Metabolic Syndrome in obese children – clinical prevalence and risk factors

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Research

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Abstract

**Background:** Prevalence of childhood obesity increases worldwide. Some of the obese children develop metabolic syndrome (MetS), who of them—remains to be determined. The aim of this study was indicate predisposing factors for metabolic syndrome, especially those which can be modified.

**Methods:** The study comprised 591 obese children aged 10-12 years. Clinical examination, anthropometry, biometric impedance analysis, blood works (incl. OGGT and insulinemia) as well as dietary evaluation and physical activity were estimated.

**Results:** The risk factors of MetS or feature of this are: male, parent's especially father's obesity, low body mass at birth as well as omitting breakfast or dinner.

**Conclusions:** There are few risk factors of metabolic syndrome in obese subjects, also in obese children. Some of these predictors can be modified, especially those referring to lifestyle. Indicating and then influencing these factors can be one way to diminish metabolic syndrome development, such improving health and quality of life. Besides certain socioeconomic effects could be gained too.

**Background**

Prevalence of obesity is rapidly increasing. According to World Health Organization (WHO) in 2016 it affected as many as 650 million people and 2 billion adults were overweight. At the same time 41 million children younger than 5yrs were overweight or obese and over 340 million children and adolescents aged 5-19yrs were overweight or obese. Number of children with obesity increases and one should expect that complications of obesity in this age group will increase too.

Obesity, defined as the excess of fat tissue, is widespread all over the world and it affects all age groups. Obesity, among other, is well known risk factor of metabolic syndrome (MetS) which comprises cardiovascular diseases (CVD), diabetes mellitus (DM), hypertension, atherosclerosis as well as other complications. Although etiology of obesity is complex, genetic predisposition is permissive and, actually, interacts with environmental agents including physical activity and diet. Heritable factors seem to have 40–85% contribution in obesity’s etiology. Apart from genetic predisposition, other recognized constituents such as: metabolom, metabolic programming during both gestational and post gestational period can be modified to some extent. Consequently development of obesity and its complications might be reduced.

Metabolic syndrome is recognized consequence of obesity and it can occur as early as in adolescence. Certainly, not all obese children will develop all or any complications of obesity. Which one of children living with obesity are mostly prone to MetS remains to be fully elucidated.

In the systematic review of 85 studies in children, median prevalence of metabolic syndrome in all populations was 3.3% (range 0–19.2%), in overweight children it was 11.9% (range 2.8–29.3%), and in
obese subjects – 29.2% (range 10–66%). For non-obese, non-overweight populations the range was 0–1% [6]. Almost 90% of obese children and adolescents have at least one feature of the metabolic syndrome. On the basis of NHANES 1999 to 2002 data, the prevalence of metabolic syndrome in adolescents 12 to 19 years old ranged from 0–9.4%; variation in this estimate was the result of different criteria used to define metabolic syndrome. In the report from BIOSHARE-EU, prevalence of metabolic syndrome in obese subjects ranged from 24–65% in females and from ≈ 43% to ≈ 78% in males and substantially exceeded the prevalence in metabolically healthy obese ones. The divergences were conditioned by the country.

In the light of child’s dynamic growth and maturation population of children is unique. Obesity is diagnosed on the basis of percentile charts, when BMI ≥ 95th centile. Moreover, according to IDF consensus - commonly used by most of the authors - metabolic syndrome may be recognized in children not younger than 10yrs old. It takes some time before metabolic syndrome complicates obesity. Nevertheless the younger the child becomes obese the earlier in life he or she might suffer from its complications. However one must remember that not all children suffering from obesity will develop MetS.

The aim of our study was to identify factors favoring the presence of one or all compounds of metabolic syndrome in obese children. Secondly, we analyzed the results in order to indicate which of them are modifiable.

Material And Methods

This study was a part of the “6–10–14 for Health” integrated weight management program for children with overweight and obesity from Gdansk, Poland, previously described. 12–14

Analyzed data included children aged 10-12yrs attending the interventional program in 2011–2015. Children were screened in primary schools and if overweight or obesity was diagnosed they were invited to multidisciplinary, 12-month-long program. Patients flow is presented in Fig. 1.

All the children during first interventional visit were examined by pediatrician (incl. weight, height, waist circumference measurement), and bioelectric impedance analysis (BIA) was performed. All children were referred to blood works within 4 weeks from the first visit. Body mass, BMI centile, waist circumference centiles, blood pressure centiles were assessed using Polish centile charts, as recommended by WHO. 15–17 Medical history was taken and collected data included: body mass at birth (below 2,5 kg was assumed as hypotrophy, more than 4,0 kg – macrosomy), parents’ BMI, any metabolic disease in family members, feeding pattern (original questionnaire, specific questions regarding breakfast and supper time and quality). Lifestyle and diet were evaluated too. Waist circumference (WC) over 90th percentile and waist-hip –ratio (WHR) > 0.8 for girls and > 0.9 for boys were interpreted as abnormal.
For children younger than 10 years old waist-hip-ratio (WhtR) seems to be more accurate than WC. Abnormal WhtR was defined when WhtR ≥ 0.5.

In our study, although all the participants were at least 10 years old, WhtR was also calculated.

Overweight was diagnosed if BMI centile was ≥ 85th and obesity was diagnosed when BMI was ≥ 95th centile on recommended centile charts. \(^{15}\)

Central obesity was recognized when WC was above 90th or WhtR was > = 0.5.

The results of biometric impedance analysis were assessed according to standard values. \(^{18}\)

Blood tests included: aminotransferases, lipid fractions, thyroid stimulating hormone, tyrosine, Hb1c, oral glucose tolerance test (OGTT) along with insulin level at the same time points and the results were compared to standard values for appropriate age and sex.

Physical activity was evaluated by means of Kash Pulse Recovery Test \(^{20-21}\) and classified as excellent, very good, good, moderate, poor and very poor.

Nutritional habits were evaluated by the dietitian on the basis of data given by children and parents. Special attention was paid on breakfast (first course within 2hr after wake up) and dinner (last meal eaten 2 hr before sleep).

Metabolic Syndrome (MetS) was diagnosed according to IDF, \(^{22}\) in children with WC > 90th centile and at least two out of the following metabolic features: HDL < 40 mg/dl, TG > 150 mg/dl, glycemia > 100 mg/dl and blood pressure ≥ 130/85 mmHg.

**Statistical analysis included:**

Normal distribution of continuous variables was verified with the Shapiro-Wilk test. Descriptive statistics are presented as the mean or median and standard deviation from the mean. Between-group comparisons were carried out using the Mann-Whitney U test and ANOVA Kruskal-Wallis test. Nonparametric tests were chosen because of the large number of significant Shapiro tests, which were used for normality assumption assessment. All statistical tests were 2-tailed and performed at the 5% level of significance. Statistical analysis was performed using Statistica 10 software (TIBCO Software Inc., Tulsa, USA 2014).

This study was accepted by the Independent Bioethics Committee for Scientific Research at Medical University of Gdańsk. The study is registered in clinicaltrials.gov (NCT number): NCT04143074

**Results**
591 children aged 10-12ys who entered the program and fulfilled questionnaire and had blood works done were assessed in this study. None of the children had any chronic disease which could influence investigated parameters as well as no infection on the day of examination.

The girls were younger ($p = 0.031$), shorter ($p = 0.028$), had lower WC ($p < 0.0001$), lower WHR ($p < 0.0001$), lower WhTR ($p = 0.002$) and lower DBP ($p = 0.044$) compared to the boys. Moreover, higher BMI centile ($p < 0.001$) and higher fat tissue content were characteristic for girls. Elevated systolic blood pressure (SBP) was found in 10% of children, with no difference between girls and boys (Table 1).

