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The comprehensive assessment of the prevalence of metabolic syndrome in obese children and adolescents

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Abstract: *childhood obesity is recognized as a significant health concern by the WHO, but not all obese individuals face the same risk of cardiometabolic disorders. This study aims to diagnose metabolic syndrome (MetS) in obese children according to various known definitions and to determine the influence of all five definitions of MetS on insulin resistance using logistic regression models. The observational cross-sectional study on 82 children aged 12 to 17 with obesity was conducted at the Children's Clinical Hospital No.6 in Kyiv. MetS was established according to five main definitions. All biochemical analyses were performed using the enzymatic colorimetric method by Cobas 6000, Roche Diagnostics (Switzerland). The prevalence of MetS among children with obesity was higher using the de Ferranti et al. (76.8%) definition and the lower using Viner et al. definition (29.3%), p=0.023. The construction of a logistic regression model showed that having all the components of MetS according to different definitions, children and adolescents are likely to have a HOMA-2 above 2.26 (AUC more significant than 0.5, p<0.05). Different prevalence of MetS was found, depending on the different approaches to diagnosis. The construction of a logistic regression model showed that the parameters of the metabolic syndrome influence the risk of high HOMA-2 IR using four of five definitions.*

Keywords: Body Mass Index, Insulin Resistance, Metabolic Syndrome, Paediatric Obesity, Waist Circumference

Introduction

According to WHO estimates in 2016, more than 340 million children and adolescents aged 5-19 were overweight or obese (WHO, 2021). This rapid rise in obesity prevalence is attributed to increased consumption of high-energy foods high in fat and sugar, growing urbanization, and changing modes of transport (Jebeile et al., 2022). Childhood obesity is associated with a high risk of disability and premature mortality in adulthood (DeBoer, 2019). As the prevalence of obesity increases, the number of comorbidities associated with this condition also increase (Lim & Boster, 2023). However, not all obese people have an equivalent risk of cardiometabolic disorders such as hypertension, dyslipidemia, hyperglycemia, etc (Drozdz et al., 2021). Studies are showing that about 50% of obese adults are «metabolically healthy» if health is assessed by the absence of any criteria of the metabolic syndrome (MetS) and only 5% are «metabolically healthy» if any of the components of the MetS are absent and insulin sensitivity is normal (Smiths et al., 2019). In a previous study of clustering children with MetS, it was shown that 20% of children did not have insulin resistance (IR), although they had other cardiometabolic disorders such as dyslipidemia or hypertension (Aliusef et al., 2022). Although there

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is no single definition for a complication of obesity as metabolic syndrome in children (Reisinger et al., 2021). However, basically, all the definitions include at least three of the following criteria: obesity (central or abdominal), dyslipidemia, high blood pressure, impaired glucose tolerance, or insulin resistance (Aguilar-Gomez et al., 2020; Fernandez-Aparicio et al., 2021).

Aim

The aim of this study is to define the metabolic syndrome in obese children according to various known definitions and to identify a group that does not belong to the metabolic syndrome and which can be classified as «metabolically healthy obese» because it has one or two cardiometabolic disorders. In this article, we use a logistic regression model to consider which of the five definitions of diagnostic of MetS most affects the development of insulin resistance.

Materials and methods

The observational cross-sectional study on 82 children aged 12 to 17 with obesity was conducted at the Rheumocardiology Department of Children's Clinical Hospital No.6 in Kyiv. Inclusion criteria: alimentary obesity which body mass index (BMI)≥95 percentiles according to reference standards depending on age and gender (CDC, 2022). Exclusion criteria: patients with obesity, associated with genetic syndromes (Littleton et al., 2020). Metabolic syndrome (MetS) was established according to the criteria of five different sources: Adult Treatment Panel III (ATPIII) criteria modified for age (hereafter referred to as Cook et al.), Viner et el., de Ferranti et al., Ford et al., IDF Consensus Group (Aguilar-Gomez et al., 2020; Fernandez-Aparicio et al., 2021).

