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ABSTRACT

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NUTRIGENETICS AND PERSONALIZED NUTRITION IN PEDIATRIC METABOLIC DISORDERS: GENETIC DETERMINANTS OF OBESITY AND DIABETES MELLITUS

Introduction. In recent years, the prevalence of metabolic diseases, particularly obesity and diabetes mellitus, in the pediatric population has been steadily increasing. Modern scientific research proves that the formation of metabolic disorders is due to the complex interaction of genetic, epigenetic mechanisms, as well as environmental factors. A special role in this process is played by genetic polymorphisms that affect appetite regulation, energy metabolism, insulin sensitivity and lipid metabolism. Identification of genetic determinants of obesity and diabetes mellitus opens up new opportunities for the implementation of personalized preventive and therapeutic strategies.

Materials and methods. The study was conducted as an analytical review of the scientific literature in order to summarize and critically analyze current data on the nutrigenetic mechanisms of obesity and type 1 and type 2 diabetes mellitus in children. For this purpose, a systematic search and analysis of publications in international scientific databases, including PubMed, Google Scholar, Scopus and Web of Science for the period from 2017 to 2025, was conducted.

Results. A review of current studies confirmed the significant role of genetic factors in the development of obesity and diabetes in children. The most stable associations with increased body mass index were demonstrated for variants of the FTO and MC4R genes, which affect appetite regulation and energy balance. For type 1 diabetes, immunogenetic predisposition is the leading one, while in the development of type 2 diabetes in adolescents, the combination of polygenic predisposition (in particular, TCF7L2, KCNJ11 variants) with obesity and environmental factors is important. It has

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been shown that polygenic risk scores can be used for early risk assessment, but their predictive value depends on population characteristics and lifestyle. The integration of genetic, epigenetic and metabolic data opens up prospects for personalization of nutrition in pediatrics, but requires further clinical validation and standardization.

Conclusions. Nutrigenetics deepens the understanding of the individual predisposition of children to obesity and diabetes, and explains how nutrition and lifestyle interact with genetic variants in shaping metabolic disorders. At the same time, most genetic markers are characterized by a moderate effect, which is significantly modified by environmental factors. Further development of the direction requires standardization of methodology, accumulation of high-quality pediatric studies and development of clear clinical recommendations for the substantiated integration of nutrigenetic data in the prevention and treatment of metabolic diseases in children.

Keywords: child, genetic polymorphism, metabolic syndrome, obesity, diabetes mellitus, nutrigenetics, nutrigenomics, personalized nutrition.

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НУТРИГЕНЕТИКА ТА ПЕРСОНАЛІЗОВАНЕ ХАРЧУВАННЯ ПРИ ПЕДІАТРИЧНИХ МЕТАБОЛІЧНИХ РОЗЛАДАХ: ГЕНЕТИЧНІ ДЕТЕРМІНАНТИ ОЖИРІННЯ ТА ЦУКРОВОГО ДІАБЕТУ

Вступ. Протягом останніх років поширеність метаболічних захворювань, зокрема ожиріння та цукрового діабету, серед дитячого населення безперервно зростає. Сучасні наукові дослідження доводять, що формування метаболічних порушень зумовлене складною взаємодією генетичних, епігенетичних механізмів, а також факторів навколишнього середовища. Особливу роль у цьому процесі відіграють генетичні поліморфізми, які впливають на регуляцію апетиту, енергетичний обмін, чутливість до інсуліну та ліпідний метаболізм. Виявлення генетичних детермінант ожиріння та цукрового діабету відкриває нові можливості для впровадження персоналізованих профілактичних і лікувальних стратегій.

Матеріали та методи. Дослідження виконано у форматі аналітичного огляду наукової літератури з метою узагальнення та критичного аналізу сучасних даних щодо нутригенетичних механізмів ожиріння та цукрового діабету 1-го і 2-го типів у дітей. З цією метою було проведено систематичний пошук і аналіз публікацій у міжнародних наукових базах даних, зокрема PubMed, Google Scholar, Scopus і Web of Science за період із 2017 по 2025 рік.

Результати. Огляд сучасних досліджень підтвердив значущу роль генетичних чинників у розвитку ожиріння та цукрового діабету у дітей. Найбільш стабільні асоціації з підвищеним індексом маси тіла продемонстровані для варіантів генів FTO та MC4R, що впливають на регуляцію апетиту й

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енергетичний баланс. Для цукрового діабету 1-го типу провідною є імуногенетична схильність, тоді як у розвитку діабету 2-го типу в підлітків значення має поєднання полігенної схильності (зокрема варіанти TCF7L2, KCNJ11) з ожирінням і середовищними факторами. Показано, що полігенні ризикові індекси можуть використовуватися для раннього виявлення ризику, однак їх прогностична цінність залежить від популяційних особливостей і способу життя. Інтеграція генетичних, епігенетичних і метаболічних даних відкриває перспективи персоналізації харчування в педіатрії, проте потребує подальшої клінічної валідації та стандартизації.

Висновки. Нутригенетика поглиблює розуміння індивідуальної схильності дітей до ожиріння та цукрового діабету, а також пояснює вплив харчування і способу життя на формування метаболічних порушень, залежно від генетичних варіантів. Водночас для більшості генетичних маркерів характерний помірний ефект, який істотно модифікується середовищними чинниками. Подальший розвиток напряму потребує стандартизації методології, накопичення якісних педіатричних досліджень та розробки чітких клінічних рекомендацій для обґрунтованої інтеграції нутригенетичних даних у профілактику й лікування метаболічних захворювань у дітей.

Ключові слова: діти, поліморфізм генетичний, метаболічний синдром, ожиріння, цукровий діабет, нутригенетика, нутригеноміка, персоналізоване харчування.

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INTRODUCTION

Metabolic disorders in children, such as obesity and type 1 and type 2 diabetes mellitus, represent one of the most pressing medical and social challenges of modern healthcare. Over recent decades, the prevalence of childhood obesity has increased to the level of a global epidemic, contributing to the early development of cardiometabolic complications [1]. At the same time, within the structure of pediatric diabetes, an increase is observed both in the incidence of autoimmune type 1 diabetes and in the growing number of early-onset type 2 diabetes cases among adolescents [2, 3].

Standard dietary recommendations have proven to be insufficiently effective, as they fail to account for the substantial interindividual variability in responses to nutritional factors. One of the key explanations for this variability lies in genetic characteristics that shape nutrient metabolism, appetite regulation, and energy balance [4]. Nutrigenetics, in particular, investigates the interactions between genomic variations and dietary factors, thereby enabling the development of individualized nutritional strategies [5, 6].

The aim of this review is to summarize current evidence on the genetic determinants of obesity and type 1 and type 2 diabetes mellitus in children, as well as to analyze the opportunities and limitations of applying nutrigenetics in pediatric clinical practice.

MATERIALS AND METHODS

The study was conducted as an analytical review of the scientific literature with the aim of summarizing and critically analyzing current evidence regarding nutrigenetic mechanisms underlying obesity and type 1 and type 2 diabetes mellitus in children.

To this end, a systematic search and analysis of publications in international scientific databases, including PubMed, Google Scholar, Scopus, and Web of Science, was performed for the period from 2017 to 2025. The search employed combinations of the following keywords: *nutrigenetics, nutrigenomics, childhood obesity, type 1 diabetes, type 2 diabetes, genetic polymorphism, FTO, MC4R, polygenic risk score, pediatric*.

The review included review articles, meta-analyses, prospective cohort studies, and clinical research focusing on genetic factors contributing to pediatric metabolic disorders such as obesity and diabetes, as well as on the potential application of genotype-based dietary interventions.

Literature selection was based on criteria of scientific relevance, including the recency of publication, quality of the evidence, and alignment with current international clinical guidelines. A formal PRISMA protocol was not applied, consistent with the narrative review design.

The literature analysis aimed to compare findings across studies, identify consistent and conflicting data, and assess the clinical translatability of nutrigenetic approaches in pediatric practice. In addition, ethical and practical aspects of implementing nutrigenetic technologies in pediatrics, as well as potential barriers to their widespread use, were analyzed.

The synthesis of the results allowed for the identification of current trends in nutrigenetics and outlined prospects for its integration into pediatric medical practice to optimize nutrition and prevent metabolic disorders.

Nutrigenetics: Current Concepts and Clinical Relevance in Childhood

Nutrigenetics is a scientific discipline that studies the relationship between genetic variation in nutrition-related genes, the body's response to nutrients and bioactive compounds, their metabolism, and the likelihood of disease development. Nutrigenetics investigates the effects of genetic variability on dietary influences on health. Nutrigenomics, in turn, analyzes the impact of nutrition on gene expression and the associated molecular processes.

Although these fields employ different methodological approaches, they are increasingly considered complementary in contemporary research, as they allow a comprehensive assessment of the interaction between genotype, diet, and metabolic outcomes [7, 8].

