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Probiotic Supplementation in Infantile Colic: A Comparative Literature Review Between Breastfed and Formula-Fed Infants

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ABSTRACT

Background: Infantile colic is a functional gastrointestinal disorder in infants under five months, marked by excessive, unexplained crying, and is increasingly linked to gut dysbiosis and intestinal inflammation. Probiotics have been proposed as a therapeutic option to modulate the gut microbiota and alleviate symptoms, though their efficacy may differ between breastfed and formula-fed infants. **Objective:** This study aims to evaluate the effectiveness of probiotics in managing infantile colic, with a focus on differences in outcomes between exclusively breastfed and formula-fed infants. **Methods:** This literature review identifies randomized controlled trials and cohort studies involving infants aged 0–12 months that are diagnosed with colic and receiving probiotics. The outcomes are crying frequency and duration, or symptom improvement, and compared effects between exclusively breastfed and formula-fed infants. Seven databases were searched using combinations of relevant keywords, limited to publications from the past five years. Data were synthesized using narrative qualitative analysis. **Results:** From 1,886 initially identified records, 29 studies met the eligibility criteria after screening and full-text assessment. Among these, 13 focused on probiotics alone, 15 examined probiotics in breastfed infants, and 5 involved formula-fed infants. Most studies supported the efficacy of *Lactobacillus reuteri* DSM 17938 in reducing crying duration and frequency, particularly in breastfed infants. Formula-fed infants showed variable outcomes, potentially influenced by probiotic strain, feeding composition, and study design. **Conclusion:** Probiotics, especially *Lactobacillus reuteri*, demonstrate promising effects in alleviating colic symptoms, predominantly among breastfed infants. Feeding type may act as a modifier of probiotic efficacy, highlighting the need for tailored interventions based on nutritional context.

Keywords: Breastfeeding, Formula feeding, Infantile colic, Lactobacillus reuteri, Probiotics

1. Introduction

Infantile colic is recognized as a functional gastrointestinal disorder, characterized by recurrent and prolonged episodes of inconsolable crying or fussiness in infants younger than five months, occurring without any identifiable medical cause. According to the Rome IV criteria, the condition is defined by symptoms that persist for at least three hours per day, on a minimum of three days per week, and lasting for at least one week [1]. Epidemiologically, the prevalence of infantile colic varies considerably worldwide, with global estimates ranging from 1.9% to 19.2%, and a median prevalence of approximately 17.7% based on the Rome IV criteria [2]. In Indonesia, a cross-sectional study involving 433 infants aged 6 weeks to 4 months reported a 16.8% prevalence of colic symptoms consistent with Rome IV criteria. The comparable rates of infantile colic in Indonesia and worldwide stress the significance of prompt diagnosis and effective treatment strategies [3].

Infantile colic is generally self-limiting and resolves by six months of age, yet excessive crying in early infancy remains a leading cause of pediatric visits and emergency consultations, imposing significant healthcare burdens. Persistent crying is associated with adverse psychosocial impacts, including strained family relationships, maternal mental health disorders, early breastfeeding cessation, and, in severe cases, non-accidental injury. Current management focuses on parental reassurance, but no consensus exists on effective therapies, with most interventions showing limited efficacy, uncertain outcomes, or safety concerns [4].

Emerging evidence suggests that neonatal gut microbiota alterations may influence nociceptive neurobiological pathways, contributing to infantile colic pathogenesis. Affected infants exhibit reduced microbial diversity, elevated fecal calprotectin, and

increased neutrophil-derived antimicrobial peptides, indicating low-grade intestinal inflammation. Probiotics have been proposed as a preventive or therapeutic strategy by modulating central pain perception; however, their efficacy and safety are strain-specific [5,6].

Research by Partty et al. demonstrated that early administration of *Lactobacillus rhamnosus* GG was associated with a reduced incidence of infantile colic, alongside beneficial modulation of gut microbiota composition and inflammatory biomarkers [7]. Additionally, findings from Angela Pierina et al (2021) indicated that ddministration of *Lactobacillus reuteri* DSM 17938 at a daily dose of 10^8 CFU in exclusively breastfed infants was associated with a significant reduction in symptoms of infantile colic [8].

