НЕОНАТОЛОГІЯ, ХІРУРГІЯ ТА ПЕРИНАТАЛЬНА МЕДИЦИНА
NEONATOLOGY, SURGERY AND PERINATAL MEDICINE
ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)
Т. XVI, №1(59), 2026
VOL. XVI, №1(59), 2026
KEY TITLE: NEONATOLOGÌÂ, HÌRURGÌÂ TA PERINATAL'NA MEDICINA (ONLINE)
ABBREVIATED KEY TITLE: NEONATOL. HÌR. PERINAT. MED. (ONLINE)

UDC: 616.12-008.46-06:616.61-008-12-33
DOI: 10.24061/2413-4260.XVI.1.59.2026.33

MODERN IMMUNOLOGICAL AND BIOMOLECULAR FOUNDATIONS OF METABOLIC SYNDROME IN CHILDREN

Sh. Mukhamedova, Sh. Ganiyeva, O. Boboyeva, D. Hayotova

Bukhara State Medical Institute
(Bukhara, Republic of Uzbekistan)

Summary.

Metabolic syndrome in children is a multifactorial disorder characterized by obesity, insulin resistance, and other cardiometabolic risk factors, the pathogenesis of which involves complex immunological and biomolecular mechanisms. Chronic low-grade inflammation and immune system dysregulation are hallmarks of the condition, fostering insulin resistance and vascular dysfunction. Among the key molecular signaling pathways implicated in this process, the nuclear factor-kappa B (NF-κB) cascade and the NLRP3 inflammasome are aberrantly activated in adipose tissue, linking nutrient excess to inflammatory responses. Toll-like receptor 4 (TLR4) serves as a critical upstream sensor connecting innate immune signaling with metabolic stress, triggering NF-κB activation and promoting fatty acid–induced insulin resistance. This sustained innate immune activation leads to overproduction of pro-inflammatory cytokines (e.g., TNF-α, IL-1β) and altered adipokine profiles, whereby leptin levels rise while adiponectin falls – an imbalance that further exacerbates subclinical inflammation and insulin resistance. Genetic predispositions – such as polymorphisms in immunoregulatory genes (e.g., NLRP3, STAT3) – and epigenetic modifications, including diet-induced changes in DNA methylation and gene expression, further shape these immune–metabolic interactions. Emerging evidence in pediatric populations underscores that immunometabolic crosstalk – encompassing adipose tissue macrophage infiltration and adipokine signaling – contributes to the early development of metabolic syndrome. Understanding these mechanisms provides a foundation for identifying biomarkers and developing targeted interventions to prevent or mitigate pediatric metabolic syndrome and its long-term cardiometabolic complications.

Keywords: *Pediatric Metabolic Syndrome; Chronic Inflammation; Immune Dysregulation; Immunometabolism; Epigenetics; Adipokines.*

Introduction

Metabolic syndrome (MetS) in children is characterized by a constellation of cardiometabolic risk factors – typically central obesity, insulin resistance, dyslipidemia, and hypertension – that often co-occur even in youth [1]. Its prevalence has been rising in parallel with pediatric obesity rates [2], and recent data indicate that approximately 10% of adolescents meet pediatric MetS criteria [3] – figure that exceeds even the prevalence of common childhood conditions such as asthma. Children with MetS are at heightened risk of progressing to type 2 diabetes and cardiovascular disease in adulthood [4], a trajectory that underscores the importance of understanding the mechanistic foundations of MetS early in life.

Objective: to investigate the pathogenetic mechanisms and patterns of metabolic syndrome development in children.

Materials and methods: A systematic review of international literature was conducted using the MEDLINE and PubMed databases, covering publications from the past 5 years (2021-2025).

Results. Current research emphasizes that the pathogenesis of MetS extends beyond metabolic derangements to encompass chronic low-grade inflammation and immune dysregulation [5]. Obesity-related MetS is now viewed through the lens of immunometabolism – the interplay between metabolic and immune processes [6] – encompassing evolutionarily conserved interactions between the immune and metabolic systems, the balance of which is crucial for health. Disruption of this balance through overnutrition, for instance, can trigger a state of persistent inflammation and metabolic stress that is central to MetS pathophysiology [6]. In children, this crosstalk is particularly salient: the developmental windows that pattern metabolic physiology overlap with those guiding immune system maturation. Early-life nutritional and environmental factors can thus exert lasting effects on both metabolic homeostasis and immune function, which helps explain why childhood-onset metabolic syndrome so frequently tracks into adult disease [7].

This literature review synthesizes current findings on the immunological and biomolecular foundations of Met S. The analysis focuses on the role of chronic inflammation, immune system dysregulation, molecular signaling pathways, and genetic and epigenetic factors, as well as metabolism–immune interactions in children. Particular attention is given to studies and reviews published over the last decade, together with landmark discoveries foundational to the field [8].

Metainflammation – a sustained, systemic low-grade inflammatory state – is now recognized as a hallmark of obesity and MetS across all age groups. Even in children and adolescents, excess adiposity provokes a significant inflammatory response. Far from a passive fat depot, adipose tissue functions as an active endocrine and immune organ. In the context of overnutrition, hypertrophic adipocytes in white adipose tissue secrete pro-inflammatory cytokines – including tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) – as well as adipokines, while recruiting immune cells to tissue sites [9]. Clinical studies in obese youth demonstrate

that circulating markers of inflammation – such as C-reactive protein (CRP), IL-6, and TNF-α – are frequently elevated and correlate with insulin resistance and early vascular changes [10]. Notably, high-sensitivity CRP levels correlate directly with the homeostatic model assessment of insulin resistance (HOMA-IR) and carotid intima-media thickness in overweight children, thereby linking inflammation with metabolic and cardiovascular risk. Visceral fat accumulation is particularly associated with a pro-inflammatory milieu in youth [11]. This This subclinical inflammation is characterized by a shift in immune cell balance and the chronic release of pro-inflammatory mediators that interfere with normal metabolic signaling [12].

In pediatric obesity, studies have documented elevated circulating levels of TNF-α and IL-6, accompanied by a decrease in the anti-inflammatory adipokine adiponectin. TNF-α and IL-6 are not merely biomarkers; they exert direct pathogenic effects on metabolism. TNF-α binds to its receptors on insulin-sensitive tissues, triggering serine phosphorylation of insulin receptor substrate and reducing GLUT4 glucose transporter translocation, thereby inducing insulin resistance [13]. IL-6, produced in substantial quantities by visceral fat, similarly inhibits insulin receptor expression and suppresses adiponectin levels, further impairing insulin action. Together, these mechanisms create a vicious cycle in which inflammation drives insulin resistance, which in turn promotes compensatory hyperinsulinemia and broader metabolic disturbances – core components of MetS [14].

The inflammatory state in obese children is systemic, affecting multiple organs. The liver may develop steatosis and inflammation (pediatric non-alcoholic fatty liver disease, NAFLD), while the vasculature exhibits early endothelial dysfunction – both linked to inflammatory pathways. Chronic inflammation in adipose tissue can likewise spill over to reduce immune competency. Obese children frequently present with an altered baseline activation state of immune cells and may exhibit impaired responses to certain infections and vaccines [15]. This is evidenced by the higher risk of severe infections – such as complicated influenza or COVID-19 – in youth with obesity [16]. The inflammatory burden of obesity thus compromises normal immune surveillance, underscoring immune dysregulation that extends beyond metabolic control.

Not all obese children exhibit metabolic syndrome – a concept known as metabolically healthy obesity (MHO) – and inflammation appears to be a key differentiator. Obese youth who maintain normal insulin sensitivity tend to have less ectopic fat and lower levels of inflammatory markers than their metabolically unhealthy counterparts. This suggests that early intervention aimed at reducing inflammation – through dietary modification, physical activity, or possibly anti-inflammatory agents – could improve metabolic outcomes even where weight loss is modest. Lifestyle interventions in children have been shown to reduce CRP and IL-6 levels and improve insulin sensitivity concurrently [17], reinforcing the view that mitigating inflammation represents a therapeutic target in pediatric Met S.

Obesity drives broad dysregulation of immune system homeostasis, affecting both innate and adaptive immunity. In adipose tissue, this is accompanied by immune cell infiltration and phenotypic shift. Macrophages are the prototypical mediators: in lean adipose tissue, they are relatively sparse and tend toward an anti-inflammatory M2 phenotype, supporting tissue remodeling and insulin sensitivity. In obesity, however, macrophage content in adipose tissue increases dramatically – macrophages may constitute 40-50% of all cells in obese adipose tissue – and shifts toward a classically activated M1 phenotype [18]. These M1 macrophages secrete TNF-α, IL-1β, and other cytokines, and form multicellular crown-like structures around dead or stressed adipocytes. The chemokine CCL2 (monocyte chemoattractant protein-1, MCP-1), overproduced by hypertrophic adipocytes, attracts circulating monocytes via CCR2 signaling, thereby perpetuating macrophage recruitment. These findings are supported by pediatric studies of subcutaneous fat biopsies and blood samples: obese children exhibit higher circulating levels of sCD163 – a marker of pro-inflammatory M1 macrophage polarization – compared to lean children [19], indicating increased M1 polarization in vivo.

Other innate immune cells are likewise affected. Neutrophils may be elevated and contribute to adipose inflammation through the release of elastase and reactive oxygen species, while mast cells and natural killer (NK) cells in adipose tissue can modulate macrophage activity and insulin sensitivity. Invariant NKT cells, which normally help maintain adipose immune homeostasis, are reduced in obese children. This reduction in anti-inflammatory NKT cells – which characteristically produce IL-4 and IL-10 – further exacerbates the inflammatory imbalance [20].

Adaptive immunity is similarly altered: T lymphocytes infiltrate adipose tissue at the early stages of obesity development. In adults, a shift toward pro-inflammatory Th1 and cytotoxic $CD8^+$ T cells – which produce interferon-γ (IFN-γ) and promote M1 macrophage activation – alongside a concurrent decrease in regulatory T cells (Tregs), has been documented in obese adipose tissue. Although pediatric adipose T-cell profiles remain less studied, blood analyses indicate that obese children have higher levels of Th1-associated cytokines and lower IL-10 levels, suggestive of a comparable Th1/Treg imbalance. B lymphocytes may contribute as well, secreting obesity-induced IgG capable of activating macrophages. The net effect is a state of chronic immune activation [21].

This immune dysregulation is reflected in systemic inflammatory indices. The Systemic Immune-Inflammation Index (SII) – a composite of neutrophil, platelet, and lymphocyte counts – is significantly elevated in obese children with MetS compared to those without. A recent study demonstrated that SII has diagnostic value for distinguishing MetS among obese youth, with an area under the curve of 0.84. Such blood-based indices reflect the heightened innate immune activity accompanying metabolic risk. Detailed leukocyte phenotyping has revealed increases in pro-inflammatory monocyte subsets – such as $CD14^+CD16^+$ monocytes – in obese adolescents, with these subsets correlating with insulin resistance. Innate lymphoid cells (ILCs), particularly ILC2s, which

normally help maintain metabolic homeostasis, are altered in obesity as well [22].

Obesity-driven immune changes can impair host defense and tissue repair. Obese children show evidence of chronic inflammatory pre-activation of leukocytes even at baseline. While this baseline activation contributes to insulin resistance, it may paradoxically render the host less capable of mounting robust acute immune responses to true pathogens [23]. During the COVID-19 pandemic, clinical reports identified pediatric obesity as a risk factor for severe infection outcomes, attributable in part to this immune dysfunction. Vaccine studies have similarly found reduced antibody responses in obese populations. These observations underscore that in pediatric MetS, the immune system is not only aberrantly overactive – promoting inflammation in metabolic tissues – but also functionally dysregulated, with a diminished capacity to respond appropriately to external immunological challenges [24].

At the molecular level, several key signaling pathways connect nutrient excess to inflammatory responses. One pivotal mechanism involves innate pattern recognition receptors, notably Toll-like receptor 4 (TLR4) on immune cells. Nutrient-related molecules – such as free fatty acids or bacterial endotoxin (lipopolysaccharide, LPS) translocated from the gut – can engage TLR4 and related receptors on tissue macrophages and adipocytes. This triggers downstream inflammatory cascades, most notably activation of the transcription factor NF-κB, which induces expression of genes encoding TNF-α, IL-6, and other cytokines. In obesity, adipose tissue and liver exhibit chronic NF-κB activation, contributing to systemic insulin resistance. The c-Jun N-terminal kinase (JNK) pathway, another stress-responsive signaling mechanism, is similarly overactivated in obesity and phosphorylates insulin signaling intermediates, thereby impairing their function [25]. These pathways were identified in foundational studies demonstrating that deletion of TLR4 or JNK in mice confers protection against high-fat-diet-induced insulin resistance. In children, these molecular events are more difficult to measure directly; however, elevated circulating LPS in obese youth – a phenomenon termed metabolic endotoxemia – provides evidence of TLR4 engagement. A study conducted in adolescents demonstrated that plasma LPS and soluble CD14 (an LPS co-receptor) levels were significantly higher in obese compared to lean individuals, and that both normalized with weight loss. These findings suggest increased gut permeability and endotoxin-driven TLR4 stimulation in pediatric obesity, linking gut microbiome dysbiosis to systemic inflammation [26].

The NLRP3 inflammasome is another molecular complex recognized as a central mediator of obesity-induced inflammation. NLRP3 is a nutrient-sensing inflammasome that, when activated by signals such as excess fatty acids, ceramides, or LPS/TLR4-derived stimuli, triggers the maturation of IL-1β and IL-18 via caspase-1. Children and adolescents with obesity show evidence of inflammasome activation: gene expression of NLRP3 and its adapter molecules – including ASC and caspase-1 – is upregulated in blood immune cells, and circulating IL-1β and IL-18 levels are elevated compared to lean peers [27]. Rainone et al. (2016) demonstrated that obese children had significantly higher LPS-stimulated expression of inflammasome-related genes – including NLRP3, NOD-like receptors, and IL-1β – alongside higher baseline IL-1β and IL-18 concentrations, both of which decreased following lifestyle intervention and weight loss. IL-1β is particularly detrimental from a metabolic standpoint, as it impairs both insulin secretion and action. These findings parallel adult studies in which NLRP3 knockout mice are protected from insulin resistance [28], highlighting the role of the inflammasome as a metabolic trigger of inflammation.