Modern approaches in nutrigenetics increasingly involve the integration of systems-level data, including genomics, epigenomics, metabolomics, and characterization of the gut microbiota. This enables a comprehensive modeling of the mechanisms underlying metabolic phenotypes, regulation of nutrient homeostasis, and differential responses to specific dietary factors [9].

One fundamental concept is the gene–diet interaction, whereby specific alleles can modulate the body's sensitivity to macro- and micronutrient intake, influence appetite, regulate energy balance, and affect adipose tissue accumulation and dynamics, thereby shaping individually variable metabolic profiles [9].

According to recent reviews, single nucleotide polymorphisms (SNPs) are a central focus in nutrigenetics: they can modulate metabolism, nutrient absorption, and folate cycle functioning, as exemplified by variants in the *MTHFR* gene (methylenetetrahydrofolate reductase) [10].

In pediatrics, nutrigenetics is of particular importance, as childhood represents a critical period for the development of metabolic regulation and dietary habits [11]. Nutrient exposures in early life can, via genetic and epigenetic mechanisms, determine long-term risk for obesity and carbohydrate metabolism disorders. This underscores the importance of considering genetic variants already in the perinatal period, as the genotype may influence how a child responds to maternal nutrition, breastfeeding, or complementary feeding [12].

Contemporary research integrating genomics, epigenomics, and the gut microbiota is opening new avenues for the personalization of nutrition. At the same time, the implementation of this knowledge into pediatric practice presents certain challenges, including the need for standardization, the development of ethical frameworks, and professional education. To fully realize the potential of nutrigenetics in supporting child health, further research, systematic approaches, and interdisciplinary collaboration are required [13, 14].

In particular, the standardization of genetic testing panels, harmonization of clinical protocols, and the development of educational programs for healthcare professionals (including dietitians and pediatricians) would enable the evidence-based integration of nutrigenetic approaches into pediatric practice and facilitate their translation into practical clinical guidelines.

Special attention should be given to ethical considerations, including the establishment of clear policies regarding informed consent, the storage and use of children's genetic data, and the appropriate communication of results with parents and pediatric patients [15].

Genetic Mechanisms Underlying Childhood Obesity

Obesity is a multifactorial condition in which both environmental and genetic factors play a significant role. In contemporary settings, childhood obesity represents not only a medical but also a socio-psychological concern. According to scientific evidence, obesity contributes to numerous health disorders during childhood and later in adulthood. The metabolic disturbances associated with obesity may reduce both quality of life and life expectancy at the population level [16].

Recent reviews emphasize that the heritability of body mass index (BMI) in childhood ranges from approximately 40% to 70%, indicating a substantial genomic contribution [1, 17].

Although the evidence base regarding gene–diet interactions in childhood is expanding, findings remain inconsistent, underscoring the need for larger-scale and more standardized studies [18].

Nutrient exposure during the first 1,000 days of life is of particular importance, as it may program long-term metabolic risk. Perinatal factors such as breastfeeding, maternal nutrition, and gut microbiota composition influence the trajectory of obesity development [19].

In rare cases, obesity is caused by mutations in single genes (e.g., MC4R [melanocortin 4 receptor], LEP [leptin], and LEPR [leptin receptor]); however, in the majority of children, the condition exhibits a polygenic nature. Within polygenic obesity, two phenotypic variants are commonly distinguished. The first is metabolically healthy obesity (MHO), characterized by the absence of clinically significant metabolic dysfunction. The second is metabolically unhealthy obesity (MUO), defined by metabolic abnormalities and complications reflecting an adverse metabolic profile.

The development of obesity results from a prolonged imbalance between energy intake and energy expenditure. A number of genes play a key role in the regulation of energy consumption and appetite control, including GHRL, LEP, LEPR, FTO (fat mass and obesity-associated gene), MC4R, and GLP-1 (encoding glucagon-like peptide-1) [20].

Polymorphisms in the *FTO* gene (rs9939609) and *MC4R* (melanocortin 4 receptor) (rs12970134) demonstrate the most consistent associations with increased body mass index (BMI) and obesity risk across different age groups [20, 21].

The identification of novel loci is also of considerable importance. According to studies by Bradfield & Loos (2021) and Vogelezang & Felix (2020), genome-wide association study (GWAS) meta-analyses have identified additional variants influencing childhood obesity risk [22, 23]. Further investigations have shown that genetic effects may vary depending on age: certain loci exert stronger effects in early childhood, whereas others become more prominent during adolescence [4, 24].