Table 1 summarizes five definitions of metabolic syndrome in children and adolescents.

Waist circumference (WC) was determined according to growth charts for British children (Rigamonti et al., 2023). Ambulatory blood pressure monitoring was performed using ABM-04 («Meditech», Hungary) and was estimated according to percentile tables (Brady et al., 2019). Measurement of lipid metabolism parameters included total cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL-C), low-density lipoproteins (VLDL-C), very low-density lipoproteins (VLDL-C), atherogenic coefficient (AC) (Sanin et al., 2022).

Insulin resistance was determined by an update homeostatic model of insulin resistance (HOMA-

Table 1. Definitions of metabolic syndrome

	Cook et al.	**Viner et al.**	**de Ferranti et al.**	**Ford et al.**	**IDF**
Age, years	12-19	2-18	12-19	12-17	10-16
Absolutely required					WC≥90^{th} percentile
Criteria	Any three of the criteria below	Any three of the criteria below	Any three of the criteria below	Any three of the criteria below	Obesity plus two of the criteria below
Obesity	WC≥90^{th} percentile	BMI ≥ 95 percentile	WC>75^{th} percentile	WC≥90^{th} percentile	WC≥90^{th} percentile
Dyslipidemia	TG≥1.24 mmol/L or HDL-C< 1.03 mmol/L	TG ≥1.75 mmol/L or HDL-C< 0.9 mmol/L or high TC ≥95^{th} percentile	TG≥1.1 mmol/L or HDL-C≤ 1.3 mmol/l	TG≥1.24 mmol/L or HDL-C< 1.03 mmol/L	TG≥1.24 mmol/L or HDL-C< 1.03 mmol/L
Hypertension	systolic BP or diastolic BP≥90^{th} percentile	systolic BP≥95^{th} percentile	systolic BP>90^{th} percentile or diastolic BP > 90^{th} percentile	systolic BP>90^{th} percentile or diastolic BP > 90^{th} percentile	systolic BP≥130 mmHg or diastolic BP≥85 mmHg

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Table 1. (continued).

	Cook et al.	Viner et al.	de Ferranti et al.	Ford et al.	IDF
Hyperglycemia or hyperinsulinemia	FG≥6.11 mmol/L	fasting hyperinsulinemia: pre-pubertal period it is >15 mU/l, mid-puberty >30 mU/l, post-pubertal hyperinsulinism >20 mU/l; impaired FG≥6.1 mmol/L; impaired glucose tolerance: glucose at 120 min≥7.8 mmol/L	FG ≥6.1 mmol/L	FG ≥ 5.6 mmol/L	FG ≥ 5.6 mmol/L (or known type 2 diabetes mellitus)

WC – waist circumference, BMI – body mass index, TG – triglycerides, HDL-C – high-density lipoproteins, BP – blood pressure, FG – fasting glucose.

2 IR), which include beta-cell function (%B) and insulin sensitivity (%S), and calculated on [http://www.ocdem.ox.ac.uk/]. The HOMA-2 IR cut-off value was proposed > 2.26 (Aliusef et al., 2022). All biochemical analyses were performed using the enzymatic colorimetric method by Cobas 6000, Roche Diagnostics (Switzerland). The statistical analysis was performed using EZR version 1.61 (November 11, 2022). The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee of the institution mentioned in the work. Informed consent of the child's parents was obtained for the study.

Results

A total of 82 children and adolescents aged 12-17 years old (mean age 14.8±0.14) underwent assessments. The study group consisted of more males – 84.1% (n=69) than females – 15.9% (n=13). Median BMI was found to be 30.56±0.69 (95% CI 29.63-31.26) and median WC was 92.5±1.45 (95% CI 91-95) (Table 2).

The percentage prevalence of MetS found for the five definitions is shown in Table 3.

