

Impact of Vaginal Seeding on Microbial Development in Cesarean Births: A Review

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ABSTRACT

Aim/Background: This review examines the influence of vaginal seeding on microbial development in infants born via Cesarean section, highlighting concerns about altered microbial colonization and the potential benefits of early microbial exposure. The rising global Cesarean section rates have prompted a closer look at the role of vaginal seeding in restoring microbial diversity in infants.

Materials and Methods: From an initial identification of 891 articles, six (6) studies from 2020 to the present were analyzed to compare microbial composition differences among delivery modes and assess the effects of vaginal seeding on infant microbiota. Literature research was conducted using reputable academic databases like Google Scholar, PubMed, ScienceDirect, JSTOR, and Cochrane Library. **Results:** Vaginal seeding was found to establish specific microbial taxa in Cesarean-delivered infants, including taxa from the gut, oral, and skin microbiota, indicating a convergence of microbial compositions. The analysis revealed conflicting results on the effectiveness of vaginal seeding in restoring microbial diversity, emphasizing the need for further research and larger-scale randomized controlled trials. **Conclusion and Recommendations:** While some studies suggest positive effects of vaginal seeding on gut and skin bacteria, safety concerns and a lack of definitive benefits have led reputable organizations to discourage its practice. Extensive, well-designed trials are needed to validate findings, understand specific microbial strains transferred during seeding, and assess the long-term health implications of vaginal seeding.

Keywords: Vaginal Seeding, Microbirthing, Cesarean, Microbiota, Infants, Neonates, Maternal Microbes, Microbial Colonization, Microbial Seeding, Vaginal Swabbing, Infant Gut Microbiome, Vaginal Birth.

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INTRODUCTION

Recent World Health Organization (WHO) data highlights a global rise in Cesarean section deliveries, exceeding 20% of all births and anticipated to reach nearly 30% by 2030.^[1] Amid this surge, heightened research attention converges on the pivotal role of the microbiome in early-life health, particularly among

neonates born through Cesarean section. While C-sections are essential in numerous medical settings, they are associated with substantial alterations in the early microbial colonization of infants as compared to those delivered vaginally. It is also associated with reduced levels of various cytokines, as well as an elevated risk of neonatal infections, immune disorders, and obesity.^[2]

The birth environment plays a crucial role in shaping microbial outcomes, particularly noticeable in neonates born in hospital settings. These infants exhibit distinct microbiota composition in their initial month of life. For instance, infants delivered via Cesarean section (C-section) impair the journey through the vaginal

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canal, resulting in the absence of exposure to the initial live microbes that are inherent during vaginal delivery.^[3] Compared to infants born through typical labor, the sterile fetal gastrointestinal tract of C-section newborns hinders the initial acquisition of microbes crucial for building immune defenses. Early-life microbiota colonization is essential for the formation and maturation of metabolic and developmental pathways. Any disruption with the development of microbial communities during this time may increase the lifetime risk of developing a number of different illnesses. Furthermore, neonates born in hospitals exhibit lower levels of key microbial composition such as *Bacteroides*, *Bifidobacterium*, *Streptococcus*, and *Lactobacillus*, contributing to a delayed establishment of the expected normal intestinal colonization.^[4] Numerous studies highlight significant variations in the acquisition and maturation of the microbiota between infants delivered naturally and those via C-section, concluding a lower diversity of microbial features in the latter group.^[5]

In response to this concern, “vaginal seeding” has emerged as a potential intervention to address the altered microbiota development in neonates delivered through C-section. Vaginal seeding is a procedure wherein the indigenous microorganisms from the maternal vagina are introduced to the newborn’s mouth, nose, or skin using cotton gauze or a swab.^[6] In an attempt to mimic the microbial transfer that takes place after vaginal birth, this method entails exposing infants born through Cesarean section to maternal vaginal microbes. However, despite its increasing popularity, scientific literature on the effectiveness and possible implications of vaginal seeding is still varied and developing.

Previous studies suggest that the gut microbiome of neonates delivered via Cesarean Section (CS) may not have significant changes through the practice of vaginal seeding. Nonetheless, certain studies suggest that administering vaginal seeding to babies delivered by C-section shortly after birth may potentially reduce variations in gut microbiota compared to infants born through natural delivery.^[7] However, despite numerous clinical trials, conclusive evidence supporting observable health benefits related to neonatal vaginal seeding remains elusive.^[8] The American College of Obstetricians and Gynecologists (ACOG, 2017)^[9] takes a cautious stance on the practice of vaginal seeding. They do not recommend or endorse this procedure unless it is part of a research protocol approved by an Institutional Review Board (IRB). They emphasized the importance of sufficient data since there is a lack of established standards for screening mothers, and the existing trials have been relatively small. While observational studies

indicate that interventions such as maternal-infant microbial transfer in C-section-delivered newborns may contribute to restoring microbial development, a critical research gap exists in the absence of comprehensive evidence demonstrating the specific impact of vaginal seeding on the infant microbiome. This gap highlights the need for a well-designed summary of trial results to provide a robust understanding of the efficacy and safety of maternal-child microbial seeding, addressing its potential role in mitigating health risks associated with C-section delivery.

