

REVIEW

Gut Microbiota Composition in Indian and Western Infants (0–24 Months): A Systematic Review

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Abstract: Gut microbiota starts colonizing from birth and reach the adult gut microbial profile by around three years of age. There are scarce data on the gut microbial profiles of Indian infants. Moreover, there are insufficient data comparing the types of gut microbiota in Indian and Western infants, at different stages of their growth between 0 and 24 months. Also, with increasing globalization, infants of one country of origin are born in another country or travel to another country during infancy. Hence, these infants are exposed to changing environment and food practices that often causes dysbiosis or imbalance in the healthy gut microbiota profile. Dysbiosis has been linked, directly or indirectly, with many neurodevelopmental, gastrointestinal, respiratory, and other health issues. Early probiotic supplementation is associated with the return to the gut microbiota profile to a healthy state at one year and beyond. The changing global scenarios warrant the availability of a probiotic that can be used across nations. However, this is possible only if the gut microbiota profile of Indian and Western infants is similar enough to encourage the use of same probiotic in both populations. Hence, a systematic literature search was carried out to assess if the microbiota profile of the Indian and Western infants was comparable. This systematic review included 29 studies (10 Indian and 19 Western) and found that despite some differences, the gut microbiota of Indian and Western infants aged 0-24 months are largely similar, with implications for probiotic supplementation.

Keywords: gut microbiota, Indian, Western, 0.24 months, infants

Introduction

Gut microbiota start colonizing from birth and reach the adult gut microbial profile by around three years of age. 1 The terminology 'gut microbiota' includes bacteria, archaea, eukarya, microeukaryotes, viruses, fungi, and protozoans colonizing the gastrointestinal tract.²⁻⁴ However, the significance of archaea, eukarya and microeukaryotes in infants (0-24 months) is not well understood, and these microbiota are either reported as absent, transient, or detected in limited samples.^{3,5,6} Very few studies report appreciable presence of these microbiomes in infancy.⁷ On the other hand, bacteria constitute the major portion of gut microbiota during infancy and various taxonomic groups have been reported across studies. 3,4,6,8

In a healthy infant, gut microbiota are in a state of eubiosis or harmonious commensulization towards formation of a healthy human gut. 9 Right from the neonatal phase, gut microbiota play a major role metabolic (digestion and metabolism), protective (act as barrier against pathogenic microorganisms) and trophic (growth and differentiation of intestinal epithelial cells and immune system homeostasis) role. 1,8,9

Any delay or disturbance in the development of the age appropriate healthy gut microbiota can lead to dysbiosis, defined as an imbalance between healthy commensal and pathogenic organisms leading to disease. 1,8,10 The mode of delivery, vaginal (VD) or cesarean (CSD) is known to impact the diversity and colonization of gut microbiota and has a direct impact on infant health. 11-13 Similarly, feeding practices (breastfed, bottle fed, weaning etc.) affect the diversity and colonization of gut microbiota. 14,15

Dysbiosis has been linked, directly or indirectly, with many neurodevelopmental, gastrointestinal, respiratory, and other health issues. 8-10 Hence, it is important to prevent dysbiosis and correct it at the earliest. Probiotics are live

microbiota (especially bacteria and yeast) given as a supplement to prevent and/or correct dysbiosis as they help in normalizing the gut microbiota towards eubiosis. 10,16–19

Traditionally, Indians have been moving to Western world countries for better education, career and health prospects.²⁰ Today, globalization has resulted in rampant movement of individuals from one country to another.²¹ The change in geographical location, local environment, diet patterns of mother and local weaning food and supplementary milk options can impact the colonization and diversity of gut microbiota in infants.^{14,15} Thus, these infants born in another country or travelling to another country are at risk of dysbiosis due to changes in their local environment.²² Hence, there is a need for probiotics that can correct dysbiosis across infants of different geographies. However, this is possible only if the gut microbiota profile of Indian and Western infants is similar enough to encourage the use of same probiotic in both populations.

In this context, little is known about the gut microbial profiles of Indian infants. Infant gut microbiota profiles from advanced Western world are abundant. However, data comparing the gut microbiota of Indian and Western infants is lacking.⁴ Hence, this systematic review was conducted to extract data on gut microbiota profile (gut bacterial profile) of Indian versus Western infant populations aged 0–24 months, compare their gut microbiota profile/composition, and assess if there are enough similarities between the gut microbiome of the two populations to encourage use of same probiotics for these infants. Since mode of delivery and feeding practices have been shown to impact the gut microbiome across geographies, we aimed to compare the gut microbiota of Indian and Western infants by mode of delivery and by feeding practices.

Methods

Aim

To compare the gut microbiota profile/composition of Indian versus the Western infants 0–24 months old. An additional aim was to see if there was any similarity between the gut microbiotas between the Indian and Western infants.

Protocol

This systematic literature review followed a pre-determined, non-registered protocol and was conducted in accordance with the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA)^{23,24} guidelines. We included the articles that determined the gut microbiota of healthy Indian/Western well-nourished infants between the age of 0–24 months according to the predetermined inclusion/exclusion criteria. Even though the term "Western world" can mean different regions depending on the location of the index country, in general, the current understanding of Western world includes regions from America, Europe, Canada and Australia. Hence, the protocol clubbed all these countries under the "Western world" countries.

Bacteria can be classified in many ways. We used the Integrated Taxonomic Information System (IT IS) for the taxonomic classification of bacteria.²⁶ In addition, information on the taxonomic classification was taken from the article included, if it was available.

Criteria for Including Studies

The systematic review included any clinical trial from India or Western world evaluating gut microbiota (bacteria) in healthy full-term, vaginally delivered or delivered by cesarean section, well-nourished infants aged 0–24 months. The mothers were healthy and not under any medication for any comorbid condition. Trials pulling gut microbiota data from longitudinal cohorts or population databases were included, but only the data for the 0–24 months age group was considered. Only those trials that extracted data on the fecal microbiota profile were included.

Criteria for Excluding Studies

The systematic review excluded clinical trials that evaluated the gut microbiota in preterm infants; malnourished infants; stunted infants; obese infants; or pediatric studies in age group above 24 months; or the evolution of gut microbiota during a disease, gastrointestinal disorder, neurological or metabolic disorder; or in response to an intervention (vaccine,

synbiotics, supplements, antibiotics or probiotics), allergen, or a particular diet type (protein rich, carbohydrate rich, Mediterranean, etc.) Studies evaluating only oral microbiota and not fecal microbiota were also excluded. Studies reporting just the diversity index without specifying the individual bacteria, comparing Indian infants with infants of countries other than those covered under Western world, or studies analyzing the effects of different factors on the infant gut microbiota were also excluded.

Method of Literature Search and Selection of Articles

Free literature databases like MEDLINE (PubMed) were independently searched on August 1, 2022 by two investigators for English language human trials published between 1970 until July 31, 2022, using the following search terms ("infants") AND ("gut" OR "intestinal" OR "fecal" OR "stool") AND ("microbiota" OR "microflora" OR "microbiome"). A total of 2007 records were retrieved.

The two investigators (Dr Nidhi Gupta and Dr Kokil Mathur) independently screened the retrieved records for duplicates and removed the duplicates using a reference manager. The retrieved records were then analyzed for inclusion/exclusion by the title of the study and abstract, and then finally the 114 full texts were screened by them. The records being considered for inclusion during screening were segregated as Indian and Western depending on the country of the trial. A total of 104 were excluded after mutual discussion and deliberations.

Finally, the two investigators agreed to include 10 records through online search (two Indian and eight Western).

Since the number of retrieved studies were very few, the two investigators decided to supplement the search by manually sourcing the bibliography of the 42 excluded review articles and systematic reviews and meta-analysis and the Google Scholar. Nine studies meeting the inclusion criteria that were missed during the online search were added from the bibliography and 10 studies were added from Google Scholar.

Finally, of the 2017 records retrieved, 29 studies (10 Indian and 19 Western) met the inclusion criteria. Figure 1 outlines the detailed search and selection criteria of the records through the PRISMA flow chart. The studies were further segregated by mode of delivery and by feeding practices as outlined in the respective study inclusion criteria.

The details of the 29 studies included in the systematic review are captured in Table 1. Of the 19 Western studies, 14 studies were from Europe, 12,27-39 two were from America, 6,40 two from Canada, 41,42 and one from Australia 43.

Quality of Evidence and Risk of Bias

Two researchers independently assessed the records using the Cochrane Collaboration's tool for risk of bias assessment, which includes seven domains of bias stratifying the risk of bias as low, high or unclear.⁴⁴ The two researchers then discussed their findings and resolved any discrepancy through discussion and consensus.

The scientific quality of individual studies included was generally high with well-designed methodology and statistical analysis. All the studies assessed the fecal microbiota in infants and clearly defined the technique used for assessing the microbiota. The infant age group, mode of delivery, and feeding practices were captured by most studies.

Data Analysis and Its Limitations

Despite the high quality of evidence of individual studies, proper statistical comparison and analysis of the studies could not be carried out due to many inconsistencies in the way the data was presented in different studies.

None of the studies compared the gut microbiota between Indian and Western infants (0–24 months). In five studies (Albert et al, Dinh et al, Sharma et al, Balamurugan et al, Chernikova et al)^{39,45–48} the healthy infants were not the main study population but were used as controls. The controls also differed by age as shown in Table 1. Similarly, there was no consistency in the age group considered by mode of delivery/breastfeeding/weaning as shown in Table 1. It is a known fact that the gut microbiome rapidly develops between birth and first two years of life, ¹ and therefore there can be marked difference in colonizations.

Further, though the method for assessing microbiota type and the bacterial count method were clearly described, the methods used across the studies were not consistent (Table 1). The various methods used were by both Indian and Western studies were culture, DNA extracted using 16S rRNA, colony counts of organisms were expressed as log 10 count, plate-dilution technique, small subunit ribosomal deoxyribonucleic acid (SSU rDNA) microarray design,

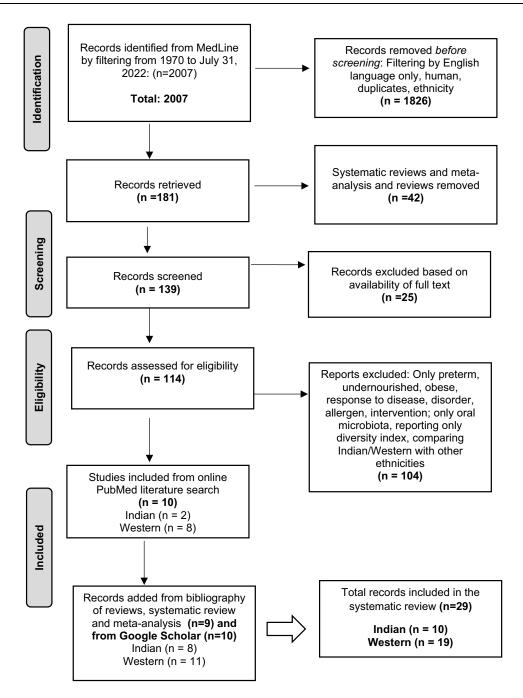


Figure 1 PRISMA flow diagram for literature search and selection.

Notes: Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ;2021:n160. Creative Commons.²⁴

fluorescent in situ hybridization (FISH), FISH combined with flow cytometry (FISH-FC), DNA extracted using MoBio kit, DNA extracted using an automated KingFisher DNA extraction system and through Polymerase chain reaction (PCR), DNA extracted using 16S rRNA, qPCR and FISH, 16S rRNA gene amplicon sequencing and high-resolution metagenomics, and metagenomic analysis. Different methods of identifying the microbiotas have their own sensitivity and specificity and thus their capability of identifying the microbiota differs. However, 14 of the 29 studies used the "DNA extracted using 16S rRNA" method and thus have the same sensitivity and specificity towards capturing the microbiota types.

Table I Studies Included in the Systematic Review

| an | | | | | |
|--|---|--|---|--|--|
| Study Size (N) | | Study Population | Age | Bacterial Count Method | |
| Albert (1978) ⁴⁵ | 78 | Full term with 1–5 days diarrheal disease requiring hospital admission (n=49); full term healthy infants used as controls (n=29) | 0–24 months | Culture | |
| Balamurugan et al (2010) ⁴⁷ | 14 | Full term neonates under surveillance for rotavirus infection; full term healthy infants used as controls (n=7); both VD and CSD | 0–I month | DNA extracted using I6S rRNA | |
| Pandey et al (2012) ⁵⁰ | 24 | Healthy full term breastfed vaginal (n=12) delivery versus cesarean (n=12) | 0–7 days | DNA extracted using I6S rRNA | |
| Sharma et al (2012) ⁴⁸ | 91 | Preterm (n=62); full term healthy infants used as controls (n=29) | 0-21 days | Colony counts of organisms were expressed as log 10 count | |
| Kabeerdoss et al (2013) ⁵¹ | 83 | Vaginal delivery; CS (n=10); colonization by mode of delivery and weaning at 4, 5 and 6 months | 0–6 months | DNA extracted using I6S rRNA | |
| Dinh et al (2016) ⁴⁶ | 20 | Stunted (n=10); full term healthy infants used as controls (n=10) | 3–24 months | DNA extracted using 16S rRNA | |
| Attri et al (2018) ⁵² | 10 | Full-term, breast-fed and vaginally delivered | 0–4 months | DNA extracted using 16S rRNA | |
| Huey et al (2020) ⁴⁹ | 53 | Vaginally delivered, breastfed, undernourished; approximately 30% cohort healthy vaginally delivered breastfed | 10–18 months | DNA extracted using I6S rRNA Rectal swabs taken instead of fecal samples | |
| Kumbhare et al (2020) ⁶⁴ | 20 | Full term healthy | 0–6 months | DNA extracted using 16S rRNA | |
| Shivakumar et al (2021) ¹⁶ | 41 | Non-breastfed term healthy | 18–24 | DNA extracted using 16S rRNA | |
| Western | | | | | |
| Mata et al(1972) ⁴⁰ | 33 | Breastfed healthy full term | 0–12 months* | Plate-dilution technique | |
| Rotimi and Duerden (1981) ²⁷ | 23 | Normal healthy full term | 0-7 days | Culture | |
| Stark and Lee (1982) ⁴³ | 14 | Healthy breast-fed and bottle-fed | 0–12 months | Culture | |
| Grönlund et al (1999) ²⁸ | 64 | Healthy full term vaginal (n=34) delivery versus cesarean (n=30) | 3-180 days | Culture | |
| Palme r et al (2007) ⁶ | 14 | Healthy full term | 0–12 months | Newly developed SSU rDNA microarray design | |
| Huurre et al (2008) ²⁹ | 165 | Healthy full term vaginal (n=141) delivery versus cesarean (n=24) | I-6 months | FISH | |
| Mitsou et al (2008) ³⁰ | 82 | Healthy full term exclusively breastfed vaginal delivery versus cesarean | 4–90 days | DNA extracted using 16S rRNA | |
| | Albert (1978) ⁴⁵ Balamurugan et al (2010) ⁴⁷ Pandey et al (2012) ⁵⁰ Sharma et al (2012) ⁴⁸ Kabeerdoss et al (2013) ⁵¹ Dinh et al (2016) ⁴⁶ Attri et al (2018) ⁵² Huey et al (2020) ⁴⁹ Kumbhare et al (2020) ⁶⁴ Shivakumar et al (2021) ¹⁶ Western Mata et al(1972) ⁴⁰ Rotimi and Duerden (1981) ²⁷ Stark and Lee (1982) ⁴³ Grönlund et al (1999) ²⁸ Palmer et al (2007) ⁶ Huurre et al (2008) ²⁹ | Study Study Size (N) Albert (1978) ⁴⁵ 78 Balamurugan et al (2010) ⁴⁷ 14 Pandey et al (2012) ⁵⁰ 24 Sharma et al (2012) ⁴⁸ 91 Kabeerdoss et al (2013) ⁵¹ 83 Dinh et al (2016) ⁴⁶ 20 Attri et al (2018) ⁵² 10 Huey et al (2020) ⁴⁹ 53 Kumbhare et al (2020) ⁶⁴ 20 Shivakumar et al (2021) ¹⁶ 41 Western Mata et al(1972) ⁴⁰ 33 Rotimi and Duerden (1981) ²⁷ 23 Stark and Lee (1982) ⁴³ 14 Grönlund et al (1999) ²⁸ 64 Palmer et al (2007) ⁶ 14 Huurre et al (2008) ²⁹ 165 | Study Study Size (N) Study Population Albert (1978) ⁴⁵ 78 Full term with 1–5 days diarrheal disease requiring hospital admission (n=49); full term healthy infants used as controls (n=29) Balamurugan et al (2010) ⁴⁷ 14 Full term neonates under surveillance for rotavirus infection; full term healthy infants used as controls (n=7); both VD and CSD Pandey et al (2012) ⁵⁰ 24 Healthy full term breastfed vaginal (n=12) delivery versus cesarean (n=12) Sharma et al (2012) ⁴⁸ 91 Preterm (n=62); full term healthy infants used as controls (n=29) Kabeerdoss et al (2013) ⁵¹ 83 Vaginal delivery; CS (n=10); colonization by mode of delivery and weaning at 4, 5 and 6 months Dinh et al (2016) ⁴⁶ 20 Stunted (n=10); full term healthy infants used as controls (n=10) Attri et al (2018) ⁵² 10 Full-term, breast-fed and vaginally delivered Huey et al (2020) ⁴⁹ 53 Vaginally delivered, breastfed, undernourished; approximately 30% cohort healthy vaginally delivered breastfed Kumbhare et al (2020) ⁶⁴ 20 Full term healthy Western Mata et al(1972) ⁴⁰ 33 Breastfed term healthy Western Mata et al(1972) ⁴⁰ 33 Breastfed healthy full term Rotimi and Duerden (1981) ²⁷ 23 Normal healthy full term Stark and Lee (1982) ⁴³ 14 Healthy breast-fed and bottle-fed Grönlund et al (1999) ²⁸ 64 Healthy full term vaginal (n=34) delivery versus cesarean (n=30) Palmer et al (2007) ⁶ 14 Healthy full term | Study Size (N) Study Population Age Albert (1978)*5 78 Full term with 1–5 days diarrheal disease requiring hospital admission (n=49); full term with 1–5 days diarrheal disease requiring hospital admission (n=49); full term healthy infants used as controls (n=29) Balamurugan et al (2010)**7 14 Full term neonates under surveillance for rotavirus infection; full term healthy infants used as controls (n=7); both VD and CSD Pandey et al (2012)**0 24 Healthy full term breastfed vaginal (n=12) delivery versus cesarean (n=2) Sharma et al (2012)**8 91 Preterm (n=62); full term healthy infants used as controls (n=29) 0–21 days Kabeerdoss et al (2013)**1 83 Vaginal delivery: CS (n=10); colonization by mode of delivery and weaning at 4, 5 and 6 months Dinh et al (2016)**4 20 Stunted (n=10); full term healthy infants used as controls (n=10) 3–24 months Attri et al (2018)**2 10 Full-term, breast-fed and vaginally delivered Huey et al (2020)**9 53 Vaginally delivered, breastfed, undernourished; approximately 30% cohort healthy vaginally delivered breastfed Kumbhare et al (2020)**4 20 Full term healthy Kumbhare et al (2020)**4 14 Non-breastfed term healthy Shivakumar et al (2021)**4 15 Non-breastfed healthy full term O-12 months** Patri and Duerden (1981)**7 23 Normal healthy full term O-7 days Stark and Lee (1982)**3 14 Healthy full term vaginal (n=34) delivery versus cesarean (n=30) 3–180 days Palmer et al (2009)**9 165 Healthy full term vaginal (n=141) delivery versus cesarean (n=24) 1–6 months Huurre et al (2008)**9 165 Healthy full term vaginal (n=141) delivery versus cesarean (n=24) 1–6 months | |

