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# The State of Intestinal Microbiota in Preterm Newborns: Impact on Adaptive Capabilities and Optimization of Therapeutic and Diagnostic Approaches

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**Abstract:** Preterm newborns present unique challenges in the development of intestinal microbiota, which significantly influences their immune system, metabolic processes, neurological development, and overall adaptive capacity. This article, based on a systematic literature review, examines the role of intestinal microbiota in preterm infants, highlights the clinical consequences of dysbiosis, explores its impact on neuropsychological development via the gut-brain axis, and discusses modern therapeutic and diagnostic strategies. Findings indicate that breastfeeding and probiotic supplementation help stabilize the microbiota, while advanced molecular diagnostic technologies enable early detection of complications and the implementation of personalized therapeutic approaches (Tamburini et al., 2016; Warner & Hamvas, 2018).

**Keywords:** Preterm infants, intestinal microbiota, neonatal adaptation, probiotics, breastfeeding, diagnostics, gut-brain axis, NEC.

**Introduction:** Preterm birth continues to be one of the leading causes of neonatal morbidity and mortality worldwide (WHO, 2023). The World Health Organization (WHO) reports that over 15 million babies are born preterm annually, with nearly one million deaths directly attributable to complications of prematurity. Survivors often face long-term health consequences, including chronic lung disease, cerebral palsy, neurodevelopmental impairment, and gastrointestinal dysfunction (Walker, 2017). The burden of preterm birth disproportionately affects low- and middle-income countries, where healthcare resources are limited.

The intestinal microbiota, often referred to as the “second genome,” has emerged as a critical determinant of neonatal development (Milani et al., 2017). It contributes to digestion, nutrient absorption, immune system maturation, and protection against pathogens. In preterm infants, however, microbial colonization is disrupted due to cesarean deliveries, antibiotic exposure, and prolonged hospitalization. These factors lead to reduced microbial diversity, a lower prevalence of beneficial species such as Bifidobacterium and Lactobacillus, and dominance of opportunistic pathogens including Enterobacteriaceae and Staphylococcus.

The implications of this imbalance extend beyond gastrointestinal health. The “gut-brain axis” and “gut-immune axis” highlight the interconnectedness of microbial communities with neurological development and immune regulation (Arrieta et al., 2014; Tamburini et al., 2016). Disruptions during this critical window may predispose infants to adverse outcomes later in life, ranging from impaired cognitive function to increased susceptibility to immune-mediated and metabolic disorders. Understanding these dynamics is essential for developing interventions that support neonatal adaptation and long-term well-being.

## Methods

This article is based on a systematic literature review.

Databases including PubMed, Scopus, Web of Science, and Google Scholar were searched for articles published between 2000 and 2023. Keywords used included preterm infants, intestinal microbiota, neonatal adaptation, probiotics, diagnostic strategies. Inclusion criteria were: (1) studies focused on preterm infants; (2) research addressing associations between microbiota and clinical outcomes; and (3) evidence on probiotics, breastfeeding, or diagnostic approaches. Articles were analyzed in two stages: first, assessing their main findings and objectives; second, evaluating methodological quality and limitations. The final synthesis was organized into three themes: microbiota composition, impact on adaptive capabilities, and clinical strategies.

## Results

The review indicates that preterm infants display significantly reduced microbial diversity compared to full-term infants (Patel & Denning, 2015). Opportunistic bacteria such as Enterobacteriaceae and Staphylococcus often dominate, while beneficial commensals like Bifidobacterium and Lactobacillus are markedly underrepresented (Milani et al., 2017). This imbalance, or dysbiosis, adversely affects both immune maturation and nutrient absorption. The consequence is not limited to immediate health issues but extends to long-term vulnerability. Dysbiosis not only increases the risk of necrotizing enterocolitis (NEC) and sepsis but is also associated with slower postnatal growth trajectories and impaired physical development (Neu & Pammi, 2018).