Objective

This review aims to explore how vaginal seeding affects the development of the microbiota in infants delivered via Cesarean section, with emphasis on identifying any possible advantages or benefits of this procedure. The objective is to thoroughly review primary research to specifically identify the vaginal seeding effects on the variety and composition of infant microbiome, aiming to contribute valuable insights into its potential advantages for their health and development.

MATERIALS AND METHODS

Literature Search

Relevant literature was sourced from reputable academic databases, such as Google Scholar, PubMed, ScienceDirect, JSTOR, and Cochrane Library. Google Scholar and ScienceDirect is a large databases, to narrow down the studies the researchers use these systematic combinations of search terms, specifically “Vaginal Seeding” OR “Microbial Seeding” OR “Vaginal Swabbing” AND “Cesarean infants” OR “Newborns” AND “Microbial Colonization” OR “Infant Gut Microbiome” AND “Comparison” AND “Vaginal Birth,”. As for the PubMed, JSTOR, and Cochrane Library, the terms used are only “Cesarean” AND “Vaginal Seeding” AND “Microbiota” AND “Vaginal Birth”. These are the terms used to identify studies that focus on investigating the differences in infant microbiome delivered via cesarean section with vaginal seeding, Cesarean section without vaginal seeding, and those via vaginal delivery.

Table 1 was utilized to guide the literature search on vaginal seeding’s impact on microbial development in Cesarean-delivered infants, employing the PICO framework to clearly define the research focus. The framework specified the Patient/Population (infants delivered via Cesarean), Intervention (vaginal seeding), Comparison (infants delivered via Cesarean without seeding and those delivered vaginally), and Outcome

Table 1: PICO Framework for Investigating Microbial Development in Cesarean-Delivered Infants with Vaginal Seeding

Patient, Population or Problem	Intervention	Comparison Intervention	Outcome
Infants delivered via Cesarean section (CS), particularly those who may experience altered microbial colonization compared to those delivered vaginally.	Vaginal seeding, which involves transferring maternal vaginal microbes to the infant immediately after a Cesarean delivery to promote microbial diversity.	Infants delivered via Cesarean section without vaginal seeding, as well as those delivered vaginally, to assess differences in microbial development and health outcomes.	The primary outcomes include the composition and diversity of the infant's microbiome, and health implications associated with different delivery methods.

(effects on microbiome composition and health). This structured approach aimed to systematically identify and evaluate relevant studies, ensuring a comprehensive understanding of the topic and highlighting areas for further research.

Eligibility Criteria

By limiting the included studies and articles to those published primarily between 2020 and the present, this review examines the microbial development in infants delivered through Cesarean section, both with and without vaginal seeding, in addition to vaginal delivery. While full-text publications are the primary focus, articles without full-text were nonetheless included as long as they presented statistically significant data on the outcomes of vaginal seeding or were summarized in the abstract, addressing the study's primary objective. Other inclusion criteria include (a) infants born vaginally, (b) healthy infants born through C-section with seeding, and (c) infants born through C-section without seeding. The exclusions in this study are (a) emergency C-section, (b) pregnant women with infectious diseases, (c) articles that were published prior to 2020, (d) incomplete research outcomes and (e) articles sourced from predatory sites. The researchers independently examined the titles and abstracts to identify the publications of relevance.

The exclusion criteria in the review aim to enhance the eligibility of findings by eliminating cases that could introduce variability, such as emergency Cesarean sections and pregnancies complicated by infectious diseases. Additionally, excluding articles published prior to 2020 ensures that the review focuses on the most current research. Studies with unreported outcomes and from predatory journals are ineligible to maintain the validity and integrity of the articles used. These criteria collectively help ensure that the conclusions regarding vaginal seeding and its impact on microbial development in infants are based on reliable and relevant data.

