

Probiotics in gastroenteritis in children: A systematic review

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Abstract

Background and objectives: Gastroenteritis is the second leading cause of death among children worldwide. It is a preventable and treatable disease, yet it affects 3 to 5 million children and is the cause of approximately 10% of hospitalizations globally. This systematic review aims to identify the effectiveness of probiotics in treating acute gastroenteritis in children globally and also to provide results of quality research to healthcare-related communities about possible therapies of the condition.

Methods: This study follows the PRISMA guidelines for systematic reviews of 29 quantitative studies conducted between 2014-2023. A quality appraisal of the selected studies was conducted using CADIMA and a rating scale of 0 to 3 based on a few predetermined criteria.

Results: Sample sizes varied from 29 to 1811, with a median of 200. Globally, there are mixed findings about the roles and benefits of probiotics to treat acute gastroenteritis in children. This is possibly due to the type of probiotic, the type of disease, and treatment adherence.

Conclusions: Findings from this systematic review suggest that probiotics play a crucial role in improving children's health outcomes. Therefore, it is important to promote and implement the use of probiotic therapies in the treatment of acute gastroenteritis conditions in children.

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Introduction

Acute gastroenteritis is a serious illness prevalent among infants and children globally. Despite being a preventable and treatable disease, acute gastroenteritis remains a major cause of pediatric morbidity and mortality, especially in developing countries. Every year, around 3 to 5 billion children worldwide suffer from acute gastroenteritis resulting in approximately 12% of death in children aged 5 years or younger [1]. In addition, an estimated 10% of hospitalizations in children under 5 years were attributed to acute gastroenteritis globally [2]. Gastroenteritis causes a tremendous economic burden, and the cost of care could weigh heavily on affected families. According to Papadopoulos et al. [3], the five-year economic burden of acute gastroenteritis in Belgium was estimated to be €112 million in direct cost and €927 million (90% of the total costs) in indirect

cost, totaling an average cost of €103 per case and €94 per person. Gastroenteritis in children is mostly caused by rotavirus and norovirus [4]. Both pathogens account for about 58% of all acute gastroenteritis cases in the United States [5]. Due to the high rates of acute gastroenteritis and severe outcomes associated with the illness, it is imperative to identify effective treatment therapies to improve health outcomes in children with acute gastroenteritis.

Globally, the use of probiotics in treating acute gastroenteritis has been extensively studied by researchers. This has caused controversy and prompted questions about whether or not to use probiotics for treating gastroenteritis. Two clinical trials by Erdoğan et al. [6] and LaMont [7], conducted in Turkey and Europe, respectively, showed better health outcomes from probiotic use in gastroenteritis. Erdoğan et al. [6] reported that

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Saccharomyces boulardii and *Bifidobacterium lactis* probiotics had an efficacious effect in treating gastroenteritis in children. Furthermore, Lamont [7] tested the effectiveness of probiotics in the treatment of acute gastroenteritis in children and revealed beneficial effects in the hosts or patients. Results from these clinical trials [6,7] suggest the use of probiotics as an important aspect of gastroenteritis research in treating severe outcomes associated with the condition. These outcomes include death, severe dehydration, etc. In contrast, Hojsak [8], a Croatian researcher, argued that “*not all probiotic strains have the same efficacy for all clinical indications, therefore, only strains with proven efficacy and safety should be recommended*”. This contradictory finding indicates a need for further investigation into the issue of probiotic use in treating gastroenteritis in children.

Gastroenteritis among children is the second-leading cause of death worldwide [5]. Due to the poor outcomes associated with gastroenteritis in children, it is crucial to review the effectiveness of probiotics in treating acute gastroenteritis in children. It is also vital to identify new or effective therapies to improve the health outcomes of children afflicted with gastroenteritis. Furthermore, improving children's health, safety, and well-being, a goal that aligns with Healthy People 2030 in the United States, can be achieved by providing adequate medications for children afflicted by diseases such as acute gastroenteritis [9,10]. We

hypothesize that probiotics are able to treat acute gastroenteritis in children.

The aim of the systematic review was to assess the effectiveness of probiotics in treating acute gastroenteritis conditions in children and to provide quality research data to healthcare-related communities about use of probiotics as a possible treatment option in childhood gastroenteritis.

Materials and methods

The systematic review included studies following the PRISMA guidelines [11]. The study focused on published primary articles associated with the impact of probiotics on acute gastroenteritis outcomes in children. Table-1 shows the inclusions and exclusions of the review.

Search Guidelines

The primary search engines used to identify articles included in EBSCOhost, MEDLINE, APA PsychoInfo, APA Psych, Socindex, Google Scholar, and CINAHL. The studies were chosen for the review based on inclusion criteria, such as (1) articles being written in English; (2) being quantitative studies; (3) being scholarly papers; (4) using human participants between the ages of 0-17 years; (5) being associated with acute gastroenteritis; and (6) being associated with probiotics. The search was performed on 25 January 2023. The time limit for the studies was from 2008–2023. Table-2 shows the search string.

Table-1: Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Quantitative studies	Studies that were not in English
Human studies	Studies that only involved ages 18 and older
Scholarly papers	Review articles
Age group: 0-17 years	Not human studies
Acute gastroenteritis illness	
Research associated with Probiotics	

Table-2: Research thread for all databases

Search strategies	No. of studies available
Search terms used: ‘clinical trials’ OR ‘gastroenteritis’ OR ‘probiotics’ OR ‘children	22,403
Total number of studies excluded based on eligibility criteria	22,299
Total number of studies excluded due to being duplicates	3
Total number of studies excluded because they were review articles	72
Total number of studies accepted and reviewed	29

Screening guidelines

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (2009) were used as a guide to record the review process [11]. Selected abstracts were reviewed to ensure eligibility. Full-text articles of eligible abstracts were retrieved and assessed on whether they answered the research questions and fulfilled the inclusion criteria. Studies were included if a consensus was reached by the researchers.

Research Information System (RIS) formatted references were exported from the databases, where studies were automatically screened based

on the inclusion criteria and then imported into CADIMA. Total studies imported into CADIMA were accessed based on title and abstracts. The researchers assessed the studies twice before discussing if the studies should be chosen for full-text review. Conflicts were managed by group discussions between the researchers of the study. After the initial discussion, the researchers agreed that 104 studies should be selected for further screening using the inclusion criteria. During this second phase of screening for excluding review articles, the researchers independently screened the 104 articles twