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PRACA POGLĄDOWA
REVIEW

Gastrointestinal disorders associated with gut microbiota dysbiosis in children aged 0–3 years

Dysfunkcje przewodu pokarmowego powstałe w wyniku zaburzeń mikrobiomu jelitowego u dzieci w wieku 0–3 lat

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ABSTRACT

The gut microbiota plays a pivotal role in gastrointestinal and systemic health. Early childhood (0–3 years) is a critical period for microbiota development and disturbances during this time may result in functional gastrointestinal disorders such as colic, gastroesophageal reflux, and constipation and may increase the risk of chronic diseases later in life. This review analyzes the current evidence on factors which shape the gut microbiota, including mode of delivery, feeding practices, antibiotic exposure, diet, and stress. Diagnostic methods such as stool analysis, DNA microbiota testing, and the Organix Gastro test are discussed, along with preventive and therapeutic approaches. Gut dysbiosis in children aged 0–3 years is strongly associated with gastrointestinal dysfunction and may predispose the patient to allergies, autoimmune disorders, and metabolic diseases. Vaginal delivery, breastfeeding, and avoiding unnecessary antibiotic therapy have a protective role. Preventive and therapeutic strategies include probiotics, prebiotics, synbiotics, fiber-rich diets, and behavioral as well as environmental interventions. Early diagnosis and targeted interventions can significantly improve gastrointestinal health in young children and reduce the risk of long-term complications. An integrated approach combining microbiota diagnostics, nutritional management, supplementation, and parental education is essential for effective prevention and treatment.

KEYWORDS

probiotics, infants, prebiotics, synbiotics, dysbiosis, gut microbiota, functional gastrointestinal disorders

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STRESZCZENIE

Mikrobiota jelitowa odgrywa kluczową rolę w utrzymaniu zdrowia przewodu pokarmowego i całego organizmu. Wczesne dzieciństwo (0–3 lat) to okres krytyczny dla rozwoju mikroflory, której zaburzenia mogą prowadzić do dysfunkcji, takich jak kolki niemowlęce, refluks żołądkowo-przełykowy i zaparcia, a także zwiększać ryzyko rozwoju chorób przewlekłych w późniejszym życiu. W niniejszym przeglądzie analizie poddano aktualne piśmiennictwo dotyczące czynników determinujących rozwój mikrobioty, w tym sposób porodu, rodzaj karmienia, antybiotykoterapię, dietę oraz stres. Uwzględniono także metody diagnostyczne, takie jak analiza kału, testy DNA mikrobioty oraz badanie Organix Gastro, a także strategie terapeutyczne i profilaktyczne. Dysbioza jelitowa u dzieci w wieku 0–3 lat jest ściśle związana z zaburzeniami czynnościowymi przewodu pokarmowego i może prowadzić do poważniejszych konsekwencji zdrowotnych, w tym alergii, chorób autoimmunologicznych i zaburzeń metabolicznych. Istotnym czynnikiem ochronnym pozostaje poród drogą naturalną, karmienie piersią oraz ograniczenie nieuzasadnionej antybiotykoterapii. Skuteczne strategie terapeutyczne obejmują stosowanie probiotyków, prebiotyków, synbiotyków, dietę bogatą w błonnik oraz interwencje behawioralne i środowiskowe. Wczesna diagnostyka i ukierunkowane interwencje mogą poprawić zdrowie przewodu pokarmowego u dzieci i zmniejszyć ryzyko powikłań w przyszłości. Kompleksowe podejście, łączące diagnostykę mikrobioty, postępowanie dietetyczne oraz edukację rodziców, stanowi fundament skutecznej profilaktyki i terapii.

SŁOWA KLUCZOWE

probiotyki, niemowlęta, prebiotyki, synbiotyki, dysbioza, mikrobiota jelitowa, zaburzenia czynnościowe przewodu pokarmowego

Introduction

The gut microbiota, a complex community of microorganisms inhabiting the intestines, plays a fundamental role not only in the functioning of the gastrointestinal tract, but also in the overall physiology of the host. The terms “microbiota” and “microbiome” are frequently used interchangeably in the literature, although they refer to distinct but related concepts. According to recent literature [1,2], the term “microbiota” describes the community of living microorganisms – bacteria, viruses, fungi, and archaea – that inhabit a specific ecological niche, such as the human intestine [1,2]. In contrast, the “microbiome” refers to the collective genomes, genes, and metabolic activities of those microorganisms, as well as their interactions with each other and with the host organism. In other words, the microbiome represents the functional and genetic dimension of the microbiota. Recognizing this distinction is crucial, as most studies on pediatric gastrointestinal health refer primarily to the composition and diversity of the gut microbiota, whereas the microbiome encompasses its broader molecular and ecological context. The relationship between the host and the microorganisms colonizing the gastrointestinal tract is the result of a long and complex co-evolutionary process [3]. The host provides a stable habitat and protection from external environments and pathogenic microbes, while the microbiota produces bioactive compounds that influence both the digestive and immune systems [4,5]. The entire microbiome forms a dynamic ecosystem that supports digestive processes, nutrient metabolism, and defense against harmful microorganisms.

In addition to its role in digestion, the gut microbiota provides a protective function, acting as the first line of defense against pathogens. Through competition for space and nutrients, as well as the production of antimicrobial compounds, it limits the proliferation of potentially harmful microorganisms. Moreover, it influences the immune system by supporting the maturation of immune cells and regulating inflammatory responses, which is crucial for maintaining systemic homeostasis [6]. Certain microorganisms, such as *Bifidobacterium* and *Faecalibacterium prausnitzii* [7], are considered beneficial to health, although evidence supporting this remains inconclusive. At the same time, the gut community also harbors microbes capable of exerting detrimental effects due to their metabolic activity or pathogenic potential [8].

The balance of the microbiota, known as eubiosis, is essential for health. Disruptions in its composition – referred to as dysbiosis – can lead to a wide range of health issues, including gastrointestinal disorders, metabolic disturbances, and inflammatory diseases. Therefore, the gut microbiota is not only a key component of gastrointestinal function, but also a significant area of research in the field of human health.