Adipose tissue produces a variety of adipokines that modulate metabolism and immunity. Leptin, an adipocyte-derived hormone, rises with increasing fat mass and signals satiety in the hypothalamus. Beyond its metabolic role, leptin is a potent modulator of the immune system: it promotes Th1 and pro-inflammatory immune responses and enhances neutrophil and NK cell functions. Hyperleptinemia in obesity may thus contribute to the chronic inflammatory tone. Leptin has been characterized as a cytokine-like hormone; it binds to Ob-R receptors on immune cells, activating JAK-STAT and MAPK pathways, which overlap with classical inflammatory signaling. Adiponectin, by contrast, is abundant in lean individuals and exerts anti-inflammatory effects – stimulating IL-10 production and dampening TNF secretion – but its levels are suppressed in obesity [29]. The imbalance of elevated leptin and reduced adiponectin in obese children is strongly associated with components of Met S. Other adipokines of interest include resistin, chemerin, and visfatin, which further influence immune cell recruitment and activation. Chemerin is elevated in pediatric obesity and has been associated with endothelial dysfunction and inflammation, particularly when adiponectin levels are concurrently low [30].

Oxidative stress represents another important molecular mechanism: overnutrition leads to excess substrates in mitochondria, generating reactive oxygen species (ROS). ROS activate NF-κB and drive NLRP3 inflammasome activation, as ROS are a recognized danger signal for inflammasomes. In obese placentas and adipose tissue, researchers have documented mitochondrial dysfunction and oxidative damage, which correlate with increases in inflammatory markers. This oxidative stress–inflammation axis may be particularly relevant in children born to obese mothers, as discussed below [31].

The gut microbiota has emerged as a key mediator linking diet, immunity, and metabolism. Diet-induced obesity can alter gut microbial composition, favoring microbes that increase energy harvest and LPS production. In children with obesity, studies have documented dysbiosis – including an elevated Firmicutes: Bacteroidetes ratio – alongside increased bacterial metabolites that influence immune responses [32]. Enhanced translocation of LPS from the gut into the circulation, resulting from increased intestinal permeability, stimulates TLR4 on immune cells, as noted abov, and perpetuates systemic inflammation – a process termed metabolic endotoxemia. Modulation of the gut microbiota through prebiotics, probiotics, or dietary intervention may therefore reduce

inflammatory signaling and improve metabolic parameters in youth; this remains an area of active investigation [33].

Genetic susceptibility plays a significant role in the development of obesity and metabolic syndrome in children. Family studies and genome-wide analyses indicate that a substantial proportion of variance in pediatric body mass index (BMI) and MetS risk is heritable. The genetics of MetS is, however, complex and polygenic. Over the past decade, hundreds of common genetic variants have been associated with obesity and related traits, each with small effect sizes. The fat-mass and obesity-associated (FTO) gene is one notable example: polymorphisms in FTO are among the strongest genetic contributors to obesity risk. A 2025 meta-analysis by Song et al. examined FTO variants in more than 50,000 children and adolescents and found that carriers of risk alleles – such as the A-allele of rs9939609 – had significantly higher waist circumference, blood pressure, and fasting insulin levels, and were more likely to meet MetS criteria. The A allele of FTO rs9939609 was associated with increased odds of pediatric MetS, with carriers exhibiting greater central adiposity and lower HDL levels. These findings suggest that genetic differences in appetite regulation or adipocyte biology – which FTO is thought to influence via epigenetic mechanisms – may predispose children to the constellation of MetS features [34].

Beyond common variants, monogenic disorders illustrate how genetics can drive metabolic and immune dysregulation. Rare mutations in single genes regulating energy balance can lead to severe early-onset obesity – often with MetS sequelae – in childhood. Congenital leptin deficiency due to biallelic mutations in LEP, for example, causes extreme obesity from infancy, accompanied by immune impairments that render affected children more susceptible to infection, until treated with leptin therapy [35]. These cases highlight the dual role of leptin in metabolism and immunity. Mutations in the melanocortin-4 receptor gene (MC4R) – the most common monogenic cause of obesity – result in hyperphagia and obesity in childhood. Although MC4R mutations primarily affect energy balance, children with MC4R deficiency may exhibit features of MetS, including hyperinsulinemia and hepatic steatosis, at an early age, indicating how a single gene can broadly perturb metabolic homeostasis. Polymorphisms in genes encoding inflammatory cytokines and their receptors have been investigated as well Certain TNF-α promoter variants and IL-6 gene variants were hypothesized to exacerbate obesity-related inflammation; some studies found that an IL-6 promoter polymorphism (–174G/C) was associated with higher IL-6 levels, C-reactive protein (CRP), and insulin resistance in obese youth, though findings have not been consistent across populations [36].

Large-scale genomics efforts have identified loci related to lipid metabolism, adipogenesis, and insulin signaling that contribute to MetS risk in youth. These include variants in PPARG, ADIPOQ (the adiponectin gene), APOA5, and other loci that modulate triglyceride levels or adipokine production. Genetic factors rarely act in isolation, however; their penetrance is often mediated by environmental exposures. A child with a high genetic risk score for obesity is substantially more likely to manifest MetS when exposed to a calorically dense diet and sedentary lifestyle than when lean. Notable ethnic differences exist in genetic risk and MetS expression in children, with some ethnic groups exhibiting MetS at lower BMI thresholds, underscoring that genetic background and gene–environment interactions modulate immunometabolic outcomes [37].

In summary, genetics provides a predisposition to MetS by influencing baseline adiposity, fat distribution, and the propensity for inflammatory responses. Given the rapid rise of pediatric MetS in recent decades, however, genetic factors cannot be solely responsible. This has led to growing interest in epigenetic modifications and early-life programming as mediating links between genes, environment, and the development of MetS in children [38].

Epigenetics refers to heritable changes in gene expression that do not involve alterations to the underlying DNA sequence – encompassing DNA methylation, histone modifications, and non-coding RNA regulation. These mechanisms are highly responsive to environmental inputs, particularly during critical developmental periods. Substantial evidence now indicates that the origins of metabolic syndrome can be traced to early life through epigenetic programming. Nutritional and hormonal exposures in utero and in early childhood can establish metabolic and immune trajectories that persist into later childhood and adulthood [39].

