

REVIEW PAPER

The impact of intrapartum antibiotic prophylaxis on the microbiological composition of human milk and the development of the neonatal microbiota: a review of the literature

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ABSTRACT

Perinatal gut colonisation plays a crucial role in neonatal development. Microorganisms in colostrum and human milk are among the first to colonise the neonatal gastrointestinal tract, playing a key role in shaping a healthy gut microbiota. Current evidence indicates that perinatal antibiotic exposure may disrupt early microbial colonisation and modulate human milk microbiota. The most common form of this exposure is intrapartum antibiotic prophylaxis, administered to over 40% of women because of vaginal colonisation with *Streptococcus agalactiae* or the need for caesarean delivery. Despite growing interest, available studies are limited, highlighting the need to better understand factors shaping human milk microbiota and early neonatal gut development. Therefore, this review aims to summarise current evidence regarding the impact of perinatal antibiotic exposure on the microbiological composition of human milk and the establishment of the neonatal gut microbiota.

KEY WORDS:

microbiota, IAP, human milk microbiota, intrapartum antibiotics, neonatal gut microbiota.

DEVELOPMENT OF GUT MICROBIOTA AFTER BIRTH

The establishment of the infant gut microbiota is a dynamic, multistage process. It begins in utero, and is influenced by host genetic material, microbial metabolites, and microbial DNA. During the third trimester of gestation, the foetus swallows amniotic fluid, which has been shown to contain microbial components, and may contribute to the early colonisation of the gastrointestinal tract by maternal microorganisms [1]. In the early postnatal period, the gastrointestinal tract is predominantly colonised by aerobic and facultative anaerobic bacteria, and then as the infant gut proceeds toward maturity the number of strict anaerobic microorganisms increases. The maturation of the infant gut microbiota toward

a composition characteristic of the adult intestinal ecosystem takes nearly three years. Initial microbial colonisation occurs at birth as a result of contact with the maternal vaginal, intestinal, and skin microbiota, as well as with environmental microorganisms. The oral microbiota is shared almost entirely with the mother during the first several days of life [2]. The mode of delivery significantly impacts the development of the neonatal gastrointestinal microbiota. It influences not only the types of bacteria acquired by the newborn but also their overall abundance. During vaginal delivery, the infant's gut is colonised with vaginal and intestinal bacteria from the mother, which leads to the early establishment of a beneficial microbial community. The initial colonisation of the neonatal gut is typically characterised by aerobic and facultative anaerobic bacteria, including *Streptococcus* spp., *Staphylococcus*

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spp., *Escherichia coli*, *Lactobacillus* spp., and *Enterobacter* spp. During the first week of life, decreasing gut oxygen levels promote colonisation by obligate anaerobes, including *Bifidobacterium* spp., *Bacteroides* spp., and members of the phylum *Firmicutes* [3]. Maternal-derived bacteria, such as *Lactobacillus* and *Bifidobacterium*, may contribute to the development of the infant gut microbiota. Many of these early colonising bacteria produce short-chain fatty acids (SCFAs), which lower intestinal luminal pH and thereby inhibit the growth of pathogenic microorganisms. Compared with infants born *via* caesarean section, those delivered vaginally generally exhibit more diverse gut microbiota, along with lower levels of *Staphylococcus* species and reduced colonisation by *Clostridioides difficile* [4]. Birth by caesarean section interrupts the microbial transmission from the mother to a child that occurs during vaginal birth. Consequently, the infant's gastrointestinal tract is initially colonised by bacteria from the maternal skin – primarily *Staphylococcus*, *Corynebacterium*, *Propionibacterium*, and *Clostridium* – as well as microorganisms from the immediate neonatal environment. The intestinal microbiota following caesarean section (CS) is characterised by delayed bacterial colonisation, reduced bacterial abundance and diversity, and an increased abundance of opportunistic pathogens related to the health-care personnel and in some cases even hospital-associated strains such as *Enterococcus*, *Klebsiella*, *Enterobacter cloacae*, and *Clostridium perfringens* [5]. After caesarean section the neonatal gut microbiota is dominated by Firmicutes (*Enterococcus*, *Staphylococcus*, *Streptococcus*, *Clostridium*, *Veillonella*), and Proteobacteria (*Klebsiella*, *Enterobacter*, *Haemophilus*) [6]. Compared with vaginal delivery, there is a reduced amount of *Bacteroides*, *Bifidobacterium*, and *Lactobacillus*, as well as SCFAs [7]. Therefore, gut dysbiosis may be observed from the first hours of life and can persist through the following days and months, often lasting for at least two years [8].

RECOMMENDATIONS FOR ANTIBIOTIC PROPHYLAXIS AT DELIVERY

Over the past decade, a global increase in antibiotic consumption has been observed, including their use during pregnancy [9]. It is estimated that over 40% of women received antibiotics during pregnancy as part of peripartum prophylaxis for early-onset neonatal sepsis caused by *Streptococcus agalactiae* (GBS) or for the prevention of surgical site infection (SSI) following CS [10].

Caesarean section is among the most frequently performed surgical procedures worldwide and plays a crucial role in perinatal care by preventing maternal and neonatal morbidity and mortality in selected clinical situations, such as obstructed labour or foetal distress [11]. In Poland, the proportion of births delivered by CS remains among the highest in Europe, reaching 47.9% in 2024, substantially exceeding the World Health Organisation

recommendation that CS rates should not surpass 15% [12, 13]. Although CS is a life-saving intervention when medically indicated, it is associated with a significantly higher risk of postpartum infections – up to fivefold greater compared with vaginal birth – most commonly including SSI, endometritis, and urinary tract infection [14]. Consequently, international and national guidelines recommend routine antibiotic prophylaxis for all women undergoing elective or emergency CS [15]. According to the recommendations of the Polish Society of Gynaecologists and Obstetricians (PTGiP), a single dose of a penicillin or first-generation cephalosporin should be administered intravenously 30–120 minutes prior to skin incision, in such a way that a bactericidal concentration of the agents is achieved in the serum and tissues when the incision is made, effectively reducing the risk of severe maternal infectious complications [16].