Critical role of gut microbiota established during early childhood

The development of the human gut microbiota during early life has a lasting impact on the host and disturbances in this process have been associated with health outcomes later in life [9]. Studies have demonstrated that alterations in the gut microbiota during early infancy are linked to the risk of developing childhood obesity [10], type 1 diabetes [11], non-alcoholic fatty liver disease [12], asthma [13], and allergies [14]. Infancy is a period of intense intestinal colonization by microorganisms that influence immune system development, metabolism, and gastrointestinal tract maturation. This process begins at birth, when the infant is first exposed to maternal microorganisms, and continues under

the influence of their environment, feeding practices, and their parents' health. Several early-life factors can affect the development of gut microbiota, including the mode of delivery (cesarean section vs. vaginal birth), maternal antibiotic use, breastfeeding, formula or mixed feeding, and early cessation of breastfeeding [15,16,17,18,19,20,21]. To date, relatively few studies have explored the developmental trajectories of gut microbiota during early life.

Aberrant microbiota development – resulting from premature birth, exposure to antibiotics, or a lack of breastfeeding, for example – may lead to dysbiosis. Therefore, supporting the development of the gut microbiota in early life is crucial. This can be achieved through appropriate nutrition, avoiding unnecessary antibiotic treatment, and promoting natural gut colonization. Early interventions may provide a strong foundation for lifelong health. Given the growing recognition of the microbiome's role in human development, recent perspectives suggest that microorganisms may serve as biological indicators of postnatal development [22].

Prevalence of gastrointestinal dysfunction in children aged 0–3 years

Functional gastrointestinal disorders (FGIDs) are common among infants and young children, posing a significant challenge for both parents and pediatricians. The most prevalent FGIDs in this age group include infantile colic, gastroesophageal reflux disease, and functional constipation.

Infantile colic is characterized by episodes of inconsolable crying and distress in otherwise healthy infants. Epidemiological studies indicate that colic affects between 5% and 40% of infants, depending on the diagnostic criteria and population being studied. A systematic review by Lucassen et al. [23] reported an average prevalence of approximately 20%. Colic is believed to be associated with the immaturity of the gastrointestinal system and gut microbiota. Colic is believed to be associated with the immaturity of the gastrointestinal system and gut microbiota.

Gastroesophageal reflux (GER) is characterized by the gastric contents flowing backward into the esophagus. It is estimated that around 50% of infants aged 0–3 months experience daily GER episodes, with this figure rising to 67% at 4 months of age. Most cases resolve spontaneously by 12 to 18 months of age [24]. Regurgitation and GER, resulting from the immaturity of the lower esophageal sphincter, are considered physiological in most infants. However, in some children, symptoms may persist and lead to complications.

Functional constipation is another common issue in this age group. Studies indicate that constipation affects between 0.7% and 29.6% of children worldwide, with the highest prevalence being observed in Western countries [25]. In Poland, studies have shown that constipation occurs in approximately 9% of preschool-aged children [26]. Potential contributing factors include low dietary fiber intake, changes in diet, stress, and improper toilet habits. On the other hand, diarrhea, especially in its acute form, is often of infectious origin and remains one of the leading causes of pediatric hospitalizations globally. Among chronic gastrointestinal conditions, increasing attention is being paid to irritable bowel syndrome and food allergies, which may be linked to abnormal development of the gut microbiota in early childhood.

Many of these dysfunctions are transient and resolve as the gastrointestinal system matures. However, their high prevalence highlights the importance of early prevention and proper support for gut function – particularly through ensuring appropriate nutrition and fostering healthy gut microbiota development. It is worth noting that FGIDs can significantly affect the quality of life of both children and their families, leading to more frequent medical visits, parental anxiety, and potential medical interventions. Early recognition and proper management are essential to improving the well-being of young patients and their caregivers. Contemporary research indicates that the gut microbiota plays a critical role in maintaining gastrointestinal health, especially during infancy and early childhood.

The central hypothesis of this article is that gastrointestinal dysfunction is strongly associated with gut microbiota disturbances in young children. Early infancy is a critical period for microbiota development and any disruption during this time may lead to long-term health consequences, including digestive disorders, increased susceptibility to infections, allergies, and even metabolic diseases later in life.

The aim of this study is to discuss the mechanisms, consequences, and potential strategies for preventing and managing gut microbiota disturbances in children aged 0–3 years. Understanding the relationship between the gut microbiota and gastrointestinal health in early childhood is a crucial step toward developing more effective strategies for supporting healthy development and preventing microbiota-related diseases.

Gut microbiota in children aged 0–3 years

Composition and development of the microbiota – the formation process from birth and factors influencing its maturation

The gut microbiota plays a pivotal role in human health, influencing metabolism and immune system function and protecting against pathogens. It begins forming during the prenatal period, though the most intensive colonization occurs at birth and during the first years of life. Numerous factors influence the composition and development of the microbiota, including mode of delivery, type of feeding, and antibiotic exposure.

Mode of delivery

Vaginal delivery provides the newborn with its first "microbial inoculation," exposing the infant to mater-

nal vaginal and fecal microbiota – primarily *Bifidobacterium*, *Bacteroides*, and *Lactobacillus*. A classic cohort study by Penders et al. [27] (N = 1032) demonstrated that, by the first month of life, vaginally delivered infants had over 100-fold higher concentrations of *Bifidobacterium* and *Bacteroides* and significantly lower colonization by *Clostridioides difficile* compared to those delivered via cesarean section; these differences remained statistically significant even after adjusting for confounding factors such as breastfeeding and antibiotic use.

Data from the "post-metagenomic" era confirm these findings and suggest that the effects of cesarean delivery may persist for years. In a prospective study involving 163 mother–infant pairs followed at four time-points up to 24 months of age, infants born via cesarean section showed persistently lower *Bacteroidota* and higher *Firmicutes* and *Enterococcus*; these microbial deviations were correlated with elevated markers of in-sulin resistance and a proinflammatory cytokine profile at 2 years of age [28]. Randomized metagenomic sequencing studies have further shown that gut microbiota maturation in cesarean-born infants is delayed (by approx. 1.5 months) and characterized by an abundance of antibiotic resistance genes. The clinical consequences are supported by recent meta-analyses. A large systematic review and meta-analysis by Liu et al. [29] demonstrated an increased risk of allergic diseases in children born via cesarean section compared to those born vaginally.

