ASSESSMENT OF THE NUTRITIONAL STATUS OF CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS

By

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ABSTRACT

Background: *Currently, T1D is one of the most common chronic non-communicable diseases in children and adolescents. The International Diabetes Federation (IDF) estimates that more than 1.5 million children and adolescents are living with T1D. There is increased incidence of overweight and obesity in children and adolescents in the last decades. It is particularly important to monitor the nutritional status of children and adolescents with T1D as they are still growing and may be affected by the disease and the association between BMI and glycemic control.*

Objectives: *The aim of the study is to assess the nutritional status of children and adolescents with T1D and the association between BMI-SDS and gender, age, duration of diabetes, and glycemic control.*

Materials and methods: *This are a cross-sectional study included a sample of 100 children and adolescents aged from (> 2 - < 15) years with established diagnosis with T1D from those attending the pediatric diabetes clinic, Bab El-Sharia University Hospital and Al-Obour Hospital (Health Insurance Hospital), Kafr El-Sheikh governorate during the period from April 2021 to April 2022. BMI-SDS was calculated using the World Health Organization BMI charts. Children were categorized as underweight (BMI-SDS< -2SD), overweight (+1SD < BMI-SDS ≤+2SD), obese (BMI-SDS > +2 SD. Glycemic control was assessed by HbA1c. Hierarchic regression models were applied with adjustment for sex, age, and duration of diabetes.*

Results: *The prevalence of underweight, overweight, and obesity was 3%, 26%, 5% respectively. BMI-SDS increased by diabetes duration with the lowest duration in underweight group and the highest in the obese group (P = 0.011). The current study showed that the main HbA1c was 7.83 ± 0.59 and in both genders the association between HbA1c and BMI-SDS was U-shaped with the highest HbA1c in the underweight and obese groups. There is significant difference between underweight and normal (p<0.001), significant difference between underweight and overweight (p = 0.005), significant difference between normal and overweight (p<0.001), significant difference between normal weight and obese (p<0.001), non-significant difference*

between overweight and obese (p=0.176) and non-significant difference between underweight and obese (p=0.465).

Conclusion: *The high rate of overweight and obesity (31%) emphasize the need for developing further strategies to prevent and treat excess fat accumulation in T1D and it is strongly recommended in general population.*

Key words: *Type 1 diabetes, Children, Adolescents, Underweight, Overweight, Obesity, HbA1c.*

INTRODUCTION

There is increased incidence of type 1 diabetes all over the world in the recent decades. The International Diabetes Federation estimated that in 2022, there were 8.75 million individuals worldwide with T1D. One fifth (1.9 million) of these individuals live in low-income and lower-middle-income countries. Of the total population T1D in 2022, 1.52million (17.0 %) were younger than 20 years, 5.56million (64.0%) were aged between 20 and 59 years, and 1.67million (19.9%) were aged 60 years or older. In 2022, there were 530,000 new cases of T1D diagnosed at all ages, with 201,000 of these less than 20 years of age **(IDF ATLAS REPORTS, 2022)**.

In the last decades, a rapid increase in the prevalence of obesity in children and adolescents has occurred worldwide **(Risk & Collaboration, 2017)** and **(Hu & Staiano, 2022)**.

Due to the individual needs of each patient, a universal diet does not exist. Nevertheless, every patient should follow the basic recommendations for proper nutrition. The necessary change in eating habits should include avoidance of products with a high glycemic index, high glycemic load, and easily digestible carbohydrates. At the same time, the diet should be well balanced and provide nutrients that have a beneficial effect on the nutritional status, which determines the proper growth and development of the young body. Over the past few years, an increase in the occurrence of overweight and obesity has been observed, especially among children and adolescents. The tendency to increase body weight exists not only in healthy populations, but also among young diabetics **(ADA, 2020)**.

There is association between childhood obesity, or higher BMI, and subsequent increased risk of childhood onset of type 1 diabetes mellitus **(Buzzetti et al., 2020)**.

Rapid weight gain is often observed with insulin therapy in

children with newly diagnosed type 1 diabetes mellitus **(Davis et al., 2012)**.

Intensified insulin therapy and insulin dose significantly influence the increase in BMI during the course of diabetes mellitus **(Fröhlich-Reiterer et al., 2014)**.

Obese children with type 1 diabetes mellitus have lower insulin sensitivity and a higher cardiovascular risk profile than non-obese children with type 1 diabetes **(de Ferranti et al., 2014)**.

Underweight individuals with established type 1 diabetes mellitus are more prone to diabetic ketoacidosis and severe hypoglycemia than those those with normal weight **(Li et al., 2014)**.

Therefore, the increase in the amplitude of the deviation in excess or decrease from the median BMI for age and gender is associated with increased health risk for children and adolescents with type 1 diabetes mellitus. Consequently, it is crucial to identify subjects with at risk BMI and to ensure specific care for managing children with BMI in the underweight and overweight/obesity categories as well as to prevent these conditions **(Maffeis et al., 2018)**.

AIM OF THE STUDY

This study is aiming to assess the prevalence of underweight, overweight and obesity of children and adolescents with type 1 diabetes mellitus and to investigate the association between BMI-SDS and gender, age, duration of diabetes, treatment regimen and metabolic control.

Ethical consideration:

1. A written informed consent was obtained from patients or their legal guardians.

2. An approval by the local ethical committee was obtained before the study.

3. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

4. All data of the patients and results of the study are confidential and the patients have the right to keep it.

5. The author received no financial support for the research, authorship, and/or publication of this article.

6. The patients have the right to withdraw from the study at any time.

PATIENTS AND METHODS

This is a cross-sectional study that had been conducted on 100 children and adolescents with type 1 diabetes attending the pediatric diabetes clinic, Bab El-Sharia University Hospital and Al-Obour Hospital (Health Insurance Hospital), Kafr El-Sheikh governorate during the period from April 2021 to April 2022.

Sample size justification:

Sample size was calculated using Power Analysis and Sample Size Software (PASS 2020) "NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass". The incidence of diabetes mellitus type I accounts for 8/100 000 per year in Egyptian children under the age of 15 years **(El-Ziny et al., 2014)**. The minimal total hypothesized sample size of 100 eligible pediatric patients is needed to assess the prevalence of underweight, overweight and obesity of children and adolescents with type-1-diabetes mellitus and to investigate the association between BMI-SDS and gender, age, duration of diabetes, treatment regimen and metabolic control; taking into consideration 95% level of confidence, effect size of 6.7% and precision of 5% using Z- test **(Muralidharan, 2014)**.

Inclusion criteria:

1. Age from 2-15 years.

2. Both genders.

3. Known patients with Type-1-diabetes mellitus.

4. Duration of diabetes ≥ 1 year.

Exclusion criteria:

1. Other types of diabetes rather than T1D.

2. Diabetes duration < 1 year.

3. Age < 2 years or > 15 years.

All enrolled children were subjected to the following:

I. Interview-based questionnaire:

The main researcher interviewed the guardians to collect the following data:

a. Personal data:

Data on child's age, gender, order of birth, number of siblings, area of residence, father's and mother's educational level and occupation was collected to determine the socioeconomic status of study participants.

Socioeconomic status (SES) was assessed using the (Modified scale for social level of families for usage in health research) where subjects were given a score from 54 and were further classified into 3 social classes; low, medium, or high, according

to their score **(Fahmy et al., 2015)**.

b. Diabetes history:

It included diabetes duration, insulin dose (IU/kg/day), and glycaemic control over last two years prior study determined by frequency of hypoglycaemia and or diabetic ketoacidosis.

c. Dietetic history:

A 24-hour recall of diet aimed at assessing the intake of required macro- and micro-nutrients to determine quality of diet. Protein intake over a week was assessed as well.

d. medical history:

Parents were asked if their children suffered from any chronic illness or performed any previous investigations, and whether any medications or supplements were being used at the time of study conduction.

e. Family history of type-1-diabetes mellitus.

