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THE IMPACT OF EARLY-LIFE GUT MICROBIOTA ON IMMUNE-MEDIATED DISEASES IN CHILDREN – A REVIEW ARTICLE

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ABSTRACT

Background: The gut microbiota plays a crucial role in immune system development, particularly during early life. Increasing evidence suggests its involvement in the pathogenesis of immune-mediated diseases in children.
Objective: This review aims to summarize current knowledge on the relationship between early-life gut microbiota composition and the risk of developing asthma, allergic diseases, and Crohn's disease.
Methods: A comprehensive literature review was conducted using PubMed and Google Scholar databases. Keywords included "gut microbiota", "children", "asthma", "allergy", "Crohn disease", and "dysbiosis". Recent clinical studies, systematic reviews, and meta-analyses focusing on pediatric populations were included.
Results: Early-life factors such as delivery mode, feeding practices, and antibiotic exposure significantly influence gut microbiota composition. Reduced microbial diversity and dysbiosis were consistently associated with increased risk of asthma, allergies, and inflammatory bowel diseases. Specific bacterial taxa, including reduced Bifidobacterium and increased Proteobacteria, were linked to disease development. Microbial metabolites, particularly short-chain fatty acids, were identified as key modulators of immune responses.
Conclusions: Early-life gut microbiota plays a fundamental role in immune programming. Its disruption may increase the risk of immune-mediated diseases. Modulation of microbiota through diet, probiotics, and rational antibiotic use represents a promising preventive and therapeutic strategy.

KEYWORDS

Gut Microbiota, Children, Allergies, Asthma, Crohn's Disease, Dysbiosis

CITATION

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1. Introduction

The gut microbiota constitutes a complex ecosystem of microorganisms that plays a fundamental role in shaping the immune system, particularly during early life. Gut colonization begins during the perinatal period and is influenced by numerous factors, including the mode of delivery, diet, and exposure to antibiotics. Disruptions in the composition of the gut microbiota, referred to as dysbiosis, may impair immune regulation.

An increasing number of studies indicate a relationship between gut microbiota and the development of immune-mediated diseases in children, including allergic diseases, asthma, and inflammatory bowel diseases such as Crohn's disease. These mechanisms involve modulation of inflammatory responses, effects on regulatory T cells, and the maintenance of intestinal barrier integrity.

2. Methodology

This study is a structured narrative review of the current literature on the role of the gut microbiota in the development of immune-mediated diseases in children, including asthma, allergic diseases, and Crohn's disease.

A comprehensive search of the scientific literature was conducted using the PubMed and Google Scholar databases. The search strategy included combinations of the following keywords: "gut microbiota", "infant microbiome", "children", "asthma", "allergy", "atopic disease", "Crohn's disease", "inflammatory bowel disease", and "dysbiosis".

The review included peer-reviewed original research articles, systematic reviews, and meta-analyses published in English. Studies focusing on pediatric populations and early-life microbiota development were prioritized to ensure relevance to the topic. In addition, selected animal studies were included when they provided mechanistic insights into host–microbiota interactions and immune system development.

No strict time limits were applied; however, priority was given to recent publications to reflect the most up-to-date scientific evidence. Studies were selected based on their relevance to the topic, scientific quality, and contribution to understanding the relationship between gut microbiota and immune-mediated diseases.

Exclusion criteria included non-peer-reviewed articles, studies with insufficient methodological description, and publications not directly related to gut microbiota or immune-mediated diseases in humans.

Data extraction was performed qualitatively. The findings were synthesized narratively, focusing on consistent patterns, biological mechanisms, and clinically relevant associations reported across studies.

This review does not follow a systematic review protocol and no statistical meta-analysis was performed.

3. Development of gut microbiota in children

3.1 Prenatal period

For many years, it was believed that a healthy newborn is sterile and the intrauterine environment is also physiologically sterile. However, contemporary research suggests the possibility that microorganisms of maternal origin may be present in amniotic fluid, fetal membranes, umbilical cord blood, and the placenta, without being directly associated with intrauterine infection or inflammation (Aagaard et al., 2014). These findings imply that colonization of the gastrointestinal tract may begin during the prenatal period. Moreover, the maternal gut microbiota may influence the fetus and contribute to long-term health outcomes (or disease) even before the first breath of the newborn.