At the same time, strategies are emerging to mitigate this "colonization gap." The most well-documented protective factor is breastfeeding exclusively for ≥3 months, which nearly fully restored *Bifidobacterium* abundance in cesarean-born infants and reduced the incidence of respiratory infections in the first year of life by 25% [30]. An experimental method known as vaginal microbiota transfer (also called "vaginal seeding") was evaluated in a triple-blind randomized controlled trial (RCT) [31]. A single swabbing of the newborn's skin and mucosa with maternal vaginal secretions partially restored *Bacteroides* colonization, accelerated microbiota maturation, and improved neurodevelopmental outcomes by the third month of life.

There is also growing interest in targeted probiotics. Supplementation with *Bifidobacterium longum* ssp. *infantis* EVC001 (*B. infantis* EVC001; 1×10^9 CFU/day) in the first weeks of life led to stable gut colonization in cesarean-born infants, reduced fecal pH, and decreased lipopolysaccharide (LPS) leakage; in preterm infants, this approach reduced the incidence of necrotizing enterocolitis (NEC; stage II and higher) by approximately 60% [32]. Ongoing studies are also investigating maternal fecal microbiota transplantation immediately postpartum, which – according to pilot data – is more effective than vaginal seeding in restoring *Bacteroidota* profiles and normalizing immune system development, although it requires rigorous donor screening [33].

Type of feeding

Breastfeeding remains the most important modifiable factor shaping the gut ecosystem during the first months of life. Human milk provides the infant with not only live bacteria (most commonly *Bifidobacterium* and *Lactobacillus*) and secretory IgA, but also over 150 distinct human milk oligosaccharide (HMO) structures. HMOs are indigestible in the small intestine and serve as selective substrates for infant-adapted bacteria – particularly *B. infantis* – giving the infant gut microbiota a distinctly bifidogenic character [34].

Infants fed exclusively commercial formula typically exhibit a microbiota richer in *Enterococcus*, *Clostridium*, and *Proteobacteria*, but depleted in *Bifidobacterium*. This microbial deviation can persist until at least 12 months of age [35]. As a result, synthetic HMOs have been added to infant formula. A systematic review of 26 RCTs demonstrated that formulas supplemented with 2′-fucosyllactose (2′-FL) or multi-HMO blends produced stool composition, fecal pH, and immune markers more similar to those observed in breastfed infants, without adverse effects [36]. A more recent RCT showed that supplementation with pHMOs (4 g/L) significantly increased *Bacteroides* abundance, enhanced production of beneficial metabolites, and reduced systemic inflammatory cytokines compared to formulas enriched only with 2′-FL [37].

Despite these advances, the "microbial gap" between breastfed and formula-fed infants has not been fully closed. A meta-analysis confirmed that breastfeeding exclusively for approximately 6 months is associated with lower species diversity, but greater functional stability and reduced colonization by pathobionts compared to mixed or exclusive formula feeding [38]. In high-risk populations (e.g., delivered preterm or by cesarean or with early exposure to antibiotics), early supplementation with *B. infantis* EVC001 is increasingly recommended. This strain efficiently metabolizes a broad spectrum of HMOs and can stably colonize the infant gut. In RCTs, its use in preterm infants reduced the incidence of NEC stage ≥II by approximately 60%.

Beyond the period of exclusive milk feeding, the introduction of complementary foods marks a major ecological transition in the developing gut ecosystem. In infants, the concept of a "fiber-rich diet" should therefore be interpreted differently than in adults. During the first six months of life, the main source of prebiotic substrates is human milk, which naturally contains complex HMOs that selectively promote the growth of *Bifidobacterium* and *Lactobacillus* species [39]. According to the latest technical report of the American Academy of Pediatrics [40] and the multisociety response to the WHO's complementary feeding guidelines endorsed by ESPGHAN and partner organizations [41], exclusive breastfeeding for approximately 6 months remains the gold standard for early infant nutrition. After this period, the gradual introduction of fiber-containing plant-based foods sup-

ports microbial diversification and the production of short-chain fatty acids (SCFAs), strengthening gut barrier integrity and metabolic homeostasis [42].

It is worth noting that human milk itself is a dynamic biological fluid containing not only nutrients, but also live bacteria, bioactive peptides, and immunomodulatory factors that shape early microbial colonization [43]. Its composition varies depending on the mother's health, diet, and lactation stage, making it an individualized and adaptive system that continues to influence gut microbiota development throughout infancy. Human milk is not a uniform biological fluid, but a highly dynamic and individualized ecosystem. Its composition – both nutritional and microbial – varies with the mother's health, diet, lactation stage, delivery mode, and even the time of day [44]. The milk microbiome, which includes species such as *Lactobacillus*, *Streptococcus*, and *Bifidobacterium*, contributes directly to the infant's gut colonization and immune training [43]. Beyond the biochemical properties of milk itself, early postnatal interactions such as skin-to-skin contact (SSC) play a critical role in shaping the initial microbial landscape. Infants delivered vaginally and placed on the mother's chest within minutes of birth acquire microbial communities resembling the maternal skin and breast microbiota, supporting smoother immune adaptation and eubiosis establishment [40].

Early microbial colonization and skin-to-skin contact

Early microbial colonization begins during birth and is critically shaped by postnatal maternal–infant interactions, particularly SSC. Infants delivered vaginally and placed immediately on their mother's bare chest acquire beneficial microbial communities derived from both the vaginal canal and the skin, which promote early immune maturation and intestinal eubiosis [45]. Conversely, delayed SSC, cesarean delivery, or early antibiotic exposure can disrupt this process and lead to delayed colonization by *Bifidobacterium* and *Lactobacillus* species. Longitudinal observations show that daily SSC during the first few weeks of life promotes microbial stability, higher alpha diversity, and a reduction in potentially pathogenic taxa [46].

These findings emphasize that immediate physical contact and maternal proximity in the early postnatal period play a central role in establishing a resilient gut ecosystem. Together with breastfeeding, SSC represents a cornerstone of natural microbial seeding, supporting both intestinal and immune homeostasis during infancy.

Antibiotic use

Although often life-saving, antibiotic therapy is one of the most powerful factors capable of permanently reprogramming the early gut ecosystem. A foundational study by Dethlefsen et al. [47], which monitored the gut microbiota composition of three healthy adults before and after a 5-day course of ciprofloxacin, revealed a ~30% reduction in species richness and major shifts in one third of the bacterial taxa; notably, some key anaerobes failed to recover to baseline levels even 6 months after treatment. Today's research extends these observations to the perinatal and infant periods, demonstrating that the effects of exposure to antibiotics are highly dependent on its timing.

