EURASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
Innovative Academy Research Support Center
IF = 9.2 www.in-academy.uz/index.php/ejmns

CURRENT DATA ON CLINICAL-METABOLIC AND IMMUNO-ENDOCRINE DISORDERS IN CHILDREN WITH DOWN SYNDROME: A LITERATURE REVIEW

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https://doi.org/10.5281/zenodo.20343761

ARTICLE INFO

Received: 16th May 2026
Accepted: 21st May 2026
Online: 22nd May 2026

KEYWORDS

Down syndrome, children, vitamin D, micronutrients, immunity, endocrine disorders, metabolism.

ABSTRACT

Down syndrome is a common chromosomal disorder associated with metabolic, immune, and endocrine abnormalities. This review summarizes current evidence on micronutrient imbalance, vitamin D deficiency, thyroid dysfunction, and immune dysregulation in children with Down syndrome. These disturbances contribute to increased susceptibility to infectious, autoimmune, and metabolic diseases. Early diagnosis and personalized correction are important for improving patient outcomes.

СОВРЕМЕННЫЕ ДАННЫЕ О КЛИНИКО-МЕТАБОЛИЧЕСКИХ И ИММУННО-ЭНДОКРИННЫХ НАРУШЕНИЯХ У ДЕТЕЙ С СИНДРОМОМ ДАУНА: ОБЗОР ЛИТЕРАТУРЫ

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ARTICLE INFO

Received: 16th May 2026
Accepted: 21st May 2026
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KEYWORDS

Синдром Дауна, дети, витамин Д, микроэлементы, иммунитет, эндокринные нарушения, метаболизм.

ABSTRACT

Синдром Дауна — распространённое хромосомное заболевание, сопровождающееся метаболическими, иммунными и эндокринными нарушениями. В данном обзоре представлены современные данные о дисбалансе микроэлементов, дефиците витамина D, нарушениях функции щитовидной железы и иммунной дисрегуляции у детей с синдромом Дауна. Эти изменения способствуют повышенной восприимчивости к инфекционным, аутоиммунным и метаболическим заболеваниям. Ранняя диагностика и персонализированная коррекция имеют важное значение для улучшения исходов заболевания.

Down syndrome is the most common chromosomal disorder caused by trisomy of chromosome 21 and is characterized by a complex spectrum of morphological, metabolic, immunological, and endocrine abnormalities. The global prevalence of Down syndrome is estimated at

approximately 1 in 700–1000 live births, with maternal age remaining one of the major risk factors. Advances in neonatal care, cardiac surgery, infectious disease management, and multidisciplinary rehabilitation have significantly increased life expectancy in individuals with Down syndrome, which currently exceeds 55–60 years in many countries. Consequently, increasing attention has been directed toward chronic metabolic, immune, and endocrine disturbances that substantially influence long-term morbidity, quality of life, and overall prognosis.

The pathophysiological basis of Down syndrome is associated with overexpression of genes located on chromosome 21, including genes encoding superoxide dismutase-1 (SOD1), amyloid precursor protein (APP), interferon receptors, and several immune-regulatory proteins. Gene dosage imbalance contributes to excessive production of reactive oxygen species and persistent oxidative stress, resulting in mitochondrial dysfunction, lipid peroxidation, cellular injury, and accelerated aging processes. Numerous studies have demonstrated significantly elevated oxidative stress markers in patients with Down syndrome compared with the general population, indicating a central role of oxidative imbalance in the development of metabolic and neurodegenerative complications.

Metabolic abnormalities in children with Down syndrome are systemic and multifactorial. Reduced basal metabolic rate, hypotonia, limited physical activity, endocrine dysfunction, and altered body composition contribute to an increased prevalence of overweight and obesity. According to recent studies, obesity and excessive body weight occur in approximately 30–50% of children with Down syndrome, particularly during school age and adolescence. Insulin resistance is observed in nearly one-third of patients, while dyslipidemia, characterized by elevated triglyceride levels and decreased high-density lipoprotein cholesterol, is frequently reported. These metabolic disturbances increase the risk of early metabolic syndrome and cardiovascular complications.

In recent years, vitamin D has been recognized not only as a regulator of calcium-phosphorus metabolism but also as a hormone-like immunomodulatory factor involved in multiple physiological processes. Vitamin D deficiency is highly prevalent among children with Down syndrome, with low serum 25-hydroxyvitamin D concentrations reported in up to 60–90% of patients. Reduced sunlight exposure, nutritional insufficiency, obesity, impaired intestinal absorption, and altered hepatic and renal vitamin D metabolism may contribute to this condition. Vitamin D deficiency in Down syndrome has been associated with decreased bone mineral density, osteopenia, muscle hypotonia, impaired immune response, and increased susceptibility to respiratory infections and autoimmune diseases.

Micronutrient imbalance also plays a significant role in the pathogenesis of Down syndrome–associated complications. Deficiencies of zinc, selenium, magnesium, iron, and other essential trace elements are frequently identified in affected children. Zinc

deficiency, reported in more than half of patients in some studies, is associated with impaired immune function, delayed growth, and cognitive dysfunction. Selenium deficiency contributes to reduced antioxidant defense through impaired glutathione peroxidase activity, whereas magnesium deficiency may negatively affect neuromuscular and metabolic processes. At the same time, elevated copper levels and increased Cu/Zn ratios have been described as biomarkers of oxidative stress and chronic inflammation in Down syndrome.

Immune dysregulation represents another hallmark of the syndrome. Both innate and adaptive immune responses are altered, resulting in increased vulnerability to infections and autoimmune diseases. Abnormalities include reduced numbers and impaired function of T lymphocytes, altered cytokine production, decreased antibody responses, and chronic low-grade inflammation. Elevated levels of pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), have been consistently reported in patients with Down syndrome. Recurrent respiratory tract infections remain one of the leading causes of hospitalization and morbidity during childhood.

Children with Down syndrome also demonstrate a significantly increased predisposition to autoimmune disorders. Autoimmune thyroid disease, celiac disease, and type 1 diabetes mellitus occur more frequently than in the general pediatric population. These conditions are thought to arise from impaired immune tolerance, chronic immune activation, and genetic susceptibility related to chromosome 21–encoded immune regulatory pathways.

Endocrine abnormalities are among the most common comorbid conditions associated with Down syndrome. Thyroid dysfunction, particularly hypothyroidism, represents the predominant endocrine disorder. Both congenital and acquired hypothyroidism occur at markedly higher rates compared with healthy children. Subclinical hypothyroidism is especially common and may adversely affect growth, neurocognitive development, and metabolic homeostasis if left untreated. In addition, disturbances in bone metabolism, including osteopenia and osteoporosis, are frequently observed due to the combined effects of vitamin D deficiency, hormonal imbalance, reduced physical activity, and altered skeletal development.

Emerging evidence suggests that vitamin D plays an important immunoregulatory role in Down syndrome. Vitamin D modulates T-cell differentiation, suppresses excessive production of pro-inflammatory cytokines, and promotes immune tolerance. Several studies have demonstrated inverse correlations between serum vitamin D levels and inflammatory markers, supporting the anti-inflammatory effects of vitamin D and its potential role in reducing autoimmune and infectious complications.

Therefore, Down syndrome should be considered a multisystem disorder in which genetic abnormalities closely interact with metabolic, immune,

endocrine, and oxidative stress–related mechanisms. The interplay between micronutrient deficiencies, chronic inflammation, oxidative stress, and endocrine dysfunction creates a complex pathogenetic network underlying the clinical manifestations and associated comorbidities of the syndrome.

Modern management strategies for children with Down syndrome should be based on multidisciplinary and personalized approaches. Regular assessment of vitamin D status, micronutrient balance, thyroid function, metabolic parameters, and immune status is essential for early identification of abnormalities and prevention of long-term complications. Timely correction of nutritional deficiencies and endocrine disturbances, combined with individualized rehabilitation and preventive care, may improve physical development, neurocognitive outcomes, immune function, and overall quality of life in children with Down syndrome.

Conclusion: Children with Down syndrome are characterized by significant clinical-metabolic and immuno-endocrine disturbances, including vitamin D deficiency, micronutrient imbalance, immune dysregulation, and endocrine disorders. These abnormalities are closely interconnected and contribute to the pathogenetic basis of associated comorbidities. Modern management strategies should focus on early detection and personalized correction of these disturbances in order to improve the effectiveness of preventive and therapeutic interventions.

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