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USE OF PROBIOTICS DURING PREGNANCY AND IMPLICATIONS FOR MATERNAL AND NEONATAL HEALTH: A CRITICAL REVIEW

Editor-in-Chief: Dr. Deivis O. Guimarães
Gon1 Biotech frontiersofbioscience@gon1.com.br
Av.N.S Navegantes, 955/719 Vitoria/ES CEP 29050335

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Racire Sampaio Silva
Deivis O. Guimarães

Probiotic supplementation during pregnancy has received growing attention in clinical practice and translational research due to its potential to support gastrointestinal health, regulate maternal metabolism, modulate vaginal microbiota, and positively influence neonatal outcomes. This review critically examines current evidence on the safety, mechanisms of action, clinical benefits, and limitations of probiotic use in pregnancy. Pharmacovigilance data and randomized controlled trials demonstrate an overall favorable safety profile, with adverse events typically mild and rare. However, significant gaps remain, including heterogeneity in formulations, dosing, bacterial strains, and methodological limitations across studies. We conclude that while promising, routine probiotic use in pregnancy should be guided by individualized clinical assessment, weighing potential benefits and risks, and that further high-quality research is essential to define standardized protocols and confirm efficacy across diverse populations.

Keywords: probiotics, pregnancy, maternal health, vaginal microbiota, neonatal health, pharmacovigilance.

Introduction

Pregnancy is a unique physiological state marked by profound immunological, metabolic, and gastrointestinal adaptations. During this period, any nutritional or pharmacological intervention must be carefully evaluated, given the potential impacts on both maternal and fetal health. Among proposed strategies to improve maternal digestive health, immune modulation, and metabolic outcomes, probiotic supplementation has emerged as an area of significant interest.

Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer health benefits on the host. Their growing popularity reflects both a broader trend toward personalized nutrition and the accumulation of clinical evidence suggesting potential roles in managing gestational gastrointestinal symptoms, reducing gestational diabetes risk, modulating vaginal microbiota with implications for perinatal infections, and influencing infant colonization and immunity. However, given the inherent vulnerability of pregnancy, probiotic use requires rigorous safety and efficacy evaluation.

Safety Profile of Probiotics in Pregnant Women

Multiple systematic reviews and pharmacovigilance studies suggest that probiotics have an overall favorable safety profile during pregnancy. Analyses of the FDA Adverse Event Reporting System from 2005 to 2023 indicate that the most commonly reported adverse events are mild gastrointestinal symptoms such as flatulence and abdominal discomfort. Serious adverse events, including systemic infections, endocarditis, or severe dermatitis, are exceedingly rare and typically occur in immunocompromised or hospitalized populations.

A recent meta-analysis confirmed the general safety of probiotic use during both pregnancy and lactation but emphasized the need for specific monitoring in high-risk subgroups. Isolated reports of neurological adverse events, such as tremors or increased anxiety, have been described but without robust evidence of causality.

While the overall safety profile is reassuring, professional societies and regulatory agencies emphasize that probiotic prescription during pregnancy should be individualized, considering strain specificity, dosing, duration, and the clinical context of the patient.

Mechanisms of Action of Probiotics During Pregnancy

The beneficial effects of probiotics arise through multifaceted, strain-dependent mechanisms involving interactions with the host's microbiota, immune system, and metabolism. Key mechanisms include:

Influence of Maternal Probiotics on Newborn Gut Microbiota.

Newborns of mothers who took probiotics in late pregnancy show differences in gut bacteria within days after birth. This suggests maternal probiotics can shape early infant microbiota indirectly. Such early modulation may impact immune development and reduce allergy risk later in life (Li et al., 2024, Frontiers in Nutrition).

- Modulation of intestinal microbiota through restoration of balance between commensal and potentially pathogenic microorganisms, preventing dysbiosis driven by hormonal and dietary changes during pregnancy.
- Competitive exclusion of pathogens via colonization of ecological niches and production of antimicrobial substances such as bacteriocins that limit pathogen growth.
- Enhancement of intestinal epithelial barrier integrity through stimulation of tight junction proteins and mucin production, reducing bacterial translocation and systemic inflammation.
- Immunomodulation through induction of regulatory T cells and modulation of pro- and anti-inflammatory cytokines that support maternal-fetal immune tolerance.
- Interaction with bile acid metabolism influencing the pool of bile acids with downstream effects on lipid digestion and energy metabolism.
- Effects on the gut-brain axis through production of neurotransmitters and neuroactive metabolites that may modulate maternal mood and behavior.

These mechanisms provide a biologically plausible basis for observed clinical benefits, although effects vary substantially by strain and formulation.

Maternal Clinical Benefits

Gastrointestinal symptoms are highly prevalent in pregnancy, including constipation, bloating, and flatulence. Controlled studies indicate that probiotic use can alleviate these symptoms by modulating intestinal microbiota and increasing secondary bile acid production, thereby improving motility and digestibility.

Another area of significant interest is the prevention of gestational diabetes mellitus. Meta-analyses suggest that multi-strain formulations containing *Lactobacillus acidophilus* and *Bifidobacterium* spp. may improve insulin sensitivity, reduce systemic inflammation, and optimize glycolipid profiles. Despite these promising findings, no formal consensus exists, and clinical adoption awaits confirmation through large multicenter trials.

Additionally, probiotics may support maternal mental health. Emerging evidence suggests a role in reducing anxiety and depressive symptoms during pregnancy, possibly mediated through gut-brain axis interactions and immunomodulatory effects.

Neonatal and Infant Outcomes

Maternal probiotic supplementation has direct and indirect implications for neonatal health. Evidence demonstrates that infant gut microbiota colonization can be influenced by maternal intake for up to six months postpartum, reflecting vertical transmission during birth and breastfeeding.

One of the most robust findings is the significant reduction in maternal vaginal colonization by Group B *Streptococcus*, a major cause of neonatal morbidity and mortality. Randomized controlled trials report reductions of up to 75 percent in GBS colonization with specific *Lactobacillus* strains.

Additionally, maternal probiotic use has been associated with reduced incidence of atopic eczema in infants, a lower risk of necrotizing enterocolitis in preterm neonates, and modulation of neonatal immune responses. While promising, these benefits require further definition regarding optimal strains, . dosing, and supplementation schedules.

Adverse Events and Limitations in Current Evidence

Despite their general safety, probiotics are not entirely risk-free. Most adverse events are mild and transient gastrointestinal symptoms. Rare but serious events, such as systemic infections or bacteremia, have been reported primarily in immunocompromised or critically ill patients.

Key limitations of current evidence include:

- Heterogeneity of formulations and strains studied, which complicates direct comparisons and meta-analyses.
- Lack of standardized dosing and treatment duration, making clinical recommendations challenging.
- Limited representation of low- and middle-income populations, restricting generalizability.
- Underexplored clinical outcomes such as preterm birth rates or neonatal sepsis.
- Potential publication bias related to industry sponsorship of efficacy trials.

These limitations highlight the need for cautious interpretation of results and careful consideration before widespread clinical adoption in obstetric care.

Future Perspectives

To clarify the role of probiotics in prenatal care, robust, well-designed, multicenter randomized controlled trials are urgently needed. Research priorities should include:’

- Identification of specific strains and combinations most effective for each indication.

- Safety assessment in vulnerable subpopulations such as immunocompromised pregnant women or those with severe comorbidities.

- Cost-effectiveness analyses and health system impact evaluations.

- Integration of personalized approaches based on maternal microbiome profiling.

Advances in genomic sequencing and bioinformatics offer the potential for precision nutrition strategies that tailor probiotic interventions to maximize benefits while minimizing risks.

Conclusion

Probiotic use during pregnancy represents a promising strategy to support maternal and neonatal health. Current evidence suggests potential benefits in improving gastrointestinal symptoms, regulating glucose metabolism, reducing maternal GBS colonization, and modulating neonatal immune development.

However, significant gaps remain, including variability in formulations, lack of standardized protocols, and limited high-quality evidence for certain outcomes. Clinical decisions about probiotic supplementation during pregnancy should be individualized, carefully balancing potential benefits and risks.

Future translational research and rigorously designed clinical trials will be critical to establish standardized, evidence-based guidelines that enhance maternal and neonatal health outcomes globally.

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Contacts:

frontiersofbioscience@gon1.com.br

www.gon1.com.br/frontiersofbioscience