

Проблеми екології та медицини

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ОГЛЯДИ/REVIEWS

METABOLIC SYNDROME IN PEDIATRIC PRACTICE: DEFINITION, DIAGNOSTIC CRITERIA AND PRINCIPLES OF PATIENT MANAGEMENT (OVERVIEW)

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The article comprehensively reviews epidemiological indicators, risk factors, pathophysiological mechanisms, diagnostic criteria, and contemporary management principles of metabolic syndrome in pediatric practice. The study relies on the extensive analysis of literature sources retrieved from electronic databases such as PubMed, UpToDate, Web of Science, ScienceDirect, Scopus, MedLine, and Elsevier. The literature review highlights the escalating prevalence of metabolic syndrome as an urgent medical and social concern among children and adolescents, primarily attributed to the global epidemic of childhood obesity. The article not only outlines key findings but also presents recommendations from international medical societies concerning screening strategies, diagnostics, and therapeutic approaches for the individual components contributing to metabolic syndrome in childhood. The review also focuses on pivotal studies exploring alternative therapies targeting the principal pathogenic factors of the disease. In conclusion, the authors emphasize the pressing issue of the absence of standardized criteria for diagnosing metabolic syndrome in children, highlighting the imperative role of a multidisciplinary team of specialists in the effective management of this pathology in pediatric practice.

Keywords: metabolic syndrome, obesity, insulin resistance, dyslipidemia, cardiovascular diseases, children

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Introduction

The metabolic syndrome (MS), also known as syndrome X or insulin resistance syndrome, is defined by the WHO as a pathological condition characterized by abdominal obesity, insulin resistance, hypertension and dyslipidemia, substantially increasing the risk of cardiovascular disease [1, 2, 3]. Interest among physicians across diverse specialties in understanding the

phenomenon of "metabolic syndrome" intensifies with ongoing investigations. The pathogenesis, clinical manifestations, and treatment principles of MS continue to be the focal points of research and discourse in the medical scientific community. Presently, metabolic syndrome ranks among the most critical medical and social challenges globally. The undeniable prevalence of MS and its pivotal role in precipitating comorbidities like type 2 diabetes mellitus, arterial hypertension,

dyslipidemia, and atherosclerosis underpins the urgency of extensive scientific exploration into its pathogenesis, diagnosis, prevention, and treatment [4, 5, 6]. The rapid surge in obesity rates, particularly in developing countries, contributes significantly to an increased number of children and adolescents displaying signs of insulin resistance and susceptibility to metabolic disorders. Furthermore, the elevated prevalence of other metabolic syndrome components (such as arterial hypertension, dyslipidemia, etc.) among individuals under 18 and their adverse impact on cardiovascular and endocrine health in adulthood highlight the significance of investigating metabolic syndrome in childhood.

The aim of the research is to analyze data on the prevalence, risk factors, formation mechanisms, contemporary diagnostic criteria, and management principles of metabolic syndrome in pediatric practice based on current literature.

To provide a comprehensive overview of the current literature regarding the definition, diagnosis, and treatment of MS in the pediatric population, we conducted an analytical review of randomized clinical trials and relevant publications. Our search encompassed electronic databases including PubMed, UpToDate, Web of Science, ScienceDirect, Scopus, MedLine, and Elsevier. The search terms employed were "metabolic syndrome," "abdominal obesity," "insulin resistance," "dyslipidemia," "cardiovascular disease," and "children."

The global incidence of MS is on a continual rise, mirroring the escalating rates of obesity and establishing itself as a new non-communicable pandemic in the 21st century, particularly affecting industrialized countries. According to the World Health Organization (WHO) experts (2021), approximately 39% of the global population faces overweight-related issues, marking a gradual increase in overweight prevalence among children and adolescents. Statistical analyses spanning from 1980 reveal a doubling in the prevalence of childhood obesity in over 70 countries [7].

