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OVERWEIGHT, OBESITY AND METABOLIC SYNDROM IN CHILDREN AND ADOLESCENTS WIT TYPE 1 DIABETES MELLITUS

Abstract: The influence of obesity on cardiometabolic health in the general population has been widely studied, but few studies are dealing with the problem of obesity in children and adolescents with type 1 diabetes.

Aim: The aim of this study was to determine the presence of overweight, and obese persons with metabolic syndrome in children and adolescents with type 1 diabetes and to determine the conection of nutritional status with other risk factors for cardiovascular disease, such as dyslipidemia, glycoregulation, high blood pressure , insulin dose, age, illness, length of illness.

Methods: The study included 197 children and adolescents with type 1 diabetes mellitus (103 females, 94 males). The average age of respondents was 12,71 years. Data on body weight, height, BMI was calculated according to the formula kg/m². Standard laboratory procedures were determined, total cholesterol, LDL and HDL cholesterol, AST, GHbA1c, data on a daily dose of insulin, and type of insulin therapy, age at which the disease began, duration of disease, the possible existence of microvascular complications (microalbuminuria, retinopathy, neuropathy) and hypertension were obtained.

Results: There were 77,2% patients had normal weight, 14,2% were overweight, 3,4% were obese and 5,2% nutritional had metabolic syndrome. We found statistically significant conection between nutritional impairment and total cholesterol, tryglycerides, hypertension, lenght of disease and daily insuline dose.

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Conclusion: Due to the fact that people with type 1 diabetes are at high risk for the development of vascular complications, prevention, early detection and treatment of nutritional impairment as well as other cardiometabolic risk factors are imperative.

Key words: diabetes type 1, children, obesity, metabolic syndrome

Introduction

Obesity is a multifactorial, complex disease that occurs as a result of chronic excessive energy intake supported by genetic and environmental factors (1,2). Is the most common nutritional disorder in industrialized countries and is associated with increased morbidity and mortality from cardiovascular disease (3).

Starting from the definition of the weight above the P85 for age and sex means overnutrition and obesity over the P95, it is evident that there is a dramatic increase in the incidence of nutritional disorders in all age groups and among all ethnic communities (4). Obesity epidemically occurs in all younger age. It is estimated that each year about 1.3 million of children becoming overweight in Europe and 350 thousand new obese. In Serbia, the prevalence of obesity is estimated at 19% (5,6).

Adipose tissue is not only a simple body to store fat - it is an active endocrine organ and part of the innate immune system that affects many physiological and pathological mechanisms, such as glucose homeostasis, inflammation, angiogenesis, cell proliferation and differentiation (7). This endocrine role are carrying adipocytes and activated macrophages infiltrated in adipose tissue. Altered expression of adipokines associated with obesity leads to the induction of systemic inflammation and a low degree of dyslipidemia, which together can lead to rapid and early atherosclerosis (8).

Diabetes mellitus type 1 is the most common endocrine metabolic disorder in childhood and adolescence, and also shows the increasing incidence (9). Despite the progress that has been made in the treatment of children and adolescents with type 1 diabetes, these patients still have a few times higher risk of developing coronary, cerebrovascular and peripheral arterial disease in early adulthood (10,11). Diabetic macrovasculopathy is a result of structural and functional changes in blood vessels that occur as a result of numerous pathophysiological disorders. Among them hyperglycemia has a central role, which leads to nonenzymatic glycosylation, increased oxidative stress and activation of proinflammatory signaling pathways (12,13). In poorly controlled diabetes it leads to quantitative and qualitative lipid disorders by increasing the concentration of free fatty acids, triglycerides, cholesterol, low-density lipoprotein (LDL) and decrease in high density lipoprotein (HDL), and lipoprotein glycation and peroxidation of LDL. These disorders cause endothelial dysfunction with a disturbance of the balance between vasoconstrictor and vasodilator, anticoagulant and procoagulant mediators, as well as the factors that stimulate or slow down growth and

thus lead to earlier and more frequent occurrence of atherosclerosis in diabetic patients, which shows the evolution of faster and more difficult clinical course (14) .

The influence of obesity on cardiometabolic health in the general population has been widely studied, but few studies are dealing with the problem of obesity in children and adolescents with type 1 diabetes.

Increasing number os studies suggest a direct link between the growing incidence of obesity and the increasing incidence of the two main types of diabetes mellitus (type 1 and 2) (15). Both of these types of diabetes are caused by pathogenic model of inflammation. In type 1 it is an chronic inflammation within the pancreatic islets from autoimmune antibodies detectable in the periphery, whereas in type 2 diabetes is a true model of systemic inflammation with acute phase reactants of inflammation in the circulation. Pathological obesity through activation of NF-kappaB may be responsible for the development and beta cell destruction and insulin resistance, confirming the hypothesis on the connection between obesity epidemic in young people with the emergence of a new type of diabetes: 1 and 2 - “double” or “hybrid” (16) .