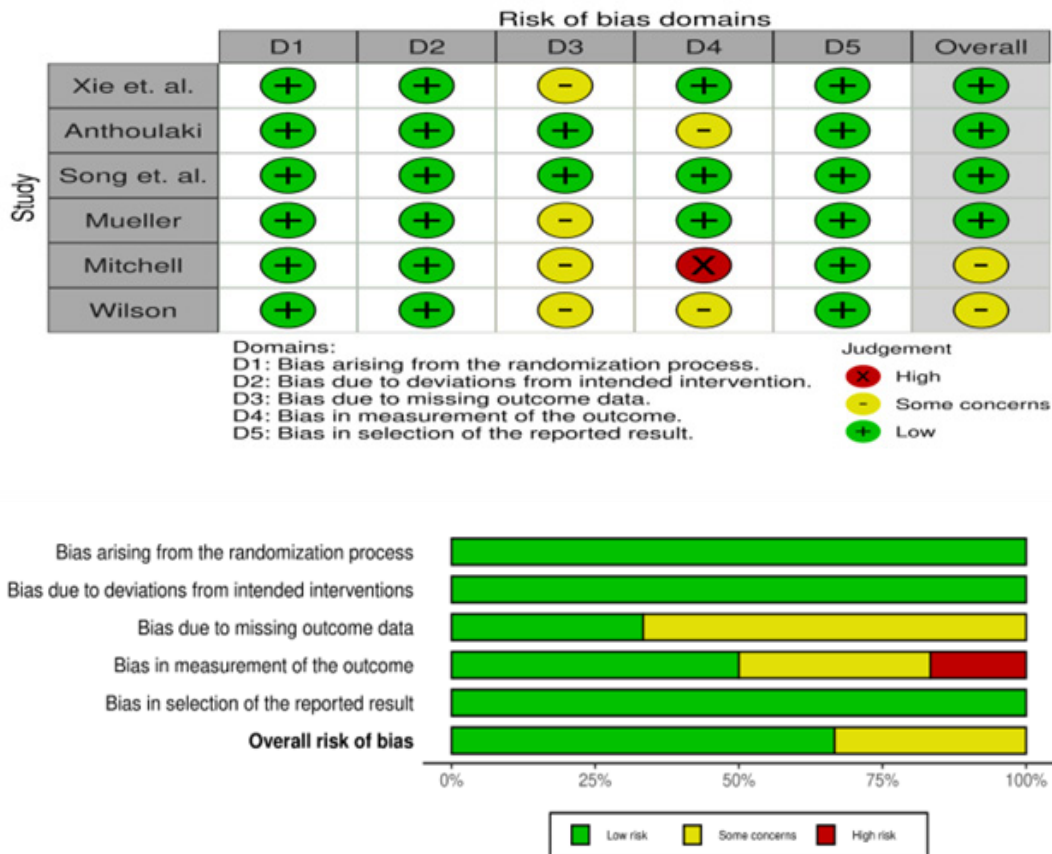
Selection Strategy

The authors independently evaluate the studies that were chosen for inclusion, taking into account their eligibility and disparities. Articles that appeared relevant were screened by two (2) researchers for full-text screening and final inclusion in the review. With the research adviser's help, all disputes and arguments were sorted out. The articles underwent a thorough review process. The authors examined the contradictions and eligibility of the chosen studies that were determined to be included. Before evaluating each potentially acceptable research article, the titles and abstracts of the studies were initially evaluated.

Risk of Bias and Quality Assessment

For the risk of bias and quality assessment of the included studies, the authors carefully selected and extracted studies and articles based on their relevance to the research topic beginning with the screening of its title, abstract, and full text. Two (2) authors utilized the CASP (Critical Appraisal Skills Programme) Systematic Review Checklist to eliminate the risk of bias and ensure study quality. Using this checklist, the studies have been assessed for their results, validity, and significance. Additionally, the authors also used RobVis's Risk of Bias Tracking Media to obtain the Risk of Bias extraction results with most of the studies having low risk (Figure 1). Two (2) other independent reviewers and the research adviser validated the data and resolved any conflict or discrepancy during data collection and extraction.

The CASP Checklist results indicate that the study effectively addressed a clear research question and utilized appropriate randomization to minimize bias. All participants were accounted for at the study's conclusion, and both participants and investigators were blinded to the interventions. The care provided was equal across study groups, ensuring fairness in treatment. The effects of the intervention were comprehensively reported, including statistical analyses that demonstrated significant benefits. Overall, the intervention appears to offer greater value than existing



treatments and is relevant for application in local healthcare settings.

Data Extraction

The authors extracted the relevant papers’ study characteristics, such as: (1) the first author’s name, (2) the year of publication, (3) title, (4) participants, (5) microbes, (6) microbiomes, (7) key findings of each study. Table 2 describes the process of extracting detailed data from publications.

Details from relevant journals were taken out, including the name of the author, the title, the year of publication, and its attributes. To further obtain and extract significant information, the abstract and discussion sections of the publications were examined. Table 2 contains a list of the eligible articles with the following details.

RESULTS

The initial search retrieved 891 articles. ZOTERO, an open-source management tool for managing resources and references in research, was utilized to identify research projects. The articles retained after the removal

of the duplicates were 130 Titles and abstracts were screened, which led to 76 articles. These were further evaluated for their eligibility. Thus, the final number of articles included in this review is 6. The selection process of this study is illustrated in Figure 2.

DISCUSSION

Delivery Mode Influence

Infant microbiota establishment is greatly influenced by a number of events throughout pregnancy, delivery, and the neonatal period. According to recent research, one of the most detrimental occurrences in early life is Cesarean Section Delivery (CSD), which significantly alters the patterns of microbiota establishment. Rios-Covian, Langella and Martin (2021)^[10] highlighted that these alterations tend to have a longer-term effect on newborn health even though they tend to lessen in the early months of life. A higher risk of infections in infancy as well as non-transmissible illnesses, including allergies, metabolic abnormalities, and inflammatory diseases has been linked to CSD. In infants delivered by C-section, microbiota is linked to reduced diversity,

Reference	Authors	Participants	Time Points	C-section seeded	Microbes C-Section only	Vaginal Birth	Findings
[12]	Xie, et al., 2023	16 CS with seeding 4 CS only 6 Vaginal births	2 months and 15 days	Bacteroides Streptococcus Clostridium Lactobacillus Escherichia-Shigella	No information included	Bacteroides Lactobacillus	Delivery mode affected newborns' gut microbiome. CS neonates with vaginal seeding showed similarities to ND babies, indicating potential attenuation of CS-induced abnormal gut microbiota by maternal vaginal microbiome exposure
[13]	Anthoulaki, et al., 2023	110 CS with seeding 85 CS only 95 Vaginal births	5 days after birth	Lactobacillus Bacteroides	Limited microbiome	Bacteroides Lactobacillus Bifidobacterium	Vaginally seeded or not, neonates delivered by CS had a similar microbiome including lactobacillus spp. and Bacteroides; in contrast, individuals lacking seeding exhibit a "limited" gut microbiota.
[2]	Song, et al., 2021	79 CS (30 were swabbed vaginal seeding) 98 Vaginal births	1st year of life	Lactobacillus Bifidobacterium	Small to limited microbiomes	Lactobacillus Bacteroides Parabacteroides	Infants born via C-section had microbiome trajectories resembling those of vaginally delivered babies. Unlike non-pregnant women in the Human Microbiome Project study, most amplicon sequence variants from maternal vaginal microbiomes on the day of birth were shared with other maternal sites.
[14]	Mueller, et al., 2023	20 CS with seeding	30 days after birth	Bacteroides Bifidobacterium	No information included	Bacteroides	Vaginal seeding altered neonatal skin and stool microbiota, leading to reduced bacterial diversity similar to vaginally delivered and breastfed infants. However, there was no significant increase in Bacteroides and Bifidobacterium
[15]	Mitchell, et al., 2020	40 Vaginal births 19 Pre-labor CS 16 Non-elective CS	2 weeks	Not effective	Low Bacteroides	Bacteroides (B. fragilis and B. thetaiotaomicron)	Maternal seeding doesn't directly transfer the vaginal microbiome to the infant's gut. Thus, the "vaginal seeding" approach, giving CS- delivered newborns maternal vaginal secretions, may not be effective.
[6]	Wilson, et al., 2021	12 CS with seeding 13 CS with sterile water seeding 22 Vaginal births	1 month & 3 months after birth	Low Bacteroides	Low Bacteroides Enriched in Haemophilus spp. and Streptococcus group	Bacteroides	No significant changes in gut microbiome occurred at one and three months for infants receiving C-section seeding versus placebo, despite the presence of living microbial cells. Both C-section groups differed from vaginal birth microbiomes, with low Bacteroides abundance affecting biosynthetic pathways

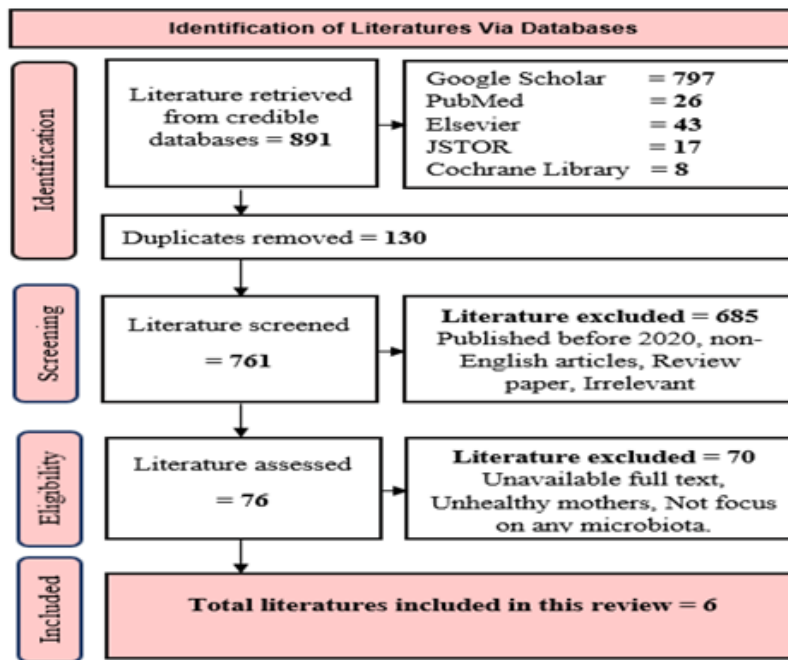


Figure 2: Schematic diagram of the literature selection process.

potentially leading to dysbiosis. This condition can impact immune development and increase susceptibility to certain immune disorders, such as allergies.^[11]

In terms of microbial composition, newborns delivered vaginally typically show increased levels of *Bacteroides*, *Bifidobacteria*, and *Lactobacillus* in their early days, followed by increased microbial diversity in the following weeks. The maternal vaginal microbiota introduces a diverse range of colonizing microorganisms to newborns, crucial for shaping and adapting their immune systems. In contrast, the microbiota of C-section infants closely resembles the microbial composition of the mother's skin and the hospital setting. The microbiota in C-section-born infants is less diverse, primarily consisting of *Staphylococcus*, *Streptococcus*, and *Clostridium*. Additionally, several research indicates that infants delivered by C-section have reduced levels of *Bifidobacterium*, *Enterobacteriaceae*, and *Bacteroides* compared to those born vaginally.^[12]

Effect of Vaginal Seeding to Gut Microbiome

Based on the collected studies, the concept of “vaginal seeding” shows a potential intervention for infants born via Cesarean Section (CS). In the study on vaginal seeding by Dominguez-Bello *et al.* (2016),^[13] it demonstrates that this intervention only shows a partial development for infant microbiome during early life. In this simple observational study, infants delivered by C-section without vaginal seeding showed an underrepresentation of vaginal bacteria. In contrast, the

gut, skin, and oral microbiome of the four C-section-delivered infants who underwent seeding were enriched with vaginal bacteria, similar to those born vaginally. However, with only four infants undergoing vaginal seeding, the study lacks the statistical power to draw definitive conclusions, make recommendations, or confirm its safety. In more comprehensive follow-up studies, researchers identified that newborns who underwent vaginal seeding exhibited microbiome trajectories more closely aligned with those born vaginally rather than infants delivered via C-section without vaginal seeding.

