Physical Growth and Body Composition of Controlled Versus Uncontrolled Type 1 Egyptian Diabetic Children

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Abstract

BACKGROUND: Type 1 Diabetes Mellitus (T1DM) is one of the most common chronic endocrine disorders of childhood. Data on growth parameters of diabetic children is scarce.

AIM: To assess growth and body composition in a group of diabetic children.

SUBJECTS AND METHODS: 427 T1DM children (age 2-10 years) were recruited from Diabetic Paediatric Unit, outpatients' clinic of Abou El-Rish Hospital. Anthropometric and body composition parameters were taken and HbA1c was measured for all subjects.

RESULTS: Highly significant difference was detected between controlled and uncontrolled groups as regard to weight/age z-score, height/age z-score, BMI z-score, triceps skin fold thickness, subscapular skin fold thickness, midupper arm circumference, fat mass, fat %, lean mass, and body water (p < 0.001). All values are higher in the controlled group than in the uncontrolled group. Uncontrolled subjects were significantly more at risk of being underweight and short, with odds ratio of 15.131 and 16.877 and 95% confidence interval 1.972-116.130 and 3.973-71.694 respectively. However, controlled subjects were significantly more at risk of being obese than the uncontrolled with an odds ratio 0.116 and 95% confidence interval 0.045-0.302.

CONCLUSION: Growth was compromised in uncontrolled T1DM children. This is of utmost importance since most of the clinical features are reversible with better glycemic control and appropriate insulin management.

Introduction

Type 1 diabetes mellitus (T1DM) is the most common chronic metabolic disorder in youth and its incidence is increasing worldwide [1]. It is a complex disease, resulting from multiple genetic and environmental etiological factors. The long preclinical prodrome raises the possibility of intervention to delay or prevent clinical onset of disease [2]. It is characterized by chronic hyperglycemia and body composition is important in the disease control [3].

T1DM accounts for 5-10% of the total number of cases of diabetes mellitus worldwide. There has been a steady increase in type 1 diabetes incidence in children <15 yr [2, 4]. It appears to have been particularly pronounced among children <5 years of age [5]. Diabetes prevalence in some Eastern Mediterranean countries is among the highest in the world. The highest rates are reported in Egypt, Kuwait, Lebanon, Oman and Qatar where the incidence of type 1 diabetes is reported to be 8-10 per 100.000 population per year in children aged <15 years [6]. T1DM incidence and prevalence showed a progressive increase over a period of 18 years among children aged from 0 to 18 years living in the Nile Delta region (Egypt). In 2011, incidence and prevalence in Egypt was $3.1/10^5$/year and $26.8/10^5$ Egyptian children from 0-18 years old respectively [7].

T1DM affects children of all ages, both sexes, and all ethnic groups [2]. In the pediatric age group, the growth is a good indicator of health, and consequently achieve normal growth speed is one of the goals of doctors who treat diabetic children [8]. Low portal insulin concentrations, documented in children with T1D, result in low circulating levels of IGF-I and IGFBP-3, and high circulating levels of IGFBP-1 with subsequent increased risk of developing growth failure [9].

Several studies have suggested growth retardation in children with type 1 diabetes with

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suboptimal diabetes control whereas other studies have demonstrated normal growth in children with good metabolic control [10]. Insulin is used to control blood glucose but may have an adverse effect on the amount and distribution of fat mass [11] and hence body composition. Available literature on body composition in children and adolescents with type 1 diabetes is scarce. Intensification of insulin therapy may result in leptin resistance and excessive gains in fat mass, particularly in girls [12].

The aims of this study are: 1) to assess growth of the diabetic children and their body composition, and 2) to realize the difference in anthropometric and body composition variables between diabetic uncontrolled and diabetic controlled children.

Subjects and Methods

The present study was a cross-sectional study comprising 427 diabetic children. They were recruited from Diabetic Endocrine Metabolic Paediatric Unit, (DEMPU) outpatients' clinic of Abou El-Rish Hospital, Cairo University in the period from May 2013 to May 2014. They were divided into 2 groups: 212 diabetic uncontrolled and 215 diabetic controlled (214 boys and 213 girls) according to the average of their glycated Haemoglobin (HbA1c) during the last year (cutoff value is < 8 %). The parents and students' approval were taken as a written consent. The study was approved by Ethical and Research Committee of the Council of Children Department, Cairo University, as well as by Ethical Committee of the National Research Centre. The sample has been chosen from pre-adolescents to avoid the physiological and psychological changes accompanying growth and pubertal development, all of them were from the same low to middle socioeconomic class.