Streptococcus agalactiae (group B *Streptococcus*, GBS) remains a leading cause of neonatal morbidity and mortality worldwide. Current recommendations in Poland, based mainly on guidelines from the Centers for Disease Control and Prevention and adopted by the PTGiP advise universal screening for GBS colonisation between 35 and 37 weeks of gestation using vaginal and rectal cultures [17]. Women with a positive result are candidates for intrapartum antibiotic prophylaxis (IAP), which has been shown to reduce the incidence of early-onset neonatal GBS sepsis by approximately 80% [18]. Intrapartum prophylaxis should be administered at least four hours prior to delivery, and intravenous penicillin (penicillin G, ampicillin) or a first-generation cephalosporin is recommended. Intrapartum antibiotic prophylaxis is also indicated for women with unknown GBS status who deliver preterm, for those with a history of a previous infant affected by invasive GBS disease, for women with GBS bacteriuria during any trimester, preterm rupture of membranes, prolonged rupture of membranes (> 18 hours), signs of chorioamnionitis or maternal intrapartum fever (> 38°C). Approximately 30% of pregnant women are colonised with GBS, and vertical transmission occurs in roughly 50% of cases, with about 1% of neonates developing invasive disease [19]. The introduction of IAP has significantly reduced early-onset GBS disease, from one case per 200 births to approximately one per 4,000 births, although it does not affect the incidence of late-onset GBS disease, which is typically acquired perinatally or from the environment. While IAP is effective in preventing early neonatal sepsis, it does not entirely prevent maternal-to-neonate transmission of GBS or the occurrence of late-onset disease [20].

IMPACT OF INTRAPARTUM ANTIBIOTIC PROPHYLAXIS ON INFANT GUT MICROBIOTA

It is well established that the gut microbiome exerts a variety of functions within the human organism, such

as vitamin synthesis and the production of SCFAs, which serve as an energy source for the host and help maintain an acidic intestinal environment. It also protects against pathogens, participates in the regulation of intestinal permeability and interacts with the immune system, for example by influencing the balance between regulatory T-cells and Th17 responses. Therefore, concerns have arisen about the potential impact of IAP on the neonatal gut microbiome. A growing body of evidence demonstrates that IAP substantially influences the early development of the infant gut microbiota. Across observational and cohort studies conducted over the last two decades, maternal exposure to antibiotics during pregnancy or labour has been consistently associated with alterations in microbial composition, reduced microbial richness, and delayed establishment of key commensal taxa in offspring. Intrapartum antibiotic prophylaxis used for the prevention of GBS mainly targets Gram-positive bacteria, while surgical antibiotic prophylaxis affects both Gram-positive and Gram-negative bacteria. As a result, commensal Gram-positive bacteria, including *Lactobacillus* species are markedly reduced after IAP administration [21]. One of the most consistent observations across studies is a reduction in *Bifidobacterium* abundance among infants exposed to IAP. This effect has been reported across different delivery modes, antibiotic classes, and analytical techniques, including culture-based methods, quantitative polymerase chain reaction (qPCR), and high-throughput sequencing. Several studies indicate that IAP exposure leads to both lower absolute and relative abundances of Bifidobacteria, particularly *Bifidobacterium longum*, *B. breve*, and *B. bifidum*, during the first weeks to months of life. Although partial recovery may occur over time – especially in breastfed infants – some alterations persist for up to one year or longer, suggesting a lasting imprint on microbiota development. Furthermore, recent research regarding microbial deviations following IAP in vaginally delivered term infants consistently reports a reduction in *Bacteroides*. Moreover, IAP exposure is frequently associated with an increased abundance of Proteobacteria and facultative anaerobes, including members of the *Enterobacteriaceae* family, *Enterococcus*, and *Clostridium*. These shifts reflect a delay in the transition toward a microbiota dominated by obligate anaerobes and are often accompanied by reduced microbial diversity and richness. Beyond taxonomic changes, functional consequences of IAP-related dysbiosis have also been described. These include reduced SCFA production, altered metabolic pathways, and an increased carriage of antimicrobial resistance genes in the infant gut microbiome. Importantly, the magnitude and persistence of these effects appear to be modified by factors such as mode of delivery, duration and timing of antibiotic exposure, and infant feeding practices, with breastfeeding exerting a partially protective effect. Table 1 summarises selected studies that investigated the impact of IAP on

the composition of the infant gut microbiota. A literature search was conducted in the PubMed database to identify relevant studies. Additionally, the reference lists of selected articles were screened to identify further relevant publications. This review is narrative in nature and does not represent a formal systematic review.

IMPACT OF INTRAPARTUM ANTIBIOTIC PROPHYLAXIS ON HUMAN MILK MICROBIOTA

The impact of IAP on the human milk microbiome is much less understood than its effect on the infant gut microbiota. However, available evidence suggests that perinatal antibiotic exposure may also alter its microbial composition. Human milk microbiota is a dynamic ecosystem, comprising both commensal and potentially pathogenic bacteria, and serves as one of the sources for neonatal gut colonisation. Hermansson *et al.* [47] investigated the composition of breast milk microbiota in 84 healthy mothers, 1 month after delivery, with a focus on the effects of delivery mode and IAP. Among the participants, 61 mothers delivered vaginally (23 of whom received IAP), 13 delivered by non-elective CS (7 received IAP), and 10 delivered by elective CS without IAP. The antibiotics administered included penicillin G, cephalothin, cephalixin, cefuroxime, and combinations with metronidazole, depending on the delivery mode and clinical indication. Despite the similarity in relative abundances, both delivery mode and IAP were significantly associated with changes in overall breast milk microbial composition as assessed by ANOSIM ($p = 0.001$). When analysed independently, IAP alone did not show statistically significant differences in breast milk composition by ANOSIM. However, redundancy analysis indicated that when delivery mode and IAP were considered simultaneously, both factors independently influenced the composition of breast milk microbiota one month postpartum (delivery mode: $p = 0.001$; IAP: $p = 0.015$). Interestingly, intrapartum antibiotic exposure was associated with higher α diversity and richness in breast milk when analysed as a single variable. Furthermore, when samples were separated based on antibiotic exposure, *Bifidobacterium* was detected exclusively in the breast milk of mothers who had not received antibiotics. Overall, the effects of IAP on breast milk microbiota were modest but independent, suggesting a detectable, though not substantial, impact at 1 month postpartum. The underlying mechanisms remain unclear, and the study authors note that changes in breast milk microbiota might be more pronounced in earlier stages of lactation. They also highlight that relying on a single time point is a limitation, emphasising the need for serial sampling in future research.

