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Research Article

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Effect of Prebiotic-Added Foods on Infant Health: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Objective: In cases where breastfeeding is not possible, one of the recommended strategies to change the composition of the nutritional baby's gut microbiota and bring it closer to breastfed infants is to enrich the infant's food with prebiotics. The aim of this study was to systematically review the results of its effect on growth, gait and gastrointestinal (GI) system in infants fed with prebiotic-added formula and to perform a meta-analysis of the available evidence.

Materials and Methods: The literature review for this systematic review was conducted between January and February 2023 using five electronic databases: PubMed, CINAHL, Scopus, WOS and ULAKBİM. Articles were scanned using MeSH-based keywords. Only Randomized Controlled Trials conducted in the last five years were included. The data were analyzed using the Review Manager computer program (Version 5.3).

Results: The analysis included six studies involving 1399 formula-fed infants. In the post-intervention analysis of the included studies, there were no significant differences in weight (SMD: −0.21 95% CI: −0.45 to 0.03, Z=1.68, p=0.09), stool frequency (SMD:0.34 95% CI:−2. 89 to 3.58, Z=4.58, p=0.84), but there was a significant difference in the stool consistency (SMD:−0.50 95% CI:−0.73 to −0.27, Z=4.24, p<0.00001).

Conclusion: This systematic review and meta-analysis confirmed that prebiotic-enriched infant formulas are likely to provide benefits for healthy infants. The studies indicate that the inclusion of prebiotics in formulas improves stool consistency. However, no significant effects were found on growth or stool frequency. These findings suggest that further research is needed to better understand the effects of prebiotics on infant gastrointestinal health.

Keywords Prebiotics · formula · newborn · anthropometric · gastrointestinal symptoms

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INTRODUCTION

Breastfeeding and nutrition with human milk are the source of nutrition of choice for infants and have been proven to provide a range of short- and long-term benefits for the infant's nervous, immune, metabolic, and GI system (1). Where breastfeeding and nutrition with human milk are not possible or are interrupted, breast milk counterparts should aim to provide nutritional and functional properties as close as possible to breast milk (2,3).

It has been reported that breastfeeding is beneficial for colonization in the intestines of babies after birth (4). While the composition and function of the gut microbiota play vital roles in digestion, metabolism, and activation of the immune system in infants, all of these affect the later stages of life (5,6). Prebiotics are the third most common component of breast milk; in cow's milk and infant formula, it is significantly less than breast milk (7). In cases where breastfeeding is not possible, one of the recommended strategies to change the composition of the nutritional baby's gut microbiota and bring it closer to breastfed infants is to enrich the infant's food with prebiotics (8). Infant formula supplemented with prebiotics is reported to reduce a more adult-like microbiota diversity, reduced atopic eczema, and the occurrence of inflammatory bowel diseases in adulthood (7). In the literature, the evidence for the infant health outcomes of prebiotic-enriched formulas is limited.

MATERIALS AND METHODS

In this study, it was aimed to systematically review the results of its effect on growth, feces and GI system in prebiotic-added formula-fed infants and to perform a meta-analysis of the available evidence. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement) was complied with in the preparation of the systematic review and meta-analysis (9).

Eligibility Criteria

The following criteria (PICOS) were considered in the selection of the studies to be included in the study:

Participant (P): Healthy infants. The infants included in the study had the following criteria for inclusion. (1): 0-6 months old and (2) formula-fed infants.

Intervention (I): Prebiotic-added food.

Comparison(C): (1) Placebo (2) Breastfed infants reference group (3) Formula without prebiotics.

Outcomes (O): (1) Anthropometric measurements (2) Stool characteristics (3) Gastrointestinal characteristics.

Study design (S): Double-blind, randomized controlled trials, placebo, and controlled groups were included. Articles given prebiotics, preterm, with health problems were excluded from traditional and systematic reviews were not included.

