

EFFECTIVENESS OF PREBIOTICS ADMINISTRATION IN CHILDREN UNDER FIVE WITH DIARRHEA

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ABSTRACT

Background: Diarrhea in children under five is caused by viral and bacterial infections in the digestive tract system characterized by liquid feces, frequent bowel movements or more than 3 times a day, and accompanied by both blood and mucus or just one of them.

Method: This study used a literature review method to collect data related to the effectiveness of prebiotics administration in children under five with diarrhea. Articles or journals were obtained from some databases, both national and international such as Google Scholar and Research Gate. Search for articles using keywords of "effectiveness", "children under five diarrhea" and "prebiotic administration".

Results: Based on the results of a review conducted on 10 articles, 7 articles revealed that the administration of prebiotic bacteria and yogurt containing prebiotics and plain yogurt (non-prebiotics) could reduce the frequency and duration of diarrhea as well as prevent diarrhea in children. However, some other articles stated that there was no significant difference between the group given prebiotics and the control group without given prebiotics.

1. Introduction (*Heading 1*) (bold, 11pt)

Children under five or children aged 0-59 months are passing the growth and development period. The process of growth and development for each child is different either fast or slow due to some factors such as heredity, nutrition, infection, immunological disorders, environment, and socio-economics. Toddlers are susceptible to infection with diseases and immune disorders as their specific and non-specific immune systems are not functioning properly. Children under five need an immune system, especially in the digestive tract so that they can reduce infectious diseases such as diarrhea. Diarrhea in children under five occurs due to viral and bacterial infections in the digestive tract system characterized by liquid feces and more frequent bowel movements more than 3 times a day and accompanied by both blood and mucus or just one of them [1].

World Health Organization (WHO) reported that the prevalence of under-five mortality due to diarrhea reached 42% in Nigeria and India with the morbidity rate of diarrhea reaching 39%. However, the Ministry of Health of the Republic of Indonesia reported that in 2018, 40.9% of diarrhea sufferers are children under five [1].

Prebiotics can complement the gut microbiota and improve the characteristics of the microbiota. Effects of prebiotics cover increased mucosal barrier function, increased visceral hypersensitivity, effects on gastrointestinal gas motility, and regulation of immune responses. Some different probiotic strains have been reported to improve various gastrointestinal ailments, especially diarrhea and other related symptoms. Prebiotics offer a promising therapeutic solution for a variety of health conditions like gastrointestinal ailments covering diarrhea, ulcerative colitis, and Crohn's disease [2].

Prebiotics are microorganisms that can give a positive impact on human health if consumed orally and are normal intestinal flora strains that can be isolated from healthy human feces [3]. In

Indonesia, the incidence of diarrhea in Indonesia reached 1,078 (1996) to 1,278 per 1,000 children (2000). It was estimated that in 2003, 8 out of 10 deaths in children under 2 years occurred in children with diarrhea with a morbidity rate of 374 per 1,000 population, and episodes in toddlers were 1.08 times per year. Patients with diarrhea in Semarang City are 29,943 per year and one-third are children under five [3].

The Indonesian diarrhea morbidity survey data showed that a total of 270/1,000 people were affected by diarrhea in 2014 and the incidence increased to 6,897,463 in 2016 and it continued to increase every year [4]. In puskesmas in Central Java, the diarrhea cases in children under five reached 191,107 cases or 45.4% of all diarrhea sufferers. Semarang City shows a similar figure for this case, namely 43.33% (Wuryanto, 2006). The age group most prone to diarrhea is 2-3 years old, although some report aged 6 months–12 months [5]. Studies on the administration of probiotics have been conducted to reduce cases of diarrhea such as the length of illness or shorten the length of hospitalization due to diarrhea.

2. Materials and Method

This study used a literature review method to collect data related to the effectiveness of probiotic administration in children with diarrhea. Data were obtained from databases, both national and international such as Google Scholar and Research Gate. Search for articles using keywords such as "effectiveness", "children under five diarrhea" and "probiotic administration".

Searches were carried out according to keywords and obtained 260 articles consisting of 160 articles from Google Scholar and 100 articles from Research Gate. The articles obtained were specified according to the inclusion criteria and exclusion criteria, namely IC1: published journals, IC2: published in 2018-2023, IC3: using quantitative research type, and IC4: non-duplicate journals published on Google Scholar and Research. After matching IC1-IC4, only 40 articles remained. Then IC5 was selected based on the compatibility of the article title and abstract with the aim of this literature review, namely "effectiveness", "children under five diarrhea", and "probiotic administration" and obtained 7 articles for further review. The process of article identification is presented in Figure 1.

