabetic children in comparison with healthy children. Particularly, those patients with an age of onset ofT1DM between 5 and 10 years had a greater loss of stature in comparison with healthy children. In the past decade, many studies reported growth disorders in diabetic patients with high serum concentrations of HbA1c [33]. However, the management of T1DM has improved with time, and it manifests as a healthier growth and development in these patients. Currently, the growth of patients with T1DM has been evaluated through the final height without performing an annual growth rate analysis, which could help to minimize the alterations of growth during their evolution [30]. Some earlier studies [14] **and** [15] have also shown that children who had better metabolic control had higher HVZ scores, underlining the importance of improving metabolic control. Children on the basal-bolus regime had better HVZ score and lower HbA1c; promoting the use of basal-bolus regime may help to optimize growth. These studies reported that patients diagnosed before 5 years of age showed the greatest height loss, and need more attention towards growth [22].

In our study, there was an insignificant correlation of weight to disease duration, while there was a significant positive correlation of height to disease duration. **Khadilkar *et al.*** [22] and **Aljuhani *et al.*** [21] reported that there was no correlation between height, weight, and BMI z-scores and the duration of diabetes in their cases. **Parthasarathy *et al.*** [34] suggest that the longer disease duration with poor metabolic control was associated with low height velocity Z (HVZ) scores. The height velocity of children diagnosed at younger years was the least across adolescent years and the majority of them fell short of target height [34]. **Elamin *et al.*** [9] found that there was a positive correlation between retardation in physical growth and pubertal development with the duration of diabetes before the onset of puberty. Weight gain was found to be independent of weight at diagnosis and the duration of diabetes but positively correlated with the daily dose of insulin and HbA1cconcentration [9].

In our study, there was a significant negative correlation between HbA1c and tanner staging, but there was no relation between HbA1c and sex or family history. **Rohrer *et al.*** [35] reported that pubertal onset is delayed in children with type 1 diabetes, sexual maturity (Tanner stage 5) was not delayed in either sex. And so elevated HbA1c and decreased BMI SDS were associated with significantly delayed onset of pubertal but not sexual maturity.

In conclusion: the findings of the present study suggest that most children in our locality had uncontrolled TIDM and those uncontrolled children are more at risk of being underweight and short. And so it is important to investigate the causes of poor glycemic control and to improve it as most of the clinical features are reversible with better glycemic control.

Limitation of the study: a small number of patients in this study as well as the high range of patient age.

ABBREVIATIONS

- **ADA**: American Diabetes Association
- **BMI**: body mass index
- **HbA1c**: hemoglobin A1c
- **HPLC**: High-performance liquid chromatography
- **HVZ**: height velocity Z
- **IGF**: insulin-like growth factor
- **IGFBP**: insulin-like growth factor binding proteins
- **SD**: standard deviation
- **T1DM**: Type 1 diabetes mellitus.

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