Maternal obesity and overnutrition during pregnancy have been linked to a higher risk of obesity and MetS features in the offspring, independent of genetic inheritance. The developing fetus in an obese mother is exposed to excess metabolic substrates – including glucose and free fatty acids – as well as pro-inflammatory cytokines crossing the placenta, which can lead to fetal hyperinsulinemia and an altered developmental milieu. Epigenetic analyses of cord blood and placental tissue from such pregnancies have demonstrated changes in DNA methylation at genes related to insulin signaling, appetite regulation, and inflammation [40]. Genes regulating adipogenesis or the hypothalamic appetite pathway may, for example, be hypomethylated – resulting in higher expression – thereby predisposing the child to adiposity. Maternal obesity is associated with increased inflammation in the placenta as well, including NF-κB activation and macrophage infiltration, which may induce epigenetic changes in the placenta and fetus that affect immune system development in the offspring. This concept falls under the Developmental Origins of Health and Disease (DOHaD) framework, which posits that early environmental conditions can have lasting effects on disease risk. Epigenetic marks established in utero – such as DNA methylation at specific loci – have been correlated with later adiposity and metabolic profile in the child [41].

Beyond the prenatal period, early infancy and childhood nutrition exert epigenetic effects as well. Rapid infant weight gain and high-protein diets in the first years of life have been linked to differential DNA methylation patterns in genes related to energy balance and inflammation – including the pro-opiomelanocortin gene (POMC), which is involved in satiety signaling. Environmental chemicals

such as endocrine disruptors, as well as psychosocial stress, can likewise alter the epigenome of metabolic tissues and immune cells. Multiple studies have identified associations between epigenetic markers and pediatric obesity phenotypes; meta-analyses, in particular, have identified consistent DNA methylation changes at several genomic loci in blood cells of obese compared to lean children. Profiles of circulating microRNAs – small non-coding RNAs that regulate gene expression post-transcriptionally – differ in obese children: Carolan et al. reported that microRNA-33a and microRNA-33b were upregulated 3-4-fold in obese children compared to non-obese peers [42]. These miR-33 molecules are known to target pathways involved in cholesterol and fatty acid metabolism; their elevation may represent either a compensatory response or a pathogenic mechanism linking obesity to disturbed lipid homeostasis. Additional microRNAs – including miR-122 and miR-146b – have been proposed as biomarkers reflecting inflammation and insulin sensitivity in youth [43].

Some epigenetic changes may be reversible with targeted interventions. Weight loss in children has been shown to partially normalize obesity-associated DNA methylation changes and microRNA levels. Exercise in adolescence can beneficially modulate epigenetic marks in muscle and adipose tissue related to insulin signaling. Evidence from animal models and human cohorts suggests that improvements in maternal nutrition and metabolism – such as treatment of gestational diabetes and adequate micronutrient supplementation – can result in healthier epigenetic profiles in offspring. These findings offer hope that breaking the cycle of intergenerational obesity and MetS may be achievable through early preventive measures [44].

Epigenetic mechanisms thus serve as a bridge between early-life environmental exposures and the later development of metabolic syndrome. They help explain why, even among children with similar genetic predispositions, those with adverse early-life environments – characterized by overnutrition, inflammation, and psychosocial stress – have a higher propensity to develop Met S. Ongoing research continues to unravel specific epigenetic markers as both predictors of risk and potential targets for intervention, including pharmacological agents that modify epigenetic enzymes and lifestyle interventions timed to critical developmental windows [45].

The relationship between metabolic regulation and immune function is bidirectional and deeply intertwined – a fact particularly evident in the context of metabolic syndrome. In children, whose immune systems are still developing, the impact of metabolic disturbances on immunity, and vice versa, can shape health trajectories for decades. Obesity and its metabolic sequelae constitute a state of chronic immune activation – sterile inflammation in the absence of infection – that is directed at restoring homeostasis but instead contributes to pathology [46]. The term «immunometabolic setpoint» has been used to describe how the body establishes a new equilibrium in obesity: immune cells adapt to an environment of excess nutrients by altering their energy utilization and activation state, while metabolic tissues adapt to persistent inflammation by becoming insulin resistant [47]. This aberrant setpoint underlies Met S. Under conditions of energy excess, immune cells such as macrophages shift to glycolytic metabolism – a hallmark of inflammatory activation – thereby producing cytokines that impair insulin signaling. Concurrently, insulin-resistant tissues emit distress signals – including free fatty acids and reactive oxygen species – that further activate immune cells. A feed-forward loop between metabolic stress and immune signaling is thus established.

Pediatric studies illustrate several of these interactions. In one cohort, higher systemic IL-6 levels in obese adolescents were associated with lower expression of insulin receptors on mononuclear cells and adipose tissue, linking an immune mediator to a metabolic effect [48]. Another study found that the degree of glycemic control in obese youth with impaired glucose tolerance correlated with T-cell cytokine profiles, suggesting that hyperglycemia itself can skew immune responses. The presence of metabolic syndrome in children has been correlated with reduced gut microbiome diversity and altered microbial metabolites – such as short-chain fatty acids – that influence both metabolism and immune education [49].

Childhood represents a plastic period for both metabolic and immune systems. Positive interventions – including improved diet quality, physical activity, and adequate sleep – have been shown not only to improve metabolic parameters but also to reduce inflammatory markers and normalize immune cell distributions [50]. A 12-week exercise program in obese adolescents, for example, can increase anti-inflammatory cytokines such as IL-10, reduce pro-inflammatory monocytes, and improve NK cell function, concurrently with reductions in visceral fat. These findings reinforce the concept that targeting immunometabolic inflammation at an early stage can alter disease trajectory. Chronic psychosocial stress in childhood, which activates stress hormone pathways, has been linked to central fat deposition and a higher inflammatory burden, potentially seeding MetS via immune mechanisms [51].

Developmental timing is central to these interactions. As noted, immune system maturation – from the neonatal Th2-skewed profile toward a balanced immune repertoire – overlaps with the period during which a significant proportion of children begin to accumulate excess weight, such as during the adiposity rebound in early childhood. Obesity developing during this critical window may durably shift the patterning of immune responses toward a pro-inflammatory profile. This may partly explain why adolescent-onset type 2 diabetes can follow a more aggressive clinical course than adult-onset disease – the immune-metabolic crosstalk has been perturbed earlier and sustained over a longer proportion of that individual's life. The presence of MetS in childhood may accelerate immunological aging, or inflammaging, as low-grade inflammation drives cellular senescence in the immune system [52].

Several specific immune-metabolic intersections merit consideration. Adipose tissue Tregs normally

restrain inflammation and promote insulin sensitivity; their reduction in childhood obesity removes a critical check on metabolic inflammation. . B cells in obesity can produce autoimmune-like antibodies against modified self-antigens – such as oxidized low-density lipoprotein (LDL) – thereby linking dyslipidemia to immune activation. The liver's Kupffer cells, resident macrophages that become activated in insulin-resistant states, contribute to hepatic inflammation; non-alcoholic fatty liver disease in children is now considered the hepatic manifestation of MetS, driven by immune cell recruitment to the liver. Each organ system implicated in MetS – adipose tissue, liver, muscle, pancreas, and vasculature – exhibits an immunometabolic dialog in which immune cells respond to metabolic stress and, in turn, exacerbate or modulate that stress [53,54].

The pediatric immune and metabolic systems do not operate in isolation; they constitute a coupled axis. Current research demonstrates that chronic inflammation and immune dysregulation are not merely byproducts of pediatric MetS but fundamental drivers of its development. Effective interventions may therefore need to be two-pronged, targeting both the improvement of metabolic parameters and the restoration of healthy immune function. As understanding in this area advances, new therapeutic possibilities emerge – including the use of anti-inflammatory agents or nutraceuticals such as omega-3 fatty acids, which exert immune-modulating effects, as adjuncts to lifestyle modification in high-risk obese youth. Identifying immunological and biomolecular markers in childhood – such as cytokine profiles or specific epigenetic signatures – could improve early identification of children at risk of developing severe MetS, enabling more timely and personalized intervention [55].

Conclusion

Metabolic syndrome in children is a multifactorial condition arising from complex interactions among excess nutrition, genetic predisposition, and immune system dysregulation. Contemporary evidence highlights that inflammation and immune dysregulation are central to the pathogenesis of pediatric Met S. In an obese child, adipose tissue becomes an immune organ that secretes cytokines and recruits immune cells, leading to insulin resistance and organ damage. Molecular pathways – ranging from TLR4/NF-κB activation by lipids to NLRP3 inflammasome-driven IL-1β release – generate a state of chronic inflammation that underlies every component of MetS, including glucose intolerance, hypertension, and dyslipidemia. Genetic factors such as FTO variants may establish a predisposition by increasing the propensity for adiposity or heightened inflammatory responses, while epigenetic modifications – shaped by maternal and early-life influences – modulate gene expression in ways that can either protect against or predispose a child to Met S. MetS is increasingly characterized as an immunometabolic disorder: an inappropriate inflammatory response to caloric excess and sedentary lifestyle, superimposed on individual genetic and epigenetic backgrounds.

These insights into the immunological and biomolecular foundations of pediatric MetS have practical implications. They suggest that effective prevention and treatment should incorporate strategies to reduce inflammation – such as improving diet quality to lower gut endotoxemia and provide anti-inflammatory nutrients, encouraging physical activity for its anti-inflammatory effects on adipose tissue and muscle, and potentially using pharmacological agents that target inflammatory pathways – including IL-1 antagonists or inhibitors of NF-κB activation – in the highest-risk youth. These findings equally highlight the importance of early-life interventions: optimizing maternal health and nutrition, promoting breastfeeding, and avoiding rapid weight gain in infancy may establish an epigenome and microbiome that confer resistance to the development of Met S.

Research is ongoing into pediatric-specific aspects of MetS, including how the maturing immune system may offer unique opportunities for resetting the immunometabolic balance. As the mechanisms by which inflammation and metabolism co-evolve in a child with MetS become better understood, more nuanced approaches to risk prediction emerge – encompassing inflammatory biomarkers and epigenetic testing for early MetS – alongside innovative interventions that extend beyond dietary restriction and increased physical activity to address the inflammatory overdrive of the immune system. Such integrated approaches are essential to mitigating the growing epidemic of pediatric metabolic syndrome and reducing its progression to serious adult disease.

Prospects for Further Research. Further research should prioritize large-scale, multicenter longitudinal studies aimed at identifying early immunological and biomolecular predictors of metabolic syndrome progression in children. Particular attention should be directed toward epigenetic regulation, gut microbiota–immune system interactions, and the role of chronic low-grade inflammation in metabolic programming.

The integration of multi-omics approaches – encompassing genomics, transcriptomics, proteomics, and metabolomics – may yield deeper insights into individualized risk stratification and personalized therapeutic strategies. Future investigations should explore targeted immunomodulatory interventions and preventive strategies aimed at modifying inflammatory pathways in pediatric populations at high risk for metabolic syndrome.

Author Contributions: All authors contributed substantially to the conception and design of the study. Conceptualization – Mukhamedova Shakhnoza; Literature review and data analysis – Ganiyeva Shakhzoda; Drafting of the manuscript – Boboyeva Ogiloy; Critical revision of the manuscript for important intellectual content – Hayotova Dilafruz; Final approval of the version to be published – All authors. All authors agree to be accountable for all aspects of the work and have approved the final manuscript.

Conflict of Interest. The authors declare that there are no conflicts of interest regarding the publication of this article.

Funding. This research received no external funding.

ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)

References:

1. Zimmet P, Alberti KG, Kaufman F, Tajima N, Silink M, Arslanian S, et al. The metabolic syndrome in children and adolescents – an IDF consensus report. Pediatr Diabetes. 2007;8(5):299-306. DOI: http://doi.org/10.1111/j.1399-5448.2007.00271.x PMID: 17850473.

2. Davlatov S, Khamdamov B, Khakimov M, Khamdamov A, Khamdamov I. Modified method of laparoscopic longitudinal gastric resection in surgical treatment of patients with metabolic syndrome against the background of gastroesophageal reflux disease. Neonatology, Surgery and Perinatal Medicine. 2025;15(1(55)):126-38. DOI: https://doi.org/10.24061/2413-4260.XV.1.55.2025.20

3. Friend A, Craig L, Turner S. The prevalence of metabolic syndrome in children: a systematic review of the literature. Metab Syndr Relat Disord. 2013;11(2):71-80. DOI: http://doi.org/10.1089/met.2012.0122 PMID: 23249214.

4. Magnussen CG, Koskinen J, Chen W, Thomson R, Schmidt MD, Srinivasan SR, et al. Pediatric metabolic syndrome predicts adulthood metabolic syndrome, subclinical atherosclerosis, and type 2 diabetes mellitus but is no better than body mass index alone: the Bogalusa Heart Study and the Cardiovascular Risk in Young Finns Study. Circulation. 2010;122(16):1604-11. DOI: http://doi.org/10.1161/CIRCULATIONAHA.110.940809 PMID: 20921439; PMCID: PMC3388503.

5. Jiang Z, Tabuchi C, Gayer SG, Bapat SP. Immune dysregulation in obesity. Annual Review of Pathology: Mechanisms of Disease. 2025 Jan 24;20(1):483-509. DOI: https://doi.org/10.1146/annurev-pathmechdis-051222-015350

6. Hotamisligil GS, Erbay E. Nutrient sensing and inflammation in metabolic diseases. Nat Rev Immunol. 2008;8(12):923-34. DOI: http://doi.org/10.1038/nri2449 PMID: 19029988; PMCID: PMC2814543.

7. Inoyatova FI, Yusupalieva GA, Begmanov RB, Bekimbetov KN, Akhralov SF. Possibilities of modern echography technologies in the diagnostics of chronic viral hepatitises in children. International Journal of Pharmaceutical Research (09752366). 2020;12(3):4040-3. DOI: http://doi.org/10.31838/ijpr/2021.13.01.595

8. Hoffman DJ, Powell TL, Barrett ES, Hardy DB. Developmental origins of metabolic diseases. Physiol Rev. 2021;101(3):739-95. DOI: http://doi.org/10.1152/physrev.00002.2020 PMID: 33270534; PMCID: PMC8526339.

9. Reisinger C, Nkeh-Chungag BN, Fredriksen PM, Goswami N. The prevalence of pediatric metabolic syndrome-a critical look on the discrepancies between definitions and its clinical importance. Int J Obes (Lond). 2021;45(1):12-24. DOI: http://doi.org/10.1038/s41366-020-00713-1 PMID: 33208861; PMCID: PMC7752760.

10. Makki K, Froguel P, Wolowczuk I. Adipose tissue in obesity-related inflammation and insulin resistance: cells, cytokines, and chemokines. ISRN Inflamm. 2013;2013:139239. DOI: http://doi.org/10.1155/2013/139239 PMID: 24455420; PMCID: PMC3881510.

11. Accacha S, Barillas-Cerritos J, Srivastava A, Ross F, Drewes W, Gulkarov S, De Leon J, Reiss AB. From childhood obesity to metabolic dysfunction-associated steatotic liver disease (MASLD) and hyperlipidemia through oxidative stress during childhood. Metabolites. 2025 Apr 24;15(5):287. DOI: https://doi.org/10.3390/metabo15050287

12. Bielach-Bazyluk A, Bossowski F, Skorupska M, Mysliwiec H, Bossowski AT, Flisiak I. Psoriasis in Obese Adolescents with Diabetes – From Common Molecular Background to Vicious Circle of Metabolic Syndrome – Case Report and Review of Literature. Cells. 2025 Apr 17;14(8):610. DOI: https://doi.org/10.3390/cells14080610

13. Cinti S, Mitchell G, Barbatelli G, Murano I, Ceresi E, Faloia E, et al. Adipocyte death defines macrophage localization and function in adipose tissue of obese mice and humans. J Lipid Res. 2005;46(11):2347-55. DOI: http://doi.org/10.1194/jlr.M500294-JLR200 PMID: 16150820.

14. Lumeng CN, Bodzin JL, Saltiel AR. Obesity induces a phenotypic switch in adipose tissue macrophage polarization. J Clin Invest. 2007;117(1):175-84. DOI: http://doi.org/10.1172/JCI29881 PMID: 17200717; PMCID: PMC1716210.

15. Kanda H, Tateya S, Tamori Y, Kotani K, Hiasa K, Kitazawa R, et al. MCP-1 contributes to macrophage infiltration into adipose tissue, insulin resistance, and hepatic steatosis in obesity. J Clin Invest. 2006;116(6):1494-505. DOI: http://doi.org/10.1172/JCI26498 PMID: 16691291; PMCID: PMC1459069.

16. Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance. Science. 1993;259(5091):87-91. DOI: http://doi.org/10.1126/science.7678183 PMID: 7678183.

17. Mukhamedova S, Ganieva S, Rustamov B, Murtazayeva Z. Features of immunological blood markers in premature newborns. Neonatology, Surgery and Perinatal Medicine. 2025;15(2(56):73-8. DOI: https://doi.org/10.24061/2413-4260.XV.2.56.2025.10

18. Ganieva ShSh, Ergasheva MU, Panoev KhSh. Immuno-inflammatory markers of syntropic cardiovascular diseases. Medical Immunology. 2023;25(4):933-8. DOI: https://doi.org/10.15789/1563-0625-IIM-2763 (in Russian)

19. Solinas G, Becattini B. JNK at the crossroad of obesity, insulin resistance, and cell stress response. Mol Metab. 2016;6(2):174-84. DOI: http://doi.org/10.1016/j.molmet.2016.12.001 PMID: 28180059; PMCID: PMC5279903.

20. Zhang B, Shi H, Cai W, Yang B, Xiu W. Metabolic syndrome in children and adolescents: definitions, epidemiology, pathophysiology, interventions, and challenges. Front Endocrinol (Lausanne). 2025;16:1512642. DOI: http://doi.org/10.3389/fendo.2025.1512642 PMID: 40568560; PMCID: PMC12187684.

21. Song Y, Li S, Liu H, Liu X, Li J, Wang Y, et al. Higher risk of metabolic syndrome in children and adolescents and polymorphisms in the fat mass and obesity-associated gene: a systematic review and meta-analysis. Pediatr Res. 2025. DOI: http://doi.org/10.1038/s41390-025-04020-1 PMID: 40169741.

22. Frăsinariu OE, Lupu VV, Trandafir LM, Streanga V, Jechel E, Bararu-Bojan I, et al. Metabolic syndrome therapy in pediatric age – between classic and modern. From diets to pipeline drugs. Front Nutr. 2024;11:1475111. DOI: http://doi.org/10.3389/fnut.2024.1475111 PMID: 39723164; PMCID: PMC11669255.

23. Nicoară DM, Munteanu AI, Scutca AC, Mang N, Juganaru I, Brad GF, et al Assessing the Relationship between Systemic Immune-Inflammation Index and Metabolic Syndrome in Children with Obesity. Int J Mol Sci. 2023;24(9):8414. DOI: http://doi.org/10.3390/ijms24098414 PMID: 37176120; PMCID: PMC10179406.

24. Kim KE, Cho YS, Baek KS, Li L, Baek KH, Kim JH, et al. Lipopolysaccharide-binding protein plasma levels as a biomarker of obesity-related insulin resistance in adolescents. Korean J Pediatr. 2016;59(5):231-8. DOI: http://doi.org/10.3345/kjp.2016.59.5.231 PMID: 27279888; PMCID: PMC4897159.

25. Rainone V, Schneider L, Saulle I, Ricci C, Biasin M, Al-Daghri NM, et al. Upregulation of inflammasome activity and increased gut permeability are associated with obesity in children and adolescents. Int J Obes (Lond). 2016;40(6):1026-33. DOI: http://doi.org/10.1038/ijo.2016.26 PMID: 26876434.

26. Carolan E, Hogan AE, Corrigan M, Gaotswe G, O'Connell J, Foley N, et al. The impact of childhood obesity on inflammation, innate immune cell frequency, and metabolic microRNA expression. J Clin Endocrinol Metab. 2014;99(3): E474-8. DOI: http://doi.org/10.1210/jc.2013-3529 PMID: 24423308.

27. Koller AM, Săsăran MO, Mărginean CO. The Role of Gut Microbiota in Pediatric Obesity and Metabolic Disorders: Insights from a Comprehensive Review. Nutrients. 2025;17(11):1883. DOI: http://doi.org/10.3390/nu17111883 PMID: 40507152; PMCID: PMC12158192.

28. Cabiati M, Guiducci L, Randazzo E, Casieri V, Federico G, Del Ry S. Circulating and Exosomal microRNA-33 in Childhood Obesity. Biomedicines. 2023;11(8):2295. DOI: http://doi.org/10.3390/biomedicines11082295 PMID: 37626791; PMCID: PMC10452681.

29. Vandanmagsar B, Youm YH, Ravussin A, Galgani JE, Stadler K, Mynatt RL, et al. The NLRP3 inflammasome instigates obesity-induced inflammation and insulin resistance. Nat Med. 2011;17(2):179-88. DOI: http://doi.org/10.1038/nm.2279 PMID: 21217695; PMCID: PMC3076025.

30. Wen H, Ting JP, O'Neill LA. A role for the NLRP3 inflammasome in metabolic diseases – did Warburg miss inflammation? Nat Immunol. 2012;13(4):352-7. DOI: http://doi.org/10.1038/ni.2228 PMID: 22430788; PMCID: PMC4090390.

