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Restoring Gut Health in C-Section Infants: Exploring the Role of Nutrition Modulators

Globally, there has been a significant increase in the rate of caesarean section (CS) deliveries.[1] Current data shows that 21% of women globally undergo CS delivery and this rate is projected to reach 30% by 2030.[2] Such a trend raises significant concerns as studies have shown that CS delivered infants have a gut microbial imbalance which is associated with increased risk for infections, allergies and metabolic disorders.[3,4]

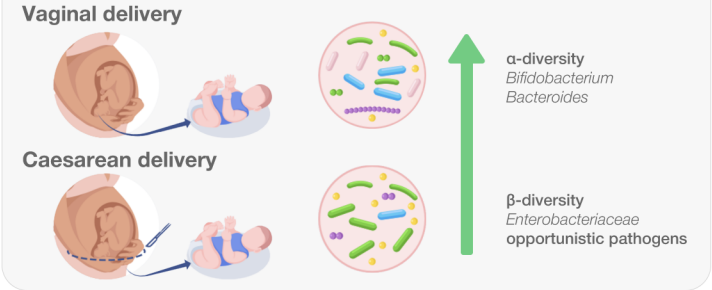
Impact of C-Section on the Infant Gut Microbiota Development

The mode of delivery significantly influences the development of an infant's gut microbiome. Vaginal delivery facilitates the transfer of maternal intestinal and vaginal microbiota, enriching the infant's gut with beneficial bacteria like *Bifidobacterium* and *Bacteroides*, as illustrated in Figure 1.[3-7] These microbes play a vital role in fermenting human milk oligosaccharides (HMOs), creating an optimal gut environment that inhibits opportunistic pathogens such as *Enterobacteriaceae*.[7-9]

In contrast, CS-born infants primarily acquire microbes from the mother's skin and the hospital environment. This results in reduced levels of beneficial bacteria and increased colonization by opportunistic pathogens such as *Enterococcus, Enterobacter*, and *Klebsiella* (Figure 1). Furthermore, colonization of Bacteroides in CS-born infants is often delayed, with disruptions persisting up to one year.[5,8,9]

This **microbial dysbiosis**, underlines the importance of addressing the long-term implications of cesarean delivery on infant gut health and development.[10,11]

Figure 1: CS birth eliminates the normal mother-to-infant transmission of beneficial microbes.[7]



Adapted from: Rios-Covian, 2021.

Other Factors Affecting Gut Microbiota Development

In addition to the mode of delivery, various external factors such as diet and antibiotic exposure can also negatively impact the development of gut microbiota.[9,12] Diet is a key modifiable factor influencing the composition of the gut microbiota.[13] Non-exclusive breastfeeding and formula feeding in infants during the early stages of life have been shown to be associated with alterations in the gut microbiota and a dysregulated gut environment.[14]

The gut microbiome of infants who received perinatal antibiotics appears to be less diverse. Infants born to mothers who receive intrapartum antibiotic prophylaxis may have lower levels of *Bifidobacterium* and *Bacteroidetes*, while showing a higher relative abundance of *Clostridium leptum*.[9,12]

While the administration of intrapartum antibiotics is a recommended practice to prevent infections from CS delivery, it is likely to cause dysbiosis in the infant's gut microbiome and is associated with adverse later-life outcomes such as infections and metabolic disorders.[9,10]

Health Risks Associated with Infants Born via Cesarian Section

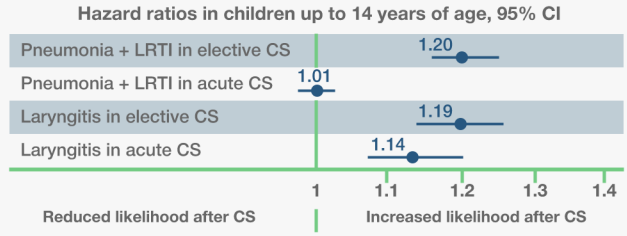
Early-life gut microbiota is a key driver to promote the development and maturation of the immune system as 70% to 80% of immune cells are present in the gut hence dysbiosis can put the child at risk for disease conditions.[12,15]

A meta-analysis revealed that CS-born infants have a higher risk of developing asthma compared to those born through vaginal delivery (Figure 2).[16]

Figure 2: CS increases the likelihood of developing asthma by 23%.[16]

A population-based study showed that CS birth is associated with a 20% increased risk of lower respiratory tract infections, pneumonia and laryngitis during the first 14 years of life (Figure 3).[17]

Figure 3: Increased risk of lower respiratory tract infection in acute and elective CS-delivered children.[17]