II. General examination:

Anthropometric evaluation included weight in kilograms (Kg) and height in centimeters (cm) as follows:

Weight: was measured on digital scale in kilograms and to the nearest 0.1 kg with the subjects standing motionless without shoes and with minimal clothing.

Height: was measured to the nearest 0.1 cm on a wall mounted stadiometer without shoes. The participants were asked to stand with their back against the wall-mounted stadiometer with their back (scapulae), buttocks and both heels touching the wall-plate. The shoulders are relaxed, and arms are relaxed and hanging loosely at the sides. The head should be in the "Frankfort Horizontal Plane" in which the lowest point on the inferior orbital margin and the upper margin of the external auditory meatus form a horizontal line and the participant was asked to look straight ahead.

Body mass index (BMI): It was calculated using the standard equation (the body mass in kilograms divided by the square of the body height in meters).

To allow comparisons, weight, height and BMI Z scores were measured using the World Health Organization charts **(WHO, 2008)**.

III. Systemic examination:

This included:

- Cardiac examination for hemic murmur and to exclude any underlying illness.

- Chest examination for dyspnea and to exclude any underlying illness.

- Abdominal examination for hepato-splenomegaly and to exclude any underlying illness.

IV.Laboratory investigations:

Glycosylated hemoglobin (HbA1c) for all patients was assessed: a well-trained nurse had withdrawn the samples by pricking a finger and collecting finger capillary blood sample then the blood sample was added to the buffer and was shacked well to mix the blood with the buffer and through fluorescent immune-chromotography analyzing system with fine care TM FIA meter plus device the result was collected **(Mustafa et al., 2019)**.

Statistical Analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

The used tests were:

1. Chi-square test.

For categorical variables, to compare between different groups

2. Monte Carlo correction

Correction for chi-square when more than 20% of the cells have expected count less than 5

3. F-test (ANOVA)

For normally distributed quantitative variables, to compare between more than two groups

4. Kruskal Wallis test

For abnormally distributed quantitative variables, to compare between more than two studied groups.

RESULTS

Our results will be demonstrated in the following tables and figures:

Table (1): Distribution of the studied cases according to demographic data

	No. (%)
Sex	
Male	50 (50)
Female	50 (50)
Age (years)	
≤10	33 (33)
>10	67 (67)
Min. – Max.	6.30 – 14.90
Mean ± SD.	11.13 ± 2.83
Median (IQR)	11.50(8.05 – 13.95)

Table (2): Distribution of the studied cases according to anthropometric measurement (n = 100)

Anthropometric measurement	No. (%)
BMI (kg/m^2)	
Underweight	3 (3)
Normal	66 (66)
Overweight	26 (26)
Obese	5 (5)
Mean ± SD.	19.55 ± 3.10
Median (IQR)	19.12(17.20 – 21.62)
Weight (kg)	
Min. – Max.	20.20 – 73.0
Mean ± SD.	42.52 ± 14.23
Median (IQR)	42.20(28.80 – 55.75)
Height (cm)	
Min. – Max.	113.80 – 173.10
Mean ± SD.	145.08 ± 17.42
Median (IQR)	147.55(127.55 – 159.15)

This table shows the prevalence of underweight, overweight, and obesity of the studied cases according to BMI-SDS for age and sex.