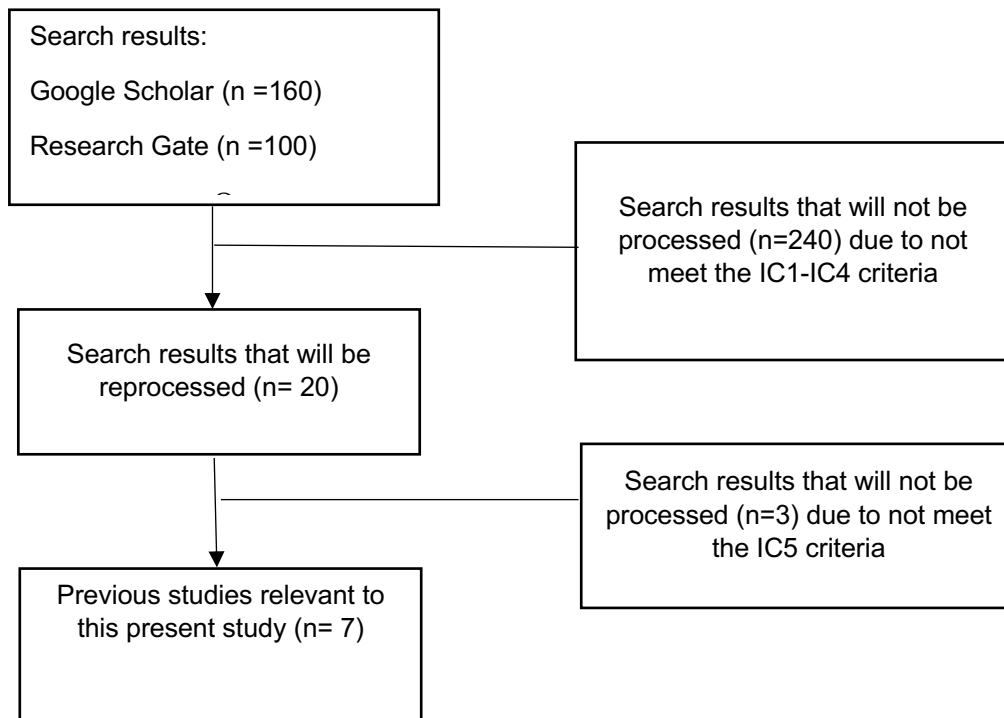


Figure 1. Article Identification Process

3. Results and Discussion

3.1. Results

This study involved 7 articles for further review consisting of 2 articles from national journals and 5 articles from international journals. The summary of the results of the review is presented in Table 1 below.

Tabel 1. Article Analysis Tale

No.	Author	Title	Method	Sample	Results
1.	Fujie Wanga, Ting Zhaoa, Weiwei Wang, Qianqian Daic, Xianghua Maa	Meta-analysis of the Effectiveness of Probiotics for Treating Diarrhea	Systematic literature review	A total of 16 experiments and involved 1,585 patients	The results of the meta-analysis showed that compared with the plain Western medicine or placebo treatment groups, the use of probiotics can improve feces frequency and morphology, and associated irritable bowel syndrome symptoms.
2.	Loukia Vassilopoulou, Panagiota Spyromitrou Xioufi, Fani Ladomenou	The effectiveness of prebiotics and synbiotics in reducing the duration of acute infectious diarrhea in pediatric patients in developed countries	Systematic literature review	The population of this study is 20 experiments with a total of 3,469 eligible patients	The results showed that probiotics do not show sufficient clinical impact in reducing the duration of diarrhea in children in developed countries. The comparison reveals moderate probiotic efficacy in low-risk unbiased studies (MD = \ddot{y} 13.45 h; 95% CI \ddot{y} 24.26, \ddot{y} 2.62; p = 0.02, Bayesian meta-analysis of combined effects MD = \ddot{y} 0.38, 95% CrI \ddot{y} 2.3, 1.58) and a significant effect in studies with high/unclear risk of bias (MD = \ddot{y} 19.70 h; 95% CI \ddot{y} 28.09, \ddot{y} 11.31; p = 0.0004). In the optimal methodological quality trial (n = 1989), the probiotic effect is absent (MD = -3.32 h; 95% CI - 8.78, 2.13, p = 0.23).
3.	Hao Fan, Lei Gao, Zidan Yin,	Probiotics and Rifaximin for	Systematic literature review	A total of 17 RCT in the analysis [12-28] with 6,012 participants	Both rifaximin and probiotics are better than placebo, and rifaximin has a better treatment effect than probiotics in reducing the diarrhea incidence. Various types of probiotics show