Antibiotics administered to the mother during the third trimester or at the time of cesarean section disrupt the transmission of the initial "starter pack" of microbes to the newborn. In a murine model, prenatal exposure to broad-spectrum β-lactams led to reduced sIgA concentrations in breast milk, offspring dysbiosis, and increased susceptibility to early-onset bacterial sepsis [48]. In humans, routine intrapartum antibiotic prophylaxis against group B *Streptococcus* has been associated with a more than twofold increase in *Enterococcus* and a significant decrease in *Bifidobacterium* and *Bacteroides* in transitional neonatal stools; these alterations persisted through at least the first month of life [49].

When antibiotics are administered directly to the newborn, the outcomes are more variable and depend on the drug spectrum and duration of therapy. A prospective study of 323 full-term infants showed that a 4-day course of amoxicillin caused only transient changes: the microbiota composition returned to baseline within a month, especially in infants who were exclusively breastfed [50]. However, a Danish analysis found that a single exposure to macrolides or cephalosporins doubled the abundance of antibiotic resistance genes and mobile plasmids; this enriched resistome profile persisted for at least 1 year after treatment [51].

Although the general structure of the gut microbiota often returns to baseline within 4 to 8 weeks, key butyrate-producing taxa such as *Faecalibacterium* and *Roseburia* may fail to reestablish, suggesting that antibiotics can shift the microbiota into an alternative, stable equilibrium with reduced metabolic capacity. Moreover, the accumulation of resistance genes in the gut favors the selection and amplification of harmful bacterial strains with each subsequent course of antibiotics [51].

The immunological cost of early antibiotic exposure is becoming increasingly apparent. A multicenter study showed that loss of *Bifidobacterium* at the time of vaccination correlated with lower antibody titers in response to PCV-13 and Hib vaccines [52]. In mice, this effect could be partially reversed by supplementation with a three-strain *Bifidobacterium* mixture.

These findings collectively highlight the importance of optimizing both the timing and spectrum of antibiotic use during the perinatal period. Strategies such as limiting group B *Streptococcus* prophylaxis to a single dose, promoting exclusive breastfeeding, and providing early targeted supplementation with *B. infantis* EVC001 in infants with significant antibiotic exposure currently represent the most promising approaches to mitigating the long-term consequences of dysbiosis and antibiotic resistance.

Functions of the gut microbiota

The gut microbiota plays a key role in maintaining human health by participating in digestion, metabolism, and immune system development. Microorganisms residing in the gut are involved in the fermentation of undigested food residues – particularly dietary fiber – resulting in the production of SCFAs such as butyrate, propionate, and acetate. These substances serve as an important energy source for intestinal epithelial cells and contribute to the regulation of glucose and lipid metabolism in the body [53]. In addition, the gut microbiota contributes to the synthesis of certain essential vitamins, such as vitamin K and B-group vitamins, which are critical for proper physiological function [54].

The gut microbiota also plays a vital role in the development and regulation of the immune system. Through direct interactions with immune cells, intestinal microorganisms influence the maturation and activity of lymphocytes and the production of cytokines, helping to maintain a balance between pro-inflammatory and anti-inflammatory responses [55]. Disruptions in microbiota composition – referred to as dysbiosis – can lead to abnormal immune activation and increase the risk of developing autoimmune diseases and allergies [56].

Disturbances of the gut microbiota and their consequences

Causes of gut microbiota imbalance

The gut microbiota plays a fundamental role in maintaining human health by influencing digestive processes, metabolism, and immune system function. Disruptions in its balance – commonly referred to as dysbiosis – can lead to a wide range of health issues. The main factors contributing to dysbiosis are described below.

Infections and the gut microbiota

Previous infections – especially those involving the gastrointestinal tract – are among the most significant external factors disrupting intestinal eubiosis. Acute bacterial or viral diarrhea can reduce ecological diversity by 30%–40%, and a complete recovery of the native microbiome in adults may take 6–12 months on average [57]. The mechanisms of disruption include direct competition for mucosal surfaces (mucin and carbohydrates), secretion of epithelial-damaging toxins, increased intestinal oxygen levels during inflammation, and the use of antibiotics, which intensify selective pressure and favor persistent microbiota imbalances.

Toxigenic strains of *Clostridioides difficile* strongly shift the microbial balance toward Proteobacteria while depleting key butyrate producers such as *Faecalibacterium* and *Roseburia*. A recent double-blind randomized trial (N = 153) found that oral encapsulated fecal microbiota transplantation did not significantly reduce the risk of recurrent *Clostridioides difficile* infection compared to placebo (absolute difference = 3%, 95% CI: −11.7 to 17.7), indicating no statistically significant effect [58]. These findings contrast with the 2023 Cochrane meta-analysis [59], in which traditional colonoscopic fecal microbiota transplantation showed a number needed to treat (NNT) of approximately 3 for preventing recurrences – highlighting that the efficacy of restorative therapies depends on the route of administration, microbial viability, and prior antibiotic exposure.

Salmonella enterica can actively modulate the intestinal environment to promote its colonization and persistence, including the induction of inflammation and disruption of host–microbiota interactions [60]. A similar "strategic" pattern is observed in pathogenic *Escherichia coli* (enterohemorrhagic *E. coli* [EHEC], enteropathogenic *E. coli* [EPEC]), where secreted virulence factors suppress immune protein expression by Paneth cells, facilitating the entry of bacteria into the mucosal biofilm.

A comprehensive literature review showed that acute norovirus infection can reduce species richness by up to 50%, preferentially depleting *Bifidobacterium* and *Lactobacillus* – bacteria which are capable of binding histo-blood-group antigens – thereby competing with the virus for mucosal receptors [61]. In immunocompromised patients, chronic viral shedding may occur. In small RCTs, supplementation with *Lactobacillus rhamnosus* GG reduced the duration of noroviral RNA shedding in stool by an average of 38%.

In the case of SARS-CoV-2 infection and post-acute sequelae of SARS-CoV-2 infection (PASC), a recent review identified a long-lasting decrease in butyrate-producing bacteria (*Faecalibacterium* and *Roseburia*) and a concurrent rise in opportunists such as *Enterococcus* and *Streptococcus*, even 6–12 months after infection [62]. This dysbiosis correlated with elevated levels of kynurenic acid and IL-6, suggesting a gut–brain axis contribution to the symptom of "brain fog."