| Feature                  | Girls (n = 275) | Boys (n = 316) | p  |
|--------------------------|-----------------|----------------|----|
| Age [years]              | 10.36 0.74      | 10.5 0.8      | 0.031 |
| Height [cm]              | 148.3 7.89      | 149.7 7.7     | 0.028 |
| Body mass [kg]           | 53.12 9.88      | 54 9.46       | 0.074 |
| BMI [kg/m$^2$]           | 24.01 2.88      | 24.1 2.73     | 0.541 |
| BMI centile              | 94.18 3.91      | 92.9 3.81     | 0.000 |
| WC [cm]                  | 76.46 7.34      | 78.85 7.58    | 0.000 |
| Hip circumference [cm]   | 87.99 7.5       | 87.72 6.7     | 0.952 |
| WHR                      | 0.87 0.07       | 0.9 0.09      | 0.000 |
| WHtR                     | 0.52 0.05       | 0.53 0.05     | 0.002 |
| SBP [mmHg]               | 112.61 11.77    | 112.87 11.4   | 0.820 |
| DBP [mmHg]               | 68.87 8.41      | 70.11 8.38    | 0.044 |
| Fat tissue [%]           | 33.08 4.56      | 27.61 5.42    | 0.000 |

$p < 0.05$ Mann-Whitney U test analysis.

Based on BMI percentile criterion there were 401 overweight (67.9%) and 190 obese children (32.1%).

Obesity was diagnosed in 85 (30.9%) girls and in 105 (33.2%) boys whereas, 190 (69.1%) girls and 211 (66.82%) boys were overweight. Girls had higher BMI centile compared to boys ($p < 0.0001$).

Results of laboratory tests:
Although there were statistically significant differences between mean concentrations of glucose, triglycerides and HDL, these values were within normal ranges (See Supplementary Table 1, Additional File 1). However, boys had more often pathological glycemia and normal TG and HDL concentration in comparison to girls (See Supplementary Table 2, Additional File 1).

Prevalence of MetS and features of MetS in the studied population.

For the use of this study we distinguished three subgroups in study population:

**Group I** – with diagnosis of MetS (+) i.e. WC > 90th centile and at least two out of the following: glycemia ≥ 100 mg/dl, BP ≥ 130/85 mmHg and dyslipidemia (HDL < 40 or TG > 150 mg/dl)

**Group II** – none compound of MetS, no diagnosis of that (MetS-)

**Group III** – only one feature typical for MetS, but not enough to meet criteria of MetS (MetS +/-)

These groups were determined for distinction of children with any feature of MetS in order to look for predisposing factors to MetS.

| Number of compounds of metabolic syndrome (N) | Total | Girls | Boys | p   |
|---------------------------------------------|-------|-------|------|-----|
| n                                           | %     | n     | %    | n   | %   |
| 0                                           | 243   | 41.1  | 119  | 43.3 | 124 | 39.2 | 0.239 |
| 1                                           | 272   | 46    | 126  | 45.8 | 146 | 46.2 |
| 2                                           | 66    | 11.2  | 24   | 8.7  | 42  | 13.3 |
| 3                                           | 10    | 1.7   | 6    | 2.2  | 4   | 1.3  |

p < 0.05 Chi square test analysis.

Among 76 (12.9%) children with metabolic syndrome there were 30 girls and 46 boys.
Table 3
Number of girls and boys in Groups I, II and III

| Group   | Total | Girls       | Boys       | p     |
|---------|-------|-------------|------------|-------|
|         | n     | %           | n          | %     | n   | %      |
| MetS+   | 76    | 12.9        | 30         | 10.9  | 46  | 14.6   | 0.349 |
| MetS−   | 243   | 41.1        | 119        | 43.3  | 124 | 39.2   |
| MetS+/− | 272   | 46          | 126        | 45.8  | 146 | 46.2   |

p < 0.05 Chi square test analysis.

73.4% of children with MetS had elevated blood pressure in comparison with 1.1% of children from group II and III (p = 0.005).

Reduced level of HDL (< 40 mg/dl) was found in all the children with MetS and in 27.6% of the remaining (ie group II and III), which was significantly different (p = 0.029). More than half of participants with MetS (55.3%) had increased TG concentration compared to 4% of the remaining (p = 0.001).

Analysis of prevalence of proposed risk factors of MetS
To reach this aim we compared children constituting group I (MetS+) to the rest of the children i.e. group II and group III (Met− and MetS+/−).

According to medical history, hypotrophy at birth was 3 times more prevalent in boys with MetS than in boys without MetS. Discerning gender it showed that low birth weight was more prevalent in boys with MetS (p = 0.034). All the girls with MetS were eutrophic at birth.

Further analyses revealed that 47.3% of fathers of children with MetS were obese and 14.5% fathers had normal body mass. Mother’s BMI did not differ between the groups.

There was no difference between all the subgroups in terms of analyzed metabolic diseases (DM2, hypothyroidism, MetS or dyslipidemia) in children’s parents. Similarly, prevalence of cardiovascular diseases in parents was not significant.

The correlation between metabolic syndrome and it’s compounds was significant for:
• Father’s obesity (p = 0.023)
• Obesity in at least one parent (p = 0.046)
• Low body mass at birth in boys (p = 0.046)

Nutrition analysis based on medical history and questionnaire
The results provided that children with MetS (44.7%) omitted breakfast more often than children from group II (35%) and group III (28.7%) (p = 0.030). This phenomenon was especially distinctive in boys.

Thereby not eating breakfast was a risk factor of not only MetS (p = 0.027, OR = 1.74; 95%CI: 1.06–2.87) but also a risk factor of at least one of its components (p = 0.036) (OR = 1.46; 95%CI: 1.02–2.09).
Omitting dinner was more prevalent in children from group I and III (OR = 1.63; 95%CI: 1.13 – 2.35) as well as in boys (OR = 2.66; 95%CI: 1.56 – 4.55) (See Supplementary Table 3, Additional File 1). Not eating dinner seems to be another risk factor of MetS.

On the other hand there were no differences in eating fruit or vegetables (in terms of quantity and frequency) between children with MetS and the rest of the study population.

Physical activity
The results of physical performance (evaluated by Kash Pulse Recovery Test) are presented in Supplementary Table 4, Additional File 1 It shows that children with MetS had very poor physical performance, three times more than the rest of the children. Besides, boys with MetS had significantly worse physical performance than the rest of males (p = 0.15).

The correlation between metabolic syndrome and it’s compounds was significant for:
• Omitting dinner: in whole population (OR = 1.63; 95%CI: 1.13–2.35), especially in boys (OR = 2.66; 95%CI: 1.56–4.55)
• Not eating breakfast (p = 0.036) (OR = 1.46; 95%CI: 1.02–2.09)

Biochemical assessment
Elevated levels of insulin were most common in children with MetS; twice as much as in children from group III and fourfold than in group III. Obese children without MetS had significantly more often normal insulin level (p = 0.001).

Insulin resistance was also more common in children with MetS compared to the remaining.
Table 4
Fasting insulin level [Ins], one and two hours after glucose intake (OGTT) in study population

|                  | MetS+ | MetS− | MetS+/− | MetS+ vs MetS− vs MetS+ & +/- vs MetS− & +/- | p-value |
|------------------|-------|-------|---------|---------------------------------------------|---------|
| **Fastiing insulin level** |       |       |         |                                             |         |
| Elevated (≥ 15 ng /ml) | 37    | 48.6  | 32      | 13.2 | 59 | 21.7 | 0.001 | 0.001 | 0.001 |         |
| Normal (< 15 ng /ml) | 39    | 51.4  | 211     | 86.8 | 213 | 78.3 |       |       |       |         |
| [Ins] after 1 hr OGTT | n    | %     | n       | %     | n    | %    | 0.015 | 0.076 | 0.831 |         |
| Elevated         | 6     | 7.9   | 3       | 1.2   | 14   | 5.1  |       |       |       |         |
| Normal           | 70    | 92.1  | 240     | 98.8  | 258  | 94.9 |       |       |       |         |
| Eleva ted        | 23    | 30.3  | 19      | 7.9   | 39   | 14.3 |       |       |       |         |
| Normal           | 53    | 69.7  | 224     | 92.1  | 233  | 85.7 |       |       |       |         |

p < 0.05 Kruskal-Wallis test analysis.
### Table 5
Glucose concentration in study population during oral glucose test