Recent data confirmed the severity of the issue, indicating that in 2019, around 38.2 million children under the age of 5 were either overweight or obese, with an alarming 12.9% of children aged 5 to 9 diagnosed with obesity [8]. In the European Union Member States, nearly one in five adolescents aged 15 met the criteria for overweight or obesity in 2018 (OECD. Health at a Glance: Europe 2020. State of Health in the EU Cycle). According to the Centers for Disease Control and Prevention (CDC) in the United States, the prevalence of obesity stands at about 18%, impacting approximately 13 million children. This rate varies with the age of the

child, ranging from 13.9% in the 2-5 age group to 20.6% in the 12-19 age group [9]. Moreover, the study highlighted disparities in the United States, revealing higher obesity rates among Hispanic and non-Hispanic black populations compared to whites. Notably, it observed a significant correlation between elevated obesity rates and children from families with lower incomes and limited educational attainment. Experts estimate the prevalence of metabolic syndrome in the United States to be around 4.5%, with nearly all affected children falling into the categories of obesity or overweight [10]. In India, studies investigating obesity prevalence among children in 16 states disclosed that approximately 19.3% of children and adolescents suffer from this pathology. Simultaneously, the overall prevalence of metabolic syndrome among children in Srinagar was found to be 3.8%, demonstrating a relatively even gender distribution. In the Northern region of India, specifically in Chandigarh, this figure increased to 4.2% among adolescents aged 12 to 17 years [11].

The epidemiology of MS across various European countries exhibits statistical variations, potentially stemming from differences in diagnostic criteria applied to children. These criteria, subject to change over time, contribute to discrepancies in MS diagnoses. For clarity and convenience, we present statistical data based on the latest criteria from the International Diabetes Federation (IDF), aligning closely with clinical practice. For instance, in Poland, the prevalence of MS in the pediatric population, calculated according to IDF criteria, displayed variability with age — ranging from 12.9% in children aged 10-12 years to 20.0% in children/adolescents aged 5-18 years [12]. In Italy, MS prevalence according to IDF criteria reached up to 19.9% in children/adolescents aged 5-20 years [13]. Slovakia reported a range from 2.75% in children under 14 years [14] to 5.5% in overweight and obese adolescents (14-18 years). Meanwhile, a study in the Czech Republic, involving a sample of 274 Czech children/adolescents aged 10-17 years, revealed a notably high prevalence of MS — 37% in obese children [15]. A comprehensive study in Ukraine, encompassing 314 children aged 10 to 18 years with diagnosed obesity, found that around 34% exhibited manifestations of MS according to IDF criteria [16]. Unfortunately, the current stage lacks sufficient research on the epidemiological indicators of metabolic syndrome in the pediatric population. However, even existing study results indicate that this issue remains underestimated and pertinent in pediatric practice.

Currently, the scientific community is engaged in ongoing discussions regarding the exploration of potential causes, or risk factors, for metabolic syndrome. At the present stage, considerable

attention is devoted to both maternal/hereditary factors and acquired risk factors, often referred to as "lifestyle factors." Research findings highlight the undeniable influence of maternal/hereditary factors on metabolic syndrome, particularly concerning the child's nutrition in the early years. Notably, the duration of breastfeeding and the use of high-quality, highly adapted formulas emerge as critical elements ensuring the harmonious growth and development of the child [17, 18]. Studies affirm the close association between childhood metabolic syndrome and gestational diabetes mellitus, as well as variations in birth weight [17]. Researchers observe that inadequate or excessive nutrient availability during prenatal development can induce metabolic and hormonal changes in the child's body, impacting the leptin-to-adiponectin ratio and contributing to insulin resistance and metabolic syndrome later in life [19].

Furthermore, the risk of obesity more than doubles if one parent suffers from this pathology. Research indicates that children with at least one parent exhibiting metabolic syndrome manifest a significantly higher body mass index and elevated rates of insulin resistance compared to a control group of children [20]. The role of genetic predisposition in shaping the components of metabolic syndrome and childhood obesity is acknowledged but remains incompletely understood to date.