Xie *et al.* (2023)^[14] revealed that incorporating vaginal seeding in Cesarean section (CS)-born infants led to a gut microbiota profile closely resembling that of naturally delivered infants, suggesting a potential correction of the atypical microbial composition associated with CS. Among these, the genus *Bacteroides* showed similarities to those found in vaginally delivered infants (14.95%), a significantly higher proportion compared to neonates born via C-section (0.15%). The analysis at the genus level identified a post-vaginal seeding microbial community in CS-born infants, predominantly composed of *Bacteroides* (12.10%), *Lactobacillus* (6.38%), and *Escherichia-Shigella* (6.03%), similar to vaginally delivered infants. There was no significant difference in beta diversity observed in the gut microbiome between neonates born via Cesarean section with vaginal seeding and those delivered vaginally. In other words, the gut microbiota of these

two groups were more similar to each other than to the gut microbiota of neonates born via C-section without vaginal seedings.

Anthoulaki *et al.* (2023)^[15] emphasized a comprehensive analysis of neonatal microbial colonization across various delivery modes, including elective Cesarean Section (CS) with vaginal seeding, CS without seeding, and vaginal delivery. The research emphasized the potential clinical significance of vaginal seeding in reshaping the gut microbiome of CS-born neonates, revealing a microbial composition closely resembling that of vaginally born infants, marked by the presence of *Lactobacillus* species and *Bacteroides*. Notably, CS with seeding introduced certain microbes, such as *St. aerius* and *St. epidermidis*, at statistically significant levels compared to vaginal delivery. The study further highlighted distinctive microbial profiles in ocular, rectal, ear, umbilical, and nasal regions for CS-born infants with seeding, underscoring the impact of delivery mode on neonatal microbiome composition. The intermediate variability in fecal, oral, and skin samples of seeded infants suggested that vaginal seeding might contribute to a more stable microbiome development.

The results aligned with Song *et al.* (2021)^[2] which explores the efficiency of vaginal seeding in establishing microbial taxonomies in infants, particularly those delivered via Cesarean Section (CS). The study introduces a seeding effectiveness score for various microbial taxa, with a score of 0 indicating poor seeding and a score of 1 indicating effective seeding of. The efficiently seeded microbes are those that are transferred to C-section-delivered infants through seeding. Many associated with CS-seeded infants scored above 0.8, indicating effective microbial establishment. It notes the successful introduction of missing microbes in CS-born infants, including the enrichment of specific gut-associated bacteria like *Bacteroides*, *Streptococcus*, and *Clostridium*. In the oral microbiota, CS-seeded infants had a higher effectiveness associated with *Haemophilus*, *Gemellaceae*, and *Streptococcus*. These taxa were effectively seeded in the CS-seeded group and observed at all ages. In the skin microbiota, CS-seeded infants showed an association with *Streptococcus*, *Thermus*, *Neisseria*, and *Neisseriaceae*. The consistent association of *Bacteroides* with vaginal seeding is observed with the highest enrichment. Vaginal seeding not only impacts the gut but also leads to a convergence of microbial compositions in infants. Overall, the analysis revealed

that vaginal seeding was able to effectively introduce specific microbial taxa in CS-seeded infants, including taxa from the gut, oral, and skin microbiota.

Effect of Vaginal Seeding on Skin Microbiota

In a comprehensive study by Mueller *et al.* (2023)^[16] vaginal seeding fostered the enrichment of bacterial communities, with a notably higher bacterial load on the seeding gauze (62,000 copies/ μ L) compared to the control group (180 copies/ μ L; $p = 5.1 \times 10^{-9}$). The bacterial load on the seeding gauze demonstrated an enrichment in *Lactobacillus* (19,000 copies/ μ L compared to 33 copies/ μ L in the control; $P=0.0003$) and *Bifidobacterium* (109 copies/ μ L compared to 48 copies/ μ L; $p = 0.0078$), emphasizing the significant influence of vaginal seeding on bacterial load and specific microbial compositions. The results indicated a significant increase in microbiota transmission, while reducing the abundance of *Enterobacteriaceae*. While bacterial levels on the skin showed a statistically significant increase in seeded infants (32 copies/ μ L) compared to the control group (14 copies/ μ L; p -value=0.033), this effect was localized to the skin and did not extend to stool samples collected on day 30 ($p=0.32$). Moreover, it did not significantly increase *Bacteroides* and *Bifidobacterium* levels, which some studies have previously shown to be higher in infants who were born vaginally seeded. These results underscore how vaginal seeding can influence bacterial levels and specific microbial compositions, leading to alterations in neonatal skin and stool microbiota that resemble those seen in vaginally delivered infants, characterized by lower bacterial diversity.