Long-term consequences of infections include post-infectious irritable bowel syndrome, recurrent diarrhea, and gut–brain axis disturbances (e.g., brain fog or depression). In clinical practice, it is advisable to:

1. monitor the microbiota (e.g., metagenomic profiling) following severe or recurrent infections;
2. consider fecal microbial transplantation, next-generation bacterial consortia, or postbiotics in documented dysbiosis, while acknowledging the currently inconclusive efficacy data; and
3. limit antibiotic use, as it amplifies the risk of post-infectious dysbiosis.

Low-fiber diet

A diet low in dietary fiber and high in processed foods can lead to reduced diversity of the gut microbiota. Dietary fiber serves as a primary energy source for many beneficial gut bacteria, and its deficiency may promote the development of dysbiosis [63]. In particular, fermentable plant fibers such as fructooligo-

saccharides (FOS) and inulin stimulate the growth of probiotic bacteria. A lack of these fibers may result in decreased production of SCFAs, which play a key role in maintaining and protecting the intestinal barrier [64]. Recommended daily fiber intake varies by age, as shown in Table I.

For infants under 2 years of age, a simple guideline – "age (in years) + 5 g" – is still commonly applied, resulting in approximately 8–10 g/day for toddlers in their second year of life [41]. Interventional studies suggest that microbiota-related benefits typically emerge at intake levels above ~30 g/day (a mix of soluble and insoluble fiber fractions). In a 14-day RCT involving overweight individuals, daily supplementation with 30 g of inulin increased the abundance of *Bifidobacteriaceae* and SCFA production [65]. Key fiber fractions beneficial to the gut microbiota and their effects are summarized in Table II.

Table I. Recommended daily fiber intake

Age group	Minimum daily intake according to the latest guidelines
Adults	≥25 g of naturally occurring dietary fiber
Children 2–5 years old	≥15 g
Children 6–9 years old	≥21 g
Over 10 years old	≥25 g

Table II. Key fiber fractions beneficial to the gut microbiota

Fraction	Key microbiotic effects	Evidence from 2023–2025
Inulin and fructans (FOS/GOS)	↑ *Bifidobacterium*	30 g of inulin for 14 days – significant shift in microbiota composition and metabolic function [66]
Resistant starch (RS2/RS3)	↑ *Ruminococcus bromii*, ↑ *Bifidobacterium*, ↓ insulin resistance	8-week RCT, RS (40 g/d) → −2.8 kg body mass, improved HOMA-IR [67]; 2023 review on RS degradation [68]
Beta-glucans (oats or barley)	↑ *Roseburia*, ↑ *Faecalibacterium*, pH modulation	6.8 g β-glucan/d – enterotype-dependent effects; patients showed lower pH and higher SCFAs [69]
Pectins / arabinoxylans	↑ *Prevotella*, ↑ propionate	2024 observational studies showed stronger *Prevotella* enterotype response to these fibers [69]

FOS – fructooligosaccharides; GOS – galactooligosaccharides; RCT – randomized controlled trial; RS – resistant starch; RS2/RS3 – types of resistant starch (type 2/type 3); SCFAs – short-chain fatty acids; HOMA-IR – homeostatic model assessment of insulin resistance.

Fermentable fiber fractions are considered the most beneficial, as they lead to the production of SCFAs, primarily butyrate, propionate, and acetate. These metabolites strengthen the intestinal barrier, regulate blood glucose levels, and reduce inflammatory responses. However, the microbiome's response is largely individual. A 2024 clinical study by Pihelgas et al. [69] demonstrated high microbiota resistance in certain individuals, even after several months of supplementation with various types of fiber. Therefore, fiber diversity and consistency over time are more important than occasional high total intake.

Stress

Chronic activation of the hypothalamic–pituitary––adrenal (HPA) axis under prolonged psychological stress leads to a marked release of corticotropin--releasing factor (CRF) in the hypothalamus, increased cortisol secretion by the adrenal cortex, and stimulation of the sympathetic nervous system. An observational study from 2023 demonstrated that, even after a few days of stress exposure in animal models, gastrointestinal motility was impaired, mucin and IgA secretion declined, and the microbiota composition shifted toward Proteobacteria at the expense of butyrate-producing species [70]. Similar patterns have been confirmed in humans. In a study by Madison and Bailey [71], increases in inflammatory markers (e.g., IL-6) were correlated with elevated serum zonulin levels and reduced bacterial diversity within the first weeks of chronic stress.

CRF also acts peripherally through CRHR1/2 receptors located on intestinal epithelial cells and mast cells, enhancing myosin light chain kinase phosphorylation, leading to endocytosis of ZO-1 and occludin proteins, and ultimately disrupting tight junctions. This increases intestinal permeability ("leaky gut"), allowing LPS and other pathogen-associated molecular patterns – such as peptidoglycans and flagellin – to translocate into systemic circulation, thereby promoting Th1/Th17 immune responses [72]. In a water avoidance stress model, pharmacological modulation of the CRF––CRHR2 axis using lidocaine restored barrier integrity and reduced plasma diamine oxidase and LPS levels, confirming the central role of this pathway in the pathophysiology of stress-induced gut dysfunction [73].

Barrier dysfunction results in a decline of *Lactobacillus* and *Bifidobacterium* abundance, reduced butyrate production, and a higher proportion of LPS-producing *Proteobacteria*. In the RCT called "Feed Your Microbes", a four-week diet rich in fermented foods and prebiotics restored microbiota stability and reduced perceived stress levels by 32%, despite only modest taxonomic changes; this highlights the importance of microbiota-derived metabolites (e.g., SCFAs and tryptophan-derived indoles) as key mediators of the gut–brain axis [74].

At the immuno-neuronal level, chronic stress promotes low-grade inflammation (via IL-6 and TNF-α), reduces the Treg cell population, and activates microglia. Simultaneously, it inhibits vagal tone, which under

physiological conditions suppresses inflammatory responses [72]. Clinically, this may result in stress-related irritable bowel syndrome and gut–brain axis symptoms such as anxiety and "brain fog." Randomized trials from 2025 showed that one month of supplementation with psychobiotics – containing a mix of nine diverse bacterial strains – led to reductions in negative affect and gut permeability. However, improvements in psychometric scales were moderate [75].