MetS is defined by the presence of 3 or more criteria, including obesity. In this study the prevalence of MetS among children with obesity was higher using the de Ferranti et al. (76.8%) definition and the lower using Viner et al. definition (29.3%). A comparison of the different criteria for

Table 2. Characteristics of the study group

Subject variables	Me±m	95%CI
BMI (kg/m^2)	30.56±0.69	29.63-31.26
WC (cm)	92.5±1.45	91-95
TC (mmol/L)	3.8±0.16	3.59-4.06
TG (mmol/L)	1.06±0.11	0.87-1.21
HDL-C (mmol/L)	1.11±0.05	1.05-1.2
Glucose (mmol/L)	4.78±0.08	4.08-4.92
Insulin (mIU/mL)	19.22±2.39	16.46-22.9
HOMA-2 IR	2.44±0.20	2.09-2.83
%B	208.95±13.39	169.7-231.6
%S	41.15±5.34	34.8-48.6
Average daily systolic BP (mmHg)	132±2.5	127-135
Average daily diastolic BP (mmHg)	68±1.57	65-72

Table 3. Prevalence of MetS according to different definitions

Definition	Prevalence % (n=82)
de Ferranti et al.	76.8% (n=63)
Cook et al.	70.7% (n=58)
Ford et al.	69.5% (n=57)
IDF	53.7% (n=44)
Viner et al.	29.3% (n=24)

**Analysis* of variance. A chi-square (X^2) test of multiple comparisons (Chi-square=14.18, k=4, p=0.007).

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defining MetS showed a significant difference in the prevalence of MetS between Viner et al. and de Ferranti et al. (Chisquare=11.29, p=0.023). No significant difference was found when other combinations of criteria were analyzed (p>0.05).

The prevalence of MetS criteria using different definitions is shown in Fig.1.

Most of the obese children, i.e. 28% (n=23) had just one criterion by Viner et al. definition. In opposition, the most obese children with all five criteria were found according to de Ferranti – 17% (n=14). The prevalence of the children who have two criteria according to the definition of Viner et al. was 42.7%, by Ford's et al. – 29.2%, Cook et al. – 25.6%, IDF – 24.4% and de Ferranti et al. – 18.3%. Using the logistic regression model the dependence of HOMA-2 IR> 2.26 (Y) and metabolic syndrome parameters (X_1, X_2…X_5) according to five different definitions was established. ROC curves were plotted with all definitions (AUC greater than 0.5) (Table 4). The quality of the models was assessed according to the following classification: excellent (AUC≥0.9), very good (0.8≤AUC ≥0.9), good (0.7≤AUC ≥0.8), satisfactory (0.6≤AUC ≥0.7), unsatisfactory (0.5≤AUC ≥0.6) (Jaswal & Kishore, 2021).

The quality of the model was assessed as «unsatisfactory» by de Ferranti et al. (Figure 3), «satisfactory» by Cook et al. (Figure 2) and Ford et al. (Figure 4), and «good» by Viner et al. (Figure 5) and IDF (Figure 6).

Table 4. The characteristics of the ROC-curve five-factor logistic regression model of the dependence of HOMA-2 IR> 2.26 and different definitions of MetS

Definition	AUC	95% CI
Cook et al.	0.676	0.513 - 0.84*
Viner et al.	0.741	0.587 - 0.896*
de Ferranti et al.	0.598	0.423 - 0.773
Ford et al.	0.676	0.513 - 0.84*
IDF	0.757	0.611 - 0.902*

* $p<0.05$

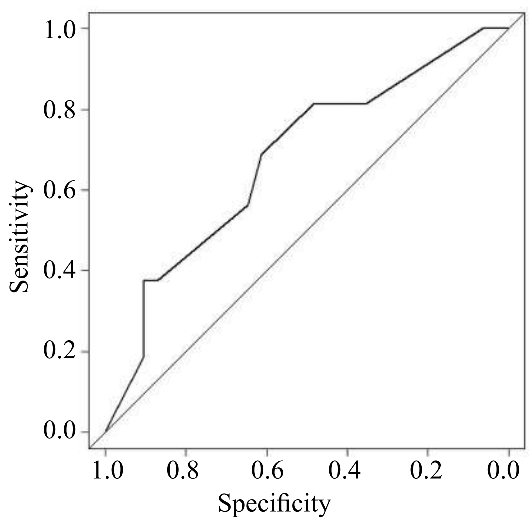

Figure 2. ROC-curve five-factor logistic regression model the dependence of HOMA-2 IR>2.26 and Cook et al. definition of MetS (AUC=0.676 95% CI 0.513–0.84)