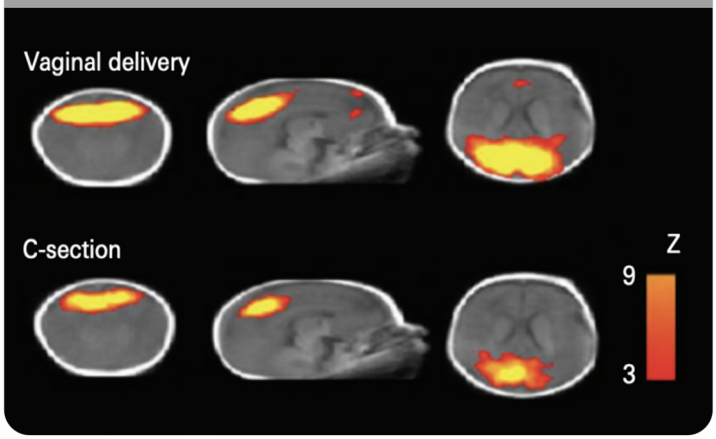
Moreover, CS delivery may predispose to allergic disorders in early infancy.[18,19] A prospective birth cohort study showed a 3-fold higher odds of developing food allergy in CS-born infants.[18]

Similarly, CS born infants demonstrate a higher vulnerability to immune-related diseases ranging from 25% to 50% throughout their first 14 years of life.[17]

C-Section may Directly Impact Brain Development

A longitudinal cohort study revealed that CS delivery significantly reduces white matter integrity, lowers functional connectivity at 2 weeks (Figure 4), and reduces myelination at 6 months. This may have an implication on neurodevelopmental outcomes such as communication, learning, and motor skills.[20]

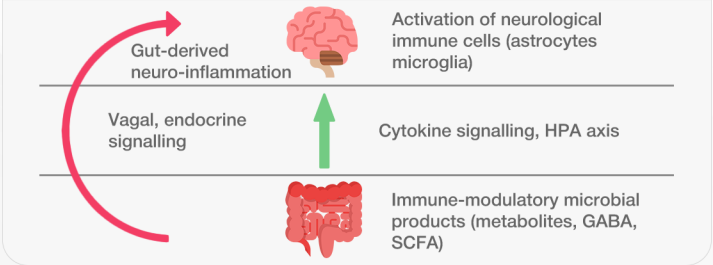
Figure 4: CS group has lower brain functional connectivity compared to those born vaginally.[20]



C-section Affects the Gut-Brain Axis

C-section affects the brain directly and through the gut. Gut dysbiosis can have effects on the brain, through the gut–brain axis connection The disruption in the delicate balance of gut microbiota due to gut dysbiosis can result in abnormal signaling to the brain, affecting both structure and function of the brain (Figure 5).[20,21]

Figure 5: Mechanistic pathways by which the gut microbiota influences the brain function.[21]



How can Nutrition Support Healthy Gut Microbiota Development in CS-delivered Infants?

The Role of Breast Milk in Shaping a Healthier Gut Microbiota

Breastmilk plays a crucial role in shaping the infant gut microbiota by promoting the growth and proliferation of beneficial *Bifidobacteria*, suppressing harmful microorganisms, and enhancing barrier integrity and immune function.[22] A key component driving this effect is HMOs, unique to breastmilk, selectively nourishing beneficial gut bacteria such as *Bifidobacteria*.[22]

In CS-born infants, breastfeeding supports the restoration of the gut microbiota, particularly through the enrichment of beneficial microbes like *Bifidobacteria*.[23,24] This suggests that by delivering both HMOs and other bioactive components, breastmilk supports a balanced gut microbiome in CS-born infants, promoting both gut and immune health during critical early life stages.[22,23]

Role of Prebiotics and Probiotics in Restoring Gut Dysbiosis and Supporting the Immune System

A randomised controlled trial of supplementation of formula with 2'FL and LNnt revealed that the stool composition and diversity of CS-born infants are closer to those of breastfed infants, with an abundance of beneficial gut microbiota (specifically *Bifidobacterium*) and decrease of *Escherichia* and *Peptostreptococcaceae*.[25]

In another study, infant formula with milk-derived oligosaccharides (MOS) shifted the gut microbiome and metabolic signature of CS-born infants closer to that of human milk-fed infants, reduced fecal pathogens, and improved the intestinal immune response.[26]

Of interest in the supplementation of formula with prebiotics and probiotics is the outcome of possible enhanced benefits on the immune system. In studies by Puccio and Berger, lower incidence of respiratory tract infections and bronchitis were documented in the CS group with 2 FL and LNnT.[25,27] With probiotic *B. lactis*, the finding of improved vaccine response in C-section born infants may suggest an enhanced immune system support.[28]

Key Takeaways

- **Vaginal birth promotes healthy gut microbiome development in infants through exposure to the mother's natural microbiota.**
- **CS delivery disrupts this normal process, leading to altered gut microbiota in infants and increased risks for adverse short- and long-term health outcomes.**
- **Dietary interventions can help address the altered gut microbiota and support the immune system of CS infants. Supplementation with prebiotics (e.g. HMOs, MOS), probiotics (e.g. *B. lactis*), play important roles in maintaining a balanced gut microbiome and enhancing immune support.**

References

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Abbreviations

B. Lactis: Bifidobacterium lactis; **CI:** Confidence interval; **CS:** Caesarean section; **2'-FL:** 2'-fucosyllactose; **HMOs:** Human milk oligosaccharides; **LNnT:** Lacto-N-neotetraose; **MOs:** Milk oligosaccharides; **OR:** Odds ratio.