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ORIGINAL PAPER

Analysis of selected biomarkers of obesity-related complications in the paediatric population

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ABSTRACT

Introduction: Childhood obesity is a growing global health concern, strongly associated with chronic low-grade inflammation and increased risk of metabolic, cardiovascular, and renal complications. Identifying early biomarkers of obesity-related disorders is essential for timely intervention and prevention. This study aimed to evaluate selected serum and urinary biomarkers in children and adolescents aged 8–18 years to assess their relationship with overweight and obesity and their potential as early indicators of metabolic disturbances.

Material and methods: A total of 268 participants were included: 200 children with excessive body weight (body mass index – BMI ≥ 85th percentile) and 68 children with normal weight (BMI < 85th percentile), classified according to the Polish OLAF percentile charts. Biochemical markers analysed in serum included high-density lipoprotein (HDL)-C, low-density lipoprotein (LDL)-C, creatinine (Cr), uric acid, isthmin-1, visfatin, resistin, and in urine, α-1-acid glycoprotein (α1AGP)/Cr.

Results: The study group had significantly lower HDL-C concentrations compared to their normal-weight peers. No statistically significant differences were observed in LDL-C or serum Cr levels between the groups. However, the study group exhibited significantly higher serum resistin levels and an elevated urine α1AGP/Cr. In contrast, concentrations of serum isthmin-1 and visfatin were significantly lower in the study group than in the control group. Correlation analysis using Spearman's test showed no significant associations between concentrations of adipokines and uric acid.

Conclusions: This study demonstrated significant differences in biochemical and inflammatory markers between children with overweight/obesity and their normal-weight peers, including decreased HDL-C and visfatin, lower isthmin-1, and elevated resistin and α1AGP/Cr. These findings may reflect early metabolic and inflammatory disturbances that occur even before clinical symptoms arise. The lack of correlation between adipokines and uric acid suggests distinct, independent mechanisms involved in obesity-related complications. Monitoring these biomarkers may support early detection and prevention strategies in paediatric populations at risk of metabolic disorders.

KEY WORDS:

obesity, children, biomarkers, overweight.

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INTRODUCTION

Obesity has been considered for several decades as one of the most serious civilisation and chronic diseases, posing a growing worldwide health problem. According to the World Health Organisation (WHO) report, nearly 60% of adults and one of three children in Europe are struggling with overweight or obesity. Overweight and obesity account for over 1.2 million deaths every year in the WHO European Region, making up more than 13% of all deaths. They also represent a leading cause of disability, significantly contributing to the overall burden of disease in the population [1]. In addition to their impact on health, obesity and overweight also pose a substantial economic challenge due to increased healthcare expenditures, reduced productivity and related social costs. These trends underscore the urgent need for effective prevention and intervention strategies at both national and international levels [2].

The rising percentage of children and adolescents with overweight and obesity is a growing health and social concern. Obesity leading to chronic conditions such as hypertension, type 2 diabetes, insulin resistance, dyslipidaemia, and atherosclerosis, which increase the risk of serious cardiovascular events [1–3]. Chronic kidney disease is among the numerous complications associated with obesity, and its occurrence even in paediatric populations underscores the need for early metabolic monitoring and timely intervention [4]. In recent years, growing attention has been given to the identification of biomarkers that reflect these underlying disturbances and may serve as early indicators of obesity-related complications.

The aim of this study was to examine the levels of selected biochemical biomarkers in blood, including high-density lipoprotein (HDL), low-density lipoprotein (LDL), creatinine (Cr), uric acid, isthmin-1, visfatin, resistin and in urine, the α-1-acid glycoprotein (α1AGP), in children and adolescents aged 8–18. The primary objective was to assess how these metabolic markers relate to overweight and obesity in comparison to children with normal body mass index (BMI), as determined based on BMI percentile charts. According to the OLAF criteria, children and adolescents with a BMI above the 85th percentile were included in a combined overweight and obesity group for the purposes of analysis [5].

The selected biomarkers examined in this study – such as isthmin-1, visfatin, and resistin – have been increasingly recognised in recent literature for their potential role in adipose tissue regulation, inflammatory processes, and metabolic homeostasis. In parallel, traditional biochemical markers including HDL, LDL, Cr, and uric acid provide essential information on lipid metabolism, renal function, and systemic inflammation. Additionally, α1AGP was evaluated as a potential early biomarker of obesity-related kidney dysfunction in the paediatric population [6]. By evaluating both conventional and emerging indicators, this study seeks to provide a more comprehensive understanding of the metabolic profile associated with excess body weight in the paediatric population.