In another study, Padilha *et al.* [48], investigated the impact of the maternal antibiotic prophylaxis on the human milk *Bifidobacterium* spp. and total bacteria counts, in the first week and first month after delivery.

TABLE 1. Selected studies examining perinatal antibiotics and offspring microbiota

Author, year	Study group	Antibiotic	Type of microbiome sample and technique for gut microbiota analyses	Results
Jauréguy <i>et al.</i> , 2004 [22]	50 full-term, vaginal and CS newborns; $n = 25$ antibiotic-exposed group and $n = 25$ non-antibiotic-exposed group	Amoxicillin	Fecal samples collected from 3-day-old infants; culturing	- Similar colonisation rates by aerobic bacteria and amoxicillin-resistant enterobacteria in antibiotic-exposed and non-exposed infants ($p = 0.79$) - Significantly fewer infants in the antibiotic-exposed group than in the non-antibiotic-exposed group were colonised by anaerobic bacteria, especially <i>Clostridium</i> ($p < 0.05$) β-lactam-resistant bacteria: IAP did not promote colonisation - Infants whose mothers took antibiotics during pregnancy including labour were associated with lower counts of <i>Bifidobacterium angulatum</i>
Pozo-Rubio <i>et al.</i> , 2013 [23]	55 infants (age: 4 months) among which 15 were exposed to maternal antibiotic during pregnancy and 8 during labour	No data	Fecal samples analysed by qPCR	<i>Lactobacillus</i> transfer from the mother to the infant is delayed in IAP infants
Keski-Nisula, 2013 [24]	45 mother-baby dyads	Penicillin/ amoxicillin and cephalosporin	Maternal vaginal and neonatal oral samples; culturing	- At one month of age, infants not exposed to antibiotics had significantly higher percentages ($p < 0.05$) of Bifidobacteriaceae, Streptococcaceae, unclassified Actinobacteria, and unclassified Lactobacillales and lower ($p < 0.05$) percentages of Enterobacteriaceae than infants whose mothers received IAP - Later studies confirmed, at a high taxonomic level, the previously reported effect: after 30 days IAP infants harbour lower abundances of Actinobacteria and Firmicutes, higher levels of Proteobacteria, and lower levels of acetate and total short-chain fatty acids in their gut microbiota.
Arbolea <i>et al.</i> , 2015 and 2016 [25, 26]	27 preterm infants (7 delivered vaginally and 20 by CS) compared with 13 full-term vaginally delivered infants	Penicillin ampicillin or ampicillin + erythromycin	Fecal samples; 16S rRNA amplicon sequencing, qPCR	- Significant reduction in bifidobacterial counts in the IAP group ($p = 0.001$) <i>Escherichia coli</i>, <i>Bacteroides fragilis</i>, <i>Bifidobacterium</i> were the most abundant in the control group, whereas Lactobacilli and <i>Clostridium difficile</i> were much lower - IAP newborns had decreased <i>Bifidobacterium</i> and <i>Escherichia coli</i> levels
Aloisio <i>et al.</i> , 2014 [27]	52 newborns: 26 born by mothers negative to GBS (control group) and 26 by mothers positive to GBS and subjected to the IAP group	Ampicillin	Fecal samples; qPCR, PCR-DGGE	- Significant reduction in <i>Bifidobacterium</i> spp. following IAP ($p < 0.05$) - Reduced microbial diversity and richness, leading to dominance by the Enterobacteriaceae family in the IAP group - Decreased Actinobacteria and Bacteroidetes in the IAP group, as well as overrepresentation of Proteobacteria
Aloisio <i>et al.</i> , 2016 [28]	20 full-term, vaginally delivered infants: 10 born by mothers negative to GBS and 10 by mothers positive to GBS and receiving IAP	Ampicillin	Fecal samples; 16S rRNA amplicon sequencing, qPCR	- IAP infants group: decrease in Bacteroidetes and Firmicutes and increase in Proteobacteria - Genera Parabacteroides and Bacteroides underrepresented and <i>Enterococcus</i> and <i>Clostridium</i> over-represented at 3 months following maternal IAP - Microbiota differences were especially evident following IAP with emergency CS, with some changes (increased Clostridiales and decreased Bacteroidaceae) persisting to 12 months, particularly among non-breastfed infants
Azad <i>et al.</i> , 2016 [29]	198 healthy, full-term infants at the ages of 3 months and 1 year, 85 of them were exposed to IAP	Cefazolin and penicillin	Fecal samples; 16S rRNA amplicon sequencing	

TABLE 1. Cont.