Lactobacillus reuteri DSM 17938 has demonstrated efficacy in alleviating infantile colic by modulating gut microbiota, reducing pro-inflammatory cytokine levels, and strengthening the intestinal barrier. It supports gastrointestinal maturation, enhances immune tolerance to dietary antigens, and produces antimicrobial compounds such as reuterin. Through interactions with Toll-like receptors, it modulates innate immunity, collectively reducing the frequency and duration of crying episodes, particularly in breastfed infants [9].

This paper aims to assess the efficacy of probiotics in managing infantile colic, both overall and within specific feeding subgroups, namely exclusively breastfed and formula-fed infants.

2. Method

2.1 Eligibility criteria

This literature review was conducted using the PICO framework: 1) Population: infants aged 0-12 months with infantile colic; 2) Intervention: probiotics; 3) Comparison: probiotics in exclusively breastfed infants and formula-fed infants; 4) Outcomes: infantile colic symptoms, such as crying frequency, crying duration, and other signs of clinical improvement. Study Design: only randomized controlled trials (RCTs) or cohort studies were considered, and studies published in English or Indonesian.

2.2 Search strategy and screening

A literature search will be conducted using several databases, including PubMed, Cochrane Library, ScienceDirect, ProQuest, Taylor & Francis, SpringerLink, SAGE Journals, and Google Scholar. The search will incorporate appropriate keywords: "Infantile colic" AND ("Probiotic" OR "Probiotics") AND ("Breastmilk" OR "breastfed" OR "Milk formula"). Any disagreements among reviewers will be resolved through discussion.

3. Result

3.1 Study selection and identification

A total of 1,886 articles were published across six databases following the literature search. A total of 1,335 articles were excluded as ineligible by automation tools. A total of 1212 articles were excluded for failing to meet the specified study design and inclusion criteria. Subsequently, numerous journals were excluded due to ineligible data, including review articles and books; additionally, some articles were inaccessible due to subscription barriers (n = 94). This study comprises 29 articles.

3.2 Summaries of the included studies

Among these, 13 focused on probiotics alone, 12 examined probiotics in breastfed infants, and 6 involved formula-fed infants. There are 2 studies that examined probiotics in both breastfed and formula-fed infants. Most studies supported the efficacy of *Lactobacillus reuteri* DSM 17938 in reducing crying duration and frequency, particularly in breastfed infants **(Table 1)**.

4. Discussion

Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host by supporting intestinal microbiota balance, which is essential for overall health. Probiotics support host health by influencing immune system activity, strengthening the intestinal barrier, generating antimicrobial compounds, and inhibiting pathogen colonization by competing for attachment sites and available nutrients in the gut. These mechanisms collectively support digestive health and may provide therapeutic benefits in various disorders, including inflammatory, allergic, and infectious diseases. Common genera used as probiotics include *Lactobacillus, Bifidobacterium*, and certain *Saccharomyces* species a[10].

Probiotics have been extensively investigated across various gastrointestinal disorders. Probiotic administration was associated with a reduced incidence of necrotizing enterocolitis (NEC) in pediatric populations. Furthermore, a meta-analysis by Rao Huang et al. revealed that in the context of pediatric acute diarrhea, adjunctive probiotic therapy was effective in reducing symptom duration [11]. Probiotic led to significant improvements in among patients with irritable bowel syndrome (IBS) [12].

Table 1. Included studies

No	Author, Year / Study	Sample (Probiotic/ Placebo)	Intervention	Outcome	
				Quantitative (Probiotic & Placebo)	Qualitative
Probiotics only					
1	Martinelli, 2017 / RCT [13]	59/57	*L. reuteri DSM 17938*	51/59 39/57	Administration of L. reuteri DSM 17938 are significantly more effective than simethicone in improving colic symptoms
2	Partty, 2015 / RCT [7]	81/78	*L. rhamnosus* GG (ATCC 53103) Administered via infant formula Starting from birth until 3 months of age	colic 26%/47% RR): 0.56 (95% CI: 0.33–0.95) crying duration: significantly reduced in LGG group fecal calprotectin lvl: significantly lower in probiotic group	Early-life probiotic supplementation with *L. rhamnosus* GG reduced the risk of developing colic It also favorably modified gut microbiota and inflammation markers No adverse effects reported
3	Savino, 2015 / RCT [14]	52/53 Vit D3	*L. reuteri* DSM 17938 (10^8 CFU) + 400 IU vit D_3	RR for cimetropium 0.04; simethicone 0.24; breastfeeding switch RR 0.37; fewer pediatric visits	Reduced need for medications, fewer visits; no adverse events; supports symptomatic relief
4	Savino, 2018 / RCT [15]	45/42	*L. reuteri* DSM 17938 (10^8 CFU/day)	Crying time significantly reduced; ↑ RORγ/FOXP3 expression	Reductions in crying supports immune-modulatory mechanisms via T-cells
5	Maldonado-Lobón, 2021 / RCT [16]	50 per arm (Probiotic, Combo, Control)	*B. breve* CECT7263 (2×10^8 CFU/day); Combo: *B. breve* + *L.*	Crying-time reduction: –40% to –68.5% (probiotic) vs –27% to –59% (control), significant weekly difference	Early effect, better infant sleep, improved parental mood, safe and well-tolerated