Genetic variants and epigenetic modifications (including DNA methylation and histone modifications), in combination with characteristics of the gut microbiota, collectively contribute to individual pathways of obesity development. Consideration of gut microbiota status is particularly relevant, as microbial composition may modulate metabolic responses to diet in a genotype-dependent manner. Alterations in the expression of genes involved in energy regulation, appetite control, or adipose tissue accumulation may be partially explained by gene–diet interactions. Moreover, through epigenetic mechanisms (e.g., DNA methylation), early-life nutrition may “program” future metabolic phenotypes [9].

The application of polygenic risk scores (PRS) enables the prediction of obesity risk from early childhood. Scientific evidence indicates that PRS may reflect BMI trajectories from birth to adulthood, thereby opening opportunities for early preventive interventions in high-risk children [25, 26].

An important aspect is the modulation of genetic effects by dietary factors. For example, carriers of the *FTO* risk allele demonstrate greater protection against excess weight when consuming a high-fiber diet [21]. A polymorphism near *MC4R* has been associated with increased intake of sugar-sweetened beverages, making this genetic marker a potential target for behavioral interventions [20]. Similarly, interactions between genetic predisposition and overall diet quality have been confirmed in large cohort studies [27].

A recent meta-analysis demonstrated that the *FTO* rs9939609 and rs1421085 alleles are associated with components of metabolic syndrome in children and adolescents, including increased waist circumference, elevated fasting glucose levels, higher blood pressure, and reduced HDL cholesterol concentrations [28].

In a study by Bryl et al. (2023), polymorphisms in *FTO* and *MC4R*, together with perinatal factors and exposure to adverse childhood events (ACEs), were shown to exert a combined effect on BMI, fat mass, and other anthropometric indicators in children aged 6–12 years. The authors further reported that the presence of “risk” genotypes, in combination with unfavorable environmental factors, amplified negative effects on adiposity-related parameters [29].

The *FTO* gene represents one of the loci most consistently associated with body mass index in children. The extensively studied rs9939609 polymorphism has been reliably linked to an increased risk of overweight and obesity; however, the strength of this association varies considerably across studies [21, 29].

At the molecular level, *FTO* encodes a demethylase enzyme that acts on RNA modifications (notably N6-methyladenosine, m6A) and influences adipogenesis and energy metabolism through the regulation of transcript processing and stability. These molecular functions provide a mechanistic explanation for how variants in regulatory regions of *FTO* may alter the expression of genes involved in appetite control and fat accumulation [30].

In an adolescent cohort, the *FTO* rs9930506 polymorphism was correlated with lower resistance to eating, indicating an influence on eating behavior rather than solely on metabolic pathways. Although this study

did not include younger children, it highlights the potential impact of the *FTO* genotype on behavioral components (e.g., appetite and food motivation), which is relevant for nutrigenetic modeling [31].

Analyses of pediatric cohorts further suggest that the effect of *FTO* variants is substantially modified by lifestyle factors. In children with higher levels of physical activity and better diet quality, the association between the risk allele and increased BMI is attenuated or loses statistical significance. This gene–lifestyle interaction has important practical implications for preventive programs targeting children with elevated genetic risk [32].

In several recent pediatric studies, associations between specific *FTO* SNPs and BMI did not reach statistical significance, reflecting sample heterogeneity, ethnic differences, the influence of other genetic loci, and environmental factors. Therefore, the interpretation of findings should carefully consider population characteristics and study design [33, 34].

Thus, *FTO* polymorphisms represent an important marker of genetic susceptibility to obesity in children; however, they should not be regarded as deterministic factors in obesity development. Rather, they may be interpreted as markers of increased sensitivity to adverse environmental exposures, which has practical implications for early prevention strategies [34, 30].

When describing the impact of *MC4R* (melanocortin-4 receptor) polymorphisms on childhood obesity, it should be emphasized that the *MC4R* gene plays a key role in the central regulation of appetite and energy balance [35]. The rs17782313 polymorphism, located near this gene, has been consistently associated with an increased risk of obesity in children across different ethnic groups. Study findings indicate that carriers of the risk allele tend to exhibit more rapid weight gain, a higher percentage of body fat, and a shift in dietary preferences toward high-calorie foods [36].

Population-based studies conducted in Spain, China, and Turkey demonstrate the stability of the *MC4R* effect across diverse ethnic groups. In large cohort samples, the frequency of *MC4R* variants has been associated not only with obesity but also with other metabolic phenotypes, including elevated blood pressure, insulin resistance, and components of metabolic syndrome [37–39].

Comparative analyses suggest that although *FTO* and *MC4R* polymorphisms are frequently incorporated into polygenic risk scores, their clinical significance differs. In contrast to *FTO*, *MC4R* variants are more often associated with earlier-onset and more severe forms of obesity and appear to be less modifiable through behavioral interventions. This supports consideration of *MC4R* as a marker of increased risk for severe obesity phenotypes in childhood, whereas the impact of *FTO* is substantially influenced by lifestyle factors [30, 33, 39].

This distinction has practical implications: carriers of FTO variants may derive greater benefit from behavioral and dietary interventions, whereas children with MC4R variants may require earlier and more intensive monitoring.

Genetic Aspects of Diabetes Mellitus in Children

Diabetes mellitus in childhood is most commonly represented by autoimmune type 1 diabetes (T1D) and type 2 diabetes (T2D), the latter predominantly manifesting during adolescence. In both conditions, genetic factors play a substantial role; however, their contribution and clinical implications differ. In T1D, immunogenetic susceptibility is central, whereas in T2D, disease development reflects the interaction between polygenic predisposition, obesity, and environmental influences [2, 40].

Genetic testing may be useful for clarifying the type of diabetes and predicting disease course; however, its practical value depends on the specific clinical context and should always be interpreted in conjunction with phenotype, risk factors, and the presence of comorbid obesity [2, 41].

The development of T1D results from the interplay between genetic susceptibility and environmental triggers. The most significant genetic predictors are associated with the HLA region, while additional loci (including INS and PTPN22) have also been implicated, supporting the immunogenetic nature of the disease [2].

Of particular interest in pediatrics is the impact of early-life nutrition, which may modify potential diabetes risk. The literature describes associations between gluten and cereal intake and the development of autoimmune responses in children, as well as evidence linking the timing of cereal introduction to T1D risk in prospective studies [40, 41]. High levels of gluten intake during the perinatal period have been associated with an increased risk of T1D in offspring [42]. Similar findings have been reported for maternal dietary patterns during late pregnancy [2].

Thus, the risk of developing T1D is predominantly genetically determined, whereas early-life nutritional factors may exert an additional modifying effect; however, the effectiveness of preventive strategies remains limited [43, 44].

In contrast to adults, T2D in adolescents is characterized by a more aggressive course and more rapid development of complications, underscoring the need for early risk prediction. Contemporary genetic studies indicate the involvement of loci associated with β-cell function and insulin resistance, and demonstrate that several “adult” T2D susceptibility markers (e.g.,

TCF7L2, *PPARG*, *KCNJ11*) are also relevant in pediatric populations [3, 45].

Long-term follow-up studies have shown that T2D in adolescents progresses rapidly and often requires combination therapy, highlighting the importance of developing genetically informed dietary strategies. Conclusions from recent reviews suggest that understanding the genetic characteristics of pediatric T2D enables the implementation of a personalized approach to patient management [3, 46].

Polygenic risk scores (PRS) aggregate the contribution of multiple GWAS-identified markers associated with T2D and obesity and may correlate with early BMI elevation, insulin resistance, and the risk of metabolic disturbances in children and adolescents [3, 47]. However, their predictive value remains limited due to factors such as ethnic variability of genetic markers, the requirement for large validation cohorts, and the substantial influence of environmental factors (including diet and physical activity) [48].

Particular attention has been directed toward epigenetic mechanisms. Altered DNA methylation patterns and other epigenetic modifications induced by nutritional exposures during the perinatal period may significantly increase the future risk of T2D development [47, 48].

In summary, immunogenetic susceptibility plays a central role in T1D, whereas early-life nutritional factors may modify disease risk; however, preventive dietary interventions demonstrate heterogeneous levels of evidence. In adolescents with T2D, genetic markers more commonly reflect susceptibility in combination with obesity and environmental influences, supporting the potential utility of polygenic approaches (PRS), albeit with consideration of their limitations and the need for further validation. Taken together, nutrigenetics may serve as a tool for early risk assessment, contributing to risk stratification and the individualization of preventive strategies.

Personalized Nutrition: Integration of Genetic Data into Clinical Practice and Future Perspectives of Nutrigenetics

The application of nutrigenetics in pediatrics offers opportunities to move from universal dietary recommendations toward personalized strategies. Genotype-guided nutrition may enhance the effectiveness of prevention and treatment of metabolic disorders in children [5, 49].