In a study conducted by Aagaard et al., placental samples from 320 women were analyzed, revealing the presence of bacterial DNA with a profile resembling the oral microbiota (Aagaard et al., 2014). The authors suggested that bacteria may be transferred hematogenously from the maternal oral cavity to the placenta. In another study, Collado et al. examined samples of amniotic fluid, umbilical cord blood, and meconium ($n \approx 50$) and detected bacteria such as *Enterococcus and Staphylococcus*, indicating potential microbial exposure before birth (Collado et al., 2016).

However, more methodologically rigorous studies have challenged this hypothesis. In a study by de Goffau et al., which analyzed over 500 placental samples ($n = 537$) using advanced contamination control methods, the authors demonstrated that previously detected bacterial signals were most likely the result of laboratory contamination rather than true microbial presence (de Goffau et al., 2019). Similar conclusions have been reported in studies employing highly sensitive sequencing techniques, which indicate extremely low bacterial biomass in the intrauterine environment, often below reliable detection thresholds (de Goffau et al., 2019). Therefore, the prevailing view is that a stable prenatal microbiota likely does not exist, although the issue remains controversial.

Despite the lack of definitive evidence for the presence of live bacteria in the intrauterine environment, maternal factors appear to play an important role. An experimental study by Gomez de Agüero et al. demonstrated that metabolites derived from maternal microbiota can cross the placenta and influence fetal immune system development (Gomez de Agüero et al., 2016). Although this study was conducted in animal models, the findings suggest that bacterial-derived molecules may stimulate immune cell development before birth. Additionally, maternal diet and metabolic status influence gut microbiota composition, which may indirectly determine the subsequent colonization of the infant's gastrointestinal tract (Chu et al., 2016). Epidemiological studies have also shown that children born to mothers with obesity or gestational diabetes exhibit distinct microbiota profiles after birth, which may be relevant to the development of chronic diseases.

Although evidence supporting the existence of a prenatal microbiota remains limited and controversial, there are strong indications that the intrauterine environment is not entirely microbiologically neutral. Maternal factors and microbial metabolites may play a key role in so-called "immune programming" of the fetus and in preparing the infant's organism for postnatal microbial colonization.

3.2 The impact of mode of delivery on gut microbiota development

The mode of delivery is one of the most important factors determining the initial composition of the gut microbiota in newborns. This process is crucial subsequent microbiota and immune system development because the first microorganisms initiate a cascade of immunological responses and influence the development of immune tolerance. During vaginal delivery, the newborn is colonized primarily by microorganisms originating from the maternal vaginal and intestinal microbiota, including bacteria of the genus *Lactobacillus*. In contrast, infants delivered by cesarean section are colonized primarily by microorganisms from the surrounding environment as well as from maternal skin (Dominguez-Bello et al., 2010). It has been demonstrated that these differences may persist for an extended period and are associated with an increased risk of immune-mediated diseases such as allergies and asthma.

In a classic study by Dominguez-Bello et al., the microbiota of 9 mothers and their 10 newborns (6 vaginal deliveries, 4 cesarean sections) was analyzed, revealing significant differences in microbial composition already within the first hours of life (2010). Vaginally delivered infants were predominantly colonized by *Lactobacillus, Prevotella*, and *Sneathia*, whereas cesarean-delivered infants were mainly colonized by skin-associated bacteria such as *Staphylococcus, Corynebacterium*, and *Propionibacterium*. However, it should be noted that the study was conducted on a relatively small sample, which may limit the generalizability of the findings. In a larger cohort study involving 98 infants followed during their first year of life, differences in gut microbiota composition were shown to persist for several months, although they gradually diminished with age (Yatsunenko et al., 2012). The authors also observed that infants delivered by cesarean section exhibited lower microbial diversity in early life ($p < 0.01$), which may have implications for immune system development.

Epidemiological studies further support the impact of delivery mode on microbiota development. A meta-analysis including over 20,000 children demonstrated that cesarean section is associated with an increased risk of allergic diseases, including asthma (OR ≈ 1.2–1.3) (Sevelsted et al., 2015). This effect is thought to result from the lack of exposure to maternal vaginal microbiota and delayed colonization by beneficial bacteria. An important issue is also the attempt to "restore" natural colonization in cesarean-delivered infants, for example through vaginal seeding. However, current evidence is limited and does not allow for a clear assessment of the safety and efficacy of this approach (Cunnington 2016).

Although some studies suggest that the influence of delivery mode on microbiota composition may diminish over time due to diet, environmental factors, and other influences, the first months of life represent a critical window for immune system development (Yatsunenko et al., 2012). Therefore, early differences in microbial colonization may have long-term health consequences.

3.3 The impact of infant feeding on gut microbiota development

Infant feeding practices play a key role in shaping the composition and function of the gut microbiota during early life. Breastfeeding, in particular, is considered highly beneficial, as it provides not only essential nutrients but also a wide range of bioactive components, including immunoglobulins and human milk oligosaccharides (HMOs), which promote the growth of commensal bacteria (Bode, 2012).

Observational studies conducted during the first year of life have demonstrated substantial differences in gut microbiota composition between breastfed and formula-fed infants (Yatsunenko et al., 2012). In breastfed infants, bacteria of the genus *Bifidobacterium* tend to dominate, whereas formula-fed infants exhibit

greater microbial diversity, including the presence of potentially pathogenic species such as *Clostridium difficile, Granulicatella adiacens, Citrobacter spp., Enterobacter cloacae*, and *Bilophila wadsworthia* ($p < 0.01$). Similar findings were reported in a cohort study by Pannaraj et al., which demonstrated that breast milk itself may represent a major source of microorganisms colonizing the infant gut (Pannaraj et al., 2017). It has been estimated that up to 30% of an infant's gut microbiota may originate directly from breast milk.

Human milk oligosaccharides also function as prebiotics, selectively stimulating the growth of beneficial bacteria, particularly *Bifidobacterium* (Koh et al., 2016). These bacteria are associated with the production of short-chain fatty acids (SCFAs), which exert anti-inflammatory effects and contribute to the development of the intestinal barrier.

The importance of infant feeding is further supported by long-term studies. In an analysis involving more than 1,000 children, shorter duration of breastfeeding was associated with an increased risk of allergic diseases and obesity later in life (OR ≈ 1.3–1.5) (Victora et al., 2016).

In summary, breastfeeding promotes the development of a beneficial and stable gut microbiota that supports immune system maturation. Differences associated with feeding practices may have long-term health consequences.

3.4 The impact of antibiotics on gut microbiota

Antibiotics are among the most significant factors affecting gut microbiota composition, particularly during early childhood, when the microbiome is still developing. Although their primary function is the elimination of pathogenic bacteria, antibiotics also affect commensal microorganisms, leading to a reduction in their abundance and a decrease in overall microbial diversity (Cox & Blaser, 2015).

A review by Cox and Blaser highlighted that even short-term antibiotic use may lead to long-lasting alterations in gut microbiota composition, persisting for months or even years (2015).

Experimental studies have demonstrated that antibiotic treatment results in a reduction of *Bifidobacterium* and *Lactobacillus*, accompanied by an increase in opportunistic bacteria.

These findings are supported by the study conducted by Penders et al., which included over 1000 infants and showed that early-life antibiotic exposure was associated with reduced microbial diversity and increased colonization by potentially pathogenic bacteria ($p < 0.01$) (Penders et al., 2006).

A large cohort study involving more than 11,000 children demonstrated that antibiotic exposure during infancy is associated with an increased risk of developing allergic diseases later in life (RR = 1.2–1.5) (Metsälä et al., 2015). This effect was particularly pronounced in cases of repeated antibiotic use.

Antibiotics also influence the metabolic activity of the gut microbiota, leading to reduced production of short-chain fatty acids, which play a key role in immune regulation (Arrieta et al., 2015). These alterations may contribute to chronic inflammation and increase the risk of metabolic and immune-mediated diseases.

It should be emphasized that the impact of antibiotics depends on several factors, including the type of drug, duration of treatment, and the age at which exposure occurs. However, early-life exposure appears to be of particular clinical importance, as the microbiota is most vulnerable during this period.

4. Immune-mediated diseases associated with gut microbiota

4.1 Asthma

Asthma is one of the most common chronic respiratory diseases in children and is characterized by persistent airway inflammation and bronchial hyperresponsiveness. Its etiology is multifactorial, involving both genetic predisposition and environmental influences. In recent years, increasing attention has been given to the role of gut microbiota as a key factor modulating the risk of asthma development. Early life appears to be particularly critical, as both the microbiota and the immune system undergo rapid development during this period.

One of the most significant studies in this field is a prospective cohort study analyzing gut microbiota composition in infants during the first 100 days of life and its association with later clinical outcomes. The study demonstrated that reduced abundance of *Bifidobacterium, Faecalibacterium, Lachnospira,* and *Veillonella* was associated with an increased risk of developing asthma later in childhood (Arrieta et al., 2015). Importantly, these differences were observed before the onset of clinical symptoms. The authors also performed metabolomic analyses, showing that infants with altered microbiota exhibited reduced levels of short-chain fatty acids, suggesting functional disturbances.

Another cohort study demonstrated that early colonization of the gastrointestinal tract by *Clostridium difficile* is associated with an increased risk of wheezing and asthma development (Penders et al., 2006). This finding suggests that certain microbial species may serve as markers of dysbiosis.

Antibiotic use is another important factor influencing microbiota composition. Studies suggest that antibiotic therapy may reduce microbial diversity and stability, thereby increasing the risk of asthma and other immune-mediated diseases (Korpela et al., 2016). This effect is particularly evident in cases of repeated antibiotic exposure during the first year of life. It has also been shown that macrolide use in children aged 2–7 years (n = 142) is associated with long-term alterations in gut microbiota composition and metabolic function. These changes included a decrease in *Actinobacteria*, an increase in *Bacteroides* and *Proteobacteria*, and increased macrolide resistance. In contrast, penicillins were found to have a less pronounced impact.

Microbiota metabolites also have a significant impact on the development of the immune system. Trompette et al. observed that a diet rich in fermentable fiber increases the production of short-chain fatty acids (SCFA) in the intestine, which has a protective effect against the development of allergic respiratory diseases (Trompette et al., 2014). The study involved mice. The first group was fed a diet rich in fermentable fiber, while the second group was fed a low-fiber diet. The animals fed the high-fiber diet had increased levels of circulating SCFAs, thus protecting them from the development of allergic inflammation in the lungs. In contrast, the second group had significantly lower SCFA concentrations, which had implications for an increased risk of developing allergic respiratory diseases. This mechanism is based on the influence of SCFAs on bone marrow hematopoiesis, characterized by an impaired ability to promote Th2 cell effector function, ultimately reducing the incidence of allergic reactions in the lungs. These findings support the existence of the gut-lung axis. These results suggest that not only the composition of the microbiota but also its metabolic activity plays a role in the risk of developing asthma.