TABLE 1. Distribution of children by sex in the control and excess body weight groups, including total numbers and mean body mass index percentile values

Group	Boys (*n*)	Girls (*n*)	Total (*N*)	Mean BMI percentile
Study group	103	97	200	92.5
Control group	35	33	68	54.2

BMI – body mass index

MATERIAL AND METHODS

STUDY GROUP

The children participating in the study were recruited as part of the PICTURE project – Population Cohort Study of Wroclaw Citizens [7]. The biobanking process was conducted in accordance with the Quality Standards for Polish Biobanks [8]. Prior to participation, written informed consent was obtained from each participant for both the examination and biobanking of biological material. All ethical aspects of the study were conducted in accordance with the Quality Standards for Polish Biobanks – Chapter 5: ELSI (Ethical, Legal and Societal Issues). The study included 268 children and adolescents aged 8–18 years comprising 200 children with excessive body weight (study group) and 68 children with normal body weight (control group) (Table 1). The diagnosis of overweight and obesity was based on BMI values referenced against percentile charts appropriate for age and sex. Children and adolescents with a BMI above the 85th percentile were included in a combined overweight and obesity group for the purposes of analysis. The control group was selected to ensure proportional representation of children from each age group and to match their height values with the calculated averages for age and sex of the study group (Table 2).

BIOLOGICAL MATERIAL

The biological material used in the study was stored at the Wroclaw Medical University Biobank. Two types of biological material were used in the study: urine and serum. Samples were collected following current laboratory standards to ensure their quality and integrity. All samples were immediately frozen and stored at –80°C until biochemical analyses were conducted.

URINE BIOMARKERS

The level of α1AGP was measured using the enzyme-linked immunosorbent assay (ELISA) method with the Human α1AGP ELISA Kit (SEA816Hu, Cloud-Clone Corp.). The creatinine concentration in urine was deter-

TABLE 2. Characteristics of the study group

Biomarker	Study group Median (IQR)	Control group Median (IQR)	*p*-value
HDL-C [mg/dl]	53.00 (46.00–61.00)	56.50 (48.25–67.00)	0.005
LDL-C [mg/dl]	85.50 (71.00–105.00)	79.50 (68.75–98.75)	0.115
Cr [mg/dl]	0.590 (0.5025–0.6700)	0.6050 (0.5100–0.6875)	0.376
Uric acid [mg/dl]	4.800 (4.100–5.700)	4.400 (3.600–5.075)	0.005
Isthmin-1 [ng/ml]	0.640 (0.540–0.750)	0.740 (0.520–0.842)	0.048
Visfatin [ng/ml]	126.9 (90.81–176.8)	153.8 (122.3–174.8)	0.017
Resistin [ng/ml]	9.220 (7.160–12.630)	7.910 (6.048–10.340)	0.003
α1AGP/Cr [mg/g]	540.6 (283.8–759.0)	378.6 (226.5–568.6)	0.004

a1AGP – α-1-acid glycoprotein, Cr – creatinine, HDL – high-density lipoprotein, IQR – interquartile ranges, LDL – low-density lipoprotein
Data are presented as median values with interquartile ranges.

mined using the colorimetric method with the Creatinine Assay Kit (MAK475).

SERUM BIOMARKERS

The level of isthmin-1 in serum was measured using the enzyme-linked immunosorbent assay (ELISA) method with the Human Isthmin-1 ELISA Kit (SEQ515Hu96, Cloud-Clone Corp.). The concentration of visfatin in serum was determined using the ELISA method with the Visfatin EIA Kit (RAB0377, Sigma-Aldrich). The level of resistin was measured using the ELISA method with the Human Resistin ELISA Kit (#EZHR-95K, Merck KGaA). All biomarker determinations, both in urine and serum, were performed according to the respective manufacturer's instructions and measured using the same microplate reader (Multiskan™ GO UV/Vis Spectrophotometer, Thermo Scientific, Type 1510, Ref. 51119300).

BIOCHEMICAL PARAMETERS FROM THE PICTURE STUDY

Serum biochemical parameters, including uric acid, HDL, LDL, and Cr concentrations, were assessed during routine clinical evaluations conducted as part of the PICTURE project. The analyses were carried out in accordance with standardized laboratory procedures to ensure consistency and reliability of results.

STATISTICAL ANALYSES

To compare the levels of the analysed markers between individuals with obesity and overweight and those with normal body weight, statistical analysis was performed using GraphPad Prism 10.4.1 software. The distribution of the data was assessed using the Kolmogorov-Smirnov test [9], which determined the conformity of the variables with a normal distribution. Due to the lack of normal distribution in all cases, the non-parametric Mann-Whitney *U* test [10] was used to compare differences between groups. All tests were two-tailed, and the level of statistical significance was set at $p < 0.05$. *P*-values below this threshold were considered statistically significant.