	Sheng Ye, Hua Zhao, Qi Peng	Diarrhea Prevention			heterogeneous treatment effects. A total of 17 RCTs after screening 1,119 records are included in the analysis with 9 RCTs with low risk of bias. Compared with placebo, probiotics and rifaximin are associated with a lower incidence of tetanus and diphtheria (probiotics, RR 0.85, 95% CI 0.76–0.95; rifaximin, RR 0.47, 95% CI 0.35–0.63), and rifaximin is more effective than probiotics (RR 0.56, 95% CI 0.4–0.78).
4.	Rifda Nur Achriyana Arif, Ai Mardhiyah, Henny Suzana Mediani	The Effectiveness of Yogurt Probiotics on Diarrhea	Systematic literature review	The sample of the study is pediatric patients aged < 12 years with acute diarrhea with the intervention of administration of probiotic bacterial strains and administration of yogurt	Based on the results of a review conducted on 10 articles, 8 articles stated the administration of probiotic bacteria and yogurt containing probiotics and plain yogurt (non-probiotics) can reduce the frequency and duration of diarrhea as well as prevent diarrhea in children. However, some articles stated that there is no significant difference between the group given probiotics and the control group. This review resulted in differences in research results on probiotics, probiotic yogurt, and non-probiotic yogurt. It is important to break down this issue into some sub-themes to see the differences in the effectiveness of probiotic bacteria and yogurt.
5.	Rao Huang, Hong-Yi Xing, Hong-Juan Liu, Bi-Bo Tang	Effectiveness of probiotics in the treatment of acute diarrhea in children	Systematic literature review	12 articles with 744 patients	The meta-analysis showed that the duration of diarrhea in the probiotic group is shorter than in the control group [standard mean difference (SMD) = \bar{y} 0.74, 95% CI: \bar{y} 1.11 to \bar{y} 0.37, Z= \bar{y} 3.935, P=0.000]. The efficacy of a 2-day treatment for diarrhea in the probiotic group is higher than in the control group [odds ratio

(OR) = 2.12, 95% CI: 1.47–3.05, Z = 3.998, P = 0.000]. Besides, the length of hospitalization in the probiotic group is shorter than that in the control group (SMD = \dot{y} 0.60, 95% CI: \dot{y} 0.74 to \dot{y} 0.47, Z = \dot{y} 8.781, P = 0.000). In the subgroup analysis, the combined probiotics shorten the duration of diarrhea compared to the use of a single probiotic. *Lactobacillus reuteri* and *Saccharomyces boulardii* have a better therapeutic effect than *Lactobacillus rhamnosus* or *Lactobacillus acidophilus*.

6.	Zeng Bin Li, Guixia Zhu, Chao Li, Xin Liu, Lei Zhang	What is the most effective probiotics in treating acute diarrhea in children	Cross-sectional	A total of 62 outpatients who are willing to be respondents	The results of the compliance analysis showed that 32 (51.6%) patients have a high compliance score. Besides, 34 patients (54.8%) have high confidence and 45 patients (72.6%) have high social support. Meanwhile, 33 patients (53.2%) do not experience side effects). The highest reason for patients forgetting to take their medication is feeling that their condition is fine with 14 people (46.6%). There is a significant correlation between compliance and drug side effects (p=0.002, r= -0.326).
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7.	Ngurah Nara Kusuma, Ni Ketut Sri Wahyuni	The effectiveness of prebiotics administration on the duration of diarrhea in children	Cross-sectional	A total of 40 respondents selected using a purposive sampling technique based on the predetermined inclusion and exclusion criteria.	Independent t-test results obtained a p-value of 0.001 <0.05 which means giving prebiotics is more effective than giving standard therapy for the duration of diarrhea in pre-treated children.
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Figure 2. Extraction table

3.2 Discussion

The clinical efficacy of probiotics has been widely studied in gastrointestinal diseases of various etiologies. Trials and meta-analyses support probiotics for the treatment of acute infectious diarrhea, either provided individually or in combination with other medicinal agents, immunoglobulins, and micronutrients [6]. However, the available studies show a lack of useful results or even raise safety concerns considering the side effects, lack of factual information, and existing marketing conditions. Differences in health claim legal regimes in all developed countries hinder the establishment of a commonly accepted definition framework and perpetuate the provision of probiotics as dietary supplements without formal approval by authorities as medicinal agents [7].