			fermentum; Simethicone 80 mg/day		
6	Piątek, 2021 / RCT [17]	54/33	9-strain synbiotic (*L. acidophilus* LA-14, *L. casei* R0215, *L. paracasei* Lp-115, *L. rhamnosus* GG, *L. salivarius* Ls-33, *B. lactis* Bl-04, *B. bifidum* R0071, *B. longum* R0175, Fructooligosaccharides (FOS)) vs simethicone	≥50% reduction: crying days 72% vs 18%; evening crying 85% vs 39%	Multi-strain mix significantly outperformed simethicone; no adverse events
7	Ahmadipour, 2020 / RCT [18]	48/24	Synbiotic "Pedilact" (L. rhamnosus + L. reuteri + B. infantis + FOS)	Frequency ↓ significantly ($P < 0.0001$); Crying duration ↓ significantly ($P = 0.025$)	Improved quality of life, more weight gain in probiotic group; no adverse events
8	Moreno, 2024 / RCT [19]	80/80	*L. rhamnosus GG* + *L. reuteri DSM 17938* (10^9 CFU/strain/day) for 21 days	Crying ↓ from 190 to 80 min/day (vs 122 in placebo), $P < 0.001$	Faster symptom relief; safe and well tolerated
9	Khoshnevisasi, 2022 / RCT [20]	30/30	Synbiotic (L. rhamnosus, L. reuteri, B. infantis + FOS) vs Simethicone	Crying ↓ (130 vs 80 min/day); $P < 0.001$	Synbiotic more effective and well tolerated than simethicone
10	Vandenplas, 2017 / RCT	23/23	*Lactobacillus*	Duration of crying per episode was	Effective in reducing the number and duration of

	[21]		*reuteri* SGL01 and *Bifidobacterium brevis* SGB01	significantly shorter (9.14 ± 5.34 vs 13.22 ± 5.29 min; p = 0.014)	crying episodes in infants with colic
11	Basturk, 2022 / RCT [22]	20/18	*L. reuteri* DSM 17938, 1×10^8 CFU	crying episodes: 945 ± 420 vs 1,205 ± 450 min ($p = 0.041$); restlessness: 1,005 vs 1,155 min ($p = 0.037$)	Significant reduction in crying and restlessness for both feeding types; safe and well tolerated
12	Tyrsin, 2024 / RCT [23]	45/45	*L. reuteri* DSM 17938 + FOS, 10^8 CFU/day	Crying ↓ from 185 to 78 min/day (vs 122 in placebo); P < 0.001	Synbiotic more effective than placebo; symptom improvement from day 7; safe
13	Nation, 2017 / RCT [24]	85/82	*L. reuteri* DSM 17938, 1×10^8 CFU/day	Probiotic group cried/fussed 49 min **more** at 1 month ($P = 0.02$); no difference in secondary outcomes	No clinical benefit; poor gut colonization may explain refusal; safe and well tolerated
Probiotics in the breastmilk population					
14	Savino, 2020 / RCT [25]	24/21	*Lactobacillus rhamnosus*	Probiotic (242min/day -> 104.7min/day) Placebo (247.9 min/day -> 239.6 min/day)	Reductions in crying time and faecal calprotectin levels, with increased total bacteria and *Lactobacillus* sp
15	Nocerino, 2019 / RCT [26]	40/40	*B. animalis* subsp. *lactis* BB-12 1×10^9 CFU/day	≥50% cry reduction from wk 2; crying episodes ↓ −4.7 vs −2.3 (P < 0.05); ↑ butyrate, sIgA; ↓ calprotectin	Effective in breastfed infants; immunomodulatory effects; safe and tolerated
16	Chen, 2021 / RCT [27]	48/42	*B. longum* KABP042 + *P. pentosaceus* KABP041, 1×10^9 CFU/day	Crying decreased to 14 vs 40 min/day by Day 21; higher ≥50% responder rates; fewer episodes (p < 0.001)	Synbiotic significantly reduced crying and fussing; improved stool consistency; safe and well tolerated
17	Gerasimov, 2018 / RCT [6]	84/84	Synbiotic (*L. rhamnosus* + *L. reuteri* + FOS + vit D_3)	Cry/fuss –163 vs –116 min/day (p = 0.019); Day 28: 142 vs 199 min/day (p < 0.05)	Significantly improved crying/fussing; safe; exclusively breastfed infants

18	Fatheree, 2017 / RCT [28]	20/10	*L. reuteri* DSM 17938, 1×10^8 CFU	Cry/fuss time 300 → 140 min/day in probiotic group; no significant between-group difference	Safe in infants with neutropenia; no adverse events; underpowered for efficacy outcomes
19	Mi, 2015 / RCT [29]	21/21	L. reuteri DSM 17938, 1×10^8 CFU	100% responders vs 15.7%; crying time : 32 vs 121 min/day ($P < 0.01$)	Rapid symptom relief, maternal mood improvement, safe and well tolerated
20	Baldassarre, 2018 / RCT [30]	27/26	Multi-strain probiotic (Vivomixx)	Crying: 68.4 vs 98.7 min/day by day 21 (p=0.001); responder rate Day 21: 26/27 vs 17/26 (p=0.001)	Effective in reducing colic, improved parental QoL, safe and well tolerated
21	Savino, 2024 / RCT [31]	16/16	L. reuteri DSM 17938	Urinary metabolites increased post-probiotic vs placebo	Demonstrates metabolic impact; safe and well tolerated in colicky infants (Pilot RCT → mechanistic, ocusing on **urinary metabolome changes**, **not directly measuring crying symptoms)**
22	Chau, 2015 / RCT [32]	24/28	*L. reuteri* DSM 17938, 10^8 CFU	Median crying: 60 vs 102 min/day (P = 0.045); total crying over 21 days: 1,719 vs 2,195 min (P = 0.028); responders: 71% vs 21% (RR = 3.3)	Significantly reduced crying/fussing; improved family QoL; well tolerated
23	Giglione, 2016 / RCT [33]	29/31	*B. breve* BR03 + B632 (10^8 CFU/strain	Month 3 crying: 12.1 vs 46.7 min/day ($P = 0.016$); no early benefit	Reduced colic by month 3; delayed benefit in bottle-fed infants; safe
24	Venkataraman, 2025 / RCT [34]	40/40	*L. reuteri* UBLRu-87, daily	Significant reductions in crying/fussing; high responder rates; reduced burping and facial flushing	Improved microbiome diversity; enhanced parental QoL; safe & well tolerated
25	Zoham, 2019 / RCT [35]	33/32	Pedilact synbiotic (B. infantis, L. reuteri, L. rhamnosus)	Daily crying/fuss episodes, crying days, and crying duration significantly reduced ($P \leq 0.032$ by day 21; $P \leq 0.001$ by day 30)	Effective in mixed-fed infants; early symptom relief; safe
Probiotics in the milk formula population					

26	Shulman, 2022 / RCT [36]	36 / 35 (PHF-LGG vs PHF)	PHF formula ± LGG (L. rhamnosus GG, ~10^9 CFU/day)	Crying/fussing decreased similarly in both groups; no significant group differences over 3 weeks	LGG colonized the gut and altered microbiome; safe and well tolerated; no clinical advantage
27	Jalaludin, 2022 / Cross sectional [37]	**BFI**: 760/ **FFI (with & without)** : 2,036	Formula with pre/probiotics (varied strains), compared to formula without	IGSQ scores better in FFI+probiotics (~22.1) vs FFI-noPP (~23.4); colic and crying rates lower in	Probiotic formula group had similar GI tolerance and crying frequency as breastfed group; observational data, not causal
28	Maldonado, 2019 / RCT [38]	50/50/50	*B. breve* CECT7263 (2×10^8 CFU/day) or combo *Lf+B.breve* vs simethicone	Bb: –40.3%, –59.2%, –64.5%, –68.5% by weeks 1–4; Bb + Lf: similar but later onset; control ~—27.6–59.5%	*B. breve* alone faster & more robust; improved sleep, parental mood; safe & well tolerated
29	Turco, 2020 / RCT [39]	124/117	*Lactobacillus reuteri* DSM 17938	Mean daily crying time at 28th day was significantly lower in Group B when compared to Group A [104.7 (87-122.4) versus 146.4 min (129.2-163.7), treatment effect -41.8 (95% C.I.: -66.5 to -17.1), p = 0.001]	Significantly greater reduction in daily crying time, defined as a ≥50% reduction in crying duration from baseline.
	Giglione, 2016 / RCT *same with no 23* [33]	29/31	*B. breve* BR03 + B632 (10^8 CFU/strain	Month 3 crying: 12.1 vs 46.7 min/day ($P = 0.016$); no early benefit	Reduced colic by month 3; delayed benefit in bottle-fed infants; safe
	Zoham, 2019 / RCT *same with no 25* [35]	33/32	Pedilact synbiotic (B. infantis, L. reuteri, L. rhamnosus)	Daily crying/fuss episodes, crying days, and crying duration significantly reduced ($P \leq 0.032$ by day 21; $P \leq 0.001$ by day 30)	Effective in mixed-fed infants; early symptom relief; safe

Various studies have shown the benefits of using probiotics to support digestive health and boost children immunity. Colic has been associated with gut dysbiosis, an imbalance in the gut bacteria that can lead to inflammation and digestive issues [18]. As for the efficacy of probiotics, *Lactobacillus acidophilus* (HA122), *Lactobacillus reuteri* NCIMB 30351 could promote a healthy gut which can help reduce inflammation and support better digestion [13]. Another Lactobacillus species like *Lactobacillus reuteri* DSM 17938 has been shown to have a calming effect on the gut, improving gut motility and reducing bloating [22]. Other probiotics like *Bifidobacterium breve* also help restore the balance of beneficial bacteria in the intestines [21,38].

The probiotic treatment positively affected the expression of RORγ and FOXP3, both of which are involved in maintaining immune tolerance and regulating inflammation [15]. *Lactobacillus reuteri* led to a reduction in inflammatory markers in the gut. *Lactobacillus rhamnosus* GG helps regulate the gut microbiota by promoting the growth of beneficial bacteria, which in turn helps reduce gut inflammation and improve digestion. Probiotics' effects on the microbiome likely contributed to improved digestion and a decrease in gut-related discomfort, which are common issues in infants with colic [7]. The preventive effect of *Lactobacillus reuteri* DSM 17938 was one of the most significant findings of study by Savino which infants who received the probiotic early had a lower incidence of colic symptoms compared to those who did not receive it [14].

Microbiota engage with the gut-brain axis, influencing gut sensory and motor functions by transmitting and receiving various signals to and from the brain. A modified microbiota colonization of the gastrointestinal tract may alter the bidirectional interrelation, potentially contributing to the pathogenesis of infantile colic. According to this, microbiota modulation through probiotic administration may be beneficial [30].

Infants receiving probiotics exhibited a greater increase in all immunity biomarkers (HBD-2, LL-37, and sIgA) compared to those in the placebo group, indicating that probiotics may have an immunomodulatory effect on the infant gut [40]. Probiotics influence the proliferation of human peripheral blood mononuclear cells and the expression of cytokines, providing protective effects against gastrointestinal infections in infants and children. Bifidobacteria inhibit Proteobacteria and promote butyrate production in infants experiencing colic. Bifidobacteria do not produce butyrate directly; however, by engaging in cross-feeding with other commensal bacteria [41], they can enhance butyrate levels, potentially influencing various aspects of gut physiology. Butyrate influences intestinal transit time, alters visceral and central pain perception, affects the gut-brain axis, and demonstrates significant anti-inflammatory properties [42,43].

However, some studies noted a high placebo response, such as Fatheree et al. (2017) [28], where 66% of the placebo group also improved, and Giglione et al. (2016) [33], which found no significant difference ($P = 0.14$) in outcomes between breastfed infants receiving probiotics versus controls. Nocerino et. al (2019) stated that qualitatively, probiotic use was generally safe and well tolerated, with improvements observed in stool consistency, gut inflammation markers (e.g., fecal calprotectin), and immune parameters (e.g., sIgA, defensins) [26]. Some studies also examined maternal dietary modifications, such as cow's milk elimination, as potential enhancers of probiotic efficacy [7]. While spontaneous resolution of colic over time was acknowledged in several trials, strains such as *L. reuteri* and *B. animalis* BB-12 remain consistently associated with clinically meaningful reductions in colic symptoms, especially among exclusively breastfed infants. Further studies are warranted to elucidate potential synergistic effects between probiotic supplementation and breast milk components [35].

The integration of probiotics into formula-fed regimens has been investigated across various studies to determine whether this combination yields clinical outcomes comparable to or better than probiotics alone or standard formula feeding. Evidence from randomized controlled trials and observational studies in this review provides key insights. Several studies have shown that probiotic-enriched formulas outperform standard formula in reducing colic-related symptoms. For instance, Maldonado et al. (2019) found that infants receiving Bifidobacterium breve CECT7263-enriched formula experienced a 40–68.5% reduction in crying time, significantly greater than those given simethicone (27–59.5%), alongside improvements in sleep quality and parental mood [38]. Similarly, the Happy Tummy Consortium (2022), in a large cross-sectional study involving 2,036 infants, reported better gastrointestinal tolerance and reduced colic-like symptoms in those fed probiotic-supplemented formulas [37].

However, when comparing formula-fed infants receiving probiotics to exclusively breastfed infants

supplemented with probiotics, the latter group appears to benefit more. Nation et al. (2017), which included both feeding types, found no significant reduction in colic symptoms with *Lactobacillus reuteri* supplementation and noted low probiotic colonization, particularly in formula-fed infants [24]. In contrast, studies by Savino et al. (2015, 2018) and Fatheree et al. (2017) involving exclusively breastfed infants demonstrated significant reductions in crying duration, with faster symptom relief and higher parental satisfaction. These findings suggest that the gut environment in breastfed infants may be more favorable for probiotic colonization and effectiveness, likely due to the presence of human milk oligosaccharides (HMOs) and immunomodulatory compounds in breastmilk that work synergistically with probiotics [14,15,28].

This literature review provides a comprehensive synthesis of current evidence regarding the use of probiotics for managing infantile colic, with a unique focus on feeding type as a potential modifier of treatment efficacy. A key strength of this review lies in its rigorous selection criteria, including only randomized controlled trials and cohort studies published within the last five years, ensuring relevance and methodological quality. The use of multiple major databases and independent screening by multiple reviewers also enhances the reliability of the findings. However, the review is limited by the heterogeneity of included studies in terms of probiotic strains, dosages, treatment durations, and outcome measures, which precludes quantitative meta-analysis. Additionally, the limited number of studies involving formula-fed infants restricts the ability to draw firm conclusions for this subgroup. Language restrictions and potential publication bias may also affect the generalizability of the findings.

5. Conclusion

This literature review concludes that probiotic supplementation, particularly with *Lactobacillus reuteri* DSM 17938, is associated with a reduction in the frequency and duration of crying episodes in infants diagnosed with colic. The therapeutic effect appears more consistent and pronounced in exclusively breastfed infants compared to their formula-fed counterparts. These findings suggest that the mode of infant feeding may influence the clinical efficacy of probiotics in managing colic, likely through its impact on gut microbiota composition and immune modulation. Future research should aim to standardize probiotic strains, dosages, and feeding regimens to optimize treatment outcomes across diverse infant populations.

Conflicts of Interest

The authors declare no conflict of interest.

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Author Contributions

Vira Cendana Sais and Nurlinah Amalia contributed to the conception and design of the study, as well as the technical supervision. Vira Cendana Sais, Erika Aini Putri, Aliffa Neta Yustisiani, Qoniatunnisa Nuzulul Falakhi, and Hafidhania Penadi extracted the data. Nurlinah Amalia performed an interpretation result and provided technical supervision. Erika Aini Putri, Aliffa Neta Yustisiani, Qoniatunnisa Nuzulul Falakhi, and Hafidhania Penadi drafted the manuscript. All authors critically revised the manuscript for important intellectual content, approved the final version, and agreed to be accountable for all aspects of the work.

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