In summary, chronic stress triggers a neurohormonal cascade (CRF, cortisol, and catecholamines) that increases intestinal permeability, disrupts microbiota composition, and amplifies inflammation. Early interventions – including high-fiber diets, psychobiotics, and stress reduction techniques (e.g., heart rate variability biofeedback or breathing exercises) – may interrupt this "vicious cycle" and protect both gastrointestinal and mental health.

In infants and young children, "stress" primarily refers to physiological and environmental stressors rather than psychological tension. Such stressors include perinatal hypoxia, hospitalization, invasive medical procedures, maternal separation, and chronic or oncological diseases. These early-life challenges have been shown to significantly affect gut microbial composition. For example, neonatal intensive care unit (NICU)-related procedural stress and prolonged hospitalization in preterm infants are associated with an increase in Proteobacteria and a reduction in beneficial taxa such as *Bifidobacterium* and *Lactobacillus* [76]. Likewise, maternal psychosocial stress correlates with reduced microbial diversity in infants during the first few months of life [77]. Systematic analyses confirm that early-life stress alters intestinal permeability, promotes low-grade inflammation, and may predispose children to long-term gastrointestinal and neurodevelopmental disturbances [78]. Major causes of gut dysbiosis are summarized in Table III.

Table III. Major causes of gut dysbiosis

Cause	Mechanism of action
Antibiotic therapy	Elimination of beneficial bacteria, promoting pathogen overgrowth
Infections	Pathogen competition with native microbiota, leading to imbalance
Low-fiber diet	Insufficient substrate for beneficial bacteria, reduced microbiota diversity
Stress	Gut–brain axis disturbances affecting microbiota composition and function

Gastrointestinal dysfunctions

Intestinal dysbiosis can lead to a range of gastrointestinal dysfunctions. In infants, one of the clinical manifestations of dysbiosis is colic, characterized by episodes of inconsolable crying and distress. Studies suggest that reduced microbial diversity and a lower abundance of *Lactobacillus* and *Bifidobacterium* species may be associated with the occurrence of infantile colic [79]. Dysbiosis can also present as diarrhea, resulting from disturbances in microbiota composition, which impair gut barrier function and trigger excessive immune activation [80]. Conversely, constipation may be linked to a decreased abundance of SCFA-producing bacteria, which are essential for maintaining proper intestinal motility [81]. Bloating is often a consequence of excessive intestinal fermentation by gas-producing bacteria, which may arise due to dysbiosis [82].

Long-term consequences

Prolonged gut dysbiosis can lead to more serious health complications. Alterations in the microbiota during infancy have been associated with an increased risk of developing food allergies. A deficiency of *Bifidobacterium* and *Lactobacillus* species may result in improper immune system development, thereby facilitating the onset of allergic reactions [27]. Dysbiosis has also been implicated in the pathogenesis of Crohn's disease and ulcerative colitis. Less microbial diversity and fewer anti-inflammatory bacteria may contribute to persistent intestinal inflammation [83]. Furthermore, microbiota imbalances may play a role in the development of food intolerances, such as lactose or fructose intolerance. The absence of specific bacterial strains responsible for metabolizing these sugars can lead to symptomatic intolerance [84].

The gut microbiota plays a critical role in maintaining the integrity of the intestinal barrier. Dysbiosis increases intestinal permeability, allowing pathogens and toxins to translocate into the bloodstream and trigger inflammatory responses. Studies have shown that dysbiosis can damage the gut barrier, thereby facilitating the development of inflammatory diseases [85]. Understanding the mechanisms through which dysbiosis affects the gut barrier, immune system, and inflammatory pathways is essential for developing effective therapeutic strategies to treat dysbiosis-related disorders.

Diagnostic and therapeutic methods

Stool analysis

Stool analysis is a fundamental microbiological examination used in the diagnosis of gut microbiota disturbances. It enables the identification of bacteria, viruses, or parasites that may cause symptoms like infantile colic, diarrhea, constipation, or bloating. In children aged 0–3 years, special attention is paid to the presence of bacterial pathogens such as *Salmonella*, *Shigella*, *Campylobacter*, and EPEC [86].

Microbiome DNA testing

Modern diagnostic methods such as microbiome DNA testing allow for a detailed analysis of the microbial composition in the gut. Techniques like next-gene-

ration sequencing enable the identification and quantification of bacteria in stool samples, which is particularly valuable in infants and young children, where traditional culture-based methods may be less effective [87].

Organix Gastro test

The Organix Gastro test is an indirect assessment of dysbiosis, evaluating gut microbiota composition based on the quantification of 12 organic acids – metabolites produced by intestinal bacteria. Measuring the concentrations of these compounds in urine can provide important insights into abnormal gut flora and allow for early detection of microbiota imbalance.

Table IV. Comparison of diagnostic methods for gut microbiota disorders in children

Diagnostic method	Application	Advantages	Limitations
Stool analysis	Identification of bacterial, viral, and parasitic pathogens	Widely available, fast, relatively inexpensive	May fail to detect all pathogens, especially with low microbial counts
Microbiome DNA testing	Detailed analysis of microbiota composition via stool sample	High sensitivity, broad microorganism detection	Higher cost, requires specialized equipment and software for analysis
Organix Gastro test	Urinary analysis of bacterial metabolites, indirect assessment of dysbiosis	Non-invasive, easy to perform in children, provides metabolic insight	May not reflect full microbiota composition, influenced by host metabolism

Treatment and prevention

Early identification and treatment of gut microbiota disturbances in children are crucial for preventing long-term health consequences. The selection of appropriate diagnostic tools should be tailored to the individual needs of the patient and the available medical resources. Effective treatment and prevention of conditions such as infantile colic, diarrhea, constipation, and bloating rely on several key components: the use of probiotics, prebiotics, and synbiotics; appropriate dietary interventions; and behavioral and environmental strategies.

Role of probiotics, prebiotics, and synbiotics

Probiotics are defined as specific strains of microorganisms that, when administered in appropriate doses and forms, confer a clinical benefit to the host. After two decades of research, it is now well established that the effectiveness of probiotics depends strictly on the individual strain and the specific clinical indication. The latest ESPGHAN position statement recommends that probiotic interventions should always specify the species name, strain designation, dosage, duration of therapy, and clinical evidence supporting the particular indication [88].

Table V. Main probiotic groups and indications in children aged 0–3 years

Indication	Strain/Protocol with proven efficacy (RCTs/ESPGHAN 2023–2025)	Key outcome
Infantile colic	*Limosilactobacillus reuteri* DSM 17938, 1 × 10^8 CFU/d for ≥21 days	↓ crying by 50–60 min/day; NNT ≈ 3 [88]
Acute infectious diarrhea	*Lacticaseibacillus rhamnosus* GG 2 × 10^{10} CFU/d or *Saccharomyces boulardii* CNCM I-745 250 mg × 2	↓ duration of diarrhea by 24–30 h [88]
Antibiotic-associated diarrhea	Same as above + *Lactobacillus reuteri* DSM 17938	↓ AAD risk by ~40%
NEC in preterm infants (<34 GA)	*Bifidobacterium longum* ssp. *infantis* EVC001, 1×10^9 CFU/d until 36 GA	NEC ≥ stage 2: 11% → 4% (p = 0.006) [32]
Functional constipation	*Bifidobacterium animalis* ssp. *lactis* HN019 or BB-12 (3–6 × 10^9 CFU/d for 4 weeks)	↑ stool frequency +1/week; ↓ abdominal pain
Functional abdominal pain	*Lactobacillus reuteri* DSM 17938 (≥4 weeks)	↓ pain episodes by 30%

Doses are given in colony forming units (CFU); minimum intervention duration is typically 3–4 weeks; necrotizing enterocolitis (NEC) requires ≥4 weeks; GA – gestational age; RCTs – randomized controlled trials; ESPGHAN – European Society for Paediatric Gastroenterology, Hepatology and Nutrition; DSM – Deutsche Sammlung von Mikroorganismen (German Collection of Microorganisms and Cell Cultures); NNT – number needed to treat; AAD – antibiotic-associated diarrhea; ssp. – subspecies.

Prebiotics are substances that stimulate the growth and activity of beneficial microorganisms in the gut. A diet rich in dietary fiber – particularly inulin and FOS – can promote the proliferation of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, thereby improving gastrointestinal function [63]. As of 2024, the ESPGHAN Committee expanded the definition of prebiotics to include selected HMO blends. In pediatric practice, the most commonly used include:

– galactooligosaccharides (GOS) and FOS in a ratio of 9:1 (0.4 g/100 ml of formula) – these increase *Bifidobacterium* levels and reduce stool pH; evidence supports effectiveness in both formula-fed infants and preterm neonates

– inulin or polydextrose – slower fermentation rate, which is beneficial for constipation; shown to improve stool frequency in two RCTs conducted in 2024
– 2′-fucosyllactose + lacto-N-neotetraose – studies from 2023–2024 report ~25% reduction in gastrointestinal infections among mixed-fed infants.

Synbiotics are formulations that combine probiotics and prebiotics to synergistically support gut health. They can be beneficial in managing gut dysbiosis in children by enhancing microbiota balance and gastrointestinal function [89].

The ISAPP consensus statement distinguishes between complementary synbiotics and synergistic synbiotics [90]. While Hojsak et al. [91] have not yet issued formal clinical recommendations due to study heterogeneity, a meta-analysis of 27 RCTs suggests that certain combinations (e.g., *Saccharomyces boulardii* + inulin or *Bifidobacterium animalis* ssp. *lactis* BB-12 + scGOS/lcFOS) reduce the duration of diarrhea by an additional 12 hours compared to probiotics alone.

There is a growing shift toward next-generation probiotics – strains isolated from healthy, breastfed infants or designed to restore specific microbial functions:

– *B. infantis* EVC001 – the most extensively documented next-generation probiotic
– *Akkermansia muciniphila* – early pediatric studies using pasteurized strain HB05 show improvements in metabolic and barrier markers, though no RCTs exist yet for children under 3 years of age [92]
– *Faecalibacterium prausnitzii*, *Roseburia* spp. – currently in Phase I/II trials as a microbial consortium for early inflammatory bowel disease and atopy prevention [93].

In children with severe dysbiosis (e.g., following multiple antibiotic treatments), encapsulated fecal microbiota transplantation and bacteriophage therapies targeting *Klebsiella* or *E. coli* have been explored – though current data are too preliminary to support clinical recommendations [67].

Psychobiotics represent a subgroup of probiotics or synbiotics that have shown effects on neurobehavioral parameters such as anxiety, sleep, and crying. Their mechanisms include the production of GABA, serotonin, and tryptamines, as well as the modulation of the HPA axis.

In 2025, the first RCT to use a multistrain formulation (*Lactobacillus helveticus* R0052 + *Bifidobacterium longum* R0175 + GOS prebiotic) in infants with high levels of "difficult temperament" showed a 22% reduction in night-time crying and lower salivary cortisol levels [87]. In children aged 5–10 years with attention-deficit/hyperactivity disorder, a 3-month supplementation with *Lactobacillus rhamnosus* GG improved attention scores in the Continuous Performance Test (CPT) and reduced results on the Conners' Parent Rating Scale [94].

Current international recommendations underline a targeted, evidence-based approach to probiotic therapy in pediatric populations. According to the European Society for Paediatric Gastroenterology, Hepatology and Nutrition [95] and the American Gastroenterological Association [96], probiotic supplementation should be strain-specific, used only when clinical efficacy has been demonstrated for a defined indication and administered cautiously in preterm or immunocompromised infants.

Recent studies have expanded the focus toward multistrain and synbiotic formulations, which combine complementary bacterial species and prebiotic substrates to enhance colonization stability and functional diversity. These preparations have shown superior modulation of the gut ecosystem, supporting immune tolerance and intestinal barrier function.

In neonatal intensive care, high-potency probiotic mixtures are now being applied as part of preventive strategies against NEC. A study by Bui et al. [97] demonstrated that supplementation with a multi-strain, high-dose probiotic product significantly reduced the incidence of NEC stage ≥II in very preterm infants without adverse effects, leading to its inclusion in several NICU protocols across Europe and the United States.

Together, these findings reinforce the importance of individualized, evidence-based probiotic therapy in restoring microbial balance and preventing dysbiosis-related complications in early life.