31. Sah AK, Afzal M, Elshaikh RH, Abbas AM, Shalabi MG, Prabhakar PK, et al. Innovative strategies in the diagnosis and treatment of liver cirrhosis and associated syndromes. Life. 2025;15(5):779. DOI: https://doi.org/10.3390/life15050779

32. Jorquera G, Russell J, Monsalves-Álvarez M, Cruz G, Valladares-Ide D, Basualto-Alarcón C, et al. NLRP3 Inflammasome: Potential Role in Obesity Related Low-Grade Inflammation and Insulin Resistance in Skeletal Muscle. Int J Mol Sci. 2021;22(6):3254. DOI: http://doi.org/10.3390/ijms22063254 PMID: 33806797; PMCID: PMC8005007.

33. Romeo M, Silvestrin A, Senese G, Di Nardo F, Napolitano C, Vaia P, Coppola A, Federico P, Dallio M, Federico A. From «Traditional» to «Trained» Immunity: Exploring the Novel Frontiers of Immunopathogenesis in the Progression of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Biomedicines. 2025 Aug 18;13(8):2004. DOI: https://doi.org/10.3390/biomedicines13082004

34. Vukovic R, Dos Santos TJ, Ybarra M, Atar M. Children With Metabolically Healthy Obesity: A Review. Front Endocrinol (Lausanne). 2019;10:865. DOI: http://doi.org/10.3389/fendo.2019.00865 PMID: 31920976; PMCID: PMC6914809.

35. Luo Y, Luo D, Li M, Tang B. Insulin Resistance in Pediatric Obesity: From Mechanisms to Treatment Strategies. Pediatr Diabetes. 2024;2024:2298306. DOI: http://doi.org/10.1155/2024/2298306 PMID: 40302954; PMCID: PMC12016791.

36. Zhang Q, Kong B, Zhou Z, Liu F, Wen E, Lin B, et al. Association between systemic immune-inflammation index and central obesity in pediatric populations: a cross-sectional and cohort study. Frontiers in Immunology. 2025;16:1546612. DOI: https://doi.org/10.3389/fimmu.2025.1546612

37. Zaki ME, ElGebaly H, Hassan M, Elbatrawy SR, Yousef W, Ismail AS, et al. Serum Chemerin and Apelin Levels in Obese Children: Relation to Endothelial Function and Inflammation from a Cross-sectional Case–Control Study. Open Access Maced J Med Sci. 2022;10(B):1547-54. DOI: https://doi.org/10.3889/oamjms.2022.9935

38. Pérez-Pérez A, Sánchez-Jiménez F, Vilariño-García T, Sánchez-Margalet V. Role of Leptin in Inflammation and Vice Versa. Int J Mol Sci. 2020;21(16):5887. DOI: http://doi.org/10.3390/ijms21165887 PMID: 32824322; PMCID: PMC7460646.

39. Misch M, Puthanveetil P. The Head-to-Toe Hormone: Leptin as an Extensive Modulator of Physiologic Systems. International Journal of Molecular Sciences. 2022;23(10):5439. DOI: http://doi.org/10.3390/ijms23105439

40. Öner-İyidoğan Y, Koçak H. Interaction of fetuin-A with obesity related insulin resistance and diabetes mellitus. Turkish Journal of Biochemistry. 2025 Apr 30;50(2):170-82. DOI: https://doi.org/10.1515/tjb-2024-0235

41. Marti A, Martínez I, Ojeda-Rodríguez A, Azcona-Sanjulian MC. Higher Lipopolysaccharide Binding Protein and Chemerin Concentrations Were Associated with Metabolic Syndrome Features in Pediatric Subjects with Abdominal Obesity during a Lifestyle Intervention. Nutrients. 2021;13(2):289. DOI: http://doi.org/10.3390/nu13020289 PMID: 33498461; PMCID: PMC7909441.

42. Nier A, Brandt A, Baumann A, Conzelmann IB, Özel Y, Bergheim I. Metabolic Abnormalities in Normal Weight Children Are Associated with Increased Visceral Fat Accumulation, Elevated Plasma Endotoxin Levels and a Higher Monosaccharide Intake. Nutrients. 2019;11(3):652. DOI: http://doi.org/10.3390/nu11030652 PMID: 30889844; PMCID: PMC6470572.

43. Cho KY. Association of gut microbiota with obesity in children and adolescents. Clin Exp Pediatr. 2023;66(4):148-54. DOI: http://doi.org/10.3345/cep.2021.01837 PMID: 36397257; PMCID: PMC10080385.

44. Luo Y, Li M, Luo D, Tang B. Gut Microbiota: An Important Participant in Childhood Obesity. Adv Nutr. 2025;16(2):100362. DOI: http://doi.org/10.1016/j.advnut.2024.100362 PMID: 39733798; PMCID: PMC11786877.

45. Goyal D, Limesand SW, Goyal R. Epigenetic responses and the developmental origins of health and disease. J Endocrinol. 2019;242(1): T105-19. DOI: http://doi.org/10.1530/JOE-19-0009 PMID: 31091503.

46. Denizli M, Capitano ML, Kua KL. Maternal obesity and the impact of associated early-life inflammation on long-term health of offspring. Front Cell Infect Microbiol. 2022;12:940937. DOI: http://doi.org/10.3389/fcimb.2022.940937 PMID: 36189369; PMCID: PMC9523142.

47. Sureshchandra S, Wilson RM, Rais M, Marshall NE, Purnell JQ, Thornburg KL, et al. Maternal Pregravid Obesity Remodels the DNA Methylation Landscape of Cord Blood Monocytes Disrupting Their Inflammatory Program. J Immunol. 2017;199(8):2729-44. DOI: http://doi.org/10.4049/jimmunol.1700434 PMID: 28887432; PMCID: PMC7384891.

48. Iwata H, Miyashita C, Yamaguchi T, Ikeda A, Miura R, Minatoya M, et al. Childhood obesity and DNA methylation in an epigenome-wide association study: findings from the Hokkaido Birth Cohort. Clin Epigenetics. 2025;18(1):7. DOI: http://doi.org/10.1186/s13148-025-02022-8 PMID: 41327469; PMCID: PMC12777100.

49. Llauradó-Pont J, Stratakis N, Fiorito G, Handakas E, Neumann A, Barros H, et al. A meta-analysis of epigenome-wide association studies of ultra-processed food consumption with DNA methylation in European children. Clin Epigenetics. 2025;17(1):3. DOI: http://doi.org/10.1186/s13148-024-01782-z PMID: 39773758; PMCID: PMC11706074.

50. Maguolo A, Jönsson J, Perfilyev A, Vaag A, Malchau Carlsen E, Nørgaard K, et al. Insulin levels at 18-20 gestational weeks in pregnant women with obesity are associated with newborn abdominal fat deposition and DNA methylation in cord blood. Clin Epigenetics. 2025;17(1):123. DOI: http://doi.org/10.1186/s13148-025-01923-y PMID: 40646607; PMCID: PMC12255083.