Search strategy

The literature review was conducted between April and May 2023 using five electronic databases (PubMed, CINAHL, Scopus, WOS and ULAKBİM). The keywords were "baby" OR "newborn" OR "infant" AND "formula" AND "prebiotic" AND "anthropometry" AND "stool" AND "gastrointestinal symptoms". In order to avoid bias, the articles determined as a result of the screening were examined independently by the same researchers to determine that the analysis met the inclusion and exclusion criteria, and the full texts of the studies that were not defined in the abstract were evaluated. In studies where consensus could not be reached, the researchers thought of working together. A data extraction tool developed by the researchers was used to obtain the research data.

For analysis, the effects of prebiotics on anthropometric measurements were collected as the primary outcomes, and stool characteristics and GI symptoms as the secondary outcomes.

The data analysis

Using data from the included studies, a between-group meta-analysis was conducted using continuous data and random effects models to compare the outcomes of the probiotic supplemented formula intervention with those of the control group. When included studies assessed outcomes using the same methods, the mandala painting intervention was measured using the mean difference (MD) with 95% confidence intervals (95% CI). When the included studies used different methods, the mandala painting intervention was measured using the standard mean difference (SMD) with 95% confidence intervals (95% CI). The SMD was interpreted according to Cohen's thresholds: insignificant (<0.2), small (0.2 to <0.5), moderate (0.5 to <0.8), and large (>0.8). All statistical analyses were performed using the Review Manager software (RevMan, version 5.4.1.; The Cochrane Collaboration, Copenhagen, Denmark). The significance level was set at $p<0.10$ and $p<0.05$ for all other analyses. The evidence quality for each outcome was evaluated using the GRADE approach.

RESULTS

Literature review

The PRISMA flowchart for the literature review and selection is summarized in Figure 1. The electronic database search and hand-search yielded 309 potentially relevant studies. After removing duplicate articles, 295 article titles and abstracts were scanned. Titles and abstracts were read to identify the relevant articles; 168 articles were removed because they did not meet the criteria for review articles, protocols, duplications, different populations, and inclusion. The remaining 127 full texts were evaluated for eligibility. Six RCT articles were included in the quantitative synthesis because they met the desired criteria (Figure 1).

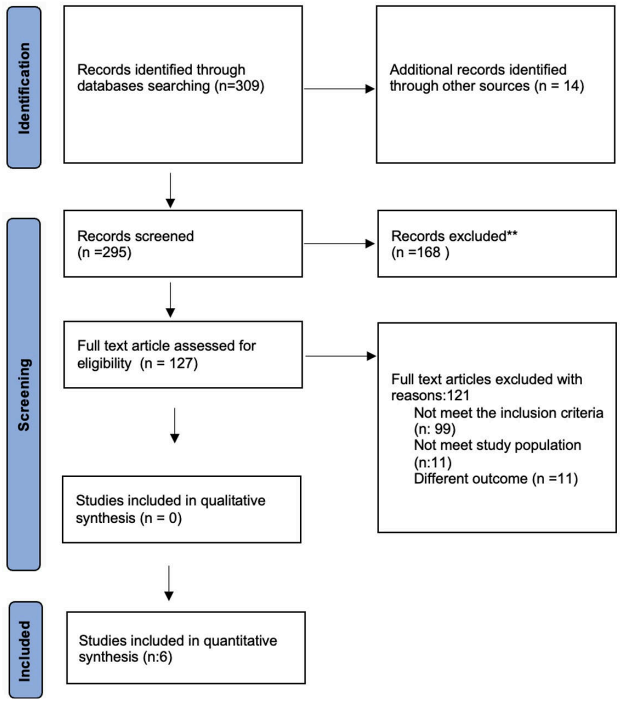


Figure 1. PRISMA flow diagram. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Study characteristics

This systematic review and meta-analysis included six studies involving 1399 formula-fed infants to assess the health outcomes of prebiotic-supplemented formula-fed infants (10-15). All studies included in the meta-analysis were double-blind RCT studies.

All of the infants included in the study were formula fed or had a requirement that their parents intended to feed them formula (10-15). The properties of prebiotics added to foods in the articles included in the study; short-chain galacto-oligosaccharides (scGOS) and long-chain fructo-oligosaccharides (lcFOS) (13), short- and long-chain inulin-type oligosaccharides to their formulas (12), polydextrose and galactooligosaccharides (10), short-chain galacto-oligosaccharides and long-chain fructo oligosaccharides ,(15) scGOS/lcFOS and large, milk phospholipid-coated lipid droplets (14) polydextrose and galacto-oligosaccharide (11).

