The Impact of Obesity Assessed by Different Criteria on the Metabolic Parameters in Children and Adolescents in Georgia

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Abstract

The aim of our study was comparative analysis of anthropometric characteristics in children and adolescents significantly correlated with the parameters of metabolic syndrome. The study group is consisted of 113 children and adolescents (study group) with excessive body weight and obesity (group 1—BMI percentile; group 2—waist circumference; group 3—waist to height ratio). The control group consisted of 113 children and adolescents without. Comparative analysis of obtained data have been carried out by multiple regression analysis. BMI percentile is more an indicator of a generalized obesity; WC and WHR percentiles better describe visceral obesity and metabolic disorders—insulin resistance, hypertension and dyslipidemia. However, the WHR Percentile may be a more useful tool. To assess obesity in children and adolescents, it is necessary to evaluate together BMI, WC, and WHR percentiles. It can be also concluded that these findings indicate the need to continue research in this direction.

Keywords

children, adolescents, obesity criteria, insulin resistance, dyslipidemia

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Background

The prevalence of excessive body weight and obesity has significantly increased in last decades. The obesity is considered to be a major risk factor for the death from cardiovascular disease at an early stage of life.[1] Despite advances in the treatment and prevention of cardiovascular disease the adolescent mortality due to obesity has not reduced.[2,3] The increase of body mass in children and adolescents is generally associated with an increase in mass of all tissues; but in the case of excessive weight and obesity the gain is mainly associated with an increase of adipose tissue[4,5] and the risk of the development of Metabolic Syndrome (MS). MS Is a coexistence of obesity and other metabolic disorders (insulin resistance, glucose intolerance, hypertension, and dyslipidemia), having the impact on the development of cardiovascular disease, during the childhood as well.[5] The severity of the MS is related to the degree of adipose tissue increase.[6] Visceral obesity is considered to be a major risk factor for the development of MS and comorbidities.[7] Thus, the assessment of the visceral obesity in children and adolescents is of great importance in the timely prevention of the MS development.[7]

There is currently no unambiguous agreement on the anthropometric and metabolic parameters that should be used to assess overweight and obesity in children and adolescents.[8] Partly, this may be due to the physiological changes developing in the childhood and adolescence that affect individual components of the MS. Physicians

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often use the modifications to the adult criteria provided by WHO and National Cholesterol Education Program's Adult Treatment Panel (ATP)—III definitions.[9,10] Also there is no consensus on the criteria for the assessment of the obesity in children and adolescents with MS, which often leads to different results.[8] According to some studies, body mass index (BMI), which is in the upper range of the norm in adolescents, is associated with an increased risk of death due to cardiovascular disease. However, the threshold after which BMI is associated with an increase of the cardiovascular risk remains unclear[2,3,11,12]; it should be also noted that other studies do not confirm such a correlation.[13] Complicating the problem is the fact that large-scale studies of childhood and adolescent obesity, which have revealed the association of the obesity with behavioral risk factors (physical activity, nutrition), are widely limited in Europe.[14-18]

Some authors consider the waist circumference (WC) is a more important criterion. It assess not only subcutaneous but also visceral fat and reveals a reliable association with lipid levels and insulin resistance.[19] Some authors prefer to use the ratio of WC to the body height (WHR) as an indicator of the risk of MS development.[8]

Taking into account the above mentioned, the search for reliable methods and criteria for the assessment of the degree of overweight and obesity in children is still relevant.

We assume that a systematic analysis of the results of studies determining the relationship between anthropometric parameters and MS in children and adolescents in the various countries will help to reach a consensus on the anthropometric and metabolic parameters that should be used to assess the risk of the overweight/obesity and their complications.

The aim of our study was to investigate anthropometric characteristics of overweight and obesity in children and adolescents which have a significant correlation with the MS parameters associated with early cardiovascular complications and death.

Methods

The study represents a single center prospective cohort investigation.

The study group consisted of 113 children and adolescents who applied to the National Institute of Endocrinology in the first 6 months of 2019 and were diagnosed overweight and/or obesity. Three subgroups were separated depending on the criteria of the definitions of excessive body mass/obesity. The control group consisted of 113 randomly selected from 197 persons of same age group who applied to the National Institute of Endocrinology in 2019 and who did not meet any of the criteria for excessive body weight. The number of girls and boys in the control and study groups was equal. The formation of the control group continued until the ratios of children and adolescents, as well as girls and boys, were equal to those of the study group. Fifty-six children aged 8 to 12 (32—girls, 24—boys) and 57 adolescents aged 13 to 15 (41—girls, 16—boys) were included in both the study and control groups. Thus, 112 children and 114 adolescents participated in the study (Table 1).

Table 1.

The content and purpose of the study have been explained to the parents/guardians of each participant. They signed the written informed consent form approved by the Board of the Ethics Committee of the National Institute of Endocrinology (protocol N 433/134 from 03.01.2019).

Excessive body weight and/or obesity were assessed by the anthropometric parameters (body mass, height, BMI, WC and WHR), using the following 3 criteria:

- BMI Percentiles ("overweight"—if BMI Percentiles range in 85‰ to 94‰; "Obesity"—if BMI Percentiles are ≥95‰)[20];
- WC Percentile ("Visceral obesity, if WC Percentile > 90‰);
- WHR ("Visceral obesity," if WHR > 90‰.

Body mass and height were measured and BMI was calculated. Blood pressure (BP) was measured 3 times in a resting position and averaged over the last 2 measurements. The levels of glucose, insulin, lipids, leptin, Total cholesterol (TC), Triglycerides (Tg), and HDL, LDL, VLDL-lipoproteins were determined in the venous blood. The determination of fasting plasma insulin (FPI) and postprandial plasma insulin (PPI) were carried out by immune fluorimetric assay based on monoclonal antibodies (Delfia), and of Leptin—by radioimmunoassay (Linco). Fasting plasma glucose (FPG) and postprandial plasma glucose (PPG) levels were measured by YSI 2700 STAT Analyzer (Yellow Springs Instruments). Insulin resistance was assessed by HOMA2 model.

All procedures were performed in accordance with the requirements of the Ethics Committee of National Institute of Endocrinology taking into account the statements of the 1964 Helsinki Declaration.

Statistical Analysis

Quantitative parameters are presented as Mean ± Standard Deviation (SD).

Table 1. The Distribution of the Children and Adolescents by Age, Sex, and Study Groups/Subgroups.

Groups Quantity, sex, age	Study group			Control group (n = 113)
	Subgroup 1 (n = 113) BMI Percentile	Subgroup 2 (n = 82) WC	Subgroup 3 (n = 65) WHR	
n=	113	82	65	113
Boys	40 (35.4%)	33 (40.2%)	29 (44.6%)	40 (35.4%)
Girls	73 (64.6%)	49 (59.8%)	36 (55.4%)	73 (64.6%)
Mean Age, years	12.0 ± 2.2	11.7 ± 2.1	11.7 ± 2.1	11.9 ± 2.1

The comparison of the quantitative parameters was performed by Student *t*-test. Correlation analysis was performed by Pearson *r*-coefficient. If the *P*-value is smaller than .05, we reject the null hypothesis (H_0); otherwise, we do not have enough. The comparison of qualitative parameters between groups has been carried out by Odds Ratio (OR) and 95% Confidence Intervals (95%CI). The statistical treatment and comparative analysis of obtained data have been carried out by multiple regression analysis and 2 models have been created.

Insulin resistance (Y1), systolic blood presure (Y2), diastolic blood pressure (Y3), Triglyceride (Y4), and HDL-cholesterol levels (Y5) were considered as outcomes in first model; the values of BMI—percentile (X1), WC-percentile (X2), and WHR-percentile (X3) were considered as outcomes in second model.