Diabetic children included in the study should be already diagnosed as T1DM and receiving insulin treatment for at least 1 year. Children with any genetic or chronic diseases that can affect their growth e.g. cardiac or renal disease were excluded. Any child with any signs of evidence of puberty was also excluded.

Simple questionnaire was done for each patient with a complete physical examination, including anthropometric measures (weight, height, midupper arm circumference, triceps and subscapular skinfold thickness). All measurements were taken according to the recommendations of International Biological programs [13]. Then, BMI was calculated as weight (kg)/height^2 (m^2). Weight, height measurements were converted to z-scores (weight-for-age, and height-for-age), based on WHO child growth standards. A cut off of ≤ –2 z scores for these indices was used for classifying children as underweight and stunting, while cut off of ≥ 2 z-scores of BMI was used for classifying obesity.

Body Composition Analysis

Body composition analysis in this study was based on the bioelectrical impedance technique. The body bioelectrical impedance was measured using body fat analyzer MODEL: BT-905. It is a device used for the estimation of body composition. It gives accurate information about: Fat percent (%), lean (%), fat mass, basal metabolic rate (BMR), target weight and target fat (%), for an individual.

Statistical analysis

Statistical analysis was carried out using the statistical package for social sciences, version 16 for windows (SPSS Inc., USA). Continuous data were expressed as mean± SD and were compared using Student's t-test. Categorical data were expressed as frequencies and percentages, and were analyzed with the two-tailed chi-square test. Pearson's correlation analysis was carried out to evaluate the association between continuous exposure and continuous covariates. The chi-square (X^2) test, odds ratio (OR) and 95% confidence interval (CI) were used to evaluate the association between diabetic control and growth deficit and obesity. Logistic regression was done to confirm the previous association after adjustment for age and sex. P value less than 0.05 was considered as statistically significant.

Results

In the present study, the mean age of the subjects studied was 6.72 ± 2.08 with a mean age at the onset of T1DM was 4.18 ± 2.16 and mean duration of the disease 2.46 ± 1.53. Two hundred fourteen were male (50.1 %) and two hundred thirteen were female (49.9 %). No significant difference between male and female were detected as regard to anthropometric parameters and glycemic control (p > 0.05). So, we considered both of them as one group for comparison.

On comparing the different anthropometric and body composition parameters between controlled and uncontrolled T1DM in all subjects and in female subjects, highly significant values were detected in controlled group than in uncontrolled except for the lean % where it was significantly higher in the

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Table 1: Comparison between controlled and uncontrolled T1DM as regard to anthropometric and body composition parameter in all subjects.

	Controlled (No 215) Mean ± SD	Uncontrolled (No 212) Mean ± SD	t-test	P
Weight/age z-score	1.203 ± 1.36	-0.873 ± 0.85	18.903	0.000*
Height/age z-score	0.763 ± 1.57	-0.921 ± 0.94	13.438	0.000*
BMI z-score	1.211 ± 0.96	0.056 ± 0.95	12.445	0.000*
TSFT (mm)	13.03 ± 3.51	11.03 ± 3.55	5.874	0.000*
SSFT (mm)	9.81 ± 4.81	7.79 ± 3.16	5.107	0.000*
MUAC (cm)	19.79 ± 2.30	17.71 ± 2.22	9.539	0.000*
Fat mass	4.82 ± 3.61	3.22 ± 2.91	5.061	0.000*
Fat %	17.67 ± 10.54	13.83 ± 9.31	3.990	0.000*
lean mass	22.41 ± 5.49	19.10 ± 4.57	6.770	0.000*
Lean %	82.46 ± 10.44	85.80 ± 9.09	-3.521	0.000*
Water	15.91 ± 4.14	13.33 ± 3.40	7.029	0.000*

P < 0.001 is highly significant; BMI = Body mass index; TSFT = Triceps skin fold thickness; SSFT = Subscapular skin fold thickness; MUAC = Midupper arm circumference.

uncontrolled than in the controlled group (p < 0.05) Table 1&2. This can be explained by the higher mean weight of the controlled group as the lean % = lean mass/body weight X 100. Same results were obtained when the same anthropometric and body composition parameters were studied in male subjects with the exception of fat % and lean %, which showed no significant difference between controlled and uncontrolled group (p > 0.05) Table 2.