Personalized nutrition aims to tailor dietary recommendations to an individual's biological characteristics—including genotype, metabolic profile, microbiome composition, and lifestyle—in order to improve health outcomes and prevent chronic diseases [6].

Nutrigenetic data already enable the identification of specific variants that modulate responses to nutrients (e.g., genetic polymorphisms associated with lipid, carbohydrate, folate, or vitamin D metabolism) and may serve as an additional tool in the development of individualized nutrition plans [5].

However, clinical implementation remains limited. Many reported associations demonstrate modest effect sizes for individual SNPs, and the overall quality of evidence is heterogeneous. Large-scale randomized controlled trials and standardized algorithms for genetic data interpretation are required for broader clinical application. Additional limitations include the ethnic specificity of GWAS findings, study heterogeneity, the lack of standardized genetic testing panels, and the absence of clear interpretative algorithms for pediatric populations. Moreover, the substantial influence of environmental factors—such as diet, physical activity, and social context—further complicates the isolated use of genetic markers in clinical decision-making [50].

The integration of genetic data with metabolomics, transcriptomics, and microbiome profiling (multi-omics approaches) represents a promising strategy to enhance predictive accuracy and develop clinically applicable biomarkers, as the incorporation of multiple parameters may better capture the complex interactions among genes, diet, and environment [51]. Such advances may facilitate the development of preventive nutrition programs in school settings and the creation of digital tools to support personalized dietetics [6, 52].

For the effective integration of nutrigenetics into both pediatric and adult clinical practice, several prerequisites must be met: clinically validated panels of genetic markers with approved interpretation algorithms; electronic clinical decision-support systems integrated into hospital discharge summaries and outpatient electronic health records; structured training for physicians and dietitians regarding the significance and limitations of genetic findings; and clearly defined ethical and legal frameworks addressing confidentiality and informed consent [51].

Economic feasibility and accessibility of testing remain additional barriers. The cost of comprehensive genetic analyses, together with the lack of standardized clinical guidelines, continues to limit widespread implementation in routine practice—particularly within resource-constrained healthcare systems [10].

The principal dietary individualization algorithms for children carrying FTO and MC4R variants include caloric intake control, increased dietary protein proportion, and restriction of sugar-sweetened beverages [20, 21]. For carriers of polymorphisms associated with an elevated risk of diabetes (e.g.,

TCF7L2, KCNJ11), a low-glycemic-index diet enriched with dietary fiber is recommended [1, 46].

CONCLUSIONS

In summary, nutrigenetics deepens our understanding of individual susceptibility to obesity and diabetes in children and helps elucidate how dietary patterns and lifestyle factors influence the development of metabolic traits.

Evidence from contemporary research indicates that, for most genetic markers, effect sizes are modest and substantially modified by environmental influences. This limits their utility as independent clinical predictors. Therefore, the greatest practical value of nutrigenetics lies in risk assessment and the individualization of preventive strategies rather than in serving as a basis for rigid dietary prescriptions.

PROSPECTS FOR FUTURE RESEARCH

Future research prospects include large-scale pediatric cohort and randomized studies to study polygenic risk indices. This will allow standardizing methods for assessing the impact of nutrigenetics and developing clinically sound personalized dietary recommendations for the prevention and treatment of metabolic diseases in children.

AUTHOR CONTRIBUTIONS

Concept and design of reseach – OS, AL, VP, data collection and analysis – OS, YM, KG, writing the first version – YM, OV, responsibility for statistical analysis – OS, VH, GR, YM, critical review – PS, YR, AL, final approval of the version for publication – VP, YM, OV, TA, agree to be responsible for all aspects of the work

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CONFLICT OF INTEREST

Olexander Smiyan (a co-author of the paper) serves as Editor-in-Chief of the East European Medical Journal. Olena Vasylieva (a co-author of the paper) serves as deputy Editor-in-Chief of the East European Medical Journal. In accordance with the journal's editorial policy and COPE guidelines, this manuscript was handled exclusively by an independent Associate Editor. The authors named above had no involvement in the peer review process, editorial evaluation, or publication decision regarding this submission. All other authors declare no conflicts of interest.

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During the preparation of this manuscript, the authors used ChatGPT (OpenAI) to assist with English language editing and proofreading, and to support literature search and organization of references. The AI tool was not used for data analysis, interpretation of results, or generation of scientific conclusions. All content was critically reviewed, revised, and approved by the authors, who take full responsibility for the accuracy, integrity, and originality of the published work.

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