Results

The anthropometric and hemodynamic characteristics, the parameters of carbohydrate and lipid metabolism in study and control groups are presented in Table 2.

The analysis of the data confirms the subgroup 1, subgroup 2, and subgroup 3 do not differ from each other by body mass, height, BMI, systolic, and diastolic blood pressure, as well as their percentiles and the parameters of carbohydrate and lipid metabolism.

Significant differences between subgroups were revealed by the following parameters:

BMI percentiles, WC, WHR and WHR percentiles are significantly lower in subgroup 1 compared to subgroup 2 (p=0.002, p=0.007, p=0.002, p<0.001; respectively), and subgroup 3 (p=0.005; p<0.001; p<0.001; p<0.001; respectively). WHR and WHR percentiles are significantly lower in subgroup 2 compared to subgroup 3 (p=0.002 and p=0.002; respectively). It indicates that all above parameters are significantly elevated in children and adolescents with visceral obesity.

Table 2

The listed below parameters in all study subgroups were significantly different compared to control group

($P < .05$): body mass, BMI, BMI percentile, WC, WC percentile, WHR, WHR percentile, sistolic BP, sistolic BP percentile, diastolic BP, diastolic BP percentile, all parameters of carbohydrate and lipid metabolism. Besides, the study and control groups did not differ by height, FPG, and PPG.

Correlation analysis revealed that in subgroup 1 BMI percentile correlates with Tg ($r=0.247$, $P=.008$) and HDL-cholesterol levels ($r=-0.257$, $P=.006$); WC percentile correlates with Tg ($r=0.219$, $P=.020$) and HDL-cholesterol levels ($r=-0.245$, $P=.009$); WHR percentile correlates with Tg ($r=0.246$, $P=.009$) and HDL-cholesterol levels ($r=-0.233$, $P=.013$).

In the subgroup 2 BMI percentile correlates with Tg ($r=0.298$, $P=.007$) and HDL-cholesterol levels ($r=-0.416$, $P<.001$); WC percentile correlates with Tg ($r=0.252$, $P=.022$) and HDL-cholesterol levels ($r=-0.306$, $P=.005$); WHR percentile correlates with Tg ($r=0.416$, $P<.001$).

In the subgroup 3 BMI percentile correlates with Tg ($r=0.286$, $P=.021$) and HDL-cholesterol levels ($r=-0.400$, $P<.001$); WC percentile correlates with Tg ($r=0.322$, $P=.009$), HDL-cholesterol levels ($r=-0.263$, $P=.034$) and with HOMA-IR ($r=0.259$, $P=.037$); WHR percentile correlates with Tg ($r=0.429$, $P<.001$) and HDL-cholesterol levels ($r=-0.399$, $P<.001$).

First **Model of Multiple Regresseion Analysis** showed that BMI percentile (X1), WC percentile (X2), and WHR percentile (X3) has not the impact on the parameters of systolic BP (Y2), diastolic BP (Y3), and Tg (Y4). When the insulin resistance was chosen as outcome (Y1), as a result of linear multiple regression, BMI percentile (X1) was excluded from the model.

The linear regression model is following: Y1=−0.714 + 0.232 X2-0.184 X3. The regression coefficient β_0 was not significant ($\beta_0=-0.714$, $P=.877$, NS), but regression coefficient of WC ($\beta_2=0.232$, $P=.049$) and WHR percentiles ($\beta_3=-0.184$, $P=.042$) were significant. It indicates that the visceral obesity assessed by WC and WHR has impact on the index of insulin resistance.

When the HDL-cholesterol level was chosen as outcome (Y5), WHR percentile (X3), and BMI percentile (X1) were excluded from the model as a result of linear multiple regression.

Table 2. Parameters Associated With the Earlier Cardiovascular Complications in Study and Control Groups.

Groups Study Parameters		Study group			Control group (n = 113)
		Subgroup 1 (n = 113) BMI Percentile	Subgroup 2 (n = 82) WC	Subgroup 3 (n = 65) WHR	
Anthropometry	Body mass, kg	73.2 ± 17.6	76.2 ± 18.4	76.4 ± 19.2	52.0 ± 10.9
	Body height, m	156.6 ± 11.0	156.4 ± 11.7	155.4 ± 11.8	162.1 ± 9.1
	BMI, kg/m2	29.4 ± 4.8	30.7 ± 4.6	31.2 ± 4.9	23.1 ± 1.6
	BMI percentile, ‰	98.8 ± 2.2	99.6 ± 0.6	99.6 ± 0.7	75.4 ± 5.2
	WC, cm	88.3 ± 12.1	92.8 ± 10.2	95.0 ± 9.9	66.8 ± 7.4
	WC percentile, ‰	90.3 ± 11.6	95.9 ± 2.3	96.5 ± 2.3	52.6 ± 5.2
	WHR	0.56 ± 0.07	0.59 ± 0.06	0.61 ± 0.05	0.41 ± 0.05
	WHR percentile, ‰	85.3 ± 17.0	93.2 ± 5.8	95.6 ± 2.5	35.4 ± 7.5
Hemodynamics	Sistolic BP, mm.Hg.	106.1 ± 9.3	106.9 ± 8.7	107.4 ± 7.9	93.7 ± 6.8
	Sistolic BP percentile, ‰	44.3 ± 25.0	45.5 ± 23.2	47.4 ± 21.8	20.4 ± 9.0
	Diastolic BP, mm.Hg.	67.1 ± 6.5	67.2 ± 6.0	67.0 ± 6.0	64.2 ± 5.1
	Diastolic BP Percentile, ‰	61.0 ± 19.2	62.2 ± 17.2	61.2 ± 17.9	51.5 + 7.9
Carbohydrate metabolism	HBA1C, %	5.2 ± 0.7	5.3 ± 0.9	5.4 ± 1.0	4.0 ± 0.5
	C-Pept, ng/ml	2.3 ± 1.1	2.6 ± 1.2	2.7 ± 1.3	1.1 ± 0.5
	FPG, mg/dl	89.7 ± 10.7	89.7 ± 10.4	90.0 ± 11.2	87.0 ± 6.7
	PPG, mg/dl	107.7 ± 22.5	107.1 ± 23.6	107.5 ± 23,6	102.4 ± 9.7
	FPI, μIU/ml	18.5 ± 14.7	19.5 ± 16.2	19.6 ± 17.6	12.6 ± 9.1
	PPI, μIU/ml	69.3 ± 52.1	74.2 ± 57.0	73.5 ± 55.0	18.3 ± 13.4
	HOMA-IR	4.0 ± 3.2	4.2 ± 3.5	4.2 ± 3.8	1.1 ± 0.3
Lipid metabolism	Tchol, mg/dl	167.6 ± 42.8	168.1 ± 46.2	165.8 ± 44,6	128.7 ± 11.0
	HDL, mg/dl	39.2 ± 12,3	37.7 ± 13.0	37.0 ± 12.7	44.1 ± 6.2
	LDL, mg/dl	101.2 ± 41.8	101.7 ± 44.7	99.4 ± 43.2	79.2 ± 10.9
	VLDL, mg/dl	27.2 ± 12.2	28.8 ± 12.7	29.3 ± 12.5	10.8 ± 3.1
	Tg, mg/dl	136.2 ± 60.9	143.8 ± 63.7	146.7 ± 62.3	54.2 ± 15.3

The linear regression model was following: $Y5 = 64.22 - 0.28\ X2$. The regression coefficient β0 ($\beta_0 = 64.22$, $P < .001$) and regression coefficient of WC percentile ($\beta_2 = -0.28$, $P = .003$) were significant. It indicates that the visceral obesity assessed by WC has impact on the HDL-cholesterol level.