Table 2: Comparison between controlled and uncontrolled T1DM as regard to anthropometric and body composition parameter in both sex.

	Controlled Mean ± SD	Uncontrolled Mean ± SD	t-test	P
Male	(No 106)	(No 108)		
Weight/age z-score	1.311 ± 1.57	-1.004 ± 0.85	13.429	0.000*
Height/age z-score	0.901 ± 1.77	-0.923 ± 0.86	9.615	0.000*
BMI z-score	1.225 ± 1.05	0.004 ± 0.92	9.050	0.000*
TSFT (mm)	12.55 ± 3.48	10.64 ± 3.36	4.088	0.000*
SSFT (mm)	8.89 ± 3.38	7.59 ± 3.09	2.938	0.004*
MUAC (cm)	19.74 ± 2.47	17.26 ± 2.23	7.718	0.000*
Fat mass	4.86 ± 3.44	3.78 ± 2.95	2.468	0.014*
Fat %	17.89 ± 10.57	16.33 ± 9.69	1.130	0.260
lean mass	23.25 ± 5.64	18.80 ± 4.63	6.309	0.000*
Lean %	82.02 ± 10.50	83.32 ± 9.42	-0.957	0.340
Water	16.51 ± 4.20	12.96 ± 3.44	6.763	0.000*
Female	(No 109)	(No 104)		
Weight/age z-score	1.097 ± 1.11	-0.737 ± .83	13.618	0.000*
Height/age z-score	0.628 ± 1.33	-0.919 ± 1.03	9.463	0.001*
BMI z-score	1.197 ± 0.876	0.112 ± 0.99	8.502	0.000*
TSFT (mm)	13.51 ± 3.49	11.44 ± 3.70	4.203	0.000*
SSFT (mm)	10.70 ± 5.76	8.00 ± 3.24	4.187	0.000*
MUAC (cm)	19.84 ± 2.13	18.176 ± 2.12	5.740	0.000*
Fat mass	4.78 ± 3.77	2.63 ± 2.76	4.735	0.000*
Fat %	17.46 ± 10.55	11.24 ± 8.18	4.793	0.000*
lean mass	21.60 ± 5.23	19.41 ± 4.50	3.258	0.001*
Lean %	82.89 ± 10.40	88.37 ± 8.00	-4.288	0.000*
Water	15.33 ± 4.01	13.72 ± 3.32	3.181	0.002*

P < 0.05 is significant; BMI = Body mass index; TSFT = Triceps skin fold thickness; SSFT = Subscapular skin fold thickness; MUAC = Midupper arm circumference.

In all subjects and in the female subjects, negative significant correlation were detected between metabolic control, detected by glycosylated Hb, and both of all anthropometric and body composition parameters except for the lean % (p < 0.05). Glycosylated Hb was significantly positively correlated with the lean % (p < 0.05) Table 3. Same results were obtained when correlating same metabolic control and anthropometric and body composition parameters in male group with the exception of fat % and lean %, where no significant correlation were detected (p > 0.05).

Table 4 showed the association between metabolic control and growth deficiency and obesity in all subjects of T1DM. Before adjustment for age and

Table 3: Correlation between metabolic control and both anthropometric and body composition parameters in all subjects and in sex groups with T1DM.

	Glycosylated Hb (%)					
	All Subjects		Male		Female	
	r	p	r	p	r	p
Weight (kg)	-0.430	0.000 *	-0.492	0.000 *	-0.370	0.000 *
Height (cm)	-0.296	0.000 *	-0.384	0.000 *	-0.220	0.001 *
BMI (kg/m²)	-0.433	0.000 *	-0.492	0.000 *	-0.383	0.000 *
TSFT (mm)	-0.274	0.000 *	-0.270	0.000*	-0.278	0.000 *
SSFT (mm)	-0.240	0.000 *	-0.198	0.004 *	-0.277	0.000 *
MUAC (cm)	-0.420	0.000 *	-0.468	0.000 *	-0.368	0.000 *
Fat mass	-0.238	0.000 *	-0.167	0.014 *	-0.310	0.000 *
Fat %	-0.190	0.000 *	-0.077	0.260	-0.313	0.000 *
Lean mass	-0.312	0.000 *	-0.398	0.000 *	-0.219	0.001 *
Lean %	0.169	0.000 *	0.066	0.340	0.284	0.000 *
Water	-0.323	0.000 *	-0.421	0.000 *	-0.214	0.002 *