Ineffective Vaginal Seeding

Mitchell *et al.* (2020)^[17] highlighted the feasibility of maternal seeding for the infant gut microbiome, clarifying that it does not entail a direct transfer of the maternal vaginal microbiome. Notably, the influence of Cesarean Section (CS) delivery on the infant gut community is not immediate; instead, it manifests as a delayed effect. This suggests that surgical delivery not only affects colonization efficiency but also introduces distinctions in the source microorganisms. Consequently, the efficacy of the “vaginal seeding” approach—which entails providing CS-delivered newborns with their mother’s vaginal secretions—may not work.

Wilson *et al.* (2021)^[6] investigated that the infant gut microbiome born through Cesarean section could be

regenerated by the mother's vaginal microbiota. A pilot single-blinded, randomized placebo-controlled trial observed no discernible differences at both the 1-month and 3-month marks after birth of CS-born infants. The vaginal microbiota solution was meticulously crafted through the collection of vaginal swabs from mothers. These swabs were then processed to isolate the essential microbiota. The subsequent solution was promptly given orally to infants in the Cesarean Section (CS)-seeded group within 2 min of their birth. The vaginal seeding method, despite its application, failed to restore *Bacteroides* levels in the infants. While the infants' stool microbiota composition significantly differed from the maternal vaginal microbiota, there were no noticeable differences in the stool microbiota of C-section from C-section newborns who went through vaginal seeding in comparison to those who received a placebo at 1 month ($p=0.90$) and 3 months ($p=0.18$). Vaginal seeding did not change the abundance of any microbial metabolic processes ($q>0.2$), and microbial diversity remained consistent across the three infant groups ($p>0.05$). Despite a distinct microbiota profile with reduced *Bacteroides* levels, C-section infants showed variations in microbiome metabolic potential, particularly in several biosynthesis pathways. The study notes the small participant number as a limitation, potentially affecting the detection of subtle differences. Overall, the findings suggest that vaginal seeding does not significantly impact gut microbiome development, growth measurements, or body composition, including total body fat, among the three infant groups at 1 or 3 months of age.

Effects on Health Outcomes

In a placebo-controlled study by Zhou *et al.* (2023)^[18] involving 68 pregnant women, the administration of vaginal swabs to their Cesarean-delivered infants showcased remarkable improvements in both the gut microbiome and metabolome of the actively treated infants. The positive impact extended to enhanced neurodevelopment at 6 months, marking a significant breakthrough. However, certain aging-associated gut microbial taxa, including pathobionts like *Staphylococcus* and *Klebsiella*, displayed a notable decline over time. These microbes are believed to affect different aspects of infant neurodevelopment, including temperament traits, cognitive and motor development, and possibly protecting against brain damage. The study not only revealed how the gut microbiota matures in infants delivered by C-section but also highlighted the potential of Vaginal

Microbiota Transplant (VMT) to speed up this complex developmental process.

Liu *et al.* (2023)^[19] found that vaginal seeding did not significantly impact the gut microbiota, body mass index (BMI), or allergies in infants over the first two years of life. The study included 120 infants, with 117 analyzed. Results showed no significant differences in BMI and BMI z-scores between the vaginal seeding and control groups at 6, 12, 18, and 24 months. For example, at 6 months, the mean BMI was 17.5 kg/m² in the vaginal seeding group and 17.8 kg/m² in the control group ($p=0.30$). The BMI z-score also remained consistent. The total allergy risk score showed no significant difference, with 1.5 in the vaginal seeding group and 2.0 in the control group ($p=0.48$). While there was a slight, non-significant increase in *Lactobacillus* and *Bacteroides* in the vaginal seeding group at birth and 6 months, there were no significant impacts on growth or allergy risks. Notably, the risk of overweight/obesity at 6 months was lower in the vaginal seeding group compared to the control group (0/57 vs. 6/59; relative risk, 0.03 [95% confidence interval, 0.00-0.57]; $p=0.03$), although this difference was not observed at later time points. No adverse events associated with the intervention were reported.

Risk of Vaginal Seeding

Due to the insufficient evidence demonstrating clear benefits and the potential risks associated with the introduction of vaginal microbes through vaginal seeding, reputable medical opinion articles, including those from organizations like the American College of Obstetricians and Gynecologists and the BJOG: An International Journal of Obstetrics and Gynaecology, advise health professionals against this practice.^[20,21] Clinicians are likely to avoid recommending or performing vaginal seeding in routine clinical settings, opting to await consensus in further research and official guidelines before considering it as a viable option.

The limitations of vaginal seeding stem from small sample sizes in case-control studies, unproven advantages, and concerns about potential harm to newborns.^[22,23] The Cleveland Clinic (2021)^[24] warns that while vaginal seeding may offer essential microbes for a healthy microbiome in C-section-born babies, it comes with inherent risks. There's a worry about exposing babies to harmful bacteria without proper safety screening and validated protocols. This could lead to unintentional transmission of various pathogens, such as Group B Streptococcus, genital herpes, chlamydia, and gonorrhea, from a compromised

vaginal microbiome. The primary focus of these trials should be on proving the safety of these therapies.^[25] Furthermore, Duar, Kyle, and Tribe (2020)^[26] questions vaginal seeding, cautioning against the practice often carried out without the supervision of healthcare professionals. This poses significant dangers for the potential transmission of opportunistic pathogens, including viruses and fungi, to the newborn, particularly when the mother may be asymptomatic.