Importance of diet in restoring microbiota balance

An appropriate diet plays a key role in shaping and maintaining a healthy gut microbiota. In infants, breastfeeding provides not only essential nutrients, but also prebiotics and probiotics that support the growth of beneficial gut bacteria [98]. The introduction of fiber-rich foods – such as fruits, vegetables, and whole grains – can promote the development of beneficial microorganisms and enhance gastrointestinal function [65,69].

Behavioral and environmental interventions

Behavioral interventions, such as parental education on proper feeding practices, hygiene, and the introduction of solid foods, can significantly influence the health of the infant gut microbiota. Promoting breastfeeding and avoiding unnecessary antibiotic use during the first months of life are particularly important [99]. Environmental factors, such as limiting exposure to environmental pollutants and toxins, also affect microbiota composition. Maintaining a clean living environment and minimizing contact with chemical substances may help support intestinal health [100].

Table VI. Recommendations for the management and prevention of gastrointestinal dysfunction in children

Intervention	Recommendations
Probiotics	Use of specific probiotic strains at recommended doses
Prebiotics	Inclusion of fiber-rich foods such as fruits, vegetables, and whole grains
Synbiotics	Consider supplementation with combined probiotic–prebiotic formulations, especially in dysbiosis
Diet	Promotion of breastfeeding and introduction of a balanced, fiber-rich diet
Behavioral interventions	Parental education on proper feeding practices, hygiene, and solid food introduction
Environmental interventions	Limiting exposure to environmental toxins and pollutants

Discussion

The findings presented in this publication underscore the critical role of the gut microbiome in the proper functioning of the gastrointestinal tract in children aged 0–3 years. A clear relationship exists between microbiota composition and the occurrence of gastrointestinal dysfunctions, as supported by the scientific literature [3,4]. Gut dysbiosis may contribute to the development of infantile colic, GER, functional constipation, and other gastrointestinal disorders [25,76]. Early identification and implementation of appropriate therapeutic strategies appear essential in reducing the risk of long-term health consequences.

One of the most significant determinants of gut microbiota composition is the mode of delivery. Infants born via cesarean section exhibit a microbial profile that is distinct from those delivered vaginally, which may predispose them to digestive and immunological complications [17]. Feeding practices are similarly impactful: human milk provides key elements that promote the growth of beneficial bacteria, whereas formula feeding has been associated with a less diverse microbiota [27]. These findings emphasize the importance of breastfeeding as a fundamental preventive measure against microbiota-related disturbances.

Another crucial factor is the impact of antibiotic therapy on microbiota balance. Overuse of antibiotics – whether administered to the mother in the perinatal period or to the child in early infancy – can significantly alter microbiota composition and increase the risk of gastrointestinal disorders [101,102]. Therefore, it is recommended that antibiotics be used only when medically indicated, and that concomitant probiotic therapy be considered to preserve the natural intestinal microbiota.

In terms of treatment and prevention, current evidence suggests that the use of probiotics, prebiotics, and synbiotics may effectively support the restoration of a healthy gut microbiome in infants and young children. Several studies demonstrate that specific probiotic strains, such as *Lactobacillus reuteri* and *B. infantis*, may reduce the severity of infantile colic and improve gastrointestinal function [79,89]. However, further research is needed to precisely determine the optimal strains and dosages tailored to specific conditions.

Dietary factors also play a central role in shaping the gut microbiome. The early introduction of fiber-rich foods and natural prebiotics into the infant's diet may promote the growth of beneficial microbes and serve as an effective preventive strategy against gastrointestinal disorders [64]. There is also evidence that reducing the intake of processed foods and simple sugars can positively influence microbiota composition [63].

The gut microbiome plays a vital role in the gastrointestinal health of children, and several key factors contribute to its development and modulation. Further research is warranted to deepen our understanding of the microbiome's role in pediatric health and to develop effective diagnostic and therapeutic strategies to support microbial balance during early childhood.

Conclusions

1. Intestinal microbiota disturbances in children aged 0–3 years may lead to a variety of gastrointestinal dysfunctions, including infantile colic, diarrhea, constipation, and bloating. Gut dysbiosis disrupts microbial balance, negatively affecting digestion, nutrient absorption, and immune system function.
2. Early diagnosis is essential for effective treatment and prevention of long-term health consequences. Modern techniques such as stool analysis, microbiome DNA testing, and the Organix Gastro test enable precise assessment of the microbiota and early detection of imbalances.
3. Therapeutic interventions – including the use of probiotics, prebiotics, and synbiotics, appropriate dietary strategies, and behavioral modifications – play a crucial role in restoring microbial equilibrium. Breastfeeding and a diet rich in dietary fiber support gut health and reduce the risk of digestive disorders.
4. Understanding the role of the gut microbiome and implementing effective diagnostic and therapeutic methods may improve the quality of life in children and help prevent the development of more serious conditions in the future.

Summary

Implications for clinical practice

Understanding the relationship between the gut microbiome and gastrointestinal dysfunction in children aged 0–3 years is of critical importance for clinical practice. Early identification of microbiota disturbances and monitoring of microbial composition allow for timely implementation of therapeutic interventions such as the administration of probiotics, prebiotics,

or synbiotics. Clinical strategies should emphasize diagnostic approaches that enable the prompt detection of intestinal dysbiosis, utilizing modern tools such as stool analysis and microbiome DNA testing. Early diagnosis and targeted interventions can significantly improve gastrointestinal health in children, helping to prevent long-term complications such as chronic inflammatory bowel disease, allergies, or digestive disorders.

Future research

Further research on the gut microbiota in early childhood is essential to better understand its role in the development of chronic conditions such as allergies, autoimmune diseases, obesity, and metabolic disorders. Although the current evidence shows a strong link between dysbiosis and various health problems in children, the underlying mechanisms remain incompletely understood. Future studies should analyze in detail how the gut microbiota influences immune system development, gastrointestinal maturation, and its interactions with environmental and genetic factors. In addition, developing more precise and accessible diagnostic tools, including microbiota profiling tests, will enable earlier detection and more effective treatment approaches.

A deeper understanding of how the gut microbiome shapes long-term health has the potential to transform preventive and therapeutic strategies for chronic diseases – particularly in children – and may serve as a cornerstone for future public health interventions.

Authors' contribution

Study design – A. Kwiatkowski, M. Kleinert

Data collection – A. Kwiatkowski, T. Lepich

Manuscript preparation – A. Kwiatkowski, J. Kwiatkowska

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