P < 0.05 is significant; BMI = Body mass index; TSFT = Triceps skin fold thickness; SSFT = Subscapular skin fold thickness; MUAC = Midupper arm circumference.

sex, uncontrolled subjects were significantly more at risk of being underweight (W/A z-score ≤ -2) and short (H/A z-score ≤ -2), with odds ratio of 15.131 and 16.877 and 95% confidence interval 1.972-116.130 and 3.973-71.694 respectively. However, controlled subjects were significantly more at risk of being obese than the uncontrolled with an odds ratio 0.116 and 95% confidence interval 0.045-0.302. Same results were obtained by using logistic regression after adjustment for age and sex.

Table 4: Association between metabolic control and growth deficiency and obesity in all subjects with T1DM before and after adjustment for age and sex.

	Metabolic control		Chi-sqaure	OR	95% CI	p
	Controlled (No)	Uncontrolled (No)				
Weight:						
W/A z-score > -2	214	198	11.868	15.131	1.972-116.130	0.001*
W/A z-score ≤ -2	1	14				
Total	215	212				
Height:						
H/A z-score > -2	213	183	25.769	16.877	3.973-71.694	0.000*
H/A z=score ≤ -2	2	29				
Total	215	212				
Obesity:						
BMI z-score < 2	178	207	26.546	0.116	0.045-0.302	0.000*
BMI z-score ≥ 2	37	5				
Total	215	212				
Logistic regression (after adjustment for age and sex)	Metabolic control					
	R²	B coefficient		OR	95% CI	p
Underweight						
W/A z-score ≤ -2	0.045	2.705		14.957	1.941-115.248	0.009*
Short Stature						
H/A z=score ≤ -2	0.069	2.831		16.955	3.991-72.030	0.000*
Obesity						
BMI z-score ≥ 2	0.086	-2.214		0.109	0.042-0.286.	0.000*

P < 0.05 is significant; W/A = Weight for age; H/A = Height for age; BMI = Body mass index; OR = Odds ratio; CI = Confidence interval.

Discussion

Type 1 diabetes mellitus (T1DM) is one of the most common endocrine and metabolic conditions in childhood. Its incidence is increasing worldwide [1]. Viral infections, hormones and stress are some of the possible causes triggering T1DM. A more frequent onset of T1DM at younger age has been described and a possible role of milk proteins, gluten or vaccinations has been speculated [14].

In the current study it was found that females

represent 49.9% and males 50.1% of the total diabetic children, which suggests a very slight predominance of male diabetic children. Similar results had been reported in some studies as Baruah et al., 2011 [10], who reported a slight male predominance (56%) found among diabetic children which is similar to that of a large epidemiologic study among Swedish (Blom et al., 1992) [15] and Swiss (Schonle et al., 2001 [16]) children. One German study [17] did not find significant difference among either sex, whereas the Hawaiian IDDM registry [16] showed a higher incidence among girls.

The present study confirmed the importance of maintaining good metabolic control to prevent any impairment of the longitudinal growth of the diabetic children.   To assess the growth of the diabetic children we had taking some anthropometric measurements, calculating the BMI and measuring the body composition. On comparing the two groups of the diabetic children together it was found that diabetic controlled children were taller and heavier with higher BMI than those of the diabetic uncontrolled children. Similar to our results several studies have suggested growth retardation in children with type 1 diabetes with suboptimal diabetic control whereas other studies have demonstrated normal growth in children with good metabolic control. Delayed development and onset of puberty in children with type 1 diabetes have been reported as well [18].

Previous studies have documented that poor metabolic control was associated with growth impairment in diabetic children [19, 20]. In contrast to our results, Bognetti et al., 1998 [21], reported that height SDS of diabetic children decreased gradually in the first 3 years after diagnosis despite adequate metabolic control as reflected by their glycosylated haemoglobin levels. Other publications also claim that the longitudinal growth is impaired in children with T1 DM, independent of metabolic control [22, 23]. Herber and Dunsmore, 1988 [24], found no correlation between the height loss from the diagnosis and the glycated hemoglobin level, during the period studied.