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Table I (Continued).

| Indian | | | | | |
|--------|--|----------------|--|--|---|
| | Study | Study Size (N) | Study Population | Age | Bacterial Count Method |
| 8 | Fallani et al (2010) ³³ | 606** | Healthy full term and correlate microbiota to country of origin, mode of delivery, feeding method, and perinatal antibiotic treatment | 0–6 weeks | FISH-FC |
| 9 | Roger and McCartney (2010) ³² | 14 | Weaning in exclusively breastfed (n=7) versus exclusively formula-fed (n=7) term infants | I-18 months | FISH and denaturing gradient gel electrophoresis |
| 10 | Fallani et al (2011) ³¹ | 605 | Healthy infants of the European project INFABIO (fully breastfed/fully formula-fed/both) | 6 weeks to 4 weeks after weaning | FISH-FC |
| П | Azad et al (2013) ⁴¹ | 24 | Healthy full term infants from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort profiled by mode of delivery and diet | 0–4 months | DNA extracted using I6S rRNA |
| 12 | Bergström et al (2014) ³⁴ | 330 | Healthy term | 9, 18 and 36 months# | DNA extracted using I6S rRNA |
| 13 | Bäckhed et al (2015) ³⁵ | 98 | Healthy full term vaginal delivery; cesarean (n=15); by mode of delivery and feeding practices | 0–12 months | Metagenomic analysis |
| 14 | Hill et al (2017) ³⁶ | 192 | Healthy full term breastfed normal vaginal delivery versus cesarean | 0-24 weeks | 16S rRNA gene amplicon sequencing and high-resolution metagenomics |
| 15 | Timmerman et al (2017) ³⁷ | 08 | Healthy full term NVD; 4 breastfed and 4 formula fed | 0–12 weeks | DNA extracted using 16S rRNA, qPCR and FISH |
| 16 | Forsgren et al (2017) ³⁸ | 118 | Late preterm (n=75) versus term (n=43) Both VD and CSD infants included but gut microbiota not reported according to mode of delivery | 0–6 months | DNA extracted using an automated KingFisher DNA extraction system and through PCR |
| 17 | Chernikova et al (2018) ³⁹ | 206 | New Hampshire Birth Cohort Study: Premature infants (n=30); Healthy full term used as controls (n=176) | 0–6 weeks | DNA extracted using MoBio kit |
| 18 | Reyman et al (2019) ¹² | 120 | Full term healthy vaginally (n=74) versus cesarean delivered (n=46) from the Microbiome Utrecht Infant Study [MUIS] | 0–12 months | DNA extracted using I6S rRNA |
| 19 | Fehr et al (2020) ⁴² | 1249 | Breast fed full term healthy infants CHILD Cohort Study | 3 months and I year | DNA extracted using I6S rRNA |

Notes: *Only 12 could be followed until 1 year, **606 infants participating in the Diet and Environment longitudinal study of the European project INFABIO, *Only 9- and 18-months results included. Abbreviations: 16S rRNA, 16S ribosomal ribonucleic acid; FISH-FC, Fluorescent in situ hybridization (FISH) combined with flow cytometry (FC); NVD, normal vaginal delivery; PCR, Polymerase chain reaction; SSU rDNA, small subunit ribosomal deoxyribonucleic acid (SSU rDNA).

The Western population was not consistent and included studies from Central America, USA, Canada, Australia, and Europe. However, 14 of the 19 studies from the Western world were from Europe, thereby ensuring that majority of the studies from the Western world were from the same region. We considered removing studies from Central America, USA, Canada, and Australia, but since a robust statistical analysis was not possible, and that there was not enough comparative European literature on gut microbiome by mode of delivery, breastfeeding and weaning practices, we decided to include these studies to understand if any inferences could be drawn regarding the similarities and differences between the gut microbiome of Indian and Western infants.

Of the two studies from America, the study by Mata et al was in indigenous Guatemalan children from Central America and the one by Palmer et al is from USA. Of the two studies from Canada, the study by Azad et al included healthy full-term infants from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort profiled by mode of delivery and diet and the study by Fehr et al included breast fed full term healthy infants from the same CHILD Cohort Study. The study from Australia by Stark and Lee included healthy breast-fed and bottle-fed infants.

There was inconsistency in the granularity of taxonomical classification reported by the studies with as some studies reported the bacteria at phyla and family level only while other studies reported more granular data by genus and species. After extracting the data, we noted a great variation at species level between the two populations. Hence, we decided to compare the gut microbiota of the two populations at the genus level. However, we built the entire taxonomical tree (Figure 2) using the IT IS system for complete understanding.

Therefore, due to differences in the methodology of microbiota classification, detection, and counting; differences in the country of origin; and inconsistency in age group captured in different studies by mode of delivery or feeding/weaning practices, the available data was described descriptively. The information extracted from the studies was discussed by the authors and synthesized with the goal to reach a logical conclusion.