At present, investigations actively explore the influence of single nucleotide polymorphisms (SNPs) in specific genes associated with regulating fundamental metabolic processes in the body. These studies encompass key genetic markers, such as the peroxisome proliferator-activated receptor gamma (*PPARG*) polymorphism Pro12Ala [21], the Glu23Lys polymorphism *KCNJ11*, and variants of *ABCC8*, *SLC2A2*, *HNF4A*, and *INS*. Notably, the intronic variant rs7903146 (allele T) of *TCF7L2*, identified as a single nucleotide polymorphism, is linked to a 41% increase in the risk of type 2 diabetes mellitus [22]. This ongoing exploration contributes to our evolving understanding of the complex genetic underpinnings of metabolic syndrome.

At the same time, some researchers emphasize the prominence of lifestyle factors in the genesis of metabolic syndrome among adolescents, positing that elements such as insufficient physical activity, a diet rich in fatty foods, an excess of easily digestible carbohydrates with inadequate vegetable intake, might carry even greater significance than hereditary factors [1, 3, 6]. In recent years, increased attention has been directed toward investigating the impact of daily (circadian) environmental rhythms on the functioning of living organisms and

the development of various pathological conditions [23, 24]. Over the past decade, this tendency has intensified due to the widespread use of gadgets by children, especially at night for educational and recreational purposes. Such practices have significantly disrupted the evolutionary adaptation of the human body to circadian rhythms, leading some scientists to posit that this disruption also exerts a negative influence on the regulatory mechanisms of metabolic processes.

The initial mechanism behind the formation of metabolic syndrome remains complex and multifactorial, lacking clear elucidation to date. Many researchers currently consider the theory of the leading role of insulin resistance in triggering a cascade of metabolic disorders and the pathophysiology of the metabolic syndrome itself in obese individuals. An alternative perspective posits the central role of visceral obesity in the development of acquired insulin resistance (IR) [3, 6, 25]. As adipose tissue weight increases, fat cell hypertrophy, commonly referred to as "adiposopathy," ensues, resulting in their dysfunction. Hypertrophied fat cells exhibit increased resistance to insulin, impeding the inhibition of lipolysis in the body. Notably, visceral adipose tissue possesses distinctive properties, being highly responsive to the lipolytic impact of catecholamines and displaying low sensitivity to the anti-lipolytic effect of insulin. Free fatty acids (FFAs) from visceral adipose tissue directly enter the portal vein, and elevated FFAs hinder insulin binding by hepatocytes, fostering insulin resistance at the hepatic level.

High concentrations of polyunsaturated fatty acids (PUFAs) stimulate lipogenesis in liver cells, resulting in excessive triglyceride (TG) formation and very low-density lipoprotein (VLDL) synthesis. This gives rise to atherogenic dyslipidemia characterized by increased TG levels and small, dense low-density lipoprotein (LDL), coupled with a decline in the anti-atherogenic fraction of high-density lipoprotein (HDL), elevating the risk of cardiovascular diseases [26]. Visceral adipose tissue is demonstrated to actively synthesize various mediators, including volatile fatty acids (VFAs), tumor necrosis factor-alpha (TNF- α), resistin, adiponectin, leptin, NO synthase (iNOS), interleukin-6 (IL-6), among others [27]. Recent studies highlight that TNF- α activates the inhibitor of kappa kinase beta (IKK β) in adipocytes and hepatocytes, disrupting insulin binding to a specific receptor. TNF- α further affects insulin receptor type 1 (IRS-1) by inducing its phosphorylation, reducing its affinity for insulin, thereby contributing to IR. Simultaneously, the quantity of the specialized transport protein GLUT-4 decreases, impeding glucose passage into cells and exacerbating hyperglycemia [28]. Thus, irrespective of whether it is a consequence or a root cause, prevailing scien-

tific consensus at this stage leans towards insulin resistance, adipose tissue "adiposopathy," and chronic inflammation as pivotal components in the pathophysiology of metabolic syndrome among overweight and obese individuals [26, 27, 29].

