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RESEARCH ARTICLE

Secular trends in BMI in a cohort of children with Type 1 diabetes in the first-year post diagnosis

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ABSTRACT

Background: Along with the global increase in the rates of overweight and obesity in the pediatric population, it is becoming more prevalent in children with type 1 diabetes. The presence of diabetes and obesity may further aggravate the long term outcome of these children.

Aims: Evaluate the secular change in BMI in children during the first year after the diagnosis of type 1 diabetes and identify variables affecting this change.

Methods: This is a retrospective cohort study conducted at the diabetes clinic at Shaare Zedek Medical Center. Demographic data was withdrawn from the patients' charts and included age, age at diagnosis, gender and ethnic origin. Clinical data included DKA at diagnosis, height, weight, and BMI at presentation and throughout the first year following diagnosis at several pre-determined time points.

Results: The study included 167 patients, 93 males. The average BMI-Z at presentation was -0.65 and increased to 0.35 after a year from diagnosis. The most pronounced increase in BMIZ occurred as expected in the first month (0.5-0.75), but it continued during the first year. At diagnosis, 16.6% of the children were underweight, 11.8% overweight and 2.7% obese. By the end of the first year, there were more overweight 28.5%, and obese 6.3% children. The lower the BMI-Z at diagnosis, the greater the weight gain observed at all-time points throughout the year. DKA at presentation was associated with a more significant weight gain in the first year using univariate analysis. No correlation was found between the patients' gender or age at diagnosis and the degree of weight gain.

Conclusions: Continuous weight gain was observed throughout the first year after the diagnosis of diabetes, with a significant increase in the rate of overweight and obesity.

Keywords: Type 1 diabetes, BMI, Children, Obesity, overweight.

Introduction

Intensive insulin therapy in patients with type 1 diabetes- T1D has led to improved glycemic control and reduced long term complications[1]. Intensive insulin regimens delivered by combinations of multiple daily injections or by continuous subcutaneous insulin infusion by a pump has been the standard of therapy for children with T1D for the past years[2]. However, several studies have shown that intensive insulin therapy has been accompanied with increased weight gain and obesity in comparison to conservative therapy[3,4].

The mechanisms underlying excessive weight gain are multiple and diverse, including a drop in the resting metabolic rate, increased fat accumulation due to insulin action, decrease in blood glucose levels below the renal threshold without compensatory reduction in calorie intake, and conscious/ unconscious increase in calorie intake due to fear of hypoglycemia[5]. Excessive weight gain may lead to adverse cardiovascular outcomes, as evidenced by its association with central obesity, dyslipidemia, insulin resistance and hypertension[6].

In a study in adolescents with type 1 diabetes the rate of hypertension and high levels of LDL and triglycerides was increased in those with overweight and obesity. These factors play a major role in cardiovascular morbidity[7].

A recent longitudinal study conducted in adults with T1D confirmed a lower survival rate than the general population, the diagnosis may also affect the partial recovery period in T1D[9]. In a study on children with type 1 diabetes, higher increase in BMISDS was associated with lower rates of partial remission, which may lead to less controlled blood glucose levels[8].

Data regarding extent of weight gain in children with T1D on intensive insulin therapy is inconclusive. In a study conducted by Baskaran with a ten year follow up of children with T1D, the incidence of intensive insulin treatment increased from 52% to 97%, but the incidence of obesity did not change[10]. On the other hand Manyanga demonstrated a constant increase in the mean BMI-Z (body mass index Z score) of patients from diagnosis to six months afterwards and at transition to adult care, with an increase in the incidence of overweight but not obesity[11]. Newfield reported a mean BMI-Z of -0.28 at diagnosis, and 0.86 ten weeks later, with almost a third of the patients with BMI above the 85th and 16% above the 95th percentile after six months[12].

The increase in weight following diagnosis may be partly explained by initial rehydration combined with the shift from catabolic to anabolic state due to the initiation of insulin therapy. However, there seems to be an over-compensation, resulting in higher rates of overweight and obesity among children with diabetes[13-15].

Several studies have tried to evaluate factors influencing the witnessed weight gain in children, such as gender, age at diagnosis, disease duration and patients keeping their disease a secret[16,17]. The data on the subject remains incomplete, inconclusive, and sometimes contradictory and further research on the topic is needed.

In this study we sought to determine the changes in BMI during the first year after diagnosis and the factors affecting these changes in a cohort of children treated in our clinic.

Materials and methods

The diabetes clinic at our center treated 273 patients with T1D at the time of study We excluded patients younger than 1 year at the time of diagnosis and patients who were not treated at the clinic for the first year following diagnosis. 167 patients met the criteria and were included in the study.

Demographic data was withdrawn from the patients' charts and included age at diagnosis, gender, and ethnic origin. Clinical data included height and weight throughout the first year after the diagnosis at several pre-determined time points: at diagnosis, at one month (2-6 weeks), three months (10-14 weeks), six months (22-26 weeks) and twelve months (50-54 weeks). Due to the patients' varying degrees of compliance to the follow-up meetings, the number of children whose data was recorded is different for each time point- at diagnosis 144 children were included, at one month 141 children, at 3 months 90, at 6 months 88, and at 12 months 63 children.

BMI-Z was calculated using the CDC growth charts. A BMI-Z of below -2 was considered underweight (UW), BMI-Z equal and/or above -2 up to and equal to 1 was considered normal weight (NW), BMI-Z above 1 overweight (OW), and above 2 obese (OB). In order to determine the effect of BMI-Z at diagnosis on weight gain in first year more accurately, we used the delta, the degree of change, instead of the actual BMI-Z values (children with higher BMI-Z at diagnosis will more likely have higher BMI-Zs throughout the year, even if they gained less weight).

The study received the local IRB approval, Number 0198-18-SZMC.

2-1 STATISTICAL ANALYSIS

The correlation between two quantitative variables was determined by the Pearson correlation coefficient. For comparing a quantitative variable with several categories of a qualitative variable, the Mann–Whitney U test was used due to the small sample size.

In order to determine the effect of multiple variables on the dependent variable (change in BMI following diagnosis), the Repeated Measures ANOVA was used.

Regression analysis was done to determine the relation between BMI at any time point, and BMI at diagnosis, and other additional factors.

Results

The patients' characteristics are presented in Table 1.

A continuous and uneven increase in patients' BMI-Z values was observed throughout the first year. The most pronounced increase occurred in the first month (an average increase of 0.5). Later the weight gain trend stabilized, with smaller differences measured at each time point. This data is shown in figure 1.

Table 1 Demographics of the study cohort at the time of diagnosis

Male N (%)	93 (55.7)
Age mean ±SD	9.97±3.77
Ethnicity N (%)	Jewish 155 (92.8) Arab 12 (7.2)
DKA at presentation	72 (43.1)
Hypothyroidism N (%)	1 (0.6)
Celiac N(%)	6 (3.6)

Fig 1 BMI-Z trend in 12 months following diagnosis

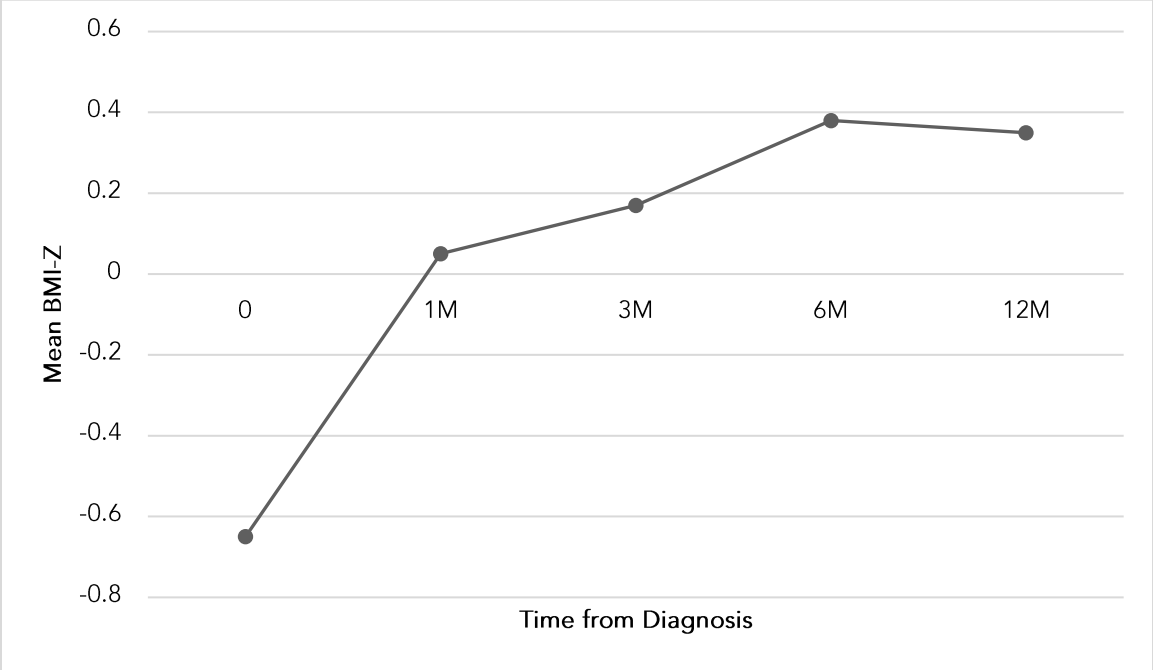

Table 2 shows the BMIZ and the percentile of BMI categories at different time scores.

Even though the weight gain trend stabilized, the percentage of children who were overweight and obese kept rising especially at six months after diagnosis. At diagnosis, 9.0% and 2.8% of the cohort were overweight and obese respectively. After six months these ratios increased to 23.9% for overweight, and 8% for obese children. By the end of the first year, 22.2% of the children were overweight, and 6.3% obese.

Table 2 BMI-Z values in first year following diagnosis

Time since diagnosis	Mean ± SD	Range	UW% (n)	NW% (N)	OW% (N)	OB% (N)
BMI-Z 0	-0.65 (1.46)	[-5.31]- [+2.42]	16.6 (24)	71.5 (103)	9.0 (13)	2.8 (4)
BMI-Z 1M	0.05 (1.04)	[-2.67]- [+2.55]	2.8 (4)	80.9 (114)	13.5 (19)	2.8 (4)
BMI-Z 3M	0.17 (1.01)	[-2.08]- [+2.46]	2.2 (2)	72.2 (65)	21.1 (19)	4.4 (4)
BMI-Z 6M	0.38 (1.07)	[-2.05]- [+2.58]	2.3 (2)	65.9 (58)	23.9 (21)	8.0 (7)
BMI-Z 12M	0.35 (1.15)	[-2.82]- [+2.44]	1.6 (1)	69.8 (44)	22.2 (14)	6.3 (4)

BMI-Z 0=at time of diagnosis, M=months; UW=underweight; NW= normal weight; OW=overweight; OB=Obese

EFFECT OF BMI-Z AT DIAGNOSIS ON WEIGHT GAIN IN FIRST YEAR FOLLOWING DIAGNOSIS

Using the paired samples T-test, we calculated the delta between BMI-Z at diagnosis (termed BMI-Z 0) and the BMI-Z measured at all other pre-determined time points (1,3, 6 and 12 months following diagnosis). Significant changes were found for all pairs (deltas) calculated, meaning a significant change was found between BMI-Z 0 and all time points examined.

To seek the correlation between weight at diagnosis and the degree of weight gain in the first year, the calculated deltas were then compared to BMI-Z 0 (at diagnosis).

For all parameters examined (between delta and BMI-Z 0), Pearson correlation coefficient was high and negative and highly significant ($p < 0.000$): ΔBMI-Z 1 -0.76, BMI-Z 3 -0.77, BMI-Z 6 -0.72, and BMI-Z 12 -0.60. This means the lower the BMI-Z 0 value, the larger the gap between it and each time point tested. The clinical significance is that the patients with lower BMI at diagnosis gained more weight during the first year.

ADDITIONAL FACTORS AFFECTING THE INCREASE IN BMI–Z IN FIRST YEAR FOLLOWING DIAGNOSIS

Patients who presented with DKA gained considerably more weight than the ones without DKA. This correlation was found to be statistically significant throughout the first 6 months after diagnosis (ΔBMI-Z for the 1, 3 and 6-months time points show a 2-tailed significance of $p<0.001$, $p<0.001$ and $p=0.007$, respectively.

Gender and age of patient at the time of diagnosis were not found to be significantly correlated to increase in BMI–Z in first year following diagnosis. We were not able to determine the effect of ethnic background on weight gain, due to the low percentage of patients from different populations included in this study.

REGRESSION ANALYSIS BETWEEN VARIOUS PATIENT PARAMETERS

We did a regression analysis using BMI at each time point (1,3,6,12 months) as a dependent factor and age, sex, DKA at presentation, BMIZ at diagnosis, the mode of therapy (CSSI Vs MDI) and HBA1c as independent factors. We did not find any correlation between BMIZ at 1 month and the independent factors. BMIZ at 3 and 6 months was related significantly to BMIZ at diagnosis. BMIZ at 12 months was not correlated to the independent factors, though we think it is related to a relative low sample size.

Discussion

The incidence of overweight and obesity is increasing among children with T1D. In a study conducted in Brazil on children with T1D the prevalence of overweight and obesity was reported to be 31.7%. In this study overweight and obese children consumed more processed food and had higher levels of HBA1c[18].

In another two large pediatric clinical registries of children with T1D in the United States and Europe, the participants' median BMI was greater than international and respective national reference values. Increased BMI in this study was associated with poor glycemic control manifested by higher HBA1c levels and increased frequency of severe hypoglycemia[19].

There is some evidence that excessive weight gain in children after the diagnosis of diabetes track to adulthood[14].

Obesity is a known risk factor for cardiovascular morbidity and mortality. In a study conducted in a large cohort of adults with T1D, 18% were found to be obese and those had a higher prevalence of other cardiovascular risk factors. The risk for hypertension in the obese with T1D was 61 % (vs 37.5% in the normal weight), dyslipidemia 63.6 % (vs 44% in the normal weight) and chronic kidney disease 38.4 % (vs 24.4 % in the normal weight). These differences were not related to sex, age or duration of diabetes or the diabetes control[20].

In the current study we sought to specify the pattern of weight gain and determine the extent and nature of the increase in BMI in the first year after diagnosis and identify the variables affecting it. We chose the first year of diagnosis, since children experience major metabolic changes during this time period, including the catabolic state before the diagnosis, the honeymoon period and final adjustment to insulin therapy.

We observed a continuous increase in patients' BMI throughout the first year after diagnosis. Although an increase in BMI is expected immediately after the diagnosis because of improvement in the dehydration and correction of the catabolic state, the children usually stabilize few weeks after diagnosis. So, the increase in the BMI in the months after the diagnosis does not seem to be related to these factors.

Previous studies show a clear upward trend in BMI throughout the first year, although there are differences in the degree and timing of the weight gain observed.

In a study in adults with T1D there was a 4.3 Kg increase in weight during the first year post diagnosis. Body composition was estimated by means of dual-energy-X-ray absorptiometry and showed a 13.3% increase in total fat mass and 4.9 % increase in lean body mass[16].

Our study is retrospective, and we do not have the exact details of the insulin dosage, calorie intake or physical activity in our patients, but the strength of our study is that all the patients were treated by the same local protocol and by the same team.

As expected, the largest increase in BMI occurred in the first month post diagnosis, which seems reasonable since most of the children at the time of diagnosis are in a catabolic state and have lost weight. On the other hand, weight gain in our cohort continued six months post diagnosis with increased rates of overweight and obesity after a year. This trend was observed both in

children (2-11 years) and adolescents (12-18) years, with 23% of children and 20.8% of adolescents being overweight one year after diagnosis. The incidence of obesity was higher in children (7.6%) than in adolescents (4.1%).

These rates are higher than the reported average rates of overweight and obesity in children in Israel (9% for overweight and 7.5% for obesity)[21]. Among adolescents the national rates are similar to what was found in our study for overweight 19.5%, while obesity was more prevalent in children without diabetes (10.7%)[22]. Our data show that after the first year of Insulin treatment, young children with diabetes suffer more frequently from overweight than their non-diabetic peers.

Regarding factors influencing the weight gain, we found a negative correlation with BMI-Z value and DKA at diagnosis. By multivariate regression analysis we found a significant effect of BMI at the time of diagnosis to BMI at 3 and 6 months.

Some previous studies show the same results as us, others show contradictory results. It should be noted that there are significant differences between the studies, including follow-up period, sample size and ethnicity of the patients. The underlying mechanism for the increased change in BMI in children with lower BMI at diagnosis may be related to the physiologic and metabolic state of the participants in the study. Children who were underweight at the time of their diagnosis were in a more severe catabolic state and had a bigger energy deficit than their peers. Therefore, they gained more weight once the cause of the catabolic state; insulin deficiency was treated.

The relation between DKA and weight gain has been described previously. Our cohort had a higher percentage of DKA at the time of diagnosis (44.6% as opposed to 22.6% and 27% at other studies) which may have affected our results.

Our results suggest that there is a need to monitor more strictly the weight of children who are severely underweight and/or suffer from DKA at time of their diabetes diagnosis, and when necessary, intervene early with diet modification and regular exercise to prevent them from becoming overweight.

We did not find a correlation between gender and age of the patients at time of diagnosis and weight gain in first year after diagnosis. Some studies have reported that older children and specifically adolescents gained more weight. Most studies show that girls gain more weight[10,14,16]. while there are some studies that show that boys gain more weight. [23] These studies have a big diversity in their population regarding the sample size and follow up period, different gender percentages and different ethnicities, which may affect treatment compliance, exercise, and nutrition.

The strength of our study is that all patients at the diabetes clinic at Shaare Zedek Medical Center who met the inclusion criteria were included in the study, which reduces the risk of selection bias. All the measurements were recorded by health care professionals with the same instruments and the same methods. No self-reported measurements were included in the study.

The limitation of our study is its retrospective design.

Conclusions:

Throughout the first year after diagnosis of diabetes, there is a continuous and uneven increase in patients' BMI-Z values, more prevalent in children with lower BMI at diagnosis. After the first year, nearly a third of patients are either overweight or obese, exceeding the overweight and obesity rates amongst their non-diabetic peers.

Conflicts of Interest Statement:

The authors have no conflict of interest to declare.

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