Results

Gut Microbiota According to Different Taxonomic Groups in the Indian versus Western Population

Gut microbiota data from all the 29 studies (10 Indian and 19 Western) were available and captured in Figure 2.

Similarities in Gut Microbiota of Healthy Full-Term Indian and Western Infants

Gut microbiota of five phyla: *Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, Fusobacteria*, and *Verrucomicrobia*, were present in both Indian and Western infants.

Proteobacteria and Firmicutes were the most represented phyla across both populations, followed by Actinobacteria. Under the phylum Proteobacteria, order Gamma Proteobacteria was the most reported order with gram-negative Escherichia, Klebsiella, Proteus and Enterobacter reported across both populations. Genus Neisseria under the order Betabroteobacteria was reported in both the populations but by one Indian and one Western study only.

Under the phylum *Firmicutes*, both gram-positive and gram-negative bacteria were reported in both the populations. The orders *Bacillales*, *Lactobacillales*, and *Clostridiales* were present in both the Indian and Western infants. At the genus level, gram-positive *Staphylococcus*, *Streptococcus*, *Enterococcus*, *Lactobacillus*, *Clostridium*, *Eubacteria* and *Blautia* were reported by multiple studies for both Indian and Western infants. Of the gram-negative bacteria, genus *Veillonella* was reported by multiple Indian and Western studies.

Under the phylum *Actinobacteria*, all the classes and orders of bacteria were seen in both Indian and Western infants, with some variance in the family and genus level. The genus *Bifidobacteria* and *Corynebacterium* were reported in both Indian and Western infants, but *Bifidobacteria* was the most reported microbiota in both the populations by majority of the records.

Under the phylum *Bacteroidetes*, the gram-positive genus *Bacteroides* was the most reported microbiota for both Indian and Western infants. Under the phylum *Verrucomicrobia*, only one genus, *Akkermansia*, was reported, and seen in both Indian and Western infants.

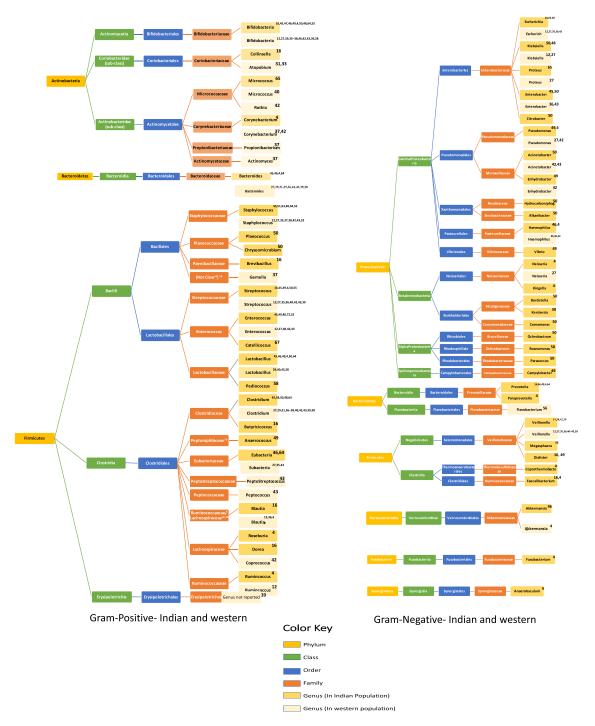


Figure 2 Gut microbiota according to different taxonomic groups in Indian versus Western infants.

Notes: *The family of genus Gemella is not clear; 65 Genus Anaerococcus is under family Peptoniphilaceae 66 as per the source cited, family details were not available at Integrated Taxonomic Information System (IT IS) used by the systematic review to classify the microbiota; Genus Blautia is reported to be under two families: family Ruminococcaceae and family Lachnospiraceae. 41.67

Differences in Gut Microbiota of Healthy Full-Term Indian and Western Infants

Two phyla, Fusobacteria and Synergistetes were reported by Indian studies only.

Under the phylum *Proteobacteria*, orders *Betabroteobacteria*, *Alpha Proteobacteria* and *Epsilon Proteobacteria* were predominantly reported for Indian infants.

Under the phylum Firmicutes, the order Erysipelotrichales was reported in Western infants by one study only.

Under the phylum *Actinobacteria*, bacteria from two families (*Propionibacteriaceae* and *Actinomycetaceae*) under the order *Actinomycetales* were not seen in Indian infants.

Under the phylum *Bacteroidetes*, the gram-negative genus *Prevotella* and *Paraprevotella* were reported only in Indian infants.

Though there were differences at the genus level between the two populations, the different genus was usually reported by one Indian or Western study only (Figure 2).

Colony Percentages of Gut Microbiota in Indian versus Western Infants According to Different Taxonomic Groups

Total 11 of the 29 included studies reported gut microbiota colony counts. However, only eight (four Indian and four Western) studies reported the colony count as percentages and were included in the analysis. Three studies by Sharma et al, Kabeerdoss et al (both Indian) and Palmer et al (Western) reported colony counts by methods other than percentages and hence they were not included in the analysis of this section Sharma reported the microbiota count as mean log colony-forming unit (CFU) per gram, while Palmer and Kabeerdoss used rRNA gene copies in the range of 10⁹ to 10¹⁰/g of stool (wet weight).

Similarities and Differences Reported at Phyla Level

When classified according to the phylum, it was seen that the colony percentage of *Firmicutes* (38.6–44.7^{16,46} vs 32.01–43.8^{6,41}) and *Bacteroidetes* (13.8–18.9^{16,46} vs 20.08⁶) was similar in both the Indian and Western populations. The percentage range for the colony percentage of *Firmicutes* and *Bacteroidetes* was narrow. On the other hand, the Western infants showed almost double the highest colony percentage of *Proteobacteria* (46.14 vs 25.89) and *Actinobacteria* (36.4 vs 17.5) compared to the Indian population. However, the range of colony percentages for both *Proteobacteria* and *Actinobacteria* was very wide.

Similarities and Differences Reported at Class Level

Under the phylum *Firmicutes*, colony counts of classes *Bacilli* (9.26⁶), *Clostridia* (19.97⁶), and *Mollicutes* (2.79⁶) were reported for only Western population and that too by one study only. Under the phylum *Proteobacteria*, bacterial count was reported for classes Gamma Proteobacteria (46.11⁶) and Beta Proteobacteria (0.03⁶) were reported by one Western study, and for order Aeromonadales (41.29⁴⁹) was reported by one Indian study.

Similarities and Differences Reported at Family Level

Under the phylum *Firmicutes*, colony count for family *Lachnospiraceae* $(8.6^{16} \text{ vs } 8-14.2^{39,41})$ and *Ruminococcaceae* $(8.5^{16} \text{ vs } 0^{41})$ were reported for both Indian and Western infants, while bacterial count for family *Erysipelotrichaceae* was reported only for Western population $(0.8-4^{39,41})$.

Under the phyla *Bacteroidetes* and *Actinobacteria* bacterial count was reported for family *Prevotellaceae* (17.6¹⁶) and *Bifidobacteriaceae* (8¹⁶) respectively, by one Indian study only and the counts were not available for Western population. Under the phylum *Proteobacteria*, bacterial count was reported for family Moritellaceae (1.19⁴⁹) by one Indian study

only and for family Enterobacterceae $(7.4-20^{39,41})$ by two Western studies.

Similarities and Differences Reported at Genus Level

When classified according to the genus, *Streptococcus, Veillonella*, and *Lactobacillus* had similar colony percentage for both the population, while Western infants had a much higher percentage range of *Bifidobacterium* ($15-40^{33,39,41}$ vs $0.57-14.85^{16,46,48,49}$) and *Bacteroides* ($11.4-19^{33,39}$ vs 6.05^{46}) than Indian infants. Figure 3 shows the similarities and differences in bacterial count reported for both the populations.

Limitations Encountered While Comparing Colony Counts

Colony percentages of various other microbiota could not be compared due to lack of data for either Indian or Western colonization.