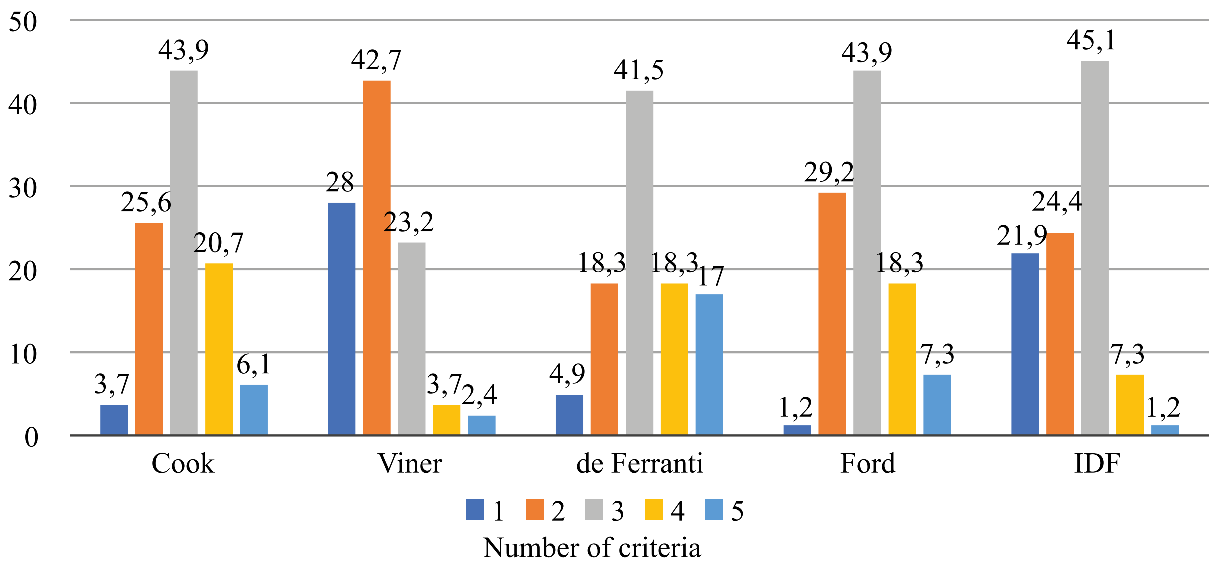

Figure 1. Number of MetS criteria (including obesity) according to different definitions

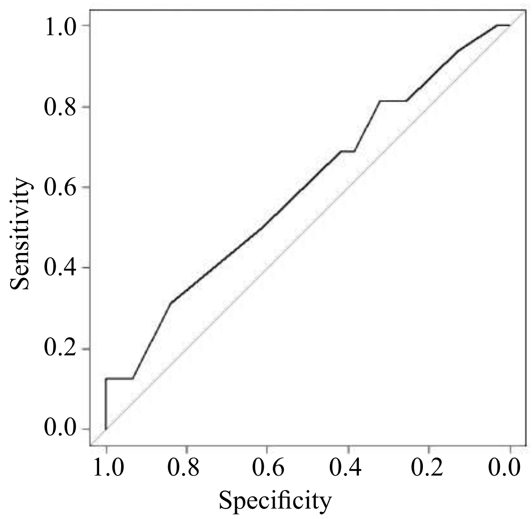

Figure 3. ROC-curve five-factor logistic regression model the dependence of HOMA-2 IR>2.26 and de Ferranti et al. definition of MetS (AUC=0.598 95% CI 0.423–0.773)

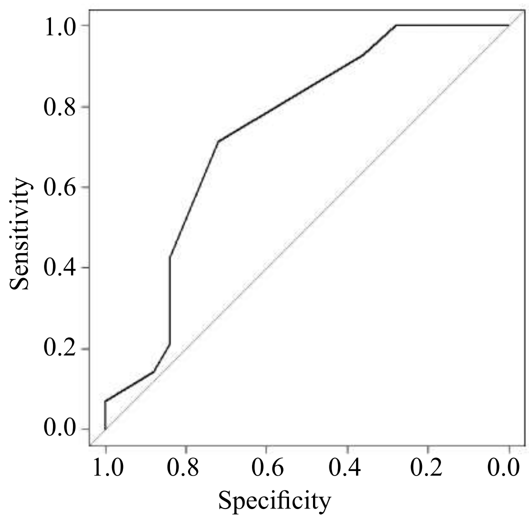

Figure 5. ROC-curve five-factor logistic regression model the dependence of HOMA-2 IR>2.26 and Viner et al. definition of MetS (AUC=0.741 95% CI 0.587–0.896)

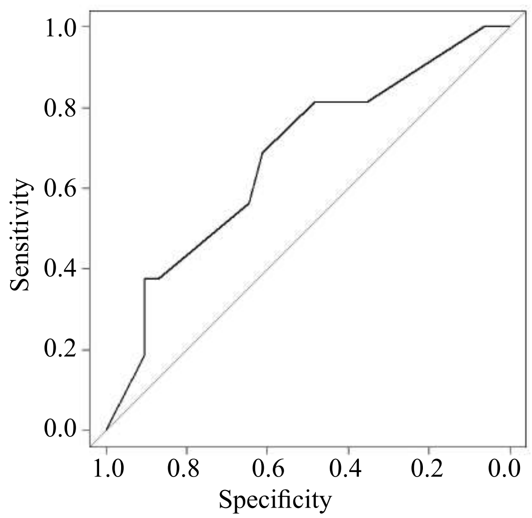

Figure 4. ROC-curve five-factor logistic regression model the dependence of HOMA-2 IR>2.26 and Ford et al. definition of MetS (AUC=0.676 95% CI 0.513–0.84)

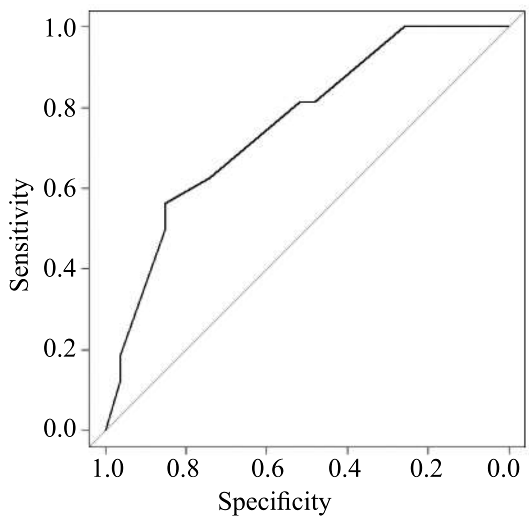

Figure 6. ROC-curve five-factor logistic regression model the dependence of HOMA-2 IR>2.26 and IDF definition of MetS (AUC=0.757 95% CI 0.611–0.902)