Environmental factors also play a significant role. The PARSIFAL (*Prevention of Allergy-Risk Factors for Sensitization in Children Related to Farming and Anthroposophic Lifestyle*) and GABRIELA (*Multidisciplinary Study to Identify the Genetic and Environmental Causes of Asthma in the European Community Advanced Study*) studies demonstrated that children growing up in rural environments, with greater exposure to diverse microorganisms, have a lower risk of developing asthma, which is associated with greater diversity of their gut microbiota (Ege et al., 2011). These observations support the so-called hygiene hypothesis, which claims that excessively sterile living conditions in developed countries, limited contact with microorganisms, and excessive hygiene in childhood lead to an increase in the incidence of allergies and autoimmune diseases. A young child's immune system requires stimulation from bacteria, viruses, and parasites; insufficient microbial stimulation may predispose the immune system to exaggerated responses to otherwise harmless antigens (predisposing to the development of allergies) or erroneously (increasing the likelihood of autoimmune diseases). This is because the fetal immune system is primarily dominated by Th2 lymphocytes, and only postnatal exposure to microorganisms activates the development of Th1 lymphocytes, which balances the immune response.

In summary, numerous studies indicate that the gut microbiota plays a significant role in shaping the risk of developing asthma in children. Disturbances in its composition and function early in life may precede the onset of clinical symptoms and constitute a significant predictor of the disease. A better understanding of these relationships could contribute to the development of effective preventive strategies.

4.2 Allergic diseases

Allergic diseases, including food allergies, atopic dermatitis, and allergic rhinitis, represent a significant health burden in pediatric populations. Their prevalence has increased markedly in recent decades, which is attributed to both environmental changes and lifestyle factors. In recent years, growing attention has been paid to the role of gut microbiota as a key factor influencing immune system development during early life. Early gut colonization plays a fundamental role in immune "programming," and disruptions in this process may promote the persistence of pro-allergic immune responses.

One of the most important studies in this field is the work by Fujimura et al. (2016), which analyzed gut microbiota composition in infants and its association with the development of multisensitized atopy later in life. The study demonstrated that infants who developed atopic sensitization exhibited distinct microbial profiles as early as the first months of life. Notably, these infants showed reduced abundance of *Bifidobacterium, Akkermansia,* and *Faecalibacterium*, along with increased relative abundance of certain fungi, including *Candida* and *Rhodotorula*. Additionally, they exhibited a distinct fecal metabolomic profile enriched in pro-inflammatory metabolites. The authors also reported differences in T-cell maturation, suggesting a

direct link between gut microbiota and immune system development. These findings suggest that microbiota composition may serve as an early biomarker of allergy risk.

Another important study by Abrahamsson et al. (2012) evaluated gut microbiota diversity in relation to the development of atopic dermatitis. The authors demonstrated that infants who later developed the disease exhibited significantly lower microbial diversity at an early stage of life. Importantly, these differences preceded the onset of clinical symptoms and persisted over time. These findings suggest that reduced microbial diversity may impair the ability of the immune system to appropriately recognize and tolerate antigens, thereby promoting allergic responses. It is also worth noting that attempts have been made to reverse dysbiosis through probiotic supplementation. However, studies have shown that supplementation with *Lactobacillus reuteri* ATCC 55730 from the perinatal period to the first year of life did not reduce the prevalence of allergic diseases at school age (7 years), despite beneficial effects observed in infancy.

The previously mentioned study by Penders et al. (2006) provides important conclusions, analyzing the influence of specific microorganisms on the development of atopy. The presence of *Clostridium difficile* in early life has been shown to be associated with an increased risk of allergic symptoms. It has been suggested that this bacterium may affect the immune system by inducing inflammation and disrupting the gut microbial balance. In contrast, the presence of bacteria from the *Bifidobacterium* genus was associated with a protective effect, further emphasizing the importance of maintaining a healthy gut microbiota balance (Penders et al. 2006).

These observations are complemented by studies on the metabolic function of the microbiota. Metabolites produced by intestinal bacteria, particularly short-chain fatty acids, play a key role in regulating the immune response. Reduced production of these metabolites is associated with increased allergic reactions and increased susceptibility to atopic diseases. It has also been emphasized that a diet that influences the composition of the microbiota may indirectly modulate the risk of allergy by influencing the synthesis of these metabolites (Trompette et al., 2014).