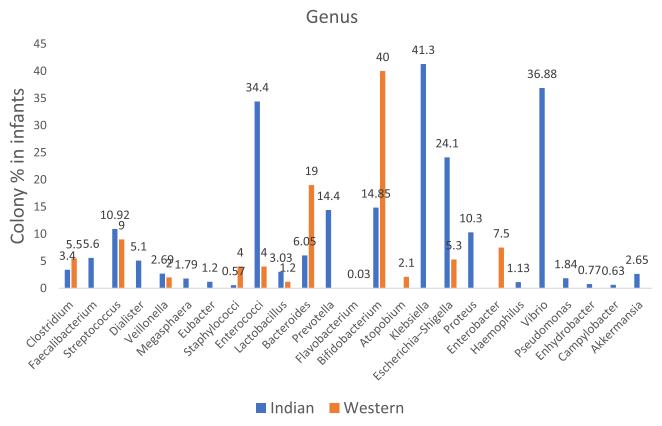


Figure 3 Colony percentages of gut microbiota in Indian and Western infants Indian; 16,46,48,49 Western 6,33,39,41

Further, a direct comparison of the colony percentages could not be made between Indian and Western infants as the studies had different probes for bacterial detection and included infants with different modes of delivery or feeding practices. Also, though all the infants were under 24 months, the gut microbiota profile was captured at different ages. Thus, a study could have reported a higher percentage of a particular microbiota during early infancy, which may have declined during later infancy resulting in a lower percentage being reported by another study.

Gut Microbiota in Indian versus Western Infants Classified According to Mode of Delivery

Table 2 and Table 3 compare the gut microbiota of infants during 0–24 months of life, classified according to the mode of delivery. Thirteen (four Indian and nine Western) studies met the inclusion criteria of reporting the gut microbiota by either mode of delivery or reported the gut microbiota in either VD or CSD infant population. There were no studies comparing the gut microbiota in Indian versus Western infants by mode of delivery. Only five studies (two Indian and three Western) compared the relative predominance of the gut microbiota by the mode of delivery in their respective population. 30,33,41,50,51

Similarities and Differences Reported in Gut Microbiota of Vaginally Delivered Infants

Table 2 shows the similarities and differences in gut microbiota profile of vaginally delivered infants of Indian vs Western population. Of the studies reporting gut microbiota in VD full-term infants *Ruminococcus*, *Clostridium*, *Streptococcus*, *Veillonella*, *Staphylococcus*, and *Lactobacillus* (*Firmicutes*); *Bacteroides* (phylum *Bacteroidetes*); *Bifidobacterium* (phylum *Actinobacteria*); *Klebsiella*, *Escherichia–Shigella*, and *Haemophilus* (phylum *Proteobacteria*) were reported by both Indian and Western studies.

Table 2 Gut Microbiota (0-24 Months) in Indian and Western Vaginally Delivered Infants

| Taxonomical Group (Genus) | Indian Vaginally Delivered | Western Vaginally Delivered | | | | |
|--|---|---|--|--|--|--|
| Phylum Firmicutes | | | | | | |
| Ruminococcus | Present ⁵² | Present ¹² | | | | |
| Clostridium | Present ⁵² | Present ^{28,29,36,41} | | | | |
| Blautia | Not reported | Present ^{12,36,37,41} | | | | |
| Coprococcus | Not reported | Present ⁴¹ | | | | |
| /Streptococcus | Present ^{50,52} | Present ^{12,36,37,41} | | | | |
| Veillonella | Present ⁵² | Present ^{12,36,41} | | | | |
| Staphylococcus | Predominant ⁵⁰ | Present ^{35,37} | | | | |
| Faecalibacterium | Present ⁵² | Not reported | | | | |
| Enterococcus | Not reported | Present ^{12,30,41} | | | | |
| Lactobacillus | Present ^{50–52} | Present ^{28–30,33,37} | | | | |
| Pediococcus; Coprothermobacter; Faecalibacterium; Roseburia; Dialister | Present ^{49,52} | Not reported | | | | |
| Phylum Bo | cteroidetes | | | | | |
| Bacteroides | Present ^{51,52} | Present ^{28,29,31,33,35,36,41} | | | | |
| Prevotella | Present ^{51,52} | Not reported | | | | |
| Paraprevotella | Present ⁵² | Not reported | | | | |
| Phylum Ac | tinobacteria | | | | | |
| Bifidobacterium | Predominant ⁵⁰ Present ^{47,51,52} | Predominant ³³ Present ^{12,28–30,35–37,41} | | | | |
| Eggerthella; Atopobium | Not reported | Present ^{31,33,41} Eggerthella ³⁷ | | | | |
| Corynebacterium | Present ⁵² | Present ³⁷ | | | | |
| Phylum Pro | oteobacteria | | | | | |
| Klebsiella | Present ⁵⁰ | Present ^{12,37} | | | | |
| Escherichia—Shigella | Present ⁵⁰ | Predominant ⁴¹ Present ^{35,36} | | | | |
| Enterobacter | Not reported | Present ^{35,36} | | | | |
| Citrobacter | Present ⁵⁰ | Not reported | | | | |
| Haemophilus | Present ⁵² | Present ^{36,37,41} | | | | |
| Acinetobacter | Predominant ⁵⁰ | Not reported | | | | |
| Neisseria; Kingella; Pseudomonas; Vibrio; Enhydrobacter | Present ^{49,52} | Not reported | | | | |
| Phylum Veru | rucomicrobia | | | | | |
| Akkermansia | Not reported | Present ⁴¹ | | | | |
| Phylum Synergistetes | | | | | | |
| Anaerobaculum | Present ⁵² | Not reported | | | | |

Table 3 Gut Microbiota (0-24 Months) in Indian and Western Cesarean Delivered Infants

| Taxonomical Group (Genus) | Indian Cesarean Delivered | Western Cesarean Delivered | | | |
|---|---------------------------|--|--|--|--|
| Phylum Firmicutes | | | | | |
| Ruminococcus | Not reported | Present ¹² | | | |
| Clostridium | Predominant ⁵⁰ | Present ^{28,29,36,41} | | | |
| Blautia | Not reported | Present ^{12,36,41} | | | |
| Coprococcus | Not reported | Present ⁴¹ | | | |
| Streptococcus | Not reported | Present ^{12,33,35,36,41} | | | |
| Veillonella | Not reported | Present ^{12,35,36,41} | | | |
| Staphylococcus | Present ⁵⁰ | Present ³⁵ | | | |
| Enterococcus | Not reported | Present ^{12,30,41} | | | |
| Lactobacillus | Present ⁵¹ | Present ^{28,29,33} | | | |
| | | Less colonized ³⁰ | | | |
| Planococcus | Present ⁵⁰ | Not reported | | | |
| Phylum Bac | teroidetes | | | | |
| Bacteroides | Predominant ⁵¹ | Present ^{28,29,31,36} Less colonized ^{33,41} | | | |
| Prevotella | Predominant ⁵¹ | Not reported | | | |
| Paraprevotella | Not reported | Not reported | | | |
| Phylum Acti | nobacteria | | | | |
| Bifidobacterium | Present ^{47,51} | Present 12,28,29,33,36,41 | | | |
| | Absent ⁵⁰ | Less colonized ³⁰ | | | |
| Eggerthella; Atopobium | Not reported | Present ^{31,33,41} Atopobium (less colonized) ³³ | | | |
| Phylum Prot | eobacteria | | | | |
| Klebsiella | Not reported | Present ¹² | | | |
| Escherichia—Shigella | Predominant ⁵⁰ | Present ^{33,36} Less colonized ⁴¹ | | | |
| Enterobacter | Present ⁵⁰ | Present ^{33,36} | | | |
| Citrobacter | Predominant ⁵⁰ | | | | |
| Haemophilus | Not reported | Present ^{33,35,36,41} | | | |
| Acinetobacter | Present ⁵⁰ | Not reported | | | |
| Roseomonas; Paracoccus; Bordetella; Kerstersia; Hydrocarboniphaga; Comamono | rs Present ⁵⁰ | Not reported | | | |
| Phylum Verru | comicrobia | | | | |
| Akkermansia | Not reported | Present ⁴¹ | | | |

Pandey et al (Indian; 0–7 days neonates) reported predominance of *Staphylococcus*, *Bifidobacterium*, and *Acinetobacter* in VD while Western studies reported predominance of *Bifidobacterium* (0–6 weeks infants)³³ and *Escherichia–Shigella* (0–4 months)⁴¹ in VD infants.