CONCLUSION AND RECOMMENDATIONS

In conclusion, the research explores the potential of “vaginal seeding” as a postpartum intervention for infants born via Cesarean Section (CS). It aims to mimic the diverse microbiota of vaginally delivered neonates, associated with enhanced immunity development and lower risks of certain health issues in the future. Currently, there is no established intervention to mitigate the impact of Cesarean Section (CS) on the establishment of the infant’s microbiota since vaginal seeding remains a debated and investigational procedure. Though there is evidence suggesting the potential benefits of vaginal seeding for the gut microbiota of CS-born infants, conflicting findings and the absence of large-scale randomized controlled studies raise concerns about its efficacy and safety. There is a significant lack of evidence demonstrating the impact of vaginal seeding on the infant microbiota associated with its influence on various health outcomes.

The authors propose further investigation into the immediate and long-term health advantages of introducing vaginal microbes to infants, highlighting whether the difference with those of infants delivered vaginally is significant. Investigating the intricate mechanisms underlying newborn diseases and their interaction with the diverse microbiota also presents a promising direction for future research. To address discrepancies in study outcomes, conducting more extensive trials with larger groups and longer study durations is crucial. Furthermore, it is imperative that safety precautions and screening procedures be established to prevent any unfavorable consequences that may arise from vaginal seeding. This is necessary to thoroughly assess the effectiveness and safety of seeding maternal-child microbes in infants born via Cesarean section.

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AUTHOR’S CONTRIBUTIONS

This study was initiated and conceptualized by Mikaela Calimon and Nathalie Lopez. Author Carlo Basilan led the group and set the cadence that resulted in the development and completion of the study. Authors Mary Lou Nogales, Mheizeli Pantanilla, and Edsel Trinidad composed the abstract of the study. Authors Mikaela Calimon, Mheizeli Pantanilla, Edsel Trinidad, and Mary Lou Nogales constructed the initial draft of the introduction. As for the Methodology, author Eriel Bernardino conducted screening and assessment of each article included in the study, with all authors contributing to the analysis and interpretation of the gathered data. Authors Mikaela Calimon and Mary Lou Nogales provided the conclusion of the study. Author Bernardino Hagojoj provided invaluable feedback, guidance, and support throughout the manuscript development process. Through collaborative efforts, all authors rigorously reviewed and approved the final manuscript version.

ETHICAL STATEMENT

The authors adhere to the ethical guidelines for conducting and collecting data from secondary sources. All references were appropriately cited and acknowledged.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. World Health Organization. Caesarean section rates continue to rise amid growing inequalities in access [Internet]. 2021 Jun 16. Available from: <https://www.who.int/news/item/16-06-2021-caesarean-section-rates-continue-to-rise-amid-growing-inequalities-in-access>.
2. Song SJ, Wang J, Martino C, Jiang L, Thompson WK, Shenhav L, *et al.* Naturalization of the microbiota developmental trajectory of Cesarean-born