According to the study, SEARCH for Diabetes in Youth, the percentage of over-nutrition (not obesity) in the group of children with type 1 diabetes is higher than in the healthy control group, suggesting the existence of different mechanisms that contribute to nutritional disorder in this population (17). Besides sedentary lifestyle, and other factors such as excessive insulin supply to optimalise glycemic control during intensified insulin therapy or increased caloric intake because of frequent episodes of hypoglycemia and nutritional liberalization (18).

Etiology and pathogenetic mechanisms of overnutrition (not obesity) are different in children and adolescents with type 1 diabetes compared to the general population. Over-nutrition and obesity as risk factors and comorbidities were the subject of several studies, which have shown contradictory results (18,19). However, the DCCT study showed that overnutrition in children and adolescents is a significant cardiometabolic risk (20).

Relationship between obesity and insulin resistance, hypertension, dyslipidemia, type 2 diabetes and other metabolic abnormalities associated with the risk of atherosclerotic cardiovascular disease in adults (Reaven et al 1988) was described as the “metabolic syndrome” (synonymous: the insulin resistance syndrome, dismetabolical syndrome or syndrome X) (21). Today it is considered that the basic disturbance in metabolic syndrome tissue resistance to the action of insulin, which leads to compensatory hyperinsulinemia, secondary disorders plasma lipids and increased blood pressure (22). For the diagnosis of the metabolic syndrome in childhood and adolescence can be used the same criteria used for the diagnosis of this syndrome in adults with the need to adjust any of the criteria for age and sex of respondents (23,24). Given the differences in children and adolescents of different ages and sexes new definition of the metabolic syndrome according to the criteria of the International Diabetes Federation (IDF) is divided into different age groups: 6 - <10, 10 - <16 and over 16 (25) (Table 1).

Table 1. The IDF consensus definition of metabolic syndrome in children and adolescents

Age group [years]	Obesity (WC)	Triglycerides	HDL-Ch	Blood pressure	Glucose
6-10	≥90 percentile	Metabolic syndrome cannot be diagnosed, but further measurements should be made if there is a family history of metabolic syndrome, T2DM, dyslipidemia, cardiovascular disease, hypertension and/or obesity			
10-16	≥90	≥ 1,7 mmol/l	<1.03 mmol/l	systolic ≥130 mmHg / diastolic ≥85 mmHg	≥5.6 mmol/l
≥16	Use existing IDF criteria for adults				

Due to the fact that people with type 1 diabetes are at high risk for the development of vascular complications, prevention, early detection and treatment of cardiometabolic risk factors is imperative (26).

The aim of this study was to determine the presence of overweight, and obese persons with the metabolic syndrome in children and adolescents with type 1 diabetes and to determine the nutritional status of connections with other risk factors for cardiovascular disease, such as dyslipidemia, glycoregulation, high blood pressure, insulin dose, age, illness, length of illness.

Methods

The study was conducted at Children's endocrinology department of Children clinic in Niš. The study included 197 children and adolescents with type 1 diabetes mellitus. The average age of respondents was 12,7 years.

By using retrospective analysis, we obtained data on body weight, height, BMI was calculated according to the formula kg/m^2 . Standard laboratory procedures were determined, total cholesterol, LDL and HDL cholesterol, AST, GHbA1c, after reviewing the medical records, data were obtained on a daily dose of insulin, and type of insulin therapy, age at which the disease began, duration of disease, the possible existence of microvascular complications (microalbuminuria, retinopathy, neuropathy) and hypertension.

Respondents were divided into 4 groups:

1. First group (N154) included patients with BMI below the 85th percentile,
2. Second group (N=28) included patients who were overweight or who had a BMI greater than the 85th percentile and less than 95th percentile
3. Third group (N=7) included the respondents who were obese or had a BMI over the 95th percentile for age and sex
4. Fourth group (N=10) is comprised of those who are references to the IDF (Table 1) had met criteria for the metabolic syndrome (MS)

Statistical processing

Data are presented as mean and standard deviation, or in the form of absolute and relative numbers. Kolmogorov-Smirnov test was used to test the data distribution. It was done to test the normal distribution of statistically significant differences between several groups we used ANOVA with post hoc analysis, if the normal normal distribution was not satisfied we Kruskal-Wallis test as a post hoc analysis, in this case we used the Mann-Whitny's U test. The statistical hypothesis was tested at the risk of significance for $\alpha = 0.05$, ie. difference between samples is considered significant if $p < 0.05$. For the analysis we used SPSS 16.0 software package.

Results

The study included 197 patients (94 boys and 103 girls). There were no significant statistical differences in sex among the groups ($p = 0.847$). The average age of all patients was 12.71 ± 4.89 . There was a statistically significant difference in age among the groups ($p = 0.023$). There was a statistically significant difference in age between the groups: first vs. fourth ($p = 0.029$), second vs. third ($p = 0.039$) and third vs. fourth ($p = 0.007$). No statistically significant differences among the groups in height.

Statistically significant difference among the groups exist in the TM ($p < 0.001$), BMI ($p < 0.001$), BMIP ($p < 0.001$), cholesterol ($p = 0.039$). It was found that a statistically significant difference exists in TM between the following groups: first vs. fourth ($p = 0.029$), second vs. third ($p = 0.039$), third vs. fourth ($p = 0.007$). The average BMI are significantly different in the following groups: first vs. second ($p < 0.001$), first vs. third ($p = 0.044$), first vs. fourth ($p < 0.001$) and second vs. fourth ($p = 0.005$). Statistically significant difference in BMIP exists between all groups ($p < 0.001$), except between the third and fourth (Table 2).

Table 2. Anthropometrical characteristics

	BMI <P85 n=152 (77,2%)	BMI <P95 n=28 (14,2%)	BMI >P95 n=7 (3,4%)	MS n=10 (5,2%)	P
Age	14,13±3,31	10,68±5,88	9,93±4,02	15,69±4,88	0,023*
Sex (M/Ž)	74/78	12/16	4/3	4/6	0,847
Height	148,96±24,97	155,18±22,19	142,40±24,52	158,19±13,47	0,307
Height P	55,68±28,63	56,79±31,15	74,43±16,11	44,80±34,02	0,252
Weight	42,42±17,92	54,05±17,54	45,64±19,14	64,00±15,89	<0,001*
BMI	18,78±3,76	22,04±3,14	21,47±3,81	25,37±3,36	<0,001*
BMI P	45,09±23,79	82,36±21,22	96,57±2,22	94,60±2,91	<0,001*

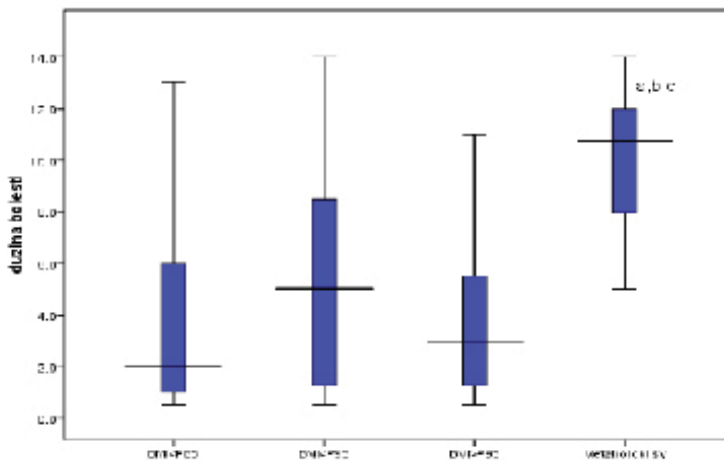
Cholesterol is statistically significantly different among the groups ($p = 0.039$), and between: the first and fourth groups ($p = 0.004$), the second and fourth ($p = 0.016$).

It is shown that there is a statistically significant difference in the presence of hypertension among the groups ($p < 0.001$). In the group with metabolic syndrome is the most common, and in group BMI $< P85$ can occur quite rarely (Table 2).

Table 3. Cardiometabolic risk factors

	BMI $\leq P85$	$P85 \leq \text{BMI} \leq P95$	BMI $\leq P95$	MS	p
Total cholesterol (mmol/l)	4,38 \pm 0,88	4,49 \pm 1,05	4,53 \pm 1,27	5,61 \pm 1,33*	0,039*
LDL-cholesterol (mmol/l)	1,41 \pm 0,38	1,58 \pm 0,84	1,43 \pm 0,21	1,37 \pm 0,24	0,407
HDL-cholesterol (mmol/l)	2,51 \pm 0,66	2,65 \pm 0,79	2,66 \pm 0,58	2,87 \pm 0,45	0,224
Triglycerides (mmol/l)	0,93 \pm 0,47	0,86 \pm 0,51	0,71 \pm 0,14	1,26 \pm 0,49*	0,050*
Age of set up (g)	8,41 \pm 4,32	8,42 \pm 3,82	5,71 \pm 4,27	5,85 \pm 4,22	0,137
Arterijska hipertenzija %	2,6	14,3	28,6	70	$< 0,001$ *