Currently, there are different versions of diagnostic criteria for MS, resulting in a divergence of results across various populations. The definitions of metabolic syndrome exhibit slight variations between adults and children at present. The roots of the modern understanding of metabolic syndrome can be traced back to the work of American endocrinologist Gerald Reaven, who, in 1988, described it as "syndrome X" or "insulin resistance syndrome." However, studies exploring the relationship between obesity, diabetes mellitus, and cardiovascular disorders date back to the 1950s. Since Reaven's initial description, several international medical societies have proposed their own criteria for defining metabolic syndrome. Despite these variations, they all share a common foundation, encompassing a combination of obesity (either general or abdominal), dyslipidemia, hypertension, and hyperglycemia. These criteria are rooted in shared pathogenetic mechanisms, including increased visceral fat mass, reduced peripheral tissue sensitivity to insulin, and hyperinsulinemia, triggering a cascade of disruptions in carbohydrate and lipid metabolism in the body [30].

For instance, the National Cholesterol Education Program for the Evaluation and Treatment of Hypercholesterolemia in Adults (NCEP-ATP III) delineates criteria for metabolic syndrome, incorporating features such as abdominal obesity, high triglyceride concentration, low high-density lipoprotein (HDL), high blood pressure, and alterations in glucose levels. Pediatric criteria for MS according to NCEP-ATP III include central obesity (waist circumference ≥ 90 th centile in both sexes), dyslipidemia (specifically, triglycerides ≥ 1.24 mmol/l and HDL ≤ 1.03 mmol/l), changes in blood pressure (systolic or diastolic) ≥ 90 th centile, and fasting blood glucose ≥ 6.1 mmol/l.

Other authors, including Cook et al [31], de Ferranti et al [32], and Weiss et al. [33], have made modifications to the NCEP-ATP III criteria for adults to enhance adaptability in diagnosing MS in children and adolescents. These modifications introduce variations in the criteria and thresholds, significantly complicating the standardization of metabolic syndrome diagnosis in pediatric practice. Notably, Cook et al. and de Ferrari et al. based their diagnosis on waist circumference, while Weiss et al. relied on a body mass index (BMI) exceeding the 95th centile. It is important to highlight that all three definitions incorporate age-specific threshold nomograms and fixed values for different components of metabolic syndrome in the pediatric population (Table 1).

Table 1
Comparison of three diagnostic criteria for metabolic syndrome given by Cook et al, de Ferranti et al and Weiss et al

MS criteria	Cook et al	de Ferranti et al	Weiss et al
Adiposity: WC or BMI	WC >90 th percentile	WC >75 th percentile	BMI z score >2.0
Fasting glycemia or at OGTT, mmol/L	Fasting glycemia >6.1	Fasting glycemia >6.1	Glycemia at OGTT of 7.8-11.1
Blood pressure	>90 th percentile	>90 th percentile	>95 th percentile
HDL Cholesterol, (mmol/L)	<1.03	<1.3 (girls), <1.2 (boys)	<5 th percentile
Triglycerides, (mmol/L)	>1.24	>1.24	>95 th percentile
<p>Note: BMI – body mass index, OGTT – oral glucose tolerance test, HDL – high-density lipoprotein, WC – waist circumference.</p>			

At present, the diagnostic criteria for MS formulated by the International Diabetes Federation have become the predominant standard in pediatric practice and research. In 2007, the IDF issued a consensus defining MS in children aged 10 to 15 years as those who are obese with abdominal fat distribution (waist circumference >90 th percentile) and exhibit any two of the following risk factors: high blood pressure, signs of dyslipidemia, and carbohydrate metabolism disorders (as outlined in Table 2). Notably, this consensus specifies that

children below the age of 10 should not be diagnosed with MS. Instead, emphasis should be placed on weight management, particularly in those with abdominal obesity or a family history of cardiovascular disease. This distinction arises from the absence of age-specific reference values for MS components in the under-10 age group. Furthermore, in alignment with the IDF consensus, children aged 16 years and older should be assessed using the criteria established for the adult population [34].