Breastfeeding emerged consistently across studies as the most critical factor in shaping a stable and protective microbiota (Ho, Groer, & Kane, 2019). Human milk is unique in its composition, containing prebiotics, lactoferrin, immunoglobulins, and a variety of bioactive compounds that foster beneficial bacterial growth and provide protection against infections (Warner & Hamvas, 2018). Probiotic supplementation, particularly with strains of Lactobacillus and Bifidobacterium, has also shown promising effects in reducing the incidence of NEC and strengthening intestinal barrier functions (Underwood, 2019). Nevertheless, ongoing debate persists regarding the optimal strains, dosages, and timing of administration, which limits the establishment of universal clinical guidelines.

Additionally, recent evidence emphasizes a striking link between gut microbiota and neurological development through the gut–brain axis (Arrieta et al., 2014). Dysbiosis in preterm infants may exert negative influences on neurodevelopmental outcomes, including reduced cognitive performance and increased vulnerability to neuropsychiatric disorders later in life. Modern diagnostic technologies such as metagenomics, 16S rRNA sequencing, and metabolomics now provide powerful tools for early identification of microbial imbalances and prediction of clinical complications, paving the way for the adoption of personalized medicine in neonatal care (Tamburini et al., 2016).

## Discussion

The results underscore the central role of intestinal microbiota in the adaptation and survival of preterm infants (Neu & Pammi, 2018; Warner & Hamvas, 2018). Dysbiosis is not simply an alteration in microbial composition; it is a major pathological factor strongly linked to severe complications such as NEC and sepsis, as well as impaired somatic growth and potentially delayed neurodevelopment (Patel & Denning, 2015). Therefore, protecting and restoring microbial health must be a priority in neonatal intensive care strategies.

Breastfeeding and probiotic therapy emerge as the most effective preventive and therapeutic interventions currently available (Underwood, 2019; Ho et al., 2019). Breast milk naturally promotes colonization with protective bacteria, while probiotics provide an additional means to reinforce mucosal defenses and restrict pathogen overgrowth. However, the absence of a clear consensus regarding the most effective probiotic strains and administration protocols emphasizes the urgent need for large-scale, randomized controlled trials (Underwood, 2019). Such research should aim to establish standardized, evidence-based guidelines for probiotic use in neonatal units worldwide.

The growing body of evidence linking microbiota to the gut–brain axis broadens the significance of this field (Arrieta et al., 2014; Tamburini et al., 2016). Supporting a healthy microbiome in the neonatal period may not only reduce immediate complications but also provide long-term benefits for cognitive and psychological well-being. The integration of advanced diagnostic tools—such as metagenomics and metabolomics—into neonatal practice represents a breakthrough, allowing for early detection of dysbiosis and enabling targeted, personalized interventions tailored to the unique microbial profile of each infant (Tamburini et al., 2016).

Altogether, these findings call for a paradigm shift: neonatal care must be viewed not only as life support but also as an opportunity to optimize microbial health, with far-reaching consequences for growth, immunity, and neurodevelopment (Walker, 2017).

## Conclusion

The intestinal microbiota of preterm newborns plays a decisive role in their adaptive capacity, immune system maturation, and long-term health outcomes (Warner & Hamvas, 2018). Literature shows that breastfeeding and probiotics reduce dysbiosis, decrease the risk of NEC and sepsis, and improve neonatal adaptation (Underwood, 2019; Ho et al., 2019). In addition, advanced molecular diagnostics provide opportunities for early detection of imbalances and the implementation of personalized therapeutic strategies (Tamburini et al., 2016).

Practical recommendations include: (1) prioritizing breastfeeding whenever possible; (2) developing national and international protocols for probiotic use; (3) gradually incorporating metagenomic and other advanced diagnostic methods into routine practice; and (4) paying greater attention to the gut-brain axis and its implications for neurodevelopment. Future research should focus on large-scale, multicenter clinical trials to define optimal probiotic regimens and evaluate long-term safety. Longitudinal cohort studies are needed to understand how early microbiota disruptions influence health outcomes into adolescence and adulthood. Additionally, equitable access to advanced diagnostics must be addressed to avoid widening disparities in neonatal care. A stronger integration of microbiota monitoring into neonatal practice has the potential to transform preterm care from reactive to preventive and personalized.

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