Table (3): Relation between BMI SDS and demographic data (n = 100)

	BMI SDS				Test of Sig.	p-value
	Under-weight (n = 3)	Normal (n = 66)	Overweight (n = 26)	Obese (n = 5)		
	No. (%)	No. (%)	No.(%)	No.(%)		
Sex						
Male (n=50)	2(4)	34(68)	12(24)	2(4)	χ^2= 0.906	0.869
Female (n=50)	1(2)	32(64)	14(28)	3(6)		
Age (years)						
≤10 (n=33)	1(3)	22(67)	8(24)	2(6)	χ^2= 0.546	1.000
>10 (n=67)	2(3)	44(66)	18(27)	3(4.5)		
Mean ± SD.	11.90 ± 2.23	11.12 ± 2.90	11.09 ± 2.83	11.06 ± 3.11	F= 0.075	0.973
Median	12.30	11.50	11.50	10.50		

This table shows statistically non-significant difference between males and females, non-significant difference between the two age groups regarding BMI-SDS.

Table (4): Relation between BMI SDS and duration of diabetes (n = 100)

Duration of diabetes (years)	BMI SDS				H	p
	Under-weight (n = 3)	Normal (n = 66)	Overweight (n = 26)	Obese (n = 5)		
Min. – Max.	1.60 – 4.0	1.70 – 8.30	2.0 – 8.30	4.50 – 8.60	11.161[*]	0.011[*]
Mean ± SD.	2.53 ± 1.29	4.36 ± 1.54	4.76 ± 1.69	6.72 ± 1.47		
Median	2.0	4.06	4.85	6.90		

This table shows statistically increased BMI-SDS with increased duration of diabetes.

Table (5): Relation between BMI SDS and HbA1c for males and females (n = 100)

HbA1c	BMI SDS				F	p
	Underweight	**Normal**	**Overweight**	**Obese**		
Total	**(n = 3)**	**(n = 66)**	**(n = 26)**	**(n = 5)**		
Min. – Max.	8.80 – 9.50	6.90 – 8.30	7.80 – 8.50	8.0 – 9.0	29.339[*]	<0.001[*]
Mean ± SD.	9.10 ± 0.36	7.57 ± 0.49	8.21 ± 0.21	8.64 ± 0.40		
Median	9.0	7.50	8.20	8.80		
Male	**(n = 2)**	**(n = 34)**	**(n = 12)**	**(n = 2)**		
Min. – Max.	8.80 – 9.0	7.0 – 8.30	7.80 – 8.20	8.0 – 8.50	13.033[*]	<0.001[*]
Mean ± SD.	8.90 ± 0.14	7.54 ± 0.44	8.06 ± 0.14	8.25 ± 0.35		
Median	8.90	7.50	8.05	8.25		
Female	**(n = 1[#])**	**(n = 32)**	**(n = 14)**	**(n = 3)**		
Min. – Max.		6.90 – 8.30	8.10 – 8.50	8.80 – 9.0	20.276[*]	<0.001[*]
Mean ± SD.	9.50	7.59 ± 0.55	8.34 ± 0.18	8.90 ± 0.10		
Median		7.55	8.40	8.90		

This table shows statistically significant increase in HbA1c in the underweight, overweight, and obese groups than in the normal weight group with no significant difference between males and females.

DISCUSSION

Our study showed that the mean prevalence of overweight and obesity was approximately 31% in the sample of children and adolescents participating in this study. This result is in accordance with the reported prevalence in the general population **(Lipsky et al., 2017)**. Therefore, it is likely that the impact of factors such as genetic predisposition and the pressure from an obesogenic environment in promoting excess body fat accumulation in children and adolescents also impact those with T1D. This is in spite of exposure to a nutritional education program and to regular clinical follow-up, which should theoretically contribute to maintenance of body weight **(Chatterjee et al., 2021)**.