Similarities and Differences Reported in Gut Microbiota of Cesarean Delivered Infants

Table 3 shows the similarities and differences in gut microbiota profile of vaginally delivered infants of Indian vs Western population. *Clostridium, Staphylococcus, Lactobacillus, Bacteroides, Bifidobacterium, Escherichia–Shigella and Enterobacter* were reported for both Indian and Western CSD full term infants.

For the CSD infants, Indian studies reported predominance of *Clostridium*, ⁵⁰ *Bacteroides* (0–6 months), ⁵¹ *Prevotella*, ⁵¹ *Escherichia–Shigella* ⁵⁰ and *Citrobacter* ⁵⁰ and absence of *Bifidobacterium*. ⁵⁰ On the other hand, Western studies reported less colonization of *Bifidobacterium*, ³⁰ *Atopobium*, ³³ *Escherichia–Shigella* ⁴¹ in CSD infants.

Relative Abundance of Microbiota in Vaginal versus Caesarean Delivered Infants

Both Indian and Western studies report predominance of in *Bifidobacterium* VD^{33,50} infants and either absence or less colonization of *Bifidobacterium* in CSD^{30,50} infants. However, the over or under representation of various other gut microbiota varied.

Gut Microbiota in Indian versus Western Infants Classified According to Feeding Practices

Tables 4–6 represent the bacteria present in the gut microbiota of infants during 0–24 months of life, classified according to the feeding practices. Twelve (four Indian and eight Western) studies reported the gut microbiota by feeding practices.

There were no studies comparing the gut microbiota in Indian versus Western infants by feeding practices. Of the Indian studies, only Kabeerdoss et al reported the gut microbiota during the weaning period. However, since Shivakumar et al reported the gut microbiota profile of 18–24 months old in infants who were not breastfed, their reported gut microbiota profile was also included in this section. On the other hand, several Western studies reported multiple genera in the infants during the weaning period. 31,32,34,34,37,40

Table 4 Gut Microbiota (0-24 Months) in Indian and Western Exclusively Breastfed Infants

| Taxonomical Group (Genus) | Indian Exclusively Breastfed | Western Exclusively Breastfed | | |
|---|---------------------------------|---|--|--|
| Phylum Firmicutes | | | | |
| Ruminococcus; Roseburia; Pediococcus; Coprothermobacter | Present ⁵² | Not reported | | |
| Clostridium | Present ⁵⁰ | Significantly lower ³³ Present ^{31,41–43} | | |
| Blautia | Not reported | Present ^{41,42} | | |
| Coprococcus | Not reported | Present ^{41,42} | | |
| Streptococcus | Present ^{49,50,52} | Present ^{40–43} | | |
| Veillonella | Not reported | Present ^{40–42} | | |
| Staphylococcus | Present ^{49,50} | Present ³⁷ | | |

(Continued)

Table 4 (Continued).

| Taxonomical Group (Genus) | Indian Exclusively Breastfed | Western Exclusively Breastfed | |
|--|------------------------------|--|--|
| Enterococcus | Present ^{49,50} | Present ^{40,41,43} | |
| Lactobacillus | Present ^{49–51} | Significantly lower ³³ Present ^{37,43} | |
| Gemella | Not reported | Present ³⁷ | |
| Planococcus | Present ⁵⁰ | Not reported | |
| Peptococcus | Not reported | Present ⁴³ | |
| PeptoStreptococcus | Not reported | Present ⁴³ | |
| Dialister | Present ⁴⁹ | Not reported | |
| Faecalibacterium | Present ⁵² | Not reported | |
| Phylum Bactero | oidetes | | |
| Bacteroidaceae/Bacteroides | Present ⁵¹ | Significantly lower ³³ Present ^{31,40–43} | |
| Prevotellaceae/ Prevotella | Present ^{49,51,52} | Not reported | |
| Prevotellaceae/Paraprevotella | Present ⁵² | Not reported | |
| Phylum Actinob | acteria | | |
| Bifidobacteriaceae/ Bifidobacterium | Present ⁵⁰ | Predominant ³³ Present ^{31,37,40–43} | |
| Coriobacteriaceael Eggerthella | Not reported | Present ⁴¹ | |
| Coriobacteriaceae/Corynebacterium | Present ⁵² | Present ³⁷ | |
| Actinomycetaceae/Actinomyces | Not reported | Present ³⁷ | |
| Propionibacteriaceae /Propionibacterium | Not reported | Present ³⁷ | |
| Phylum Proteob | pacteria | | |
| Klebsiella | Present ⁵⁰ | Not reported | |
| Escherichia-Shigella | Present ⁵⁰ | Present ^{40,41} | |
| Enterobacter | Present ⁵⁰ | Present ⁴³ | |
| Citrobacter | Present ⁵⁰ | Not reported | |
| Haemophilus | Present ⁵² | Present ^{41,42} | |
| Acinetobacter; Roseomonas; Paracoccus; Bordetella; Kerstersia; Hydrocarboniphaga; Comamonas | Present ⁵⁰ | Not reported | |
| Neisseria; Kingella; Pseudomonas; Vibrio; Enhydrobacter | Present ^{49,52} | Not reported | |
| Phylum Verrucor | nicrobia | | |
| Akkermansia | Not reported | Absent ⁴¹ | |
| Phylum Synerg | istetes | | |
| Anaerobaculum | Present ⁵² | Not reported | |
| | _ . | • | |

Table 5 Gut Microbiota (0-24 Months) in Indian and Western Not Exclusively Breastfed Infants

| Taxonomical Group (Genus) | Indian Not Exclusively Breastfed/Not Breastfed | Western Not Exclusively Breastfed/Not Breastfed | | | |
|---------------------------|--|---|--|--|--|
| Phylum Firmicutes | | | | | |
| Clostridium | Not reported | Predominant ⁴¹ Present ^{31,34,37,43} | | | |
| Blautia | Present ¹⁶ | Present ^{37,41} | | | |
| Coprococcus | Not reported | Present ⁴¹ | | | |
| Streptococcus | Present ¹⁶ | Present ^{37,41,43} | | | |
| Veillonella | Present ¹⁶ | Present ^{41,43} | | | |
| Staphylococcus | Present ⁵¹ | Present ⁴³ | | | |
| Nterococcus | Not reported | Present ^{37,41,43} | | | |
| Lactobacillus | Present ⁵¹ | Present ^{37,43} | | | |
| Peptococcus | Not reported | Present ⁴³ | | | |
| Pepto Streptococcus | Not reported | Present ⁴³ | | | |
| Dialister | Present ¹⁶ | Not reported | | | |
| Faecalibacterium | Present ¹⁶ | Not reported | | | |
| Brevibacillus | Present ¹⁶ | Not reported | | | |
| | Phylum Bacteroidetes | | | | |
| Bacteroides | Present ⁵¹ | Present ^{41,43} | | | |
| Prevotella | Present ^{16,51} | Not reported | | | |
| | Phylum Actinobacteria | | | | |
| Bifidobacterium | Present ¹⁶ | Predominant ³⁷ Present ^{41,43} | | | |
| Eggerthella | Not reported | Present ^{37,41} | | | |
| Collinsella | Present ¹⁶ | Not reported | | | |
| | Phylum Proteobacteria | | | | |
| Escherichia—Shigella | Present ¹⁶ | Predominant ⁴¹ | | | |
| Enterobacter | Not reported | Present ⁴³ | | | |
| Haemophilus | Not reported | Present ⁵² | | | |
| | Phylum Verrucomicrobia | | | | |
| Akkermansia | Not reported | Present ⁴¹ | | | |

Similarities and Differences Reported in Gut Microbiota of Exclusively Breastfed Infants

Table 4 shows the similarities and differences in gut microbiota profile of exclusively breastfed infants of Indian vs Western population. Attri et al reported all the phyla in Indian exclusively breastfed infants: *Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria, Verrucomicrobia, Fusobacteria, Synergistetes.*⁵²

For exclusively breastfed infants, the following gut microbiotas were reported for both Indian and Western infants: Clostridium, Streptococcus, Staphylococcus, Enterococcus, Lactobacillus (Firmicutes); Bacteroides (Bacteroidetes); Bifidobacterium, Corynebacterium (Actinobacteria); and Escherichia-Shigella, Enterobacter, Haemophilus (Proteobacteria). The differences in the gut microbiotas in exclusively breastfed infants are detailed in Table 4.