Table 2
International Diabetes Federation (IDF) definition of metabolic syndrome in children

Age group	Waist Circumference	Triglycerides (mmol/L)	HDL-C (mmol/L)	Blood pressure (mm Hg)	Glucose (mmol/L) or T2DM
6 to <10 yrs	≥90 th percentile	MS cannot be diagnosed, but further measurements should be made if there is a family history of metabolic syndrome, T2DM, dyslipidemia, cardiovascular disease, hypertension and/or obesity			
10 to <16 yrs	≥90 th percentile or adult cut-off if lower	≥1.69	<1.03	Systolic BP ≥130 mm Hg or diastolic BP ≥85 mm Hg	≥5.6 (If >5.6 OGTT is recommended)
≥16 yrs	Use existent IDF criteria for adults Central obesity and any 2 of the following: Central obesity: WC ≥94 cm for europid men and ≥80 cm for europid women TG ≥1.69 mmol/L HDL-C <1.03 mmol/L in males and <1.3 mmol/L in females BP: systolic BP ≥130 mm Hg or diastolic ≥85 mm Hg or previous treatment of diagnosed hypertension Impaired fasting glucose ≥ 5.6 mmol/L or previously diagnosed T2DM				

Note: T2DM – type 2 diabetes mellitus,
HDL-C – high-density lipoprotein cholesterol,
OGTT – oral glucose tolerance test,
TG – triglycerides,
BP – blood pressure, WC – waist circumference.

At the present stage, pediatric practice faces a significant challenge in the prompt identification of each component of metabolic syndrome to facilitate early prevention of cardiovascular and related pathologies linked to metabolic disturbances. The precise standardization of threshold values for specific indicators in the pediatric population remains an ongoing challenge. Contemporary suggestions advocate the use of centile values for most metabolic syndrome criteria in children, emphasizing the importance of establishing region-specific indicators, particularly for waist circumference and blood pressure. Recognizing potential variations across different ethnic groups is crucial in ensuring more precise identification of metabolic syndrome in pediatric practice.

Beyond the disruptions in carbohydrate and lipid metabolism that contribute to MS in overweight and obese children and adolescents, this group of patients is also burdened by comorbidities closely linked to metabolic dysregulation. Proposals have emerged to include certain pathologies as additional criteria for MS in pediatric practice, mirroring the approach in the adult population. Among the most prevalent comorbidities in children and adolescents diagnosed with MS are non-alcoholic (metabolically associated) fatty liver disease, polycystic ovary syndrome, obstructive sleep apnea (OSA), hyperuricemia, cholesterol gallstones (cholelithiasis), asthma, depressive disorders, chronic kidney disease, specific malignancies, and cognitive impairment (with the latter conditions being more prevalent in adults). Non-alcoholic (metabolically associated) fatty liver disease is a frequently encountered comorbidity in children with MS, with its manifestation linked to insulin resistance and defined by the presence of liver fat exceeding 5% of the organ's tissue weight,

as indicated by instrumental studies. The latest recommendations from the American Academy of Pediatrics (AAP) advocate semiannual liver disease screening, involving the measurement of blood levels of aspartate aminotransferase and alanine aminotransferase, for all children with a BMI ≥85 centile [35].

Research has demonstrated the association between obesity, insulin resistance, and polycystic ovary syndrome, showcasing heightened levels of free testosterone and hyperandrogenism from the ovaries and adrenal glands. This clinical presentation is marked by menstrual irregularities and/or ovulatory dysfunction in adolescent girls [36]. Obstructive sleep apnea syndrome (OSA) is characterized by the obstruction, partial or complete, of the upper airways, with obesity being a significant contributing factor. Obesity elevates the risk of OSA due to increased soft tissue around the airways and diminished lung volume owing to augmented abdominal fat [37].