All of the babies included in the sampling were healthy and within normal growth limits, with no health problems between 14 days and 4 months. The babies included in the study were followed between 4 and 12 months. In all of the studies, stool characteristics and anthropometric measurements were evaluated and GI symptoms (12-15), sleep and baby behavior formula (10,12,13) (Table 1).

Outcomes

Effect of prebiotics on anthropometric measurements

In the two studies analyzed, the authors reported results on weight, height and head circumference before and after treatment. The combined results of the intervention and control groups in the pretreatment period of the studies are given in Figure 2a. There was no significant difference in weight (SMD: 0.11, 95% CI:−0.13 to 0.35, Z=0.89, p=0.37). There was a significant difference in height (SMD: 0.21, 95% CI: −0.03 to 0.45, Z=1.73, p=0.08). There was no significant difference in head circumference (SMD:−0.76 95% CI:−2.16 to 0.63, Z=1.08, p=0.28).

The combined results of the intervention and control groups in the post-treatment period of the studies are given in Figure 2 b. There were no significant differences in weight (SMD: −0.21 95% CI: −0.45 to 0.03, Z=1.68, p=0.09), height (SMD: −0.05 95% CI: −0.49 to 0.39, Z=0.24, p=0.81) and head circumference (SMD: 0.27 95% CI: −0.27 to 0.82, Z=0.98, p=0.33) (Figure 2a-b)

Effect of prebiotics on the growth gap

In one study, the authors reported the results of weight, height, and head circumference before and after treatment. In the study, there was a significant difference in weight (SMD:−0.56 95% CI:−0.85 to −0.26, Z=3.71, p=0.0002) between the groups. There was no significant difference between the groups in terms of height (SMD:0.20 95% CI:−0.09 to 0.49, Z=1.35, p=0.18) and head circumference (SMD:0.04 95% CI:−0.25 to 0.32, Z=0.25, p=0.80) (Figure 3).

Effect of prebiotics on the stool frequency

In the two studies examined, the authors reported the results for stool frequency before and after treatment. The combined stool frequency results of the studies showed a significant difference between the groups in the pre-treatment period (SMD: −1.27 95% CI:−1.76 to −0.78, Z=9.06, p<0.00001) and after treatment (SMD:0.34 95% CI:−2.89 to 3.58, Z=4.58, p=0.84) (Figure 4 a-b).

Table 1. Patient demographic data, symptoms, comorbidities, and associated cranial nerve palsy