RESULTS

Figure 1 presents a comparison of biomarker concentrations between children and adolescents with excess body weight and those with normal weight. As shown in Figure 1 A, levels of HDL-C were significantly lower in the group with overweight and obesity. In contrast, LDL-C concentrations (Figure 1 B) did not differ significantly between the groups. Similarly, no significant differences were observed in Cr levels (Figure 1 C). However, uric acid concentrations (Figure 1 D) were significantly higher among individuals with excess weight. Regarding adipokines, significantly lower levels of isthmin-1 (Figure 1 E) and visfatin (Figure 1 F) were found in the overweight and obese group. Conversely, resistin (Figure 1 G) was significantly elevated in this group. Finally, α1AGP/Cr, shown in Figure 1 H, was also significantly higher in individuals with excess body weight.

DISCUSSION

The study results showed a significantly lower concentration of HDL-C in the group with overweight and obesity. This observation is consistent with the existing literature indicating that reduced HDL-C levels are a common feature of the metabolic syndrome in individuals with excessive body weight [11–13]. Lower HDL-C is considered unfavourable due to its role in reverse cholesterol transport, antioxidant activity, and anti-inflammatory effects. In the context of obesity-related chronic inflammation and dyslipidaemia, decreased HDL-C may contribute to the development of atherosclerosis, type 2 diabetes, and other metabolic complications, highlighting its importance as a clinical risk marker [14, 15].

In the conducted study, no statistically significant differences were found in LDL-C level between children and

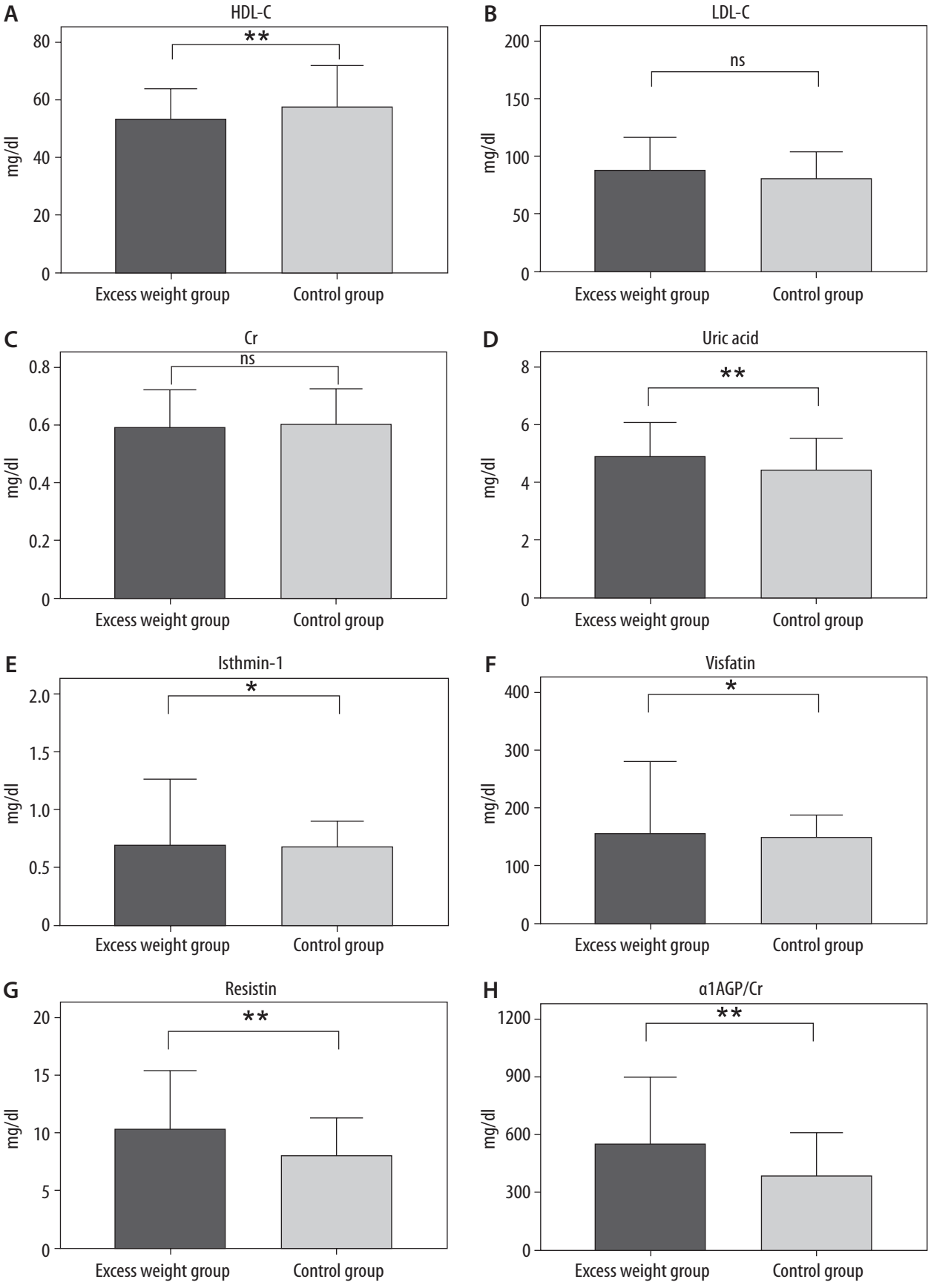

FIGURE 1. The association between excess body weight and the level of selected biomarkers compared to the control group. **A**) HDL-C (serum). **B**) LDL-C (serum). **C**) Creatinine (serum). **D**) Uric acid (serum). **E**) Isthmin-1 (serum). **F**) Visfatin (serum). **G**) Resistin (serum). **H**) α1AGP/Cr (urine)

α1AGP – α-1-acid glycoprotein, Cr – creatinine, HDL – high-density lipoprotein, LDL – low-density lipoprotein, ns – not significant
Results are presented as medians.
Statistical significance: $p < 0.05$ (*), $p < 0.01$ (**)

adolescents with overweight and obesity and those with normal body weight. The literature shows variability in findings regarding the relationship between obesity and LDL level in children. Some studies have reported elevated LDL-C values in paediatric obesity, particularly in the presence of advanced metabolic disturbances [14]. In contrast, other research suggests that early stages of overweight are more often associated with reduced HDL-C and elevated triglycerides, with LDL-C typically remaining within normal limits. These discrepancies may reflect the influence of obesity duration and the progression of metabolic dysfunction over time [16, 17].

In our study, elevated serum uric acid levels were observed in the study group. Current scientific research indicates that elevated serum uric acid levels play a significant role in the development of metabolic syndrome. Increased uric acid levels in the course of metabolic syndrome are primarily linked to excessive purine intake from diets rich in high-protein foods and fructose, as well as a sedentary lifestyle, all of which are common in individuals with obesity [18].

Based on data from numerous observational studies and meta-analyses, hyperuricemia has been shown to correlate with a higher risk of metabolic syndrome, and its severity increases with the number of components such as hypertension, visceral obesity, and dyslipidaemia. Elevated serum uric acid levels may contribute to insulin resistance and chronic inflammation, increasing the risk of cardiovascular (e.g., coronary heart disease and stroke) and metabolic diseases, as confirmed by several prospective cohort studies. These findings highlight the relevance of uric acid as a potential biomarker, particularly in individuals with obesity and other components of metabolic syndrome [19–21].

Adipokines, as molecules secreted by adipose tissue, play a key role in biological processes such as metabolism, inflammatory response, cardiovascular function, and immune regulation.

The study results indicate significant differences in the concentrations of the analysed adipokines between children and adolescents with overweight and obesity and those with normal body weight. Lower levels of isthmin-1 and visfatin, as well as elevated levels of resistin, were observed in the study group, suggesting that each of these adipokines may play a distinct role in the pathophysiology of childhood obesity and its related metabolic disturbances.

Isthmin-1 is an adipokine that amplifies glucose uptake by adipocytes and muscle cells and inhibits lipogenesis, acting independently of the insulin receptor. In addition to regulating glucose metabolism [22], it also participates in processes such as angiogenesis, apoptosis, tissue development, and the pathology of organs such as the kidneys, liver, and lungs [23, 24]. In the study, isthmin-1 levels were significantly lower in the study group compared to the control group.

Our findings are consistent with those reported by Kuwaiti researchers, who observed that reduced levels of isthmin-1 are associated with obesity and metabolic disorders, and that this adipokine may play a protective role in the development of type 2 diabetes. Its potential as a diagnostic biomarker is also emphasized, particularly for the early detection of metabolic abnormalities and assessment of the risk of related complications [25].