Second Model of Multiple Regresseion Analysis showed that when the BMI percentile was chosen as outcome (Y1), triglycerides (X4), systolic BP (X2), insulin resistance (X1), diastolic BP (X3) were excluded from the model as a result of linear multiple regression. The linear regression model was following: $Y1 = 100.78 - 0.05\ X5$. The regression coefficient β0 ($\beta_0 = 100.78$, $P < .001$) and regression coefficient of HDL-cholesterol level ($\beta_5 = -0.05$, $P = .005$) were significant. It indicates that the HDL-cholesterol level has impact on the BMI percentile.

When the WC percentile was chosen as outcome (Y2), systolic BP (X2), triglycerides (X4), insulin resistance (X1), diastolic BP (X3) were excluded from the model as a result of linear multiple regression. The linear regression model was following: $Y2 = 99.17 - 0.23\ X5$. The

regression coefficient β0 ($\beta_0 = 99.17$, $P < .001$) and regression coefficient of HDL-cholesterol level ($\beta_5 = -0.23$, $P = .010$) were significant. It indicates that the HDL-cholesterol level has impact on the WC percentile.

When the WHR percentile was chosen as outcome (Y3), systolic BP (X2), triglycerides (X4), insulin resistance (X1), diastolic BP (X3) were excluded from the model as a result of linear multiple regression. The linear regression model was following: $Y2 = 98.06 - 0.32\ X5$. The regression coefficient β0 β0 ($\beta_0 = 98.06$, $P < .001$) and regression coefficient of HDL-cholesterol level ($\beta_5 = -0.32$, $P = .013$) were significant. It indicates that the HDL-cholesterol level has impact on the WHR percentile.

Discussion

It is significant to assess excessive body weight and obesity in children and adolescents by several parameters: BMI percentile—mostly serving as an indicator of the generalized obesity; WC and WHR percentiles—better describing the visceral obesity and associated with it metabolic disorders.[8]

According to the results of our study, the BMI percentile was also higher in the patients with high WC and WHR percentiles, while, on the contrary, WC and WHR percentiles were not always high in patients with high BMI percentiles. We state the same during the comparison of WC and WHR percentiles. The analysis of study results shows that WHR is more precise indicator of visceral obesity in children and adolescents. These findings are in agreement with the results of other studies.[8,21] It was also indicated the WHR more than 0.5, is featured with 91% sensitivity and 95% specificity for both sexes and all ages of childhood and adolescence. Therefore, the researchers consider WHR = 0.5 as a threshold for the assessment of the obesity.[22-24]

Both generalized and visceral obesity are more significantly associated with fat metabolism parameters than with carbohydrate metabolism parameters and blood pressure levels.[25]

First model of multiple regression analysis showed that the WC has a significant impact on the HDL-cholesterol levels. Moreover, the correlation is negative; the higher WCs were associated with lower HDL-cholesterol levels.

Second model of our multiple regression analysis showed that the HDL-cholesterol levels has a significant impact on the BMI, WC, and WHR percentiles. Moreover, these correlations are negative; the higher HDL-cholesterol levels were associated with lower BMI, WC, and WHR percentiles.

Correlation analysis of 3 mentioned parameters—carbohydrate metabolism, lipid metabolism, BP—revealed that the relation with visceral obesity assessed by WHR is most strong compared to other assessment criteria (BMI, WC). These results are in accordance with the results of other investigators.[26-28] However, they are in partly disagreement with other authors concluded that BMI, WC, and WHR percentiles should be used equally to assess pediatric obesity.[29,30]

It is interesting to note that according to our results, the percentiles of diastolic BP are much higher than the percentiles of systolic BP in both the study and control groups. Similar data could not be found in the literature. Therefore, we think this fact needs further research.