| Glucose concentration | MetS+ | MetS- | MetS+/– | MetS+ vs MetS– | MetS+ & +/- vs MetS– | MetS+ vs MetS– & +/- |
|-----------------------|-------|-------|---------|----------------|----------------------|---------------------|
| Fastig n (%)          | n     | %     | n       | %             | n                    | %                   |
| < 100 mg/dl           | 50    | 65.8  | 243     | 100           | 244                  | 89.7                | 0.001               | 0.001               | 0.001               |
| 100–125 mg/dl         | 21    | 27.6  | 0       | 0             | 27                   | 9.9                 | 0.015               | 0.001               | 0.015               |
| >=126 mg/dl           | 5     | 6.6   | 0       | 0             | 1                    | 0.4                 | 0.015               | 0.015               | 0.010               |
| >200 mg/dl            | 0     | 0     | 0       | 0             | 0                    | 0                   |                      |                      |                      |

One hour after glucose intake

| Normal < 140 mg/dl    | 5     | 6.7   | 5       | 2.1           | 13                   | 4.7                 | 0.201               | 0.350               | 0.148               |
| Elevated 140–199 mg/dl| 71    | 93.3  | 238     | 97.9          | 259                  | 95.3                |                      |                      |                      |
| >200 mg/dl            | 0     | 0     | 0       | 0             | 0                    | 0                   |                      |                      |                      |

p < 0.05 Kruskal-Wallis test analysis.

Five children with MetS had fasting glucose > 126 mg/dl and were consulted by diabetologist.
Children without MetS had normal fasting glucose concentration, whereas children from Group I and III-pathological in 27.6% cases and 9.9% cases, respectively.

Abnormal HOMA-IR values were significantly more common in children with metabolic syndrome (p = 0.005).

Table 6
HOMA-IR values (normal and elevated) in study subgroups

| HOMA-IR | MetS+ | MetS− | MetS+/− | MetS+ vs MetS− | MetS+/− vs MetS− | MetS+ & MetS− vs MetS+/− |
|---------|-------|-------|---------|----------------|-------------------|--------------------------|
|         | n     | %     | n       | %             | n                 | %                        |
| Over > 2.5 | 58     | 76.3  | 32      | 13.2          | 86                | 31.7                     | 0.005 | 0.009 | 0.001 |
| Normal i.e. < 2.5 | 18     | 23.7  | 211     | 86.8          | 186               | 68.3                     |

p < 0.05 Kruskal-Wallis test analysis.

Although children with MetS had more often elevated aminotransferases activity, the difference was significant for ALT only (p = 0.011).

**Discussion**

Prevalence of obesity is high worldwide, some find it pandemic. This disease is known to be one of the so-called “lifestyle diseases” and it was fathered mostly upon adolescence and adults.

However, incidence of obesity in children is growing fast and the burden of its complications must be considered not only from medical but also socioeconomic point of view.

Obesity increases the risk of other diseases of affluence, such as: hypertension, dyslipidemia, glucose intolerance at the same time being a well known risk factor of CVD and MetS. 23–26.

Many authors reported that children with BMI over 75th centile have higher morbidity and mortality of DM2 and CVD in adulthood. 27–30. Thus, quality and expectancy of life certainly is and will be affected by obesity.

Metabolic syndrome became an epitome of obesity’s complications with high impact on human’s well-being.
Apart from various definitions of MetS in children, apparently not all teens with obesity develop metabolic syndrome or not even one of its components. Which of the obese children (in fact whole obese population) are especially predisposed to MetS is still not fully understood. Yet, knowing the risk factors of metabolic syndrome would allow to prevent the latter or at least minimise its prevalence and consequences.

In our study 12.9% of obese children 9–12 years old, participating in „6-10-14“ for health” had metabolic syndrome diagnosed – 10.9% of girls and 14.6% of boys. These results are similar to other publications. It seems that prevalence of obesity and metabolic syndrome in children is more or less the same all over the world.

According to Abdullah et al. young age at the onset of obesity as well as time period it lasts are essential factors of MetS in adolescence. Clearly, appropriate prophylaxis should be undertaken as soon as possible to stop his process.