In contemporary medical understanding, the interplay between obesity, type 2 diabetes mellitus, and mental health has gained prominence. This connection is underscored by an escalated susceptibility to anxiety and depression, not solely in adults but also in pediatric cases. Chronic diseases inherently serve as stressors, and the stigmatization associated with obesity can be particularly impactful during childhood and adolescence. In alignment with current AAP recommendations, mental health assessments are advised for all obese children, supplementing routine monitoring of blood pressure, glycemia, and liver function [38].

The objective in treating MS in children encompasses addressing obesity by reducing BMI and waist-to-hip ratio, along with enhancing key

parameters of carbohydrate and lipid metabolism and, if necessary, lowering blood pressure. The foremost and primary approach to managing metabolic syndrome in pediatric practice revolves around lifestyle modification. This paradigm entails alterations in eating behavior, increased physical activity, and adjustments to the child's daily routine.

A crucial element of managing MS in children involves dietary intervention, overseen by an experienced pediatric nutritionist, focusing on reducing total energy intake through caloric restriction. This approach emphasizes reducing the consumption of simple carbohydrates to mitigate excessive insulin production, increasing dietary fiber to lower the glycemic load, and substituting sweetened beverages with plain water. Dietary interventions also encompass portion control training, heightened protein, fruit and vegetable intake, reduced saturated dietary fat, sodium, and processed foods, increased fiber intake (up to 8-10 g/day), and diminished consumption of high-fructose syrups [4, 39, 40]. The initial goal of dietary intervention is to achieve a 10% reduction in body weight from baseline, with weight loss targeted at approximately 1-2 pounds per week for at least 6 months [1, 4].

Physical activity constitutes another pivotal aspect of MS treatment, involving any body movements induced by skeletal muscle contraction that elevate energy expenditure above baseline. Numerous studies affirm that physical activity enhances mitochondrial substrate metabolism in liver cells, curbing its availability for lipogenesis. Furthermore, it can alleviate insulin resistance, given the heightened sensitivity of muscle tissue to insulin compared to adipose tissue. Physical activity also contributes to improved endothelial function, resulting in reduced systolic and diastolic blood pressure. The latest guidelines from the American Academy of Pediatrics and the Endocrine Society recommend prioritizing aerobic exercise over strength training, with a suggested duration of at least 60 minutes per day, encompassing primarily short-term high-intensity exercise [41]. Additionally, physical activity bears psychological benefits for overweight and obese children, enhancing self-esteem while reducing anxiety and depression.

Lifestyle modification for children with MS extends to behavioral therapy, encompassing measures like limiting screen time, video viewing, and fostering adherence to daily routines, including a healthy approach to nighttime sleep. Extensive coordination among specialists – a pediatric nutritionist, physical therapist, psychologist, and pediatrician – is imperative for the sustained success of lifestyle modification. The American Academy of Pediatrics advises restricting screen time to less than 2 hours

per day, while the National Sleep Foundation recommends 8-11 hours of sleep per night for children and adolescents. Notably, implementing lifestyle changes necessitates a long-term commitment and collaborative efforts from various specialists, ensuring the readiness of the child and their family to embrace the proposed modifications [4, 40].

The medicinal management of metabolic syndrome in childhood constitutes a secondary line of therapy, presenting a current and not fully comprehended challenge. Many experts posit that pharmacological intervention should be contemplated only when lifestyle modifications have proven ineffective, and clear indications exist in the form of severe lipid and carbohydrate metabolic disorders, as well as arterial hypertension. It is crucial to highlight that drug therapy for pediatric obesity is currently restricted due to a paucity of sufficient evidence regarding its long-term safety. Moreover, if deemed necessary, drug therapy for obesity in children should be prescribed by experienced clinicians capable of closely monitoring its outcomes and potential side effects.