Similarities and Differences Reported in Gut Microbiota of Not Exclusively Breastfed Infants

Table 5 shows the similarities and differences in gut microbiota profile of not exclusively breastfed infants of Indian vs Western population. Seven Western and three Indian studies reported the gut microbiota profiles in not exclusively breastfed infants (formula-fed or fed with animal milk along with breastfeeding). For infants who were not exclusively breastfed, Clostridium, Blautia, Streptococcus, Staphylococcus, Veillonella, Lactobacillus (Firmicutes); Bacteroides (Bacteroidetes); Bifidobacterium (Actinobacteria); Escherichia—Shigella (Proteobacteria) were reported for both Indian and Western infants. The differences in the gut microbiotas in not exclusively breastfed infants are detailed in Table 5.

Table 6 Gut Microbiota (0–24 Months) in Indian and Western Infants During Weaning

| Taxonomical Group (Genus) | Indian Weaning | Western Weaning | | | |
|---------------------------|-------------------------|--|--|--|--|
| Phylum Firmicutes | | | | | |
| Clostridium | Not reported | Present ^{31,32,34,43} | | | |
| Blautia | Present ¹⁶ | Present ³⁷ | | | |
| Streptococcus | Present ¹⁶ | Present ^{40,43} | | | |
| Veillonella | Present ¹⁶ | Present ^{40,43} | | | |
| Enterococcus | Not reported | Present ^{40,43} | | | |
| Lactobacillus | Not reported | Decrease ³⁴ | | | |
| | | Absent ⁴³ | | | |
| Dialister | Present ¹⁶ | Not reported | | | |
| Faecalibacterium | Present ¹⁶ | Not reported | | | |
| Brevibacillus | Present ¹⁶ | Not reported | | | |
| Phylui | m Bacteroidetes | | | | |
| Bacteroides | Increased ⁵¹ | Present ^{31,40,43} | | | |
| Prevotella | Increased ⁵¹ | Not reported | | | |
| Phylu | m Actinobacteria | | | | |
| Bifidobacterium | Not reported | Decrease ^{32,34} Present ⁴⁰ | | | |
| Eggerthella | Not reported | Present ³⁷ | | | |
| Atopobium | Not reported | Present ³¹ | | | |
| Phylum Proteobacteria | | | | | |
| Escherichia—Shigella | Not reported | Present ⁴⁰ | | | |
| Enterobacter | Not reported | Present ⁴³ | | | |

Similarities and Differences Reported in Gut Microbiota of Infants During Weaning Period

Table 6 shows the similarities and differences in gut microbiota profile of infants of Indian vs Western population during the weaning period. There was lack of Indian data during weaning period with only two studies reporting microbiota profile during weaning. Eight studies from the Western world reported microbiota profile during weaning.

Despite lack of Indian literature, both the Indian and Western infants were reported to colonize *Blautia*, *Streptococcus*, *Veillonella* (*Firmicutes*); and *SeBacteroides* (*Bacteroidetes*).

Under the phylum *Firmicutes*, an increase in families of *Ruminococcaceae* and *Lachnospiraceae* and decrease in families of *Enterococcaceae* and *Lactobacillaceae* were reported by Western studies.^{32,41} Families of *Erysipelotrichaceae*; *Peptostreptococcaceae* were also reported by a Western study.⁴¹ However, the genera details of these families were not reported. Other differences in the gut microbiotas during weaning are detailed in Table 6.

Discussion

The bacterial phyla representative of the human gut microbiota are *Bacteroidetes, Firmicutes, Actinobacteria*, *Proteobacteria*, and *Verrucomicrobia*.^{6,53} Of these, the neonatal gut microflora comprises mainly of four major phyla: *Proteobacteria, Firmicutes, Actinobacteria*, and *Bacteroidetes*.^{4,11} Our systematic review also concludes that gut microbiotas of the phyla *Firmicutes, Proteobacteria, Actinobacteria, Bacteroidetes*, and *Verrucomicrobia* were present in both Indian and Western infants. The phyla *Fusobacteria* and Synergistetes were reported for only Indian infants by a single study⁵² only.

Proteobacteria and Firmicutes were the most represented phyla across both populations, followed by Actinobacteria, Bacteroidetes and Verrucomicrobia. A similar representation of phyla has also been reported Asian and Western communities by a recent review article. However, an older review of Western studies reported Firmicutes and Bacteroidetes were the most reported phyla followed by Proteobacteria and Actinobacteria. The differences in the reported predominance of the phyla are driven by the research question. Xu et al and our systematic review was focused on identifying the ethnic diversity/similarity while the review by Fang et al was focused on the gut microbiota in health and neurocognitive development.

At the genera level, Staphylococcus, Streptococcus, Enterococcus, Lactobacillus, Clostridium, Eubacteria, Blautia, Veillonella (Firmicutes); Escherichia, Klebsiella, Proteus and Enterobacter (Proteobacteria); Bifidobacteria, Corynebacterium (Actinobacteria); Bacteroides (Bacteroidetes); and Akkermansia (Verrucomicrobia) were the common genera reported for both Indian and Western healthy full-term infants. While a timeline of relative abundance according to infant's age is not possible for this systematic review due to paucity of literature, similar gut microbiotas profile has been reported for healthy full-term infants with abundance of Bifidobacterium, Bacteroides, Akkermansia, Lactobacillus, Streptococcus, Staphylococcus and Clostridium. The review by Yang et al too reported abundance of Clostridium, Enterococcus, Lactobacillus, and Ruminococcus (Firmicutes); Bacteroides and Prevotella (Bacteroidetes), which were the common genera we also found in Indian and Western studies.

The gut microbiota of the newborn undergoes developmental changes based on two primary independent factors, mode of delivery and feeding practices. 36,41,55 The gut microbiota of VD is dominated by gut microbiota derived from the mother's vagina while the gut microbiota of CSD is derived from maternal skin. 54,56 This difference is more pronounced in the first week since birth and less visible after six months of age. 11,12 Thereafter, the gut microbiotas of the VD and CSD attain almost similar profile with minor differences in the microbiotas profile along with expected delay in development and relative abundance of microbiotas in CSD as compared to VD. 28,30,33,41,50,51

Since this systematic review included the microbiota profile of both VD and CSD across different timelines between 0 and 24 months age, we found that at the genera level, *Clostridium, Staphylococcus Lactobacillus, Escherichia–Shigella, Bifidobacterium and Bacteroides* were common to both VD and CSD infants across Indian and Western population. An earlier systematic review too found that *Bifidobacteria, Bacteroides, Clostridium*, and *Lactobacillus* genera were common in both VD and CSD from the age of 6 to 12 months of life.¹¹

CSD infants have been reported to have a relative low abundance of *Bifidobacteria* and low colonization or absence of *Bacteroides*. These microbiotas are usually obtained from the mother at birth. This systematic review too reported absence of or low colonization of *Bifidobacteria* in CSD.

Compared to VD, CSD infants have a relatively lower gut microbial diversity, primarily due to delay in colonization of *Bacteroidetes*. This systematic review too found a relatively lower genera diversity for the phylum *Firmicutes* and *Proteobacteria* in the CSD infants. However, though *Bacteroides* were present in both VD and CSD, the relative difference in their abundance and timeline of appearance could not be ascertained.

The microbiota profile of both exclusively breastfed and not exclusively breastfed is also similar but the timeline of appearance and their relative abundance differs.³⁷ There is sequential colonization of intrauterine/vaginal birth associated microbiota followed by skin-derived taxa.^{35,37} Ethnic diversity in infant gut microbiota appears before the introduction of complementary feeding and is primarily due to geographic differences.⁵⁴ This is seen to some extent between the two groups, especially at the genus level. Of the phyla common between Indian and Western exclusively breastfed infants, there was ethnic diversity at the genera level. While *Ruminococcus, Roseburia, Pediococcus, Coprothermobacter, Planococcus, Dialister, Faecalibacterium, Prevotella, Paraprevotella, Vibrio, Enhydrobacter, Kingella, Neisseria, Pseudomonas, Acinetobacter, Roseomonas, Paracoccus; Bordetella, Kerstersia, Hydrocarboniphaga, Comamonas* were found in Indian infants, the genera *Blautia, Coprococcus, Veillonella, Gemella, Peptococcus, Eggerthella* were reported in Western infants. However, in general, the Indian and Western exclusively breastfed infants had the same microbial profile Box 1.

Similarly, both Indian and Western infants not exclusively breastfed also had bacteria of several genera common among them (Box 1). *Bifidobacterium* can ferment milk oligosaccharides and is therefore present in abundance in infants as they are mainly fed on milk diet.^{54,56} This systematic review too found high colony percentages of *Bifidobacterium* reported from both Indian^{16,46,48,49} and Western^{33,39,41} studies.

Box I Gut Microbiotas Common to Both Indian and Western Healthy Full-Term Infants

| General Healthy | By Mode of Delivery | | By Feeding Practices | | |
|---------------------------------------|---|-----------------|----------------------------|------------------------------|---------------|
| Full-Term Population | Vaginal | Cesarean | Exclusively Breastfed | Not Exclusively Breastfed | Weaning |
| Firmicutes | Firmicutes | Firmicutes | Firmicutes Clostridium, | Firmicutes Clostridium, | Firmicutes |
| Staphylococcus | Ruminococcus | Clostridium, | Streptococcus, | Streptococcus, | Streptococcus |
| Streptococcus | Clostridium | Staphylococcus | Staphylococcus, | Staphylococcus, Veillonella, | Veillonella |
| Enterococcus | Streptococcus Veillonella | Lactobacillus | Enterococcus Lactobacillus | Lactobacillus, Blautia | Blautia |
| Lactobacillus Clostridium | Staphylococcus | | | | |
| Eubacteria | Lactobacillus | | | | |
| Veillonella | | | | | |
| Blautia | | | | | |
| Proteobacteria | Proteobacteria | Proteobacteria | Proteobacteria | Proteobacteria | Not reported |
| Escherichia | Klebsiella, Escherichia- | Escherichia- | Escherichia—Shigella | Escherichia—Shigella | |
| Klebsiella | Shigella, Haemophilus | Shigella | Enterobacter | | |
| Proteus | | Enterobacter | Haemophilus | | |
| Enterobacter | | | | | |
| Actinobacteria | Actinobacteria | Actinobacteria | Actinobacteria | Actinobacteria | Not reported |
| Bifidobacteria | Bifidobacteria | Bifidobacterium | Bifidobacterium | Bifidobacterium | |
| Corynebacterium | | | Corynebacterium | | |
| Bacteroidetes | Bacteroidetes | Bacteroidetes | Bacteroidetes | Bacteroidetes Bacteroides | Bacteroidetes |
| Bacteroides | Bacteroides | Bacteroides | Bacteroides | | Bacteroides |
| Verrucomicrobia Akkermansia | None of the studies reporting the gut microbiota by either mode of delivery or by feeding practices reported any gut microbiota from phylum Verrucomicrobia | | | | |

Gut microbiota profile of infants fed on formula or animal milk is modified by the microbiotas present in these feeds. Staphylococcus, Streptococcus, Enterococcus and Clostridium along with Bifidobacterium have been found to dominate the gut microbiota profile of formula-fed infants. This systematic review too found these microbiotas along with Veillonella, Lactobacillus, Blautia and Bacteroides in Indian and Western infants who were not exclusively breastfed.

Complementary diet in infancy plays a major role in diversity of gut microbiota and its development into an adult gut microbiota profile.⁵⁴ Thus, the gut microbiota is dominated by genera of *Firmicutes* and *Bacteroidetes* that are also found in the adults.⁵⁴ This systematic review too found the genera *Blautia*, *Streptococcus*, *Veillonella* and *Bacteroides* in both Indian and Western infants during weaning period, despite differences in feeding practices during weaning between the Indian and Western infants. However, the gut microbiota composition during weaning was not well represented in this systematic review, especially for Indian studies, due to lack of data available from the studies that met the inclusion criteria.

Strengths and Limitations

The systematic review could not retrieve any literature that compares the gut microbiome between Indian and Western infants from birth to 24 months of age. For the first time, a systematic literature search revealed that gut microbiota of term healthy adequately nourished infants (0.24 months) is somewhat similar between Indian and Western population. However, direct agewise (at birth, 6 months, 1 year and 2 years) comparisons between the Indian and Western infants were not possible because of lack of targeted time-specific literature for the two groups. Hence, this systematic review reported the comparative gut microbiota profile for the entire time-period from birth to 2 years in Indian versus Western term healthy adequately nourished infant.

Similarly, the relative abundance of a particular gut microbiota according to a specific time period was not possible due to lack of literature. Also, no statistical analysis for the relative abundance could be conducted as the samples were collected at different time periods and analyzed using different probes and methods. Despite these shortcomings, the systematic review could retrieve and report the colony percentages of the gut microbiotas for the Indian and Western infants aged 0–24 months.

The systematic review identified the need for well-designed studies that outline the minimum requirements to report the infant gut microbiota such as (but not limited to) taxonomical classification used, granularity of data to be presented, source of swab (fecal/oral), method of detection, etc. The systematic review also identified the need for comparing gut microbiota profile between Indian and Western infants based on targeted time-period and within the targeted time-period by mode of delivery and feeding practices. Another major gap identified was lack of studies, especially Indian, during the weaning period that assessed the gut microbiota profile by the weaning feeding practices. Further, we think that larger longitudinal studies are required to see the similarities and differences in the development of gut microbiota profile between Indian and Western infants.

Clinical Implications

The systemic review showed diverse phyla colonizing the infant gut in both Indian and Western infants. Usually, a highly diverse microbial profile is advantageous for optimal health. However, the systematic review also found colonies of harmful gut microbiotas 17,18,59 such as *Klebsiella, Escherichia–Shigella, Clostridium* and *Staphylococcus* across the two populations. Probiotics containing Lactobacilli, *Bifidobacteria* and *Streptococcus* are often used to effectively alter the gut microbiota profile towards developing eubiosis. 10,16–18

These protective microbiotas were commonly present across the two populations irrespective of mode of delivery and breastfeeding practices. However, included studies did show that *Lactobacillus* population can decrease in CSD³⁰ and during weaning³⁴ and *Bifidobacteria* can decrease in CSD.^{30,50} Gut dysbiosis has been reported even in breastfed infants.⁶⁰

Gut dysbiosis has been linked to increased risk for allergic disease, asthma, inflammatory bowel disease (IBD), autoimmune disorders, obesity, and associated noncommunicable diseases (NCDs) like diabetes and cardiovascular disorders. The epigenetic link between gut dysbiosis and diseases can be explained through the perspective of the "Developmental Origins of Health and Disease (DOHaD)". The DOHaD theory gives importance to nutrition and environmental exposures and notes that proper probiotic supplementation from birth through the infancy and early childhood can favourably modulate the gut microbiota and its products and thereby reduce the risk of diseases like IBD and NCDs. Description of the cardiovascular disorders.

Early probiotic supplementation is associated with persistent eubiosis at one year and beyond.⁶⁰ Hence, since the gut microbial profile of the Indian and Western infants is largely similar with respect to clinical implications, it can be inferred that they can be supplemented with similar probiotics during infancy (0–24 months).

Therefore, infant food supplements and probiotics which have the same composition as that of the protective infant microbiota of both Indian and Western infants can be used universally for both the populations to improve the growth, health, and development of infants as desired.

Long-term follow-up studies are required to compare the gut-microbiota and its correlation with health and disease between the Indian and Western infants. Special focus is required to see the association with IBD, NCDs and autoimmune disorders and how the gut microbiota can be effectively modulated towards health.

Author Conclusions

This systematic review found that despite some differences, the gut microbiota of Indian and Western infants aged 0–24 months are largely similar (Box 1), with implications for probiotic supplementation.

However, there are no studies comparing the gut microbiota in Indian versus Western infants (0–24 months). Hence, well-designed studies with age-specific comparative populations, and according to the same timeline of development, mode of delivery, and feeding practices can better help understand the similarities and differences in the growth, development, and diversity of the gut microbiota in both the populations. This can help in clearly identifying the window of opportunity for supplementation and intervention.

Ethics Compliance

The study was a narrative synthesis of systematic literature search and hence did not require EC approval.

Acknowledgments

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work, and have given final approval for the version to be published. The authors thank Dr. Punit Srivastava, and Dr. Kokil Mathur of Mediception Science Pvt. Ltd (www.mediception.com) for providing medical writing support in the preparation of this manuscript.

Funding

There is no funding to report.

Disclosure

The authors report no conflicts of interest in this work.

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