Our main aim was to identify children who were at highest risk of developing MetS. Recognition of predisposing agents, which can be modified, may be crucial, since it is our deep believe that undertaking no prevention will lead to MetS eventually.

The results show that obese children with metabolic syndrome characterize with poor physical performance, bad nutrition habits and glucose intolerance with insulin resistance. Similarly to Mazur et.al., we also found that pathological WhtR predisposes to both MetS and syndrome’s certain components.

In our study, we found that boys with low body mass at birth had more often MetS. Obviously this fact is irreversible, nevertheless it is known that metabolic programming, which begins in fetal life is going on after birth too. There is slight opportunity to influence this process by means of “healthy” lifestyle of pregnant woman and can be achieved by education of not only doctors and health providers but also mothers. Promoting exclusively breastfeeding with recommended weaning time presents to be easy way to influence metabolic programming and weight gain in first 2–3 years of life.

Both or either parent’s obesity - especially father’s - might depict genetic predisposition to excess body mass in a child, but, on the other hand, illustrates family’s lifestyle. It is already known, that obese children more often skip breakfast. Contrary to some authors, we found that omitting dinner is related to metabolic syndrome or to components of metabolic syndrome too. This feeding pattern fits in modern model of life, characterized additionally with little physical activity and much sedentary time (at school, work and home). Similar observations have already been published.

Obviously, there is not much we can do about genetics. However, if genetic predisposition runs in the family it stands for a red flag and preventive measurements should be undertaken in order to alleviate unavoidable consequences of obesity and MetS.
Such, sound knowledge and education on energy balance (via proper diet and physical activity) as driving force against obesity should be promoted. Changes implemented for child’s prevention will cover beneficially whole family.

To our knowledge this is the first study on “factors” predisposing to metabolic syndrome” in obese children and teenagers, carried out in such a large, unanimous population (age, residency).

Taking into account genetic predisposition and environmental influences we tried to indicate modifiable risk factors
The results of our study could be used as warning signals for subjects who are genetically predisposed to obesity. In these children certain preventive measures should be undertaken.

**Conclusions**

Among many risk factors of metabolic syndrome, beside those which are irreversible (such as body mass at birth, gender genetic predisposition etc.) there are many which are dependent on lifestyle. The latter, such as proper, increased physical activity, rational nutrition (regular ‘healthy’ meals) can be modified and such the risk of metabolic syndrome in obese children can be diminished in inexpensive way.

The education and preventive companies addressed to health providers and parents are required in order to lessen morbidity of obesity and metabolic syndrome

**List Of Abbreviations**

| Abbreviation | Description                      |
|--------------|----------------------------------|
| BIA          | bioelectric impedance analysis   |
| BMI          | body mass index                  |
| CVD          | cardiovascular diseases           |
| DM           | diabetes mellitus                |
| HDL          | high density lipoprotein         |
| HOMA-IR      | homeostatic model assessment for insulin resistance |
| IDF          | International Diabetes Federation |
| MetS         | metabolic syndrome               |
| OGGT         | oral glucose tolerance test       |
| SBP          | systolic blood pressure          |
| TG           | triglycerides                    |
WC        waist circumference
WHO        World Health Organization
WhtR        waist-hip-ratio

Declarations

Ethics approval and consent to participate

This study was accepted by the Independent Bioethics Committee for Scientific Research at Medical University of Gdańsk. The study is registered in clinicaltrials.gov (NCT number): NCT04143074

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of “6–10-14 for Health” integrated weight management program for children with overweight and obesity from Gdansk, Poland

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Competing interests

"The authors declare that they have no competing interests" in this section.

Authors' contributions

AR-S design of the work; the analysis, and interpretation of data, patient recruitment, data collection and analysis, approval of the manuscript

MB design of the work, substantive revision, approval of the manuscript

AJ design of the work, patient recruitment, data collection and analysis, paper draft, revision and approval of the manuscript

ASS designed work, revision and approval of the manuscript

All authors read and approved the final manuscript
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**Figures**
Figure 1
Patient screening and qualification to the study – study flow.

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