However, it is worth noting that there are also studies in which elevated isthmin-1 levels were observed in patients with obesity [26, 27]. The observed differences in studies on the isthmin-1 level may result from a variety of factors, including biological variability, differences in metabolic status, disease stage, or the presence of coexisting conditions. To date, only a limited number of studies have investigated isthmin-1 levels in children and adolescents. One such study indicates a potential association between isthmin-1 and the pubertal stage in boys, highlighting its possible relevance during this developmental period. This highlights how many factors – such as age, sex, and developmental stage – may influence isthmin-1 concentrations, reinforcing the need for further studies to better understand its regulation and clinical relevance in childhood obesity.

The concentration of visfatin was significantly lower in the study group. Visfatin is an adipokine primarily secreted by visceral adipose tissue and exhibits insulin-like activity. Research suggests its potential involvement in the atherosclerotic process and highlights its pro-inflammatory properties due to its ability to stimulate the production of inflammatory mediators [28].

Although most studies suggest an increase in the visfatin level in the course of obesity [29–31], the results of the present study indicating a decrease may reflect the specific characteristics of the paediatric population or an early stage of metabolic disorder development. This observation may also be related to the significantly lower HDL-C levels in the study group, considering that a positive correlation between visfatin and HDL-C has been observed in obese adolescents [32]. Differences between study results may stem from multiple factors such as participants' age, the stage of obesity (early vs. advanced), the presence of other metabolic disorders, sex, as well as variations in laboratory methods and group selection criteria. Additionally, some studies show that excessive overfeeding may lead to a decrease in the visfatin level [33], and its concentration may also be reduced in response to factors such as physical activity or weight loss [34]. Due to the cross-sectional nature of the present study and the limited sample size, further prospective analyses in larger cohorts are necessary to more precisely define the role of visfatin in the pathophysiology of childhood obesity.

In turn, the concentration of resistin was significantly higher in the study group compared to the control group. As a pro-inflammatory adipokine, resistin plays an important role in regulating immune responses and is in-

volved in the pathogenesis of inflammatory, metabolic, and infectious diseases. Elevated resistin levels have previously been observed in patients with type 2 diabetes, chronic inflammatory and metabolic diseases. Through its ability to activate immune cells and stimulate the secretion of pro-inflammatory cytokines, resistin may promote disturbances in metabolic homeostasis already at the early stages of obesity. Moreover, a growing body of evidence suggests its involvement in endothelial dysfunction, increased oxidative stress, and platelet activation, which may initiate atherosclerotic processes and elevate the risk of cardiovascular events [35–37]. In light of this evidence, resistin shows promise as an early biomarker of obesity-related complications.

An elevated α1AGP/Cr was observed in children with excessive body weight. which may serve as a marker of ongoing inflammatory and metabolic processes, and its increase can reflect early pathophysiological changes accompanying obesity. α-1-acid glycoprotein is an acute-phase protein synthesized primarily in the liver, exhibiting immunomodulatory properties through the regulation of pro- and anti-inflammatory cytokines released by adipose tissue. It has also been demonstrated that α1AGP possesses anti-inflammatory potential, contributing to the maintenance of metabolic balance. Recent studies in paediatric populations have indicated that elevated α1AGP/Cr levels may appear earlier than albuminuria, suggesting its usefulness as a biomarker of early glomerular damage. α-1-acid glycoprotein is considered to be a more sensitive indicator of glomerular filtration bar-rier permeability than traditionally used albuminuria [6]. The lack of significant differences in kidney function parameters in children with overweight and obesity may result from the relatively short duration of these conditions, which has not yet allowed for the development of detectable functional changes. Due to the altered body composition in individuals with obesity, traditionally used markers such as Cr may not accurately reflect the actual glomerular filtration rate, potentially masking early kidney alterations [38].

CONCLUSIONS

This study identified significant differences in selected biochemical and inflammatory biomarkers between children and adolescents with overweight and obesity and their normal-weight peers. The observed decrease in HDL-C levels, combined with increased resistin concentrations and an elevated α1AGP/Cr level, may indicate early metabolic and pro-inflammatory disturbances occurring in the course of excessive body weight, even in the absence of overt clinical complications.

The findings underscore the importance of early screening and monitoring of non-traditional biomarkers in paediatric populations with excess body weight to identify individuals at risk of developing metabolic disorders. Further prospective studies are warranted to better understand the mechanistic roles of adipokines and inflammatory markers in the progression of obesity-related complications and to evaluate their utility in early diagnosis and targeted prevention strategies.

DISCLOSURES

1. Institutional review board statement: The project received approval from the Bioethics Committee of Wroclaw Medical University (approval no. KB 539/2024, issued on 19 September 2024).
   The study was reviewed and approved by the Bioethics Committee of the Wroclaw Medical University (approval no. KB-667/2019).
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4. Conflicts of interest: None.

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