Author, year	Study group	Antibiotic	Type of microbiome sample and technique for gut microbiota analyses	Results
Cassidy-Bushrow <i>et al.</i> , 2016 [30]	262 infants: 80 were born to GBS-positive mothers, of whom 58 received IAP	Penicillin	Fecal samples collected at 1 and 6 months of age; 16S rRNA amplicon sequencing	If IAP, no GBS associated infant gut microbiota at 1 or 6 months. If no IAP, GBS was associated with distinct microbiota at 6 months
Corvaglia <i>et al.</i> , 2016 [31]	84 healthy term infants, were divided into 2 groups: infants born to GBS-positive mothers who had received IAP versus controls	Ampicillin	Fecal samples collected at 7 and 30 days of life analysed by qPCR	- Bifidobacteria count was significantly lower in the IAP group at 7 days of life - No differences in Bifidobacteria count at 30 days or in Lactobacilli and <i>B. fragilis</i> counts at any time point were documented - Furthermore, at 7 days of life, infants who had not received IAP and were exclusively human milk-fed had higher counts of Bifidobacteria
Mazzola <i>et al.</i> , 2016 [32]	26 infants divided into 4 groups: - BF-C (7) - breast-fed infants born to mothers not receiving IAP - BF-IAP (7) - breast-fed infants born to mothers receiving IAP - MF-C (6) - mixed-fed infants control - MF-IAP (6) - mixed-fed infants born to mothers receiving IAP	Ampicillin	Fecal samples; 16S rRNA amplicon sequencing, qPCR (Bifidobacterium)	- Lower diversity in BF-IAP vs. BF-Controls. Higher abundance of bacteria in the Enterobacteriaceae family at day 7 (52% in the IAP group vs. 14% in the control group) and day 30 (44% in the IAP group vs. 16% in the control group). Actinobacteria in BF-IAP infants and absent in controls - Bifidobacterium spp. significantly reduced in IAP-exposed infants regardless of the feeding type at one week ($p = 0.001$) but recovered by day 30 (breastfed: $p = 0.025$, mixed-fed: $p = 0.013$)
Nogacka <i>et al.</i> , 2016 [33]	40 full-term vaginally delivered infants: 18 born to mothers receiving IAP and 22 as a control group	Penicillin	Fecal samples collected at 2, 10, 30, and 90 days of age; 16S rRNA amplicon sequencing, gas chromatography, PCR for resistance genes	- Proteobacteria and Firmicutes were higher in IAP exposed infants. The effect of IAP remains for at least the first months of life - Significant increase in levels of potentially pathogenic bacteria and decrease in levels of commensal bacteria following IAP ($p < 0.05$) - Increased carriage of antibiotic resistance genes conferring resistance to the antibiotics used in IAP in IAP-exposed infants vs. infants in the control group
Stearns <i>et al.</i> , 2017 [34]	74 infants: born vaginally, with no exposure to antibiotics (53), exposed to IAP for GBS (14), and born by CS (7)	Penicillin cefazolin ampicillin or cephalixin	Fecal samples; 16S rRNA amplicon sequencing	Increased Proteobacteria and reduced abundance of <i>Bifidobacterium</i> spp. at 12 weeks correlates to duration of IAP exposure: for every hour of IAP administration, there was a 7% decrease in abundance of <i>Bifidobacterium</i> spp.
Imoto <i>et al.</i> , 2018 [35]	33 healthy term infants among which 19 were exposed to IAP	Cefazolin, ampicillin	Fecal samples collected at 1 and 10 months of age; 16S rRNA amplicon sequencing	- The beta diversity index of the gut microbiota differed significantly based on maternal antimicrobial use at delivery ($p < 0.05$) - Bifidobacteria were less abundant in infants exposed to maternal antibiotics ($p < 0.05$)
Kamal <i>et al.</i> , 2019 [36]	44 infants whose mothers received IAP either before skin incision or immediately after the umbilical cord was cut	Cefuroxime	Fecal samples collected at the age of 10 days and 9 months; 16S rRNA amplicon sequencing, disk diffusion	- At day 10, the gut microbiota composition of both groups was dominated by the family Enterobacteriaceae and genus <i>Veillonella</i>, while <i>Bifidobacterium</i> spp. and <i>Clostridium</i> spp. were present in noticeable numbers, too - At 9 months, the gut microbiota of the infants was dominated by obligate anaerobes, mainly <i>Faecalibacterium</i> and <i>Blautia</i> and other Clostridiales, Lachnospiraceae, <i>Bifidobacterium</i>, <i>Bacteroides</i>, and <i>Akkermansia</i>

TABLE 1. Cont.

Author, year	Study group	Antibiotic	Type of microbiome sample and technique for gut microbiota analyses	Results
Tapiainen <i>et al.</i> , 2019 [37]	149 full-term infants including 44 born to mothers receiving IAP	Penicillin cefuroxime clindamycin	Fecal samples – daily collection before discharge from the hospital and follow-up samples at six months; 16S rRNA amplicon sequencing; metagenome sequencing	- Lower abundance of <i>Bacteroidetes</i> in the IAP group during the first days and at the age of six months compared to controls ($p < 0.01$) - At the age of 3 days and 6 months, increased Firmicutes (<i>Clostridium</i>, <i>Staphylococcus</i> genera) in the IAP group compared to controls - Significant overall increase in abundance of antimicrobial resistance genes in infants exposed to antibiotics compared with both antibiotic-exposed women and unexposed infants.
Zhou <i>et al.</i> , 2020 [38]	98 infants divided into 4 groups: full-term without antibiotic exposure (FT), full term with antibiotic exposure (FTA), preterm without antibiotic exposure (PT), and preterm with antibiotic exposure (PTA)	Cefazolin	Neonatal meconium; 16S rRNA amplicon sequencing	- Lower load of <i>Lactobacillus</i> spp. in the FTA and PTA groups - The dissimilarity between vaginal and meconium samples was higher in paired mother and newborn groups without antibiotic exposure before delivery
Coker <i>et al.</i> , 2020 [39]	266 full-term, vaginally delivered infants, 87 in the IAP group	Penicillin, cephalosporin mix	Fecal samples collected at 6 weeks, 12 months; 16S rRNA amplicon sequencing and metagenomics analysis	- Alpha diversity indices were consistently lower for infants whose mothers received any type of IAP compared to controls at both time points - IAP was significantly associated with decreased levels of <i>Bacteroides</i>, <i>Bifidobacterium</i>, <i>Blautia</i>, <i>Roseburia</i> and <i>Ruminococcus</i>; and increased levels of <i>Oscillospira</i>, <i>Pseudobacter</i> and <i>Veillonella</i> dispar - Lower representation of genes involved in γ-aminobutyric acid shunt at 6 weeks; and in an incomplete tricarboxylic acid cycle at 1 year
Dierikx <i>et al.</i> , 2022 [40]	63 healthy full-term infants born by CS received antibiotics prior to skin incision ($n = 20$) or after umbilical cord clamping ($n = 20$); a third control group of vaginally delivered infants ($n = 23$) was included	Cefuroxime	Fecal samples collected at 1, 7 and 28 days after birth and at 3 years; 16S rRNA gene sequencing and whole-metagenome shotgun sequencing	- No differences were demonstrated in the taxonomic composition at 10 days postnatally, but a significantly decreased microbial species richness was found in intrauterine antibiotic exposed infants after 9 months - At a genus and species level, no significant differences were found between antenatally antibiotic exposed and unexposed CS-born infants - Maternal antibiotic administration prior to CS does not lead to a 'second hit' on the already compromised microbiome in CS-born infants
Saturio <i>et al.</i> , 2021 [41]	43 healthy full-term babies: 16 of them delivered after IAP use	Cefazolin	Fecal samples, collected at 2, 10, 30 and 90 days of life; 16S rRNA–23S rRNA internal transcribed spacer (ITS) region sequencing and qPCR	- IAP significantly altered both the qualitative and quantitative development of the neonatal <i>Bifidobacterium</i> community during the first months of life - Antibiotic exposure was associated with reduced relative and absolute abundances of key infant-associated species, particularly <i>B. longum</i> ssp. <i>longum</i>, <i>B. breve</i>, and <i>B. bifidum</i>, especially at 1 month of age - Infants exposed to maternal antibiotics showed increased prevalence and relative abundance of species such as <i>B. dentium</i>, <i>B. adolescentis</i>, <i>B. animalis</i> ssp. <i>animalis</i>, and other low-abundance taxa (<i>B. kashiwanohense</i>, <i>B. mongoliense</i>, <i>B. parvae</i>), particularly at 1 month of life - By 3 months of age, some antibiotic-associated alterations were attenuated; however, differences persisted, with <i>B. longum</i> ssp. <i>infantis</i> and <i>B. pseudocatenulatum</i> remaining discriminant species between antibiotic-exposed and non-exposed infants