Our results were supported by the study of Maffeis et al., 2018 as they reported that BMI-SDS increased by diabetes duration (<2 years: 0.38 ± 0.05, 2 to <5years: 0.44 ± 0.05, and ≥5years: 0.50 ± 0.05, p < 0.0001). Therefore, T1D and its treatment appear to promote excess weight gain. Several factors, which are common in adolescents with or without T1D, such as sedentary behavior, reduced exercise

(especially in females), and unhealthy eating habits, may contribute to favor a positive energy balance (Lehmann et al., 2020). Other factors favoring body fat accumulation are specific to diabetes, including extra calorie intake to prevent or correct hypoglycemia, the consumption of low carbohydrate high fat foods, to reduce post-prandial glucose increase, and the chronic exposure of the peripheral tissues to non-physiologic hyperinsulinema due to the subcutaneous insulin injections **(Meissner et al., 2014)**. Nutritional strategies to reduce nocturnal hypoglycemia, include the ingestion of a bed-time snack containing carbohydrates and protein, although The American Diabetes Association (ADA) and the Endocrine Society reported the absence of consensus on this practice **(Abraham et al., 2022)**. Similar mechanisms may contribute to the frequently observed body weight gain in insulin-treated patients. Due to the strong relationship between carbohydrate intake and post-prandial glucose profile, modification of diet composition, with a reduction of carbohydrate, could be a potential strategy for limiting post-prandial glucose excursions and fluctuations at least in the short term, although appropriate carbohydrate and fat

intake was associated with lower HbA1c **(Lupoli et al., 2019)**. Moreover, a low carbohydrate intake is associated with less favorable dietary nutrient composition, leading to overconsumption of protein and fat **(Grabia & Markiewicz-Żukowska, 2021)**. Additionally, subcutaneous insulin injection exposes the body to higher peripheral insulinemia than that physiologically excreted by the pancreas in non-diabetic subjects; this chronic hyperinsulinemia promotes fat deposition **(Janssen, 2021)**.

Our study showed that half of the studied group were males (n=50) and the other half were females (50). With the mean age10.13 ± 2.83 years. There is a non-significant difference between Underweight, Normal weight, Overweight & Obese groups as regard age and sex.

However, the study of **Maffeis et al., 2018** demonstrated that in the youngest age group, the prevalence of obesity was significantly higher in males than females (M: 9.6% vs F: 6.2%; P<0.0001) whereas the opposite was found in the eldest (M: 6.2% vs F: 7.8%; P<0.0001). In children older than 10 years, the prevalence of overweight was significantly higher in females (F: 28.2% vs M: 21.5%; P<0.05) whereas the

prevalence of underweight was significantly higher in males (M: 1.65% vs F: 0.67%; P<0.0001). The difference between genders is likely the result of greater fat gain during and after puberty for girls. Three main factors may contribute to this finding: higher insulin resistance in females than males, alterations in GH/IGF-1 axis in patients with T1D, and the influence of sex steroids. Selective insulin resistance during puberty leads to compensatory hyperinsulinemia, amplifying insulin's effect on amino acid metabolism and thereby facilitating protein anabolism. This physiologic process is increased in adolescents with T1D due to lower insulin sensitivity than non-diabetic peers. Abnormalities of the GH/IGF-1 axis have been reported in adolescents with T1D, with increased GH secretion an incomplete suppression of GH by IGF-1, leading to a higher risk of hypoglycemia and weight gain. Girls seem to be more sensitive to GH/IGF-1 perturbations than boys, due to the much lower increase of testosterone.

The likely explanation of that our study showed non-significant difference between male and female children with type 1 diabetes as regard BMI is attributed to the difference in the age category included in our study (min. – max = 6.3 – 14.9years, main=11 ± 2.8) which is younger than the age of puberty with its effect on weight gain and insulin sensitivity in females which promotes BMI difference between females and males while the included age in the other studies was up to 18years. Another explanation may be the smaller sample size than that of the other studies.

The current study showed that the main HbA1c was 7.83 ± 0.59 and in both genders the association between HbA1c and BMI-SDS was U-shaped with the highest HbA1c in the underweight and obese groups. There is significant difference between underweight and normal (p<0.001), significant difference between underweight and overweight (p = 0.005), significant difference between normal and overweight (p<0.001), significant difference between normal weight and obese (p<0.001), non-significant difference between overweight and obese (p=0.176) and non-significant difference between underweight and obese (p=0.465).