The above data highlight the crucial role of the intestinal microbiota in the development of atopic diseases in children. Early disturbances in its composition, including reduced diversity and a deficiency of protective bacteria, are of paramount importance. At the same time, the presence of pro-inflammatory microorganisms and impaired metabolic functions of the microbiota may increase the risk of developing allergies. These findings suggest that the microbiota may serve as both a risk marker and a potential target for future preventive interventions.

4.3 Crohn's disease

Crohn's disease is a chronic inflammatory bowel disease with a multifactorial etiology. Its pathogenesis involves complex interactions between genetic, environmental, and microbial factors. In recent years, increasing evidence suggests that dysbiosis may not only accompany the disease but may also precede the onset of clinical symptoms.

One of the most consistently reported findings is reduced gut microbiota diversity in patients with Crohn's disease. Metagenomic studies have shown that microbial communities in these patients exhibit not only decreased diversity but also altered functional capacity (Kostic et al. 2014). This indicates that dysbiosis affects not only microbial composition but also metabolic activity, which is crucial for maintaining intestinal homeostasis.

A deficiency in anti-inflammatory bacteria also has a fundamental impact. A reduced abundance of bacteria belonging to the dominant *Firmicutes* phylum is a characteristic feature of dysbiosis in patients with Crohn's disease (Sokol et al., 2008). The composition of the intestinal microbiome associated with the mucosa of patients with CD exacerbation was analyzed at the time of surgical resection and 6 months later using FISH methods. A reduced abundance of one of the major representatives of the *Firmicutes* phylum, *Faecalibacterium prausnitzii,* was found to be associated with an increased risk of CD recurrence in the ileum after surgery. The anti-inflammatory activity of *F. prausnitzii* in mouse colitis was analyzed both in vitro (cellular models) and in vivo [after induction with 2,4,6-trinitrobenzenesulfonic acid (TNBS)] to assess the immunomodulatory properties of these bacteria. Stimulation of peripheral blood mononuclear cells with F. prausnitzii led to a significant reduction in IL-12 and IFN-gamma production and increased IL-10 secretion. Furthermore, oral administration of *F. prausnitzii* reduced the severity of colitis and restored microbiota balance disrupted by TNBS. The anti-inflammatory effects of *F. prausnitzii* are attributed to the short-chain fatty acids it produces, including butyrate, which blocks NF-κB activation and IL-8 production. In this way, these bacteria influence the proper regulation of the immune response and maintain intestinal barrier integrity.

These results suggest that modulating gut microbiota composition using *F. prausnitzii* as a probiotic may be a promising strategy for the future treatment of this condition.

At the same time, an increased presence of potentially pathogenic bacteria, particularly from the *Proteobacteria phylum*, is observed (Shin et al. 2015). An increase in their numbers is considered one of the most characteristic markers of intestinal dysbiosis and is often observed in inflammatory bowel diseases. Bacteria belonging to this group, including adherent-invasive *Escherichia coli* (AIEC), demonstrate the ability to adhere to and penetrate intestinal epithelial cells, which can lead to direct damage to the intestinal barrier. Furthermore, these microorganisms produce lipopolysaccharides (LPS), which are potent stimulators of the immune response. Excessive exposure to LPS leads to the activation of Toll-like receptors (TLRs), particularly TLR4, resulting in increased production of proinflammatory cytokines and the maintenance of chronic inflammation. Under normal conditions, the intestinal microbiota remains in balance, but an increased proportion of *Proteobacteria* can disrupt this homeostasis and promote the dominance of inflammatory processes. Research also emphasizes that the increased presence of this type of bacteria is not merely a consequence of inflammation but may actively contribute to its maintenance. Their excess has been shown to correlate with the severity of clinical symptoms and disease activity, suggesting their potential role as a biomarker of inflammatory progression. Furthermore, bacteria from the *Proteobacteria* phylum are characterized by a greater ability to adapt to an inflamed environment, providing them with a competitive advantage over commensal bacteria. As a result, dysbiosis further deepens, creating a vicious cycle in which inflammation promotes the growth of pro-inflammatory bacteria, which in turn exacerbate the inflammatory process.

These observations are complemented by functional analyses of the microbiota, which have shown that patients with Crohn's disease experience disturbances in the metabolic activity of intestinal microorganisms (Franzosa et al., 2019). Unlike traditional studies that only assess the composition of the microbiota, these analyses allow for the assessment of its actual biological function, including the ability to produce metabolites that affect the host. It has been shown that the microbiota of patients with Crohn's disease is characterized by a reduced ability to synthesize short-chain fatty acids, such as butyrate, propionate, and acetate. These metabolites play a key role in maintaining the integrity of the intestinal barrier by supporting epithelial cell function and stimulating mucus production. Their deficiency leads to increased intestinal permeability, which allows bacterial antigens to penetrate deeper layers of the intestinal wall and activate the immune system. Additionally, disturbances in the metabolism of amino acids and bile acids, which also play a significant role in regulating the immune response, have been observed. These changes may lead to exacerbation of inflammatory processes by modulating immune cell activity and affecting the intestinal environment. Studies also highlight the increased expression of metabolic pathways associated with oxidative stress and inflammation in patients with Crohn's disease. This suggests that the microbiota adapts to the inflammatory intestinal environment, but it can also perpetuate the inflammatory process. An important conclusion from these analyses is that functional disruptions of the microbiota can be as significant, or even more significant, than changes in its composition. Even with a relatively similar bacterial composition, differences in metabolic activity can lead to distinct biological effects. In the context of Crohn's disease, this indicates that microbiota assessment should include both compositional and functional analyses.

5. Discussion

The findings of this review highlight the critical role of early-life gut microbiota in shaping immune responses and susceptibility to chronic diseases. The consistency of results across multiple studies suggests that dysbiosis is not only a consequence but also a potential contributing factor in disease development.

One of the key observations is the importance of microbial diversity. Reduced diversity appears to impair immune tolerance and promote inflammatory responses. Additionally, the role of microbial metabolites, particularly short-chain fatty acids, emphasizes that not only composition but also functionality of the microbiota is essential.

Environmental and lifestyle factors, including delivery mode, diet, and antibiotic use, were identified as major modulators of microbiota composition. These findings support the concept of early-life intervention as a potential strategy for disease prevention.

However, the majority of studies are observational, limiting the ability to establish causality. Variability in study design, population size, and analytical methods also complicates direct comparisons.

Future research should focus on longitudinal studies and controlled clinical trials to better understand causal relationships and to develop targeted microbiota-based therapies.

6. Conclusions

The findings presented in this review clearly indicate that the gut microbiota plays a crucial role in shaping immune responses in children. Early life represents a critical window for immune system development, during which even subtle disturbances in microbiota composition may have long-lasting health consequences.

The available evidence consistently demonstrates that reduced microbial diversity is associated with an increased risk of immune-mediated diseases, including asthma, allergic disorders, and Crohn's disease. At the same time, differences in the role of specific microorganisms reflect the use of diverse methodological approaches, such as 16S rRNA sequencing and metagenomic analyses.

In the case of asthma, particular attention has been given to the gut–lung axis and the role of microbial metabolites such as short-chain fatty acids. Their deficiency may impair immune regulation and increase susceptibility to allergic diseases. Similar mechanisms are observed in allergies, where the balance between Th1 and Th2 responses is critical.

In Crohn's disease, both compositional and functional alterations of the microbiota are of major importance. Disruption of microbial metabolism and expansion of pro-inflammatory bacteria contribute to chronic inflammation and intestinal barrier dysfunction.

However, it should be noted that most available studies are observational in nature, which limits the ability to establish causal relationships. Additionally, many studies are based on relatively small sample sizes or animal models.

Despite these limitations, the gut microbiota represents a promising target for future preventive and therapeutic strategies. In particular, modulation of the microbiota through diet, probiotics, and more judicious antibiotic use may play an important role in preventing immune-mediated diseases in children. Future research should focus on well-designed longitudinal and interventional studies to better understand causal mechanisms and to develop personalized microbiota-based therapies in pediatric populations.

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