Discussion

In our study, there are more boys than girls among obese children. This trend is confirmed by a number of studies around the world. Thus, according to the 2019 Atlas of Childhood Obesity for children aged 10-19, the same trend was observed in 112 countries (Lobstein & Brinsden, 2019). The prevalence of MetS according to de Ferranti et al. can be explained by the widest range reference values of WC and lipid profile in this definition comparatively with the other four definitions. Conversely, the lowest prevalence according to Viner et al. can be explained by the highest cut off values. It should be noted that this definition already included the determination of total cholesterol levels which is not included in the other definitions. Special attention should be paid to the determination of hyperinsulinemia by Viner et al. For the pre-pubertal period, the reference values were higher than 15 mU/l, mid-puberty higher than 30 mU/l, and post-pubertal higher than 20 mU/l when hyperinsulinemia was diagnosed (Aguilar-Gomez et al., 2020). The mild-puberty period has the highest reference value for insulin, probably due to hormonal changes in this period. The fact that insulin resistance decreases with age was shown in our previous study, where a logistic regression model revealed the relationship between HOMA-2 IR and age (Aliusef et al., 2022). Particular attention should be paid to children who already have two components of MetS but are not yet included in the definition. These are mainly those children who, in addition to obesity, also have another complication: either high blood pressure, dyslipidemia, or hyperglycemia. The prevalence of children with one cardiometabolic risk in addition to obesity was highest according to Viner et al. and lowest according to de Ferranti et al. Logistic regression models showed that children and adolescents who had all the components of the MetS according to Viner et al., by Ford's, Cook et al., and IDF, had a HOMA-2 IR above 2.26. Consequently, children with insulin resistance with impaired pancreatic beta cell function are at a higher risk of developing diabetes in adulthood, increases cardiovascular risk and causing early endothelial dysfunction (Al-Beltagi et al., 2022). ROC-curve was also plotted by de Ferranti et al., but it was unsatisfactory and not significant.

Considering the results of this article, children and adolescents not only with MetS, but also with «metabolically healthy obesity» require special attention from pediatricians and, despite the absence of all three diagnostic criteria, should be monitored.

Conclusion

1. Different prevalence of MetS was found, depending on different approaches to diagnosis. The prevalence rate of MetS between the Viner et al. and de Ferranti et al. was significant.
2. From 18.3% to 42.7% of children had one cardiometabolic risk factor in addition to obesity, but these children were not included in the MetS group. Further longitudinal studies on a group of children with «metabolically healthy obesity» are required.
3. The construction of a logistic regression model showed that the parameters of the MetS significantly influenced the risk of high HOMA-2 IR for four of five definitions.

Financing

The study was conducted on a self-funded basis

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Consent to publication

All authors have read the manuscript and agreed to its publication.

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article

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Комплексна оцінка поширеності метаболічного синдрому у дітей та підлітків з ожирінням

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Анотація: *дитяче ожиріння визнано ВООЗ значною проблемою охорони здоров'я, але не всі особи з ожирінням стикаються з однаковим ризиком кардіометаболічних порушень. Метою цього дослідження є діагностика метаболічного синдрому (МС) у дітей з ожирінням згідно різних відомих критеріїв діагностики та визначення впливу всіх п'яти критеріїв діагностики МС на інсулінорезистентність за допомогою моделей логістичної регресії. Обсерваційне перехресне* *дослідження 82 дітей віком від 12 до 17 років з ожирінням було проведено на базі Дитячої клінічної лікарні №6 м. Києва. Метаболічний синдром встановлювали за п'ятьма основними критеріями. Всі біохімічні дослідження проводили з використанням ферментативного колориметричного методу на апараті Cobas 6000, Roche Diagnostics (Швейцарія). Поширеність МС серед дітей з ожирінням була вищою за визначенням de Ferranti et al. (76,8%) і нижчою за визначенням Viner et al. (29,3%), p=0,023. Побудова логістичної моделі регресії показала, що при наявності всіх компонентів МС за різними критеріями діагностики діти та підлітки, ймовірно, матимуть HOMA-2 вище 2,26 (AUC більше 0,5, p<0,05). Виявлено різну поширеність метаболічного синдрому залежно від різних підходів до діагностики. Побудова логістичної регресійної моделі показала, що параметри метаболічного синдрому впливають на ризик високого HOMA-2 за чотирма з п'яти критеріїв діагностики.*

Ключові слова: індекс маси тіла, інсулінорезистентність, метаболічний синдром, дитяче ожиріння, окружність талії.