Our results were supported by the study of **Maffeis et al., 2018** as they reported that in both genders, HbA1c was significantly

(p<0.05) higher in underweight and obese subjects than in normal weight persons. In males, HbA1c was significantly (p<0.05) higher in underweight and obese than in overweight subjects. In females, HbA1c was significantly (p<0.001) higher in overweight than in normal subjects.

And the large study of **Dubose et al., 2015**, which performed to examine the extent of the obesity problem and the association between BMI-SDS and HbA1c in children and adolescents with type 1 diabetes in 2 large registries in the US and Europe, reported that overall, greater BMI-SDS was associated with greater HbA1c adjusted for T1D duration, sex, age group and registry (p<0.001). When we looked at the registry-specific BMI-SDS, greater BMI also was associated with greater HbA1c within each registry (p<0.001 for both, adjusted for T1D duration, sex and age group).

In the study of **Dohan et al., 2021**, there is significantly high level of HbA1c with poor glycemic control in diabetic children with undernutrition.

Also the study of **Grabia & Markiewicz-Żukowska, 2021** reported that a connection was found between HbA1c and high accumulation of fat in the abdominal area. Good metabolic management is essential not only for normal growth and development in pediatric patients with T1D, but also for reduced or delayed progression of existing complications.

The cross-sectional design of the study did not allow assessment of the cause-effect relationship between variables. Nevertheless, in accordance with the available evidence, inadequate diabetes control leading to chronic hyperglycemia is likely associated with energy loss via glucosuria and subsequent weight reduction, spontaneous reduction of food intake promoted by ketoacidosis condition, and increased energy expenditure due to increased protein turnover and gluconeogenesis **(Maffeis et al., 2018)**.

The high HbA1c found in subjects with a high BMI-SDS may be due to chronic positive energy balance promoted by inappropriate dietary behavior and eating disorders accompanied by inadequate insulin treatment, which are more common in adolescents than in younger children **(Maffeis et al., 2018)**.

Insulin resistance and cardiovascular risk factors are associated with increased fat mass. Obese people with T1D have lower insulin sensitivity and a

higher cardiovascular risk profile than the non-obese people with T1D. Underweight affects a minority of the pediatric population. However, data in adults suggest that underweight individuals with established T1D are more prone to diabetic ketoacidosis and severe hypoglycemia than those with normal weight. Therefore, the increase in the amplitude of the deviation in excess or decrease from the median body mass index (BMI) for age and gender is associated with increased health risk for children and adolescents with T1D. Consequently, it is crucial to identify subjects with at risk BMI and to ensure specific care for managing children with BMI in the underweight and overweight/obesity categories as well as to prevent these conditions **(Dubose et al., 2015)**.

CONCLUSIONS

In conclusion, the current study showed that 31% of children and adolescents with T1D was overweight or obese whereas, 3% was underweight with no statistically significant difference between males and females. BMI-SDS statistically increased with the duration of diabetes with the lowest duration in the underweight group and the highest duration in the obese group. Underweight and obese children and adolescents

had the higher HbA1c (poorer glycemic control).

RECOMMENDATION

• Considering our results, we recommend continued nutrition education for children and parents by focusing on a healthy, balanced diet and limiting high-fat foods and increasing consumption of fiber-rich foods such as fruits and vegetables to optimize growth, maintain normal weight, reduce cardiovascular risk, and improve glycemic control in children and adolescents with T1D.

• Our results emphasize the need for developing further strategies to prevent and treat excess fat accumulation in T1D as it is strongly recommended for general population.

• Additional research is warranted to evaluate the characteristics of T1D and its management that may influence weight gain.

• Further multi-centric studies with a larger sample size should be carried out to strengthen the study results.

LIMITATIONS

The small sample size with almost the same socio-economic status. Therefore, prevalence rates are not applicable to the entire

population of children and adolescents with T1D.

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