Presently, per the recommendations of the US Food and Drug Administration (FDA), medications permitted for reducing body weight in children aged over 12 include Orlistat and Phentermine (the latter being approved for adolescents over 16 years of age). Orlistat, an intestinal lipase inhibitor, curtails the absorption of triglycerides and cholesterol but is associated with frequent gastrointestinal side effects such as severe flatulence and steatorrhea. Additionally, it may impact the absorption of fat-soluble vitamins [42]. The use of Phentermine in adults has revealed side effects such as dizziness, headache, palpitations, diarrhea, or constipation. Consequently, the effectiveness of pharmacological treatment for pediatric obesity using these drugs remains relatively limited. Other weight-loss medications, including Topiramate and Zonisamide (anticonvulsants), and Fluoxetine, along with other selective serotonin reuptake inhibitors currently undergoing experimental use for weight loss in adults, are contraindicated in pediatric practice. It is noteworthy that, as of now, the European Medicines Agency (EMA) has not sanctioned any pharmaceuticals for the treatment of obesity in children.

A crucial component of drug therapy for MS is the correction of carbohydrate metabolism disorders, a key criterion within the metabolic symptom complex. Research indicates that insulin resistance, a prominent condition, can be addressed primarily through lifestyle modifications without necessitating drug interventions. However, in clinical practice, Metformin, an oral glucose-lowering agent from the

biguanides class, may be prescribed to alleviate manifestations of insulin resistance, particularly when lifestyle modification proves challenging. Yet, a growing consensus among experts suggests that Metformin should be reserved for cases of diagnosed type 2 diabetes, considering disease symptoms, the severity of hyperglycemia, and the presence or absence of ketosis/ketoacidosis. The pharmacological objective for treating carbohydrate metabolism disorders is to achieve a glycated hemoglobin (HbA1c) level <7.0% [43].

Addressing dyslipidemia, another significant criterion for metabolic syndrome in children, is feasible through lifestyle changes and adherence to dietary recommendations. Specific signs of dyslipidemia in MS include elevated triglyceride levels and low HDL cholesterol with relatively elevated LDL cholesterol. Lifestyle modifications, such as eliminating industrially produced trans fats from the diet and incorporating plant sterols or stanol esters, are often effective. Drug treatment for dyslipidemia is rarely necessary for children responding well to weight loss through lifestyle changes. Dietary supplements may include increased fish consumption or additional supplementation with fish oil (omega-3 polyunsaturated fatty acids). Drug treatment has clear and limited indications, notably in cases of severe primary hyperlipidemia or high-risk conditions: homozygous hypercholesterolemia, primary hypertriglyceridemia with triglyceride levels ≥ 500 mg/dl, and existing cardiovascular disease in children after heart transplantation. Statins (Rosuvastatin and Atorvastatin) are approved for treating dyslipidemia in such cases, while other pharmacological agents, including fibrate and nicotinic acid, lack categorical approval by FDA experts in pediatric practice [44].

Treatment of arterial hypertension (AH), a central criterion for the metabolic symptom complex in pediatric practice, is a crucial aspect of MS management. Current therapeutic regimens have demonstrated efficacy in significantly reducing target organ damage in children with hypertension. According to the recommendations of the American Academy of Pediatrics (AAP) in 2017, initiating hypertension treatment in children with MS involves prescribing a single drug, or monotherapy, for those who still exhibit high blood pressure despite lifestyle changes over at least six months. The AAP suggests the initiation of pharmacotherapy with angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, long-acting calcium channel blockers, or thiazide diuretics. No significant differences in efficacy have been observed among these pharmacological agents in pediatric populations, and their safety has been established through studies. In cases where

hypertension coexists with type 2 diabetes mellitus, initial therapy with ACE inhibitors or angiotensin II receptor blockers is recommended. If hypertension remains uncontrolled with monotherapy, the consideration of combined treatment with multiple drug groups is warranted. The initial drug dosage is recommended in the lower range, with subsequent titration during monitoring every 2-4 weeks. The overarching goal of hypertension treatment in children with MS is to reduce blood pressure to below the 90th centile or below 130/80 mm Hg in adolescents aged ≥ 13 years [45].