So in diabetic controlled children we are in agreement with 'the accelerated hypothesis' declared by Wilkin in 2001 [25]. Indeed, during the last decade, there are some studies reporting positive growth characteristics in diabetic children [26&27]. The findings of accelerated growth are consistent with the hypothesis that increase in stature may be due to growth promoting metabolic changes prior to the onset of clinical diabetes. Hyperinsulinaemia stimulating growth in the prediabetic stage may also be a factor [28]. In addition, it has been postulated that rapid linear growth may increase insulin demand, exhaust pancreatic b cell reserve and precipitating clinical expression of the diabetes [15].

In the current study it was also found that only in diabetic uncontrolled children there was a marked declining in their growth in all parameters. Studies evaluating the course of auxological variables following the diagnosis of T1DM generally report deterioration in height SDS. These early studies were conducted on children who were receiving conventional insulin treatment. In this study, they were able to evaluate the course of height SDS only in the first 5 years of follow−up and found that no significant change in height SDS occurred in both sexes. Bognetti et al., 1998 [21], found that height SDS significantly decreased even in the first 3 years of disease in children and adolescents diagnosed between 1989 and 1992. Similarly, Donaghue et al., 2003 [27], found loss of height SDS by the 5th year of disease in T1DM patients, diagnosed between 1974 and 1991. However, Demir et al., 2010 [29], found similar to the current results that the 5th year height SDS of their patients diagnosed between 1991 and 1995 were similar to height SDS values at the time of diagnosis.

Growth deceleration during the course of the disease has been reported in various countries around the world, such as Austria, Brazil, Czech Republic, Germany, and Sudan [23, 30-32].

In agreement with the current results, Bonfig et al., 2012 [33], demonstrated no sex-specific differences as regard to anthropometric parameters, in contrast to 2 previous studies with smaller patient numbers [34, 35]. In a series of 46 patients, Du Caju et al., 1995 [34], reported a suboptimal pubertal growth spurt resulting in a loss of Ht SDS in 22 girls. Kanumakala et al., 2002 [35], found suboptimal peripubertal growth in boys; in their growth analysis of 99 children with type 1 diabetes. Against to our results, Wong et al., 2000 [36], in his study provides further evidence of sex differences in the growth of diabetic children. Boys were tall for age at presentation and they achieved average final heights. Diabetic girls attained below average adult stature and they tended to become obese. The exact reasons for such sex differences remain to be defined. Careful meal planning and exercise programs are necessary to prevent obesity especially for diabetic girls.

Increased weight and BMI in children who have developed diabetes have been reported in some studies [37-39], but were not found in others [40, 41]. Furthermore, little is known about the effect of type 1 diabetes on body composition, including fat mass (FM), lean body mass (LBM), and BMD in children and adolescents [42]. Excess body fat is the main cause for health hazards induced by obesity (metabolic and cardiovascular disorders), and the preservation of fat-free mass (FFM) is a target in the treatment of obesity. Treatments of diabetes are known to increase weight and the clinical significance of the composition of weight gain (fat or fat-free) is important. Therefore, an assessment of body composition changes is desirable as an evaluation of the procedures [43].

In the current study it was found that BMI was

significantly higher in diabetic controlled than uncontrolled children. Concerning the skin fold thickness (Triceps and sub scapular) and mid upper arm circumference, it was found that the controlled diabetic children had higher values than those of the uncontrolled in the present study. From these results we concluded that the controlled diabetic children had more central and peripheral fat distribution than the uncontrolled. Moreover, uncontrolled T1DM subjects were more at risk of being growth impaired than the controlled subjects. In a recent study evaluating 22651 children with T1DM from specialized centers in Germany and Austria, a negative significant association between growth deficit and the degree of metabolic control was detected which is in agreement with the current study [33]. Bizzarri et al. in 2013 [44] in a study of 104 T1DM children in Italy found that height velocity and BMI were inversely related to HbA1c. Same result was detected by Nansel et al., in 2013 [45] in USA, where BMI was found to be inversely related to HbA1c. The results of the previous two studies are in concordance with the results of the present study.

In conclusion, the findings of the present study suggest that children with uncontrolled T1DM are more at risk of being underweight and short, while controlled T1DM children may be susceptible to weight gain as a result of efforts to control blood glucose. Thus, healthcare planners and providers may be aware of this growth failure and especially of the molecular mechanisms characterizing growth alteration in children and adolescents with T1D. This is of utmost importance since most of the clinical features are reversible with better glycemic control and appropriate insulin management.

Acknowledgments

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