51. Louise J, Deussen AR, Koletzko B, Owens J, Saffery R, Dodd JM. Effect of an antenatal diet and lifestyle intervention and maternal BMI on cord blood DNA methylation in infants of overweight and obese women: The LIMIT Randomised Controlled Trial. PLoS One. 2022;17(6): e0269723. DOI: http://doi.org/10.1371/journal.pone.0269723 PMID: 35749371; PMCID: PMC9231808.

52. Lacagnina S. The Developmental Origins of Health and Disease (DOHaD). Am J Lifestyle Med. 2019;14(1):47-50. DOI: http://doi.org/10.1177/1559827619879694 PMID: 31903081; PMCID: PMC6933571.

53. Clarke M, Mathew SM, Giles LC, Pena AS, Barr IG, Richmond PC, et al. A Prospective Study Investigating the Impact of Obesity on the Immune Response to the Quadrivalent Influenza Vaccine in Children and Adolescents. Vaccines (Basel). 2022;10(5):699. DOI: http://doi.org/10.3390/vaccines10050699 PMID: 35632458; PMCID: PMC9142924.

54. Huang JY, Kaur BP, Seth D, Pansare MV, Kamat D, McGrath E, et al. 908 Can obesity alter the immune response to childhood vaccines? J Allergy Clin Immunol. 2019;143(2):AB299.

55. Vitoratou DI, Milas GP, Korovessi P, Kostaridou S, Koletsi P. Obesity as a risk factor for severe influenza infection in children and adolescents: a systematic review and meta-analysis. Eur J Pediatr. 2023;182(1):363-74. DOI: http://doi.org/10.1007/s00431-022-04689-0 PMID: 36369400; PMCID: PMC9652042.

СУЧАСНІ ІМУНОЛОГІЧНІ ТА БІОМОЛЕКУЛЯРНІ ОСНОВИ МЕТАБОЛІЧНОГО СИНДРОМУ У ДІТЕЙ

Ш. Мухамедова, Ш. Ганієва, О. Бобоєва, Д. Хайотова

Бухарський державний медичний інститут
(м. Бухара, Республіка Узбекистан)

Резюме.

Метаболічний синдром у дітей – це багатофакторне захворювання, що характеризується ожирінням, резистентністю до інсуліну та іншими кардіометаболічними факторами ризику. У патогенезі метаболічного синдрому задіяні складні імунологічні та біомолекулярні механізми. Хронічне, слабо виражене запалення та порушення регуляції імунної системи є основними факторами, що сприяють резистентності до інсуліну та судинній дисфункції. Ключові молекулярні сигнальні шляхи, зокрема каскад ядерного фактору-каппа B (NF-κB) та інфламасому NLRP3, аномально активуються в жировій тканині, пов'язуючи надлишок поживних речовин із запальними реакціями.Toll – подібний рецептор 4 (TLR4) служить найважливішим висхідним датчиком, який пов'язує сигналізацію вродженого імунітету з метаболічним стресом, запускаючи активацію NF-κB і сприяючи резистентності до інсуліну, викликаної жирними кислотами. Ця стійка активація вродженого імунітету призводить до підвищеної продукції прозапальних цитокінів (наприклад, TNF-α, IL-1β) і змінює профіль адипокінів. Рівень лептину підвищується, а адипонектину знижується, що спричиняє дисбаланс та посилює субклінічне запалення та резистентність до інсуліну. Генетична схильність, така як поліморфізм в імунорегуляторних генах (наприклад, NLRP3, STAT3), і епігенетичні модифікації (індуковані дієтою зміни метилювання ДНК і експресії генів) також впливають на ці імунно–метаболічні взаємодії. Нові дані, отримані в педіатричній популяції, підкреслюють, що перехресні імунометаболічні перешкоди, включаючи інфільтрацію макрофагами жирової тканини і передачу сигналів адипокінів, сприяють ранньому розвитку метаболічного синдрому. Розуміння цих механізмів забезпечує основу для виявлення біомаркерів та розробки цілеспрямованих заходів для запобігання або пом'якшення наслідків метаболічного синдрому в дітей та його довгострокових кардіометаболічних ускладнень.

Ключові слова: метаболічний синдром у дітей; хронічне запалення; порушення імунної регуляції; імунометаболізм; епігенетика; адипокіни.

Contact Information:

Shakhnoza Mukhamedova – Doctor of Medical Sciences (DSc), Associate Professor, Head of the Department of Pediatrics No. 2, Bukhara State Medical Institute (Bukhara, Republic of Uzbekistan)
e-mail: 1986neonatolog@gmail.com; shaxnoza_mukhamedova@bsmi.uz
ORCID ID: https://orcid.org/0000-0002-7874-4275

Shakhzoda Ganiyeva – Doctor of Medical Sciences (DSc), Professor of the Department of Pediatrics No. 2, Bukhara State Medical Institute (Bukhara, Republic of Uzbekistan)
e-mail: doctor.ganieva@gmail.com; shaxzoda_ganiyeva@bsmi.uz
ORCID ID: https://orcid.org/0000-0001-6090-1394
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=58532974400

Ogiloy Boboyeva – Assistant of the Department of Pediatrics No. 2, Bukhara State Medical Institute (Bukhara, Republic of Uzbekistan)
e-mail: boboyeva.ogiloy@bsmi.uz
ORCID ID: https://orcid.org/0009-0008-9535-152X

Dilafruz Hayotova – PhD, Senior Lecturer at the Department of German Philology, Bukhara State University (Bukhara, Republic of Uzbekistan)
e-mail: d.z.hayotova@buxdu.uz
ORCID ID: https://orcid.org/0000-0002-4975-9179
Researcher ID: http://www.researcherid.com/rid/LZI-0011-2025

Контактна інформація:

Мухамедова Шахноза – доктор медичних наук (DSc), доцент, завідувач кафедри педіатрії № 2, Бухарський державний медичний інститут (м. Бухара, Республіка Узбекистан)
e-mail: 1986neonatolog@gmail.com; shaxnoza_mukhamedova@bsmi.uz
ORCID ID: https://orcid.org/0000-0002-7874-4275

Ганієва Шахзода – доктор медичних наук (DSc), професор кафедри педіатрії № 2, Бухарський державний медичний інститут (м. Бухара, Республіка Узбекистан)
e-mail: doctor.ganieva@gmail.com; shaxzoda_ganiyeva@bsmi.uz
ORCID ID: https://orcid.org/0000-0001-6090-1394
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=58532974400

Бобоєва Огілой – асистент кафедри педіатрії № 2, Бухарський державний медичний інститут (м. Бухара, Республіка Узбекистан)
e-mail: boboyeva.ogiloy@bsmi.uz
ORCID ID: https://orcid.org/0009-0008-9535-152X

Хайотова Ділафруз – кандидат філологічних наук, старший викладач кафедри німецької філології Бухарського державного університету (м. Бухара, Республіка Узбекистан)
e-mail: d.z.hayotova@buxdu.uz
ORCID ID: https://orcid.org/0000-0002-4975-9179
Researcher ID: http://www.researcherid.com/rid/LZI-0011-2025

Received by the editorial office: 04 November 2025.
Approved for publication: 23 February 2026.
Published: 27 March 2026.