TABLE 1. Cont.

Author, year	Study group	Antibiotic	Type of microbiome sample and technique for gut microbiota analyses	Results
Chen <i>et al.</i> , 2021 [42]	1654 full-term infants: 375 were born vaginally following maternal IAP and 403 were delivered by CS	Penicillin cefazolin	Fecal samples collected at 3 months were profiled by 16S rRNA sequencing, qPCR (<i>Bifidobacterium</i>)	- Following vaginal birth, maternal IAP exposure was associated with reduced absolute quantities of Bifidobacteria among vaginally delivered infants as well as their lowered abundance relative to other gut microbiota including phylum Actinobacteria - Alpha-diversity analyses indicated that maternal IAP exposure significantly decreased the microbial richness
Turta <i>et al.</i> , 2022	Vaginally delivered, full-term, breastfed 24 infants exposed to IAP and 24 matched infants not exposed to IAP	No data in abstract	Fecal samples obtained at the ages of 1 and 6 months; 16S rRNA gene sequencing	- IAP was associated with reduced microbial richness but not diversity at 1 month of age - Relative abundances of <i>Clostridiaceae</i> and <i>Erysipelotrichaceae</i> were significantly altered in infants exposed to IAP compared with non-exposed infants at 1 month of age. - The observed deviations in gut microbiota composition between infants exposed and not exposed to IAP diminished by the age of 6 months
Ainonen <i>et al.</i> , 2022 [43]	100 vaginally delivered infants among which 27 were controls and 27 were exposed to IAP	Penicillin G cefuroxime	Fecal samples collected at the age of 12 months; 16S rRNA gene sequencing	- Lower abundance of the Bacteroidetes phylum in the IAP group compared to controls - The relative abundance of Firmicutes was higher in the IAP group vs. controls - Increased <i>Clostridium</i>, <i>Faecalibacterium</i>, <i>Prevotella</i> and <i>Escherichia coli</i>
Jokela <i>et al.</i> , 2022 [44]	92 full-term infants: 26 born vaginally without antibiotics and 66 exposed to IAP	Penicillin cephalosporin and other antibiotics	Fecal samples, 16S rRNA gene amplicon sequencing, integrated with qPCR	- In infants born vaginally with IAP, a significant reduction in the absolute abundance of Bacteroidaceae emerged later in infancy, becoming evident at 6 and at 9 months - Across all exposure groups, increased absolute abundances of families within the class Bacilli (including Staphylococcaceae, Enterococcaceae, Streptococcaceae, and Lactobacillaceae) as well as several Proteobacteria families were consistently observed during the first 12 weeks of life
Pivrcova <i>et al.</i> , 2024 [45]	33 neonates exposed to IAP during CS or vaginal delivery, 33 neonates as controls	Cephalosporin penicillin clindamycin	Fecal samples analysed by 16S rRNA amplicon sequencing	- IAP administration affected the abundance of several bacteria in transitional stool samples, but not in meconium samples - IAP was associated with decreased alpha diversity, decreased relative abundances of the genera <i>Bacteroides</i> and <i>Bifidobacterium</i>, and increased relative abundances of genera <i>Enterococcus</i> and <i>Rothia</i> in transitional stool samples
Teuscher <i>et al.</i> , 2025 [46]	48 infants: 26 were allocated to the control group and 22 to the IAP exposed group	Benzylpenicillin	Rectal swabs after birth, meconium and stool samples collected at one month and one year of life; 16S rRNA gene amplification, PCR	- IAP significantly reduced the relative abundance of <i>B. longum</i> in the infant gut at one month and one year of age - The microbiome of meconium samples showed minimal alterations with regard to IAP - At one month and one year of age, indicator species analysis revealed <i>B. longum</i> as a signature taxon for control infants - Indicator species for IAP exposure at one month of age were Deltaproteobacteria, Fusobacteria, <i>Lederia</i>, species <i>Cutibacterium avidum</i>, <i>Staphylococcus lugdunensis</i>, <i>Lactobacillus reuteri</i> and <i>Veillonella parvula</i> <i>Actinomycetales</i>, <i>Clostridioides</i>, <i>Murimonas</i> and the species <i>Lachnospira pectinoschiza</i> and <i>Ruthenibacterium lactatiformans</i> were associated with IAP exposure at one year of age

IAP – intrapartum antibiotic prophylaxis, CS – caesarean section, qPCR – quantitative polymerase chain reaction, PCR-DGGE – polymerase chain reaction-denaturing gradient gel electrophoresis

Human milk samples were collected from 55 healthy lactating women after vaginal delivery. Twenty-one volunteers had received maternal antibiotic prophylaxis (cefazolin, penicillin, clindamycin) and 34 had not received antibiotics during or after labour. Total DNA was isolated from milk samples, and the bacterial counts were estimated by qPCR. Lower levels of *Bifidobacterium* were observed in the IAP group in the first week after delivery, although there were no statistical differences in the total bacteria count. One month after delivery, no differences were found in *Bifidobacterium* and total bacterial counts between the groups. The findings indicate that IAP significantly affects *Bifidobacterium* levels in human milk, leading to a reduction during the first week postpartum. However, throughout the first month after delivery, the *Bifidobacterium* counts gradually increase, ultimately reaching levels comparable to those observed in the non-IAP group one month after birth.

Soto *et al.* [49] reported that the antibiotic administered during the pregnancy, labour or lactation periods can significantly reduce the frequency of *Bifidobacterium* spp. present in human milk samples.

A comprehensive evaluation of the impact of IAP on the human milk microbiota was conducted by Lo [50] in a PhD thesis based on the PregnAnZI-1 trial carried out in the Gambia. This double-blind, placebo-controlled study investigated the effects of a single 2 g oral dose of azithromycin administered during labour, originally aimed at reducing maternal and neonatal infections. The study also focused on the effects of this intervention on the human milk microbiota, a key factor in early-life microbial colonisation. The study employed a stepwise approach, including optimisation of DNA extraction for bacterial (16S rRNA) and fungal sequencing, baseline characterisation of the human milk microbiota, and longitudinal assessment of microbiota changes during early lactation. In total 7.70 breast milk samples were included in the analysis (376 in the azithromycin arm and 394 in the placebo arm). The core analysis examined the effect of intrapartum azithromycin prophylaxis on milk microbial communities. Strong evidence was found for differences in both bacterial and fungal composition between women who received azithromycin and those who received placebo. Breast milk samples from the azithromycin group exhibited higher bacterial diversity throughout the neonatal period, as well as increased fungal diversity in colostrum collected on postpartum day three. Additionally, a higher relative abundance of *Brevundimonas* was observed in the azithromycin-exposed group.

Stinson *et al.* [51] characterized the microbiota of 266 milk samples collected from 208 mothers at 3 weeks and 3 months postpartum from a multi-ethnic Asian cohort. Full-length 16S rRNA gene sequencing showed that seven of 22 operational taxonomic units showed changes in relative abundance, including an increase in *Staphylococcus epidermidis* and a decrease in *Acine-*

tobacter spp. These effects were largely time-dependent and more pronounced at three months postpartum. Intrapartum antibiotic prophylaxis use was also associated with reduced bacterial richness and Shannon diversity index. The impact varied by antibiotic class, with penicillin showing the strongest effects and cephalosporins the weakest. In contrast, antibiotic exposure during pregnancy did not affect the milk microbiota, highlighting the importance of intrapartum timing.

CONCLUSIONS

This mini-review demonstrates that IAP, although necessary for the prevention of severe perinatal infections, represents an important modifiable factor influencing early microbial colonisation in newborns. The available evidence consistently shows that IAP disrupts the establishment of the neonatal gut microbiota, leading to reduced microbial richness, delayed colonisation by key commensal bacteria such as *Bifidobacterium* and *Bacteroides*, and an increased abundance of facultative anaerobes and Proteobacteria. These alterations may persist for months and, in some cases, throughout the first year of life, particularly in infants born by CS or not exclusively breastfed. From a clinical perspective, these findings have direct relevance for neonatologists and paediatricians. Infants exposed to IAP – especially those additionally affected by caesarean delivery or early formula supplementation – should be recognised as a group at increased risk of early-life gut dysbiosis, which can alter initial intestinal colonisation. Such early disruptions of the gut microbiota have important implications for long-term health, as they have been associated with an increased risk of metabolic disorders, including obesity and type 2 diabetes, later in childhood and adulthood. This awareness may support closer clinical monitoring, informed parental counselling, and early implementation of supportive strategies aimed at promoting microbiota recovery. Breastfeeding emerges as a key protective intervention, partially mitigating IAP-associated microbial disturbances, and should therefore be actively supported and prioritised in antibiotic-exposed mother-infant dyads. Although the impact of IAP on the human milk microbiota appears more subtle than its effect on the infant gut, emerging data indicate that intrapartum timing of antibiotic administration may also influence its microbial composition and diversity. Importantly, these findings do not challenge the current indications for IAP, but rather emphasise the need for judicious antibiotic use and individualised risk-benefit assessment. For clinicians caring for newborns, integrating knowledge of perinatal antibiotic exposure into routine neonatal history-taking may help guide nutritional counselling, follow-up strategies, and future research into targeted microbiota-supporting interventions. Further longitudinal and interventional studies are needed to determine which infants would benefit most from such approaches and to translate

microbiota science into practical, evidence-based neonatal and paediatric care.

DISCLOSURES

1. Institutional review board statement: None.
2. Assistance with the article: This work was supported by a subsidy from the Wrocław Medical University, grant number SUBZ.A300.25.041
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

REFERENCES

1. Campisciano G, Quadrioglio M, Comar M, de Seta F, Zanotta N, Ottaviani C, et al. Evidence of bacterial DNA presence in chorionic villi and amniotic fluid in the first and second trimester of pregnancy. *Future Microbiol* 2021; 16: 801-810.
2. Ferretti P, Pasolli E, Tett A, Asnicar F, Gorfer V, Fedi S, et al. Mother-to-infant microbial transmission from different body sites shapes the developing infant gut microbiome. *Cell Host Microbe* 2018; 24: 133-145.e5.
3. Jost T, Lacroix C, Bragger CP, Chassard C. New insights in gut microbiota establishment in healthy breast fed neonates. *PLoS One* 2012; 7: e44595.
4. Senn V, Bassler D, Choudhury R, Scholkman F, Righini-Grunder F, Vuille-Dit-Bile RN, et al. Microbial colonization from the fetus to early childhood – a comprehensive review. *Front Cell Infect Microbiol* 2020; 10: 573735.
5. Rutayisire E, Huang K, Liu Y, Tao F. The mode of delivery affects the diversity and colonization pattern of the gut microbiota during the first year of infants' life: a systematic review. *BMC Gastroenterol* 2016; 16: 86.
6. Shao Y, Forster SC, Tsaliki E, Vervier K, Strang A, Simpson N, et al. Stunted microbiota and opportunistic pathogen colonization in caesarean-section birth. *Nature* 2019; 574: 117-121.
7. Nagpal R, Yamashiro Y. Gut microbiota composition in healthy Japanese infants and young adults born by C-section. *Ann Nutr Metab* 2018; 73: 4-11.
8. Królak-Olejnik B, Kalinka J, Sadowska-Krawczyńska I, Cedrowska-Adamus W, Cukrowska B, Mazela J, et al. Cięcie cesarskie jako czynnik ryzyka dysbiozy jelitowej u niemowląt – możliwe strategie wsparcia żywieniowego. *Stand Med* 2022; 3: 19.
9. Kuperman AA, Koren O. Antibiotic use during pregnancy: how bad is it? *BMC Med* 2016; 14: 91.
10. Pawlik K, Hryniewicz W. Antybiotykoterapia w położnictwie. *Biul Nar Pr Ochr Antybiotyk* 2017; 3: 1-4.
11. Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: systematic review and meta-analysis. *PLoS Med* 2018; 15: e1002494.
12. Available from: <https://ezdrowie.gov.pl/portal/home/badania-i-dane/zdrowe-dane/monitorowanie/porody-opieka-okoloporodowa> (accessed: 31.01.2026).
13. Betran AP, Torloni MR, Zhang JJ, Gülmezoglu AM, Aleem HA, Althabe F, et al. WHO statement on caesarean section rates. *BJOG* 2016; 123: 667-670.
14. Čopi Jerman A, Zver Skomina J, Lučovnik M, Jeverica S. Effect of universal antibiotic prophylaxis on prevalence of surgical site infection after caesarean section. *J Clin Med* 2025; 14: 7232.
15. Sanchez-Ramos L, Preis R, Romero R. Prophylactic antibiotics to prevent postcesarean infection: which antimicrobial, when, how, and why? *Am J Obstet Gynecol* 2026; 233: S483-S503.
16. Rekomendacje Polskiego Towarzystwa Ginekologów i Położników dotyczące cięcia cesarskiego. *Ginekol Perinatol Prakt* 2018; 3: 159-174.
17. Kotarski J, Heczko PB, Lauterbach R, Niemiec T, Leszczyńska-Grzelak B. Rekomendacje PTGiP dotyczące wykrywania nosicielstwa paciorkowców grupy B (GBS) u kobiet w ciąży i zapobiegania zakażeniom u noworodków. *Ginekol Pol* 2008; 79: 221-223.
18. Verani JR, McGee L, Schrag SJ. Morbidity and mortality weekly report prevention of perinatal group B streptococcal disease: revised guidelines from CDC. *MMWR Recomm Rep* 2010; 59: 1-36.
19. Szymusik I. Śródpłodowa profilaktyka zakażeń paciorkowcami grupy B (GBS): wytyczne WHO 2024 – omówienie i komentarz. *Med Dypł* 2025; 5.
20. Schrag SJ, Verani JR. Intrapartum antibiotic prophylaxis for the prevention of perinatal group B streptococcal disease: experience in the United States and implications for a potential GBS vaccine. *Vaccine* 2013; 31: D20-D26.
21. Rosen GH, Randis TM, Desai PV, Sapra KJ, Ma B, Gajer P, et al. Group B Streptococcus and the vaginal microbiota. *J Infect Dis* 2017; 216: 744-751.
22. Jauréguy F, Carton M, Panel P, Foucaud P, Butel MJ, Doucet-Populaire F. Effects of intrapartum penicillin prophylaxis on intestinal bacterial colonization in infants. *J Clin Microbiol* 2004; 42: 5184-5188.
23. Pozo-Rubio T, De Palma G, Capilla A, Olivares M, Marcos A, Acuña MD, et al. Influence of early environmental factors on peripheral lymphocyte subsets and gut microbiota in infants at risk for celiac disease. *Proc Nutr Soc* 2013; 72: E21.
24. Keski-Nisula L, Kynäjänen H-R, Kärkkäinen U, Karhukorpi J, Heinonen S, Pekkanen J. Maternal intrapartum antibiotics and decreased vertical transmission of Lactobacillus to neonates during birth. *Acta Paediatr* 2013; 102: 480-485.
25. Arboleya S, Sánchez B, Milani C, Duranti S, Solís G, Fernández N, et al. Intestinal microbiota development in preterm neonates and effect of perinatal antibiotics. *J Pediatr* 2015; 166: 538-544.
26. Arboleya S, Sánchez B, Solís G, Fernández N, Suárez M, Hernández-Barranco AM, et al. Impact of prematurity and perinatal antibiotics on the developing intestinal microbiota: a functional inference study. *Int J Mol Sci* 2016; 17: 649.
27. Aloisio I, Mazzola G, Corvaglia LT, Tonti G, Faldella G, Biavati B, et al. Influence of intrapartum antibiotic prophylaxis against GBS on early newborn gut composition and evaluation of anti-Streptococcus activity of Bifidobacterium strains. *Appl Microbiol Biotechnol* 2014; 98: 6051-6060.
28. Aloisio I, Quagliarello A, De Fanti S, Luiselli D, de Filippo C, Albanese D, et al. Evaluation of the effects of intrapartum antibiotic prophylaxis on newborn intestinal microbiota using a sequencing approach targeted to multi hypervariable 16S rDNA regions. *Appl Microbiol Biotechnol* 2016; 100: 5537-5546.
29. Azad MB, Konya T, Persaud RR, Guttman DS, Chari RS, Field CJ, et al. Impact of maternal intrapartum antibiotics, method of birth and breastfeeding on gut microbiota during the first year of life: a prospective cohort study. *BJOG* 2016; 123: 983-993.
30. Cassidy-Bushrow AE, Sitarik A, Levin AM, Lynch SV, Havstad S, Ownby DR, et al. Maternal group B Streptococcus and the infant gut microbiota. *J Dev Orig Health Dis* 2016; 7: 45-53.
31. Corvaglia L, Tonti G, Martini S, Aceti A, Mazzola G, Aloisio I, et al. Influence of intrapartum antibiotic prophylaxis for GBS on gut microbiota in the first month of life. *J Pediatr Gastroenterol Nutr* 2016; 62: 304-308.
32. Mazzola G, Murphy K, Ross RP, di Gioia D, Biavati B, Corvaglia LT, et al. Early gut microbiota perturbations following intrapartum antibiotic prophylaxis to prevent GBS disease. *PLoS One* 2016; 11: e0157527.

33. Nogacka A, Salazar N, Suárez M, Milani C, Arbolea S, Solís G, et al. Impact of intrapartum antimicrobial prophylaxis upon intestinal microbiota and prevalence of antibiotic resistance genes in vaginally delivered full-term neonates. *Microbiome* 2016; 4.
34. Stearns JC, Simioni J, Gunn E, McDonald H, Holloway AC, Thabane L, et al. Intrapartum antibiotics for GBS prophylaxis alter colonization patterns in the early infant gut microbiome of low-risk infants. *Sci Rep* 2017; 7: 16527.
35. Imoto N, Morita H, Amanuma F, Maruyama H, Watanabe S, Hashiguchi N. Maternal antimicrobial use at delivery has a stronger impact than mode of delivery on bifidobacterial colonization in infants: a pilot study. *J Perinatol* 2018; 38: 1174-1181.
36. Kamal SS, Hyldig N, Krych L, Greisen G, Krogfelt KA, Zachariassen G, et al. Impact of early exposure to cefuroxime on the composition of the gut microbiota in infants following cesarean delivery. *J Pediatr* 2019; 210: 99-105.e2.
37. Tapiainen T, Koivusaari P, Brinkac L, Lorenzi HA, Salo J, Renko M, et al. Impact of intrapartum and postnatal antibiotics on the gut microbiome and emergence of antimicrobial resistance in infants. *Sci Rep* 2019; 9: 10635.
38. Zhou P, Zhou Y, Liu B, Jin Z, Zhuang X, Dai W, et al. Perinatal antibiotic exposure affects the transmission between maternal and neonatal microbiota and is associated with early-onset sepsis. *mSphere* 2020; 5: e00984-19.
39. Coker MO, Hoen AG, Dade E, Lundgren S, Li Z, Wong AD, et al. Specific class of intrapartum antibiotics relates to maturation of the infant gut microbiota: a prospective cohort study. *BJOG* 2020; 127: 217-227.
40. Dierikx T, Berkhout D, Eck A, Tims S, van Limbergen J, Visser D, et al. Influence of timing of maternal antibiotic administration during cesarean section on infant microbial colonization: a randomised controlled trial. *Gut* 2022; 71: 1803-1811.
41. Saturio S, Suárez M, Mancabelli L, Fernández N, Mantecón L, de los Reyes-Gavilán CG, et al. Effect of intrapartum antibiotics prophylaxis on the bifidobacterial establishment within the neonatal gut. *Microorganisms* 2021; 9: 1867.
42. Chen YY, Zhao X, Moeder W, Tun HM, Simons E, Mandhane PJ, et al. Impact of maternal intrapartum antibiotics, and cesarean section with and without labor on Bifidobacterium and other infant gut microbiota. *Microorganisms* 2021; 9: 1847.
43. Turta O, Selma-Royo M, Kumar H, Collado MC, Isolauri E, Salminen S, et al. Maternal intrapartum antibiotic treatment and gut microbiota development in healthy term infants. *Neonatology* 2022; 119: 93-102.
44. Jokela R, Korpela K, Jian C, Dikareva E, Nikkonen A, Saisto T, et al. Quantitative insights into effects of intrapartum antibiotics and birth mode on infant gut microbiota in relation to well-being during the first year of life. *Gut Microbes* 2022; 14: 2095775.
45. Pivrcova E, Buresova L, Kotaskova I, Videnska P, Andryskova L, Piler P, et al. Impact of intrapartum antibiotic prophylaxis on the oral and fecal bacteriomes of children in the first week of life. *Sci Rep* 2024; 14: 18163.
46. Teuscher JL, Lupatsii M, Graspeuntner S, Jonassen S, Bringewatt A, Herting E, et al. Persistent reduction of Bifidobacterium longum in the infant gut microbiome in the first year of age following intrapartum penicillin prophylaxis for maternal GBS colonization. *Front Immunol* 2025; 16: 1540979.
47. Hermansson H, Kumar H, Collado MC, Salminen S, Isolauri E, Rautava S. Breast milk microbiota is shaped by mode of delivery and intrapartum antibiotic exposure. *Front Nutr* 2019; 6: 4.
48. Padilha M, Iaucci JM, Cabral VP, Diniz EMA, Taddei CR, Saad SMI. Maternal antibiotic prophylaxis affects Bifidobacterium spp. counts in the human milk, during the first week after delivery. *Benef Microbes* 2019; 10: 155-163.
49. Soto A, Martín V, Jiménez E, Mader I, Rodríguez JM, Fernández L. Lactobacilli and bifidobacteria in human breast milk: influence of antibiotherapy and other host and clinical factors. *J Pediatr Gastroenterol Nutr* 2014; 59: 78-88.
50. Lo CW. The human milk microbiome and the impact of intrapartum azithromycin prophylaxis among Gambian women. PhD thesis, London School of Hygiene & Tropical Medicine, London 2025.
51. Stinson LE, Pang WW, Rea A, Fok D, Chua MC, Tan KH, et al. Composition of the human milk microbiome in the GUSTO cohort is shaped by intrapartum antibiotic prophylaxis and breastfeeding exclusivity. *mSystems* 2025; 10: e0067725.