- neonates after vaginal seeding. *Medicine*. 2021;95(1):964.e5. doi: 10.1016/j.medj.2021.05.003.
3. Hoang DM, Levy EI, Vandenplas Y. The impact of Cesarean section on the infant gut microbiome. *Acta Paediatr*. 2021;110(1):60–7. doi: 10.1111/apa.15501.
 4. Korpela K. Impact of delivery mode on infant gut microbiota. *Ann Nutr Metab*. 2021;77(1):11–9. doi: 10.1159/000518498.
 5. Blanco-Rojo R, Maldonado J, Schauback M, Özener M, López-Huertas E, Olivares M. Beneficial Effects of *Limosilactobacillus fermentum* CECT 5716 Administration to Infants Delivered by Cesarean Section. *Front Pediatr*. 2022;10. doi: 10.3389/fped.2022.906924.
 6. Wilson BC, Butler EM, Grigg CP, Derraik J, Chiavaroli V, Walker N, *et al.* Oral administration of maternal vaginal microbes at birth to restore gut microbiome development in infants born by caesarean section: A pilot randomised placebo-controlled trial. *EBioMedicine*. 2021;69:103443. doi: 10.1016/j.ebiom.2021.103443.
 7. Butler EM, Chiavaroli V, Derraik JG, Grigg CP, Wilson BC, Walker N, *et al.* Maternal bacteria to correct abnormal gut microbiota in babies born by C-section. *Medicine (Baltimore)*. 2020;99(30):e21315. doi: 10.1097/md.00000000000021315.
 8. Sassan AM, Johnson GJ, Goulding AN, Aagaard KM. Crucial nuances in understanding (mis)associations between the neonatal microbiome and Cesarean delivery. *Trends Mol Med*. 2022;28(10):806–22. doi: 10.1016/j.molmed.2022.07.005.
 9. Committee on Obstetric Practice. Vaginal seeding [Internet]. American College of Obstetricians and Gynecologists; 2017 [cited 2024 Jul 8]. Available from: <https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2017/11/vaginal-seeding#:~:text=The%20American%20College%20of%20Obstetricians%20and%20Gynecologists%20does%20not%20recommend,safety%20and%20benefit%20of%20vaginal%20seeding>.
 10. Ríos-Covian D, Langella P, Martín R. From Short- to Long-Term Effects of C-Section Delivery on Microbiome Establishment and Host Health. *Microorganisms*. 2021;9(10):2122. doi: 10.3390/microorganisms9102122.
 11. Widodo AD, Juffrie M. Cesarean section and gut microbiota in children. *World Nutr J*. 2020;4(1–2):8. doi: 10.25220/wnj.v04.s2.0002.
 12. Xie J, Tang C, Hong S, Xin Y, Zhang J, Lin Y, *et al.* Maternal vaginal fluids play a major role in the colonization of the neonatal intestinal microbiota. *Front Cell Infect Microbiol*. 2023;13. doi: 10.3389/fcimb.2023.1065884.
 13. Anthoulaki X, Oikonomou E, Bothou A, Papanikolopoulou S, Nikolettos K, Damaskos C, *et al.* Comparison of Gut Microbiome in Neonates Born by Cesarean Section and Vaginal Seeding with Gut Microbiomes of Neonates Born by Cesarean Section Without Vaginal Seeding and Neonates Born by Vaginal Delivery. *Mater Sociomed*. 2023;35(3):234–43. doi: 10.5455/msm.2023.35.234–243.
 14. Mueller NT, Differding MK, Sun H, Wang J, Levy S, Deopujari V, *et al.* Maternal Bacterial Engraftment in Multiple Body Sites of Cesarean Section Born Neonates after Vaginal Seeding—a Randomized Controlled Trial. *MBio*. 2023;14(3). doi: 10.1128/mbio.00491-23.
 15. Mitchell CM, Mazzoni C, Hogstrom L, Bryant A, Bergerat A, Cher A, *et al.* Delivery Mode Affects Stability of Early Infant Gut Microbiota. *Cell Rep Med*. 2020;1(9):100156. doi: 10.1016/j.xcrm.2020.100156.
 16. Zhang C, Li L, Jin B, Xu X, Zuo X, Li Y, *et al.* The Effects of Delivery Mode on the Gut Microbiota and Health: State of Art. *Front Microbiol*. 2021;12:724449. doi: 10.3389/fmicb.2021.724449.
 17. Dominguez-Bello MG, De Jesus-Laboy KM, Shen N, Cox LM, Amir A, Gonzalez A, *et al.* Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer. *Nat Med*. 2016;22(3):250–3. doi: 10.1038/nm.4039.
 18. Zhou L, Qiu W, Wang J, Zhao A, Zhou C, Sun T, *et al.* Effects of vaginal microbiota transfer on the neurodevelopment and microbiome of cesarean-born infants: A blinded randomized controlled trial. *Cell Host Microbe*. 2023;31(7):1232–47.e5. doi: 10.1016/j.chom.2023.05.022.
 19. Liu Y, Li HT, Zhou SJ, Zhou HH, Xiong Y, Yang J, *et al.* Effects of vaginal seeding on gut microbiota, body mass index, and allergy risks in infants born through cesarean delivery: A randomized clinical trial. *Am J Obstet Gynecol MFM*. 2023;5(1):100793. doi: 10.1016/j.ajogmf.2022.
 20. Committee on Obstetric Practice. Committee Opinion No. 725: Vaginal Seeding. *Obstet Gynecol*. 2017;130:e274.
 21. Haahr T, Glavind J, Axelsson P, *et al.* Vaginal seeding or vaginal microbial transfer from the mother to the caesarean-born neonate: a commentary regarding clinical management. *BJOG*. 2018;125:533.
 22. Mueller NT, Differding MK, Ostbye T, Hoyo C, Benjamin-Neelon SE. Association of birth mode of delivery with infant faecal microbiota, potential pathobionts, and short chain fatty acids: a longitudinal study over the first year of life. *BJOG*. 2021;128(9):1293–303.
 23. Vaginal seeding after cesarean delivery [Internet]. *Natural Medicine Journal*. 2022 Oct 19 [cited 2024 Jul 8]. Available from: <https://www.naturalmedicinejournal.com/journal/vaginal-seeding-after-cesarean-delivery>.
 24. Cleveland Clinic. Vaginal seeding [Internet]. 2021 [cited 2024 Jul 8]. Available from: <https://my.clevelandclinic.org/health/treatments/22096-vaginal-seeding>.
 25. Hourigan SK, Dominguez-Bello MG, Mueller NT. Can maternal-child microbial seeding interventions improve the health of infants delivered by Cesarean section? *Cell Host Microbe*. 2022;30(5):607–11. doi: 10.1016/j.chom.2022.02.014.
 26. Duar RM, Kyle DJ, Tribe RM. Reintroducing *B. infantis* to the cesarean-born neonate: an ecologically sound alternative to “vaginal seeding.” *FEMS Microbiol Lett*. 2020;367(6). doi: 10.1093/femsle/fnaa032.

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