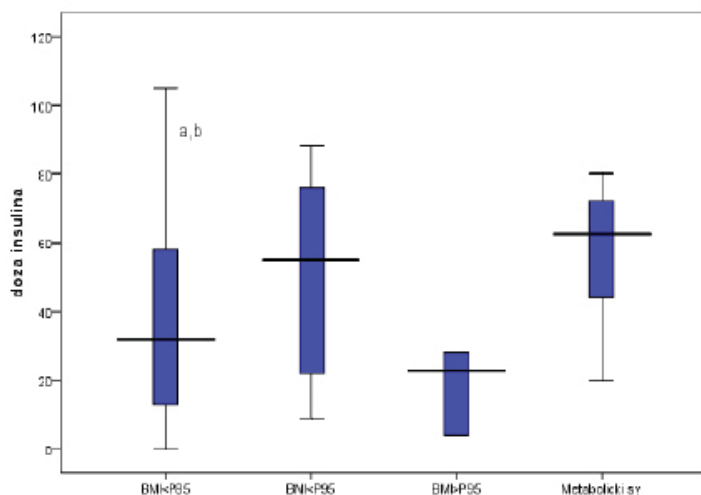
The average length of illness was 4.39 ± 4.08 . There was a statistically significant difference in the duration of disease among the groups ($p = 0.002$). The analysis showed no statistically significant difference in the length of the disease among the following groups: first vs. fourth ($p = 0.001$), second vs. fourth ($p = 0.009$), third round, fourth ($p = 0.025$) (Grafic 1).



- a – BMI $< P85$ vs metabolic syndrome, $p < 0,01$,
- b - BMI $< P95$ vs metabolic syndrome, $p < 0,05$
- c - BMI $> P95$ vs metabolic syndrome, $p < 0,05$

Grafic 1. Length of disease

There was not significant difference in glycoregulation between study group (Grafic 2).



Grafic 2. HbA1c level

The average insulin dose was 38.62 ± 35.58 . There was a statistically significant difference in the dose of insulin among the groups ($p = 0.005$), further analysis showed no statistically significant difference in insulin dose exists among the following groups: first vs. second ($p = 0.022$) and the first round, fourth ($p = 0.005$) (Grafic 3).

- a – BMI<P85 vs BMI<P95, $p < 0,05$,
- b - BMI<P85 vs metabolički sindrom, $p < 0,01$

Grafic 3. Insuline dose

Table 4 shows the distribution of late complications between the groups. Distribution of microalbuminuria are significantly different among the groups ($p = 0.001$). It is the most common in children who suffer from the metabolic syndrome. The presence of retinopathy is significantly different among the groups ($p = 0.017$). Outbreaks in patients with metabolic syndrome.

Tabela 4. Microvascular complication

	BMI<P85 n=152 (%)	BMI<P95 n=28 (%)	BMI>P95 n=7 (%)	Metabolic syndrome n=10 (%)	p
Mikroalbuminury	7 (4,6)	6 (21,4)	0	4 (40)	0,001*
Retinopatya	3 (1,9)	1 (3,6)	0	3 (30)	0,017*

Discussion

The influence of obesity on cardiometabolic health in the general population has been widely studied, but few studies are dealing with the problem of obesity in children and adolescents with type 1 diabetes

Results indicate that the prevalence of overnutrition / obesity in children and adolescents with diabetes is 22.8%, which coincides with the results of other authors (27).

Analyzing the average age in the group observes a significantly older age of the children with manifest metabolic syndrome, which speaks to the fact that in older age appears a growing number of cardiometabolic risk factors (28).

Due to the different etiology and pathophysiology of overnutrition / obesity in children and adolescents, mostly caused by excessive insulin supply, the results of our study indicate lower triglyceride levels and higher HDL cholesterol levels, although not statistically significant in children who were overweight, compared with children normal weight. Similar results were obtained in a study by Belgian (29).

Looking at the impact on the nutritional quality of glycemic control, we did not find it statistically significant. In the group of children who were overweight / obese, it is noticed even lower percentage of glycosylated hemoglobin.

It is established that the younger age of disease is an independent cardiovascular risk factor in children and adolescents with diabetes mellitus type 1 (30). Our findings indicate that children and adolescents who are overweight and have a manifest metabolic syndrome, patients are in a younger age, compared to normal weight children.

It is shown that adolescents with established metabolic syndrome have a duration of illness significantly higher, compared to the other groups, as shown in previous studies (31).

The total daily dose of insulin, and type of insulin therapy did not differ statistically in the two groups.

It is shown that there is a statistically significant difference in the presence of hypertension among the groups ($p < 0.001$). In the group with metabolic syndrome is the most common, and in the group of children who were of normal weight are the rarest occurs. The results correlate with the results of other authors (28).

As expected, microalbuminuria and retinopathy as the most common chronic complications in children who suffer from the metabolic syndrome.

Conclusion

Due to the fact that people with type 1 diabetes are at high risk for the development of vascular complications, prevention, early detection and treatment of nutritional impairment as well as other cardiometabolic risk factors are imperative.

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