According to current international guidelines, bariatric surgery in pediatric practice should be considered only as a last resort. This recommendation primarily applies to individuals who have completed their pubertal development and present clear, limited indications. These indications encompass severe concurrent complications of MS, characterized by very severe obesity with a body mass index exceeding 40 kg/m². Additionally, this surgical intervention may be warranted in cases of severe type 2 diabetes mellitus, highly frequent sleep apnea, severe liver fibrosis attributable to metabolically associated fatty liver disease, pseudotumor of the brain, or exceptionally severe orthopedic issues in children [4, 40, 41].

Conclusions

In current pediatric practice, metabolic syndrome stands as a significant and urgent medical and social concern, steadily increasing in relevance each year. The absence of a universally agreed-upon definition for the key criteria of metabolic syndrome in children, along with inadequate awareness of risk factors and the pathophysiology of this complex in childhood, poses substantial challenges in diagnosing this pathology in the pediatric population. Nonetheless, early identification of the primary components of metabolic syndrome in obese children and adolescents, coupled with prompt lifestyle adjustments and, when necessary, pharmacological interventions, holds the potential to markedly reduce the risk of cardiometabolic complications and avert other comorbidities linked to metabolic syndrome. As advocated by international medical societies, the primary treatment approach for metabolic syndrome relies on lifestyle modification, encompassing behavioral therapy, dietary interventions, and a regulated exercise regimen. Research findings indicate that diligent adherence to these recommendations, coupled with compliance between doctor and patient in pediatric practice, can effectively eliminate metabolic disorders even without pharmacological treatment. However, achieving optimal outcomes in the management of metabolic syndrome in children necessitates the coordinated efforts of a multidisci-

plinary team of experts. This collaborative approach is crucial for the timely identification and prevention of potential complications associated with this pathology, enabling the development of tailored therapeutic strategies for each patient.

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МЕТАБОЛІЧНИЙ СИНДРОМ В ПЕДІАТРИЧНІЙ ПРАКТИЦІ: ВИЗНАЧЕННЯ, КРИТЕРІЇ ДІАГНОСТИКИ ТА ПРИНЦИПИ ВЕДЕННЯ ПАЦІЄНТІВ (ОГЛЯД)

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У статті узагальнено відомості щодо епідеміологічних показників, факторів ризику, патофізіологічних механізмів,

критеріїв діагностики та сучасних принципів ведення метаболічного синдрому в педіатричній практиці на підставі аналізу літературних джерел із використанням електронних баз даних PubMed, UpToDate, Web of Science, ScienceDirect, Scopus, MedLine та Elsevier. Огляд літературних джерел з вивчення даної патології демонструє, що на сучасному етапі метаболічний синдром стає все більш поширеною медико-соціальною проблемою у дітей та підлітків у зв'язку зі зростаючою у всьому світі епідемією дитячого ожиріння. В статті наведено рекомендації міжнародних медичних товариств щодо питань по стратегії скринінгу, діагностики та принципів терапії окремих компонентів, які формують метаболічний симптомокомплекс в дитячому віці. Огляд також висвітлює основні дослідження, які були зосереджені на альтернативних методах лікування, спрямованих на основні патогенні фактори захворювання. Як висновок, автори розкривають проблему відсутності уніфікованих критеріїв діагностики метаболічного синдрому у дітей та наголошують на важливості командної роботи мультидисциплінарної групи спеціалістів з ведення даної патології в педіатричній практиці.

Ключові слова: метаболічний синдром, ожиріння, інсулінорезистентність, дисліпідемія, серцево-судинні захворювання, діти.