Reference Country	Study design	Population	The inclusion and exclusions criteria	Protocol	Comparisons	Drop out	Outcome	Results
Rodriguez et al., 2019; Italy, Spain	Çift Blind, Multicenter, RCT*	200 babies (EG*: 94; CG*: 105; BRG*: 100)	-≤28 days of term (37≥ and ≤42 GW*), Normal birth weight (10-90 percentile), Infants within +/−2 SD relative to head circumference were included. Cow's milk and soy allergy, known to have an increased risk of lactose intolerance, having any medical condition, or having a diabetic mother baby Infants who were previously fed an IF* containing is probiotics or simbiotics were not included.	- EG* infants IF* scGOS* and lcFOS 9* added The first visit occurred at ≤28 days of age, and the infants were then assessed at 4, 8, 13 and 17 weeks (5 visits) - Measurements were made at each visit.	Control: Placebo	EG*: 22; CG*: 25 BRG*: 28	GI* symptoms, growth, stool characteristics, sleep and crying behavior, AE*	No significant difference was observed in parent-reported GI symptoms. BRG* was closer and EG* stool consistency was softer than the control group. Daily weight gain was equivalent to BRG* close growth results for eachformula group. There was no clinically significant difference in AE except for the lower prevalence of infantile colic in CG* versus EG*
Neumer et al.,2021 Spain,Belgium	Dual Blind, Multi-Center, RCT*	160 babies (EG*: 81; CG*: 79)	–0-4 months old, Normal birth weight (10-90 percent according to current growth charts), - Term birth (≥37≤ and 42 weeks gestation) was included. -Parentswho do not comply with the work follow-up -The presence ofany related disease, any condition related to the immune system, which may affect the nutrition and growth of the B midwife, is an infection for 7 days before entering the study Infantswho were fed a baby food (IF) containing probiotics or synbiotics before entering the exercise were also excluded from participation.	-EG* infant rIF* short and long chain inulin-type oligosaccharides were added. -Dlasted from the day of the abortion until the baby was one year old The basic visit took place at 0-4 months of age, and the infants were then assessed at 2,4,6,9 and 12 months of age (5 visits)	Control: Placebo	EG*: 20; CG*: 17	GI*symptoms, growth measurements, microbiota analysis, AE*	Themean duration of infection was significantly lower in infants fed P-rebiotics. Babies who received prebiotic formula had softer stools.
Colombo et al., 2021; USA*	Dual Blind, RCT*	161 babies (EG*: 79; CG*: 81)	–14-35 days old, with a height weight of ≥2500 g and a normal growth history -37-42 GW* and individual infants were included. Ahistory of prenatal illicit drug use or clinically significant psychiatric illness; -A history of metabolic or chronic illness or food intake or congenital malformation in the B infant, -B A history ofbending difficulties or food intolerance; -Immunodeficiency -Infants with planned use of p-robiotics during the study period were excluded.	-EG* infants' formulas have been supplemented with polidextrose and galacto-oligosaccharides -Beginner Level (14-35 days), randomization according to the study formula (4-8 days after Basic Level), 70. Day (±7 days) and 112. Corresponds to the day (±7 days). -Basic diary and actigraphy data were taken and participants were assigned to a working formula group.	Control: Does not contain prebiotics IF*	EG*: 14; CG*: 16	Bis the behavioral state and sleep-wake of the midwife, antropometri and stool characteristics	The average duration of the crying/restlessness episodes was similar in the beginning, 70. It was significantly shorter for PDX/GOS* per day and Control and was 112. It continued in the day. Day 112 Cortisol wake-up response 70th and 112th Shown in days. Significant differences in fecal microbiome beta diversity and individual taxon abundance were observed in the PDX/ GOS* group.

Reference Country	Study design	Population	The inclusion and exclusions criteria	Protocol	Comparisons	Drop out	Outcome	Results
Wang et al., 2021, China	Dual Blind, Multi-Center, RCT*	224 babies (EG*: 112; CG*: 112, BRG: 53	• Healthy, term and ≤44 days, - 10th –90th birth weight in the percentile, - Infants without current or previous illness/condition were included. - Fully breastfed -Infants using different IF* were not included.	-EG* IF*, scGOS/lcFOS,9:1* and a symbiotic mixture of Bifidobacterium were given with the formula of partiallyh-idrolized protein (pHF). Infants were assessed at (V1), 4 (V2), 8 (V3), 13 (V4) and 17 (V5) weeks during study visits. - After the first visit, parents filled out a 7-day form before each visit, covering IF* intake, GI* symptoms, and general condition.	Control: Does not contain prebiotics IF*	EG*: 27; CG*: 22, BRG*: 2	GI* symptoms, Amsterdam Stool Scale, anthropometric measurements	EG* showed equivalence in daily weight gain (abible outcome) between BRG* and CG*. There were no clinically significant differences in GI* tolerance or AE between the formula groups.
Teoh et al., 2022, Singapore	Dual Blind, RCT*	EG1*:155, EG2*:152, CG*: 146 *,BRG: 67	• have Chinese, Malay or Indian ethnicity, 37-42 GW, ≤ 28 days -According to the Fenton growth chart, the eastern weight and head circumference are between the 3rd and 90th percentile. -S-weighted term infants were included. -Diseases that may prevent work, -Specialdietary needs, Infants with all the time atitis B or HIV were not included.	-A specific prebiotic mixture scGOS/lcFOS* and a prebiotic mixture containing large, milk phospholipid-coated lipid droplets were added to the formulas of the infants in the intervention group -Zwas performed at the age of 4, 8, 13 and 17 weeks. Daily study product intake, GI* symptoms, and stool characteristics were recorded by parents for the 7-day period prior to each individual	Control: Does not contain prebiotics IF*	EG1*:27, EG2*:117 CG*: 117, BRG*: 1	GI symptoms, Amsterdam Stool Scale, anthropometric measurements	EG2* and CG* were shown to be equivalent in daily weight gain. There were no differences in secondary growth outcomesbetween clinically relevant groups in terms of tolerance outcomes or the number, severity, or relationship of adverse events.
Hoffman et al., 2019, USA*	Double blind, Parallel Group, RCT*	142 babies (CG*: 47; ARA-25*: 48; PDX/GOS*:47)	• 10-18 days of age, with a ≥ weight of 2500 g, -Fed only with formula at least 24 hours before R andomization, -37-42 GW and individual infants were included. -GIda retrieval, normal growth and development, or a history of a disease or congenital malf formation, -Intolerance to milk-based formula during K usma or randomization, InR-andomization, <95% of the net birth weight and older infants were excluded from a diabetic motheraccording to the gestational age of the child at the time of birth.	-EG* infants' IF* PDX/GOS* prebio was broken down and different concentrations of ARA* and DHA* were added -Bbabies were randomized into three groups. -Blood and saliva samples and anthropometric measurements were taken from all babies. The infants werefollowed until they were 14 and 120 days old.	Control: Does not contain prebiotics IF*	CG*:16, ARA-25*:17, PDX/ GOS*:27	In Buccal Epithelial, PL*, RBC, anthropometric measurements, stool and gas properties	There were no statistically significant group differences in the growth rates of weight, length or head circumference. No significant group differences were detected in the frequency (number/day) of stool frequency. no significant group differences in stool consistency were detectedon days 60, 90 and 120 On day 3, precursory differences in stool consistencywere detected between the PDX/GOS* and CG* or ARA-25* groups.

ARA-25: arachidonic acid, DHA: docosahexaenoic acid and prebiotic mixed food. PDX/GOS: polydextrose galacto-oligosaccharides, PL: phospholipids, RBC: Red Blood Cell, scGOS: short chain galacto-oligosaccharides, lcFOS: long chain fructo-oligosaccharides, BRG: breastfed reference group, EG: Experimental Group, CG: Control Group, GI : Gastrointestinal, GW: Gestation Week, IF: Infantile Formula, RCT: Randomized Control Trial

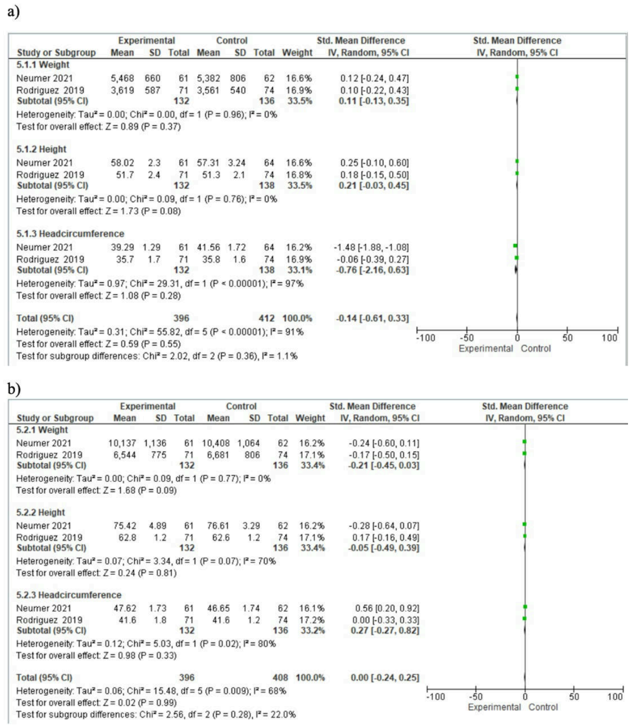


Figure 2. Meta-analysis results on the effect of prebiotics on the anthropometric measure. (a) Pre-intervention (b) Post-intervention

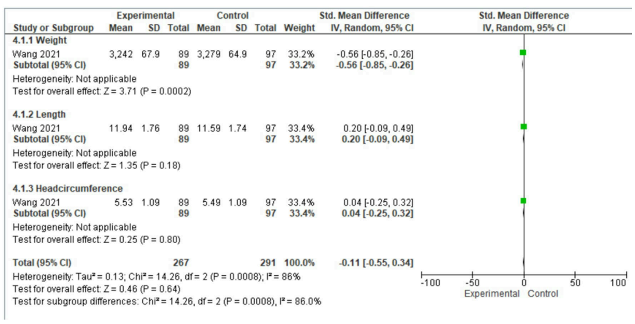


Figure 3. Meta-analysis results on the effect of prebiotics on the growth rate

Effect of prebiotics on the stool consistency

In one study reviewed, the authors reported results for stool consistency before and after treatment. Stool consistency results were significantly different between the groups in the pre-treatment period (SMD:−0.49 95% CI:−0.72 to −0.26, Z=4.13, p<0.00001) and after treatment (SMD:−0.50 95% CI:−0.73 to −0.27, Z=4.24, p<0.00001) (Figure 4 a-b).

Gastrointestinal Symptoms

In one study reviewed, the authors reported the results of vomiting and regurgitation related to GI system symptoms. The results of vomiting were found to be no significant difference between the groups in the pre-treatment period (SMD:−0.05 95% CI:−0.27 to 0.17, Z=0.45, p=0.65) and after treatment (SMD:0.00 95% CI:−0.01 to 0.01, Z=0.00, p=1.00). The results of regurgitation were found to be no significant difference between the groups in the pre-treatment period (SMD:−0.13 95% CI:−0.63 to 0.37, Z=0.51, p=0.61) and after treatment (SMD: −0.03 95% CI:−0.12 to 0.06, Z=0.65, p=0.52) (Figure 5 a-b).

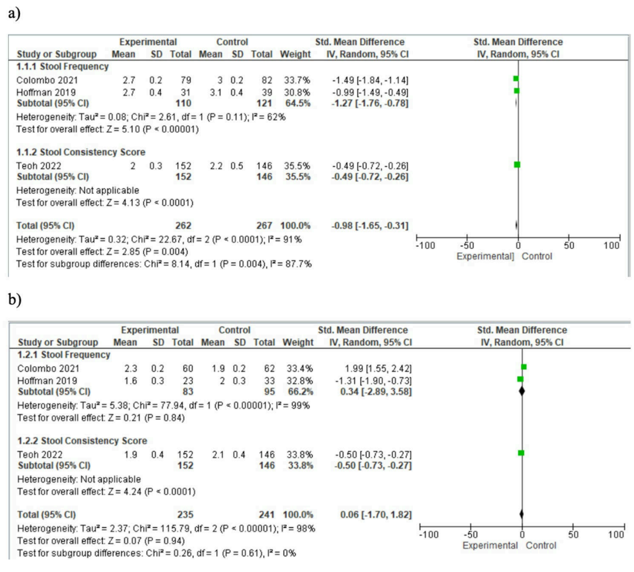


Figure 4. Meta-analysis results on the effect of prebiotics on the stool characteristics: (a) Pre-intervention (b) Post-intervention

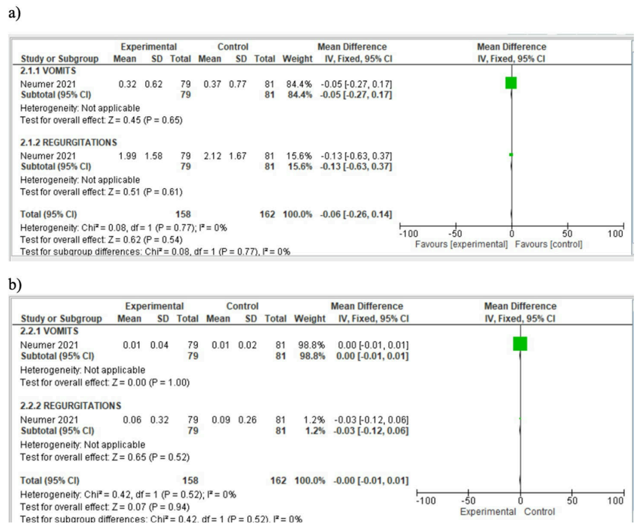
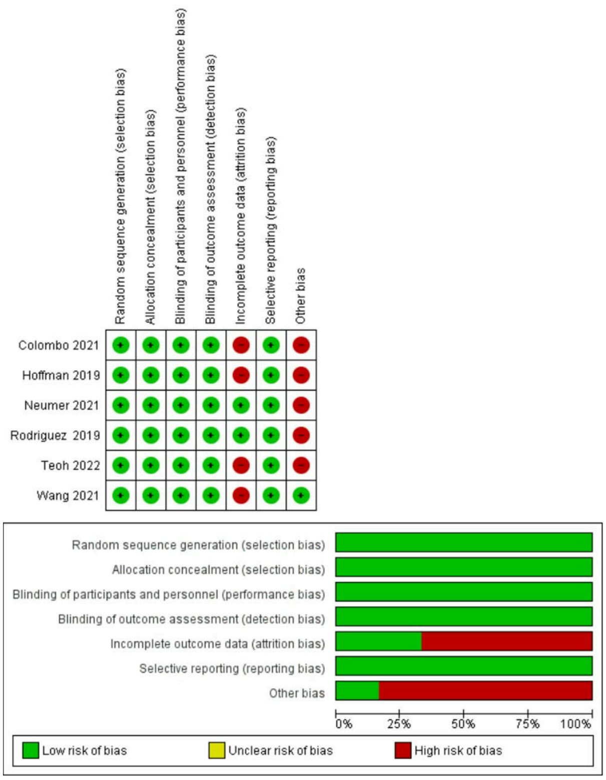


Figure 5. Meta-analysis results on the effect of prebiotics on the gastrointestinal Symptoms: (a) Pre-intervention, (b) Post-intervention

Risk of Bias Assessment

The quality of the articles in the randomized controlled trials and the Version 2 of the Cochrane Risk-of-Bias tool (RoB-2) were used for the randomized trials. The risk of bias was categorized into six domains, as outlined in the Cochrane Handbook for Systematic Reviews of Interventions. Each domain’s risk was rated "low", "high", or "uncertain" based on the predefined criteria of the bias risk tool.

All research has identified an adequate method for randomly assigning participants to treatment groups. Therefore, he rated these studies in this area as having a low risk of nepotism. All studies reported adequate distribution secrecy using sequentially numbered and sealed opaque envelopes and rated them with a low risk of favoritism error. In all studies, the risk of nepotism was low, as both participants and staff were blinded. In all studies, disability between the intervention and control groups was balanced or few enough not to affect the study. For this reason, it was concluded that the risk of attrition was low. Four studies found that the risk of reporting bias was high because anthropometric measurement data were missing or not given at all (9,10,13,14). In addition, in terms of other risks, sponsoring five studies was considered high risk (9-13). For each study included, significant concerns about other possible sources of bias that had not previously been addressed in the above categories were disclosed (Figure 6). The quality of the evidence included in this meta-analysis was assessed using the GRADE approach. Anthropometric measurements, stool characteristics and GI symptoms were the outcomes assessed. The results regarding the outcomes showed low to moderate evidence. The GRADE analysis can be seen in Figure 7.



ROB-2: Risk-of-Bias tool for randomized trials

Figure 6. Risk of bias domains: ROB-2.

DISCUSSION

The purpose of this review and meta-analysis was to summarize the available evidence regarding the infant's growth rate, defecation count and GI outcomes efficacy of probiotic supplementation given to infants compared with controls. The study results are important in terms of showing that probiotic-supported formulas can be used to promote and maintain newborn health, especially when breast milk is not an alternative.

Stool characteristics	**10.7**	**19.5**	**-0.10**	**476**	**Moderate quality**	**b.High heterojenity>97.4**
Gastrointestinal semptoms	0.09	0.06	-0.01	160	Moderate quality	a.Total population<300
*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk Ratio; [other abbreviations, eg. OR, etc]						
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.						

Figure 7. Grade analysis and sum of the findings

The results of the study found that the effect of prebiotics on the growth rates of the babies such as weight gain, head circumference and height was similar between weight gain and height compared with the control group, and the difference between head circumferences was significant. In a text-analysis that included six studies, increases in body weight, head circumference, or length between days 14 and 112 found no positive or negative effect compared with the control groups of the probiotic group. However, this study confirms that normal growth occurs when infants are given a formula containing prebiotics (16). In another study, anthropometric parameters increased in the normal range from visit to visit in the probiotic and control groups and were very similar in the two groups (17). The literature is similar to the study findings.

The results of the study showed that the effect of prebiotics on stool parameters such as stool frequency and stool consistency of infants was significantly different when compared with the control group. Two systematic reviews in China showed that prebiotics reduced the frequency of 24-h stools in infants compared with conventional treatment and that prebiotics were more effective than traditional practices. Our findings supported the claims of the two previous reviews. In a contrary study, it was found that oral probiotic supplementation given to mothers during the perinatal period did not have a significant difference in stool results compared to pesaro (18). A meta-analysis of two studies using L. reuteri ATCC 55730 and L. reuteri DSM 17938 found a statistically significant increase in the number of fecal evacuations and reported that probiotics may play an important role in the modulation of intestinal inflammation, which may also contribute (19). Two randomized controlled trials reported that soft stools predominate in infants fed 100% whey partially hydrolyzed formulas (20).

In recent years, scientists have thought that probiotics may be effective for treating GI problems, especially infantile colic (18,20). The results of the study showed that there was no significant difference between the results of vomiting and regurgitation when the effect of probiotics on vomiting and regurgitation outcomes related to GI system symptoms was compared with the control group. Karaahmet et al. (21) reported in their study that infantile colic infants whose mothers were given probiotics had reduced GI symptoms compared with the control group. Baldassarre et al. (18) found that oral probiotic supplementation given to mothers during the perinatal period did not have a significant difference on GI symptoms and stool outcomes compared with plesado. A meta-analysis of three of the six trials in a systematic review that included six randomized controlled trials investigating the efficacy of probiotic supplementation showed a statistically significant reduction in regurgitation compared with placebo in infants receiving L. reuteri DSM 17938(22,23) and the original L. reuteri ATCC 55730 (24,25) The literature is similar to the study findings.

Limitation

More work is needed, especially in formula-fed babies. Studies evaluating the efficacy of other prebiotics and prebiotics are needed, as preliminary results with some of these suggest efficacy. In cases where breastfeeding and breast milk are not an alternative, formula companies have been supporting babies with formulas similar to breast milk content in recent years. However, studies on this subject are very few. In addition, the number of participants included in the sample in the studies was negligible. Of the studies included in the meta-analysis, only two were double-blind and there were no placebo-controlled studies. Also, double-blind and placebo-controlled studies will affect the quality of the included studies.

CONCLUSION

In conclusion, this systematic review and meta-analysis confirmed that prebiotic-enriched formulas are likely to provide benefits for healthy infants. The studies indicate that prebiotic formulas have a positive effect on growth parameters, head circumference, and stool characteristics (consistency, frequency, and density). However, no significant differences were observed in growth or stool frequency. These findings suggest that while prebiotic formulas show potential for improving infant gastrointestinal health, further research is needed to address the gaps in knowledge in this area.

The healthy growth and development of infants is one of the most crucial factors influencing their lifelong health. The positive effects of prebiotics on the infant digestive system can strengthen their immune system and the development of a healthy microbiota. Therefore, prebiotic-enriched formulas can be considered an important alternative for infants who cannot be breastfed and could be an effective strategy in promoting and safeguarding infant health.

Peer Review	Externally peer-reviewed.
Author Contributions	Conception/Design of Study- D.Ç.T., A.Y.K., F.Ş.B.; Data Acquisition- F.Ş.B., A.Y.K.; Data Analysis/ Interpretation- D.Ç.T., A.Y.K., F.Ş.B.; Drafting Manuscript- F.Ş.B., A.Y.K.; Critical Revision of Manuscript- D.Ç.T.; Final Approval and Accountability- D.Ç.T., A.Y.K., F.Ş.B.
Conflict of Interest	Authors declared no conflict of interest.
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