THE INFLUENCE OF GUT MICROBIOTA ON THE IMMUNE STATUS OF FREQUENTLY ILL CHILDREN

Rabbimova Dilfuza Toshtemirovna - Doctor of Medical Sciences, Associate Professor
Head of the Department of Propaedeutics of Childhood Diseases of the
Samarkand State Medical University.

Annotation. The gut microbiota plays a pivotal role in the development and modulation of the immune system, especially in early childhood. Frequently ill children (FIC) are a vulnerable group characterized by recurrent infections, often associated with microbial imbalance (dysbiosis). This review highlights the current understanding of gut microbiota composition in FIC, its relationship with immune deficiencies, and the therapeutic potential of microbiota-targeted interventions such as probiotics, prebiotics, and dietary modification. The findings suggest that restoring microbial homeostasis may significantly improve immune responses and reduce the frequency of infections in children.

Keywords: gut microbiota, immune system, frequently ill children, dysbiosis, probiotics, immunity modulation

Introduction. In recent decades, the role of the gut microbiota in shaping the immune system has garnered growing scientific interest. The intestinal microflora consists of a complex ecosystem of bacteria, viruses, fungi, and archaea that interact with host physiology and immune defense mechanisms [1]. The term "frequently ill children" (FIC) refers to pediatric patients with ecurrent respiratory

and/or gastrointestinal infections, often due to compromised mucosal immunity and microbial dysbiosis [2].

Gut microbiota and immune development. The colonization of the infant gut begins at birth and is influenced by delivery mode, feeding practices, antibiotic exposure, and environmental factors [3]. Commensal microorganisms educate immune cells, especially T-regulatory cells, and help maintain a balance between pro-inflammatory and anti-inflammatory responses [4]. An altered microbiota may impair the development of mucosal immunity, increasing susceptibility to infections [5]. The initial colonization of the gut is a critical window for immune system programming. This process begins at birth, with significant differences noted between vaginally delivered infants—who acquire microbiota resembling maternal vaginal flora—and those born via cesarean section, who tend to harbor skin and environmental bacteria [3]. Breastfeeding further promotes the dominance of *Bifidobacterium* species, which have immunomodulatory properties and contribute to the development of gut barrier integrity [4].

The gut microbiota influences both innate and adaptive immunity. Commensal microorganisms interact with epithelial cells and dendritic cells via pattern recognition receptors such as Toll-like receptors (TLRs), leading to the maturation of immune cells and the secretion of cytokines that shape immune tolerance [1, 4]. For instance, regulatory T cells (Tregs), essential for preventing autoimmunity and controlling inflammation, are induced in the presence of short-chain fatty acids (SCFAs) produced by microbial fermentation of dietary fibers [3].

Moreover, microbial exposure during the first year of life establishes a balance between T-helper 1 (Th1) and T-helper 2 (Th2) responses. An imbalance in this developmental process has been linked to an increased risk of allergic

diseases and immune dysregulation later in life [5]. Tamburini et al. emphasize that early-life disruptions in microbial colonization, such as through antibiotic use, may alter immune maturation and predispose children to frequent infections [3].

The gut-associated lymphoid tissue (GALT), the largest immune organ in the body, is continually educated by microbial antigens, which helps fine-tune immune responses. Children with well-developed and diverse microbiota show stronger secretory IgA production, efficient mucosal defense, and more balanced cytokine profiles compared to those with altered microbial patterns [1, 4].

Dysbiosis in Frequently Ill Children. Studies have demonstrated that FIC often exhibit reduced diversity of gut microbiota, with a predominance of pathogenic species such as *Escherichia coli* and *Clostridium perfringens*, and a deficiency in beneficial bacteria like *Bifidobacterium* and *Lactobacillus* spp. [6]. This dysbiosis correlates with increased levels of inflammatory cytokines (e.g., IL-6, TNF-α) and reduced secretory IgA, suggesting impaired mucosal defense [7].

Dysbiosis is defined as a pathological alteration in the composition and function of the gut microbiota. Frequently ill children (FIC) often exhibit significant dysbiosis, characterized by reduced microbial diversity, a decreased presence of beneficial anaerobes, and an overgrowth of facultative pathogens [2, 6]. Studies by Shenderov and Manzoni et al. indicate that this microbial imbalance correlates with heightened mucosal permeability and impaired immune barrier functions [2, 6]. In FIC, there is typically a depletion of beneficial genera such as *Bifidobacterium* and *Lactobacillus*, which are known to stimulate anti-inflammatory cytokines (e.g., IL-10) and enhance mucosal immunity through IgA production [6, 9]. Concurrently, there is an increase in opportunistic organisms like *Clostridium perfringens* and *Escherichia coli*, hich produce endotoxins and stimulate excessive pro-inflammatory responses, notably IL-6 and TNF-α [7].

This dysbiotic state contributes to a chronic low-grade inflammatory environment in the gut, leading to impaired systemic immunity. Elevated levels of circulating endotoxins (lipopolysaccharides, LPS) from gram-negative bacteria can further disrupt the gut–brain and gut–lung axes, resulting in increased susceptibility to respiratory and gastrointestinal infections [6, 7].

Emerging data also suggest that dysbiosis in FIC is associated with altered metabolic profiles in the gut, including reduced levels of SCFAs such as butyrate and propionate, which are key regulators of epithelial integrity and immune signaling [1, 3]. These alterations further exacerbate immune dysfunction and reinforce a cycle of infection and immune exhaustion. Thus, understanding the mechanisms by which dysbiosis undermines immune competence in FIC is essential for developing effective microbiota-based therapies and preventive strategies.

Therapeutic Modulation of Microbiota. Probiotic and prebiotic supplementation has shown promise in restoring microbial balance and enhancing immune function in FIC [8]. For instance, *Lactobacillus rhamnosus GG* and *Bifidobacterium lactis* have been reported to reduce the frequency and severity of infections [9]. Moreover, diet rich in fiber, omega-3 fatty acids, and fermented foods supports the growth of beneficial microbiota [10].

Conclusion. The gut microbiota is a crucial determinant of immune function in frequently ill children. Dysbiosis contributes to immunodeficiency and recurrent infections. Targeted strategies to restore microbial homeostasis hold therapeutic potential and should be integrated into pediatric care protocols. Further research is needed to identify microbiota-based biomarkers and optimize treatment approaches.

References

1. Belkaid Y., Hand T.W. Role of the microbiota in immunity and inflammation. *Cell*. 2014;157(1):121–141.
2. M
3. T
4. G
5. A
6. Shendero et al. How bacterial (symbiotic) microbiota therapy in early life shapes the future of
7. Fujimura K.E. et al. Role of the gut microbiota in defining human health. *Expert Rev Anti Infect Ther*. 2010;8(4):435–454.
8. Ouwehand A.C. et al. Probiotic and other functional microbes: from markets to mechanisms. *Curr Opin Biotechnol*. 2002;13(5):483–487.
9. Kukkonen K. et al. Probiotics and prebiotic galacto-oligosaccharides in the prevention of allergic diseases: a randomized, double-blind, placebo-
10. Singh R.K. et al. Influence of diet on the gut microbiome and implications for human health. *J Transl Med*. 2017;15:73.

al. Early infancy microbial and metabolic alterations affect risk of

2016;352(6285):539–544.