Obesity in children and adolescents is significantly correlated with insulin resistance and type 2 diabetes.[31] Moreover, the degree of the obesity in the majority of diabetic adolescents is severe.[32] A sharp increase in body mass contributes to the progression of glucose intolerance in the prediabetic stage, as well as a relative decrease in insulin secretion and a physiological decrease in insulin sensitivity often taken part in puberty.[32] However, the assessment of prediabetes associated with obesity may be different in accordance with used the various definitions and criteria. When the HbA1c threshold value 5.7% was used as criterion in 12-19 year old adolescents, the prevalence of prediabetes was 5%; when the criterion was—FPG $\geq$ 100 mg/dl, the prevalence of prediabetes was 15%.[33] But when this criterion was PPG $\geq$ 140 mg/dl, the prediabetes was diagnosed in 21% of adolescents with obesity.[34] Besides, the data obtained by us are interesting to discuss in this regard. They showed that the study and control groups differed significantly in HOMA-IR rates, while there was no significant difference between FPG and PPG data.

The high content in the circulating blood of free fatty acids and pro-inflammatory factors associated with obesity leads to the peripheral and hepatic insulin resistance.[35] Increased fat deposition in the liver and visceral compartments is a significant predictor of impaired glucose tolerance and hepatic insulin resistance. The accumulation of fat in the liver and visceral areas of adolescents and adults is a more significant determinant to assess cardiometabolic health risk than total obesity determined by BMI.[36-39] The combination of dyslipidemia and insulin resistance is a major component of pediatric obesity and is characterized by elevated triglycerides and LDL and decreased HDL, which is associated with an increased risk of developing cardiovascular pathology.[40,41]

Taking into the account the correlation of a combined risk of the coronary heart disease with the factors observed in childhood such as abdominal obesity, abnormal cholesterol levels, hypertriglyceridemia, hypertension, the accurate and simple methods of screening for increased cardiometabolic risk in adolescents might be useful for monitoring and intervention measures aimed reducing the likelihood of chronic disease progression in adulthood.[42] Literature data indicate that cardio-metabolic risk increases with increased BMI, WC, and WHR percentiles. However, these screening tools had good predictive value only in the identification of the children with elevated insulin.[43,44] In addition, some differences in BMI or WC percentiles or WHR rates were observed in studies devoted to the study of the risk of developing cardiovascular pathology in different racial/ethnic and sex groups.[29] This fact confirms once again the expediency of further research of various countries/ethnic populations.

Lee et al., suggested that the BMI percentile has a relatively low predictive value for cardiometabolic risk factors despite the insulin resistance. According to some researchers, WC and WHR percentiles do not provide better identification of cardio-metabolic risk compared to BMI.[27] The results of our study also point to the urgency of this view and show that the study of the

correlation of anthropometric parameters with those parameters of the MS (in the children and adolescents with excessive body weight and obesity) associated with early (premature) cardiovascular complications should be continued.

Thus, the study of the effects of obesity on carbohydrate and lipid metabolism disorders, arterial hypertension rates requires more longitudinal and randomized studies to determine the usefulness of the above mentioned methods of obesity definition for the identification of future cardiometabolic risk.

Conclusions

Based on the results of the study, it can be concluded that in order to assess excessive body weight and/or obesity in children and adolescents, it is necessary to evaluate several parameters: BMI percentile (considered mostly as an indicator of a generalized obesity; WC and WHR percentiles (better describing a visceral obesity and metabolic disorders associated with this condition—insulin resistance, hypertension and dyslipidemia). However, the WHR Percentile may be a more useful tool when visceral obesity is suspected. Obesity defined by all 3 parameters is in a strong correlation with antiatherogenic HDL-cholesterol levels. This findings require further confirmation for the precise evaluation its prognostic ability.

Author Contributions

Concepcion and design, collection and assembly of data: Nino Tskhvedadze, Elene Giorgadze, Shota Janjgava and David Tananashvili. Data analysis and interpretation: Nino Tskhvedadze, Elene Giorgadze, Shota Janjgava, David Tananashvili. Manuscript writing: Nino Tskhvedadze, David Tananashvili. Final approval of manuscript was done by all authors. Final approval of the manuscript was done by all authors.

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