A total of 20 studies reveal information about the features of included RCTs which include 3469 participants consisting of 1,760 participants in the experimental group and 1,709 participants in the control group with a sample range from 29 to 943 patients aged 1 month to 15 years [8]. In an examination of feces samples, the most frequently identified pathogen is rotavirus. Probiotics are supplied mainly in the form of powdered sachets or capsules dissolved in a liquid solution with a dose spectrum of 107 - 10¹¹ cfu and mostly with the *Lactobacillus rhamnosus* strain [9].

A total of 1119 records were obtained from a literature search in which 905 records were screened through a review of article titles and abstracts and 93 records were obtained from a full-text review. A total of 17 RCTs were included in the analysis involving 6,012 participants [10]. The meta-analysis of differential networks of probiotics and rifaximin showed that sodium butyrate (SOB), rifaximin, *L. acidophilus* + *L. bulgaricus* + *Bifido.bifidum* + *Strept. Thermophilus* (LABST), galactooligosaccharide (GAO), *S. boulardii* CNCM I-745 (SBC) are associated with a significantly lower incidence of tetanus and diphtheria when compared with placebo. Those treatments are better than placebo and rifaximin is more effective than SBC (RR 0.56, 95% CI 0.42-0.76). The comparisons between these treatments are presented in Table 3. There is no inconsistency between the direct and indirect estimates. Heterogeneity test showed insignificant heterogeneity ($I^2 = 4.3\%$, $\tau^2 = 0.0013$, Cochran's $Q = 8.36$, $P = 0.399$) [11].

Many studies have described the mechanism of the onset of IBS (irritable bowel syndrome) as a shift from a "normal and healthy" gut to a "dysbiotic and unhealthy" gut, in which the gut microbial community plays an important role [12]. Thus, homeostasis represents a fundamental therapeutic paradigm in which probiotics can offer promising healthcare solutions for IBS. Probiotics are live bio-therapeutics that offer a promising route to treat gastrointestinal diseases such as diarrhea, digestive disorders, nutrient malabsorption, inflammatory bowel disease, ulcerative colitis, and Crohn's disease, without the risk of spreading antibiotic resistance to microorganisms [13]. The use of probiotics in the treatment of IBS (irritable bowel syndrome) has been reported to be highly effective in some trials. These studies have suggested the beneficial effects of probiotics to enhance the immune response, intestinal permeability, and altering colonic fermentation [14].

Some types of probiotics have heterogeneous treatment effects. SOB, rifaximin, LABST, GAO, and SBC are associated with a lower incidence of tetanus and diphtheria than *L. rhamnosus* GG (LRG), *Enterococcus faecium* SF68 + *S. cerevisiae* CNCM I-4444 + fructo-oligosaccharide (ESCF), *L. helveticus* ATCC33409 + *L. gasseri* ATCC4962 (LHG), and other different probiotics significantly decreased, which supports the differential effect of different probiotics. Generally, both probiotics and rifaximin are safe for the prevention of tetanus and diphtheria due to no severe side effects of either treatment have been reported. Besides, both have similar or lower rates of side effects than placebo [15]. Probiotics are considered safe in immunocompetent patients, and unwanted side effects of probiotics are rare, or maybe underreported [5].

4. Conclusion

Based on the results of the review of 10 articles, 7 articles reveal that the administration of probiotic bacteria and yogurt containing probiotics and plain yogurt (non-probiotics) can reduce the frequency and duration of diarrhea as well as prevent diarrhea in children. On the other hand, some other articles show that there was no significant difference between the experimental group given probiotics and the control group. This review shows differences in the results of studies on probiotics, probiotic yogurt, and non-probiotic yogurt. Therefore, it is important to break down this issue into some sub-themes to see the differences in the effectiveness of probiotic bacteria and yogurt.

Additional use of probiotics can improve clinical outcomes in patients with diarrhea. Meanwhile, the implementation of larger and high-quality clinical trials is needed to verify this study. Probiotics have not shown sufficient clinical impact in the reduction of the duration of diarrhea in

children in developed countries. Both rifaximin and probiotics are better than placebo, and rifaximin has a better treatment effect than probiotics in reducing the incidence of tetanus and diphtheria.

Some types of probiotics have heterogeneous treatment effects. Western medicine is simple or placebo in which supplemental use of probiotics can improve feces frequency and morphology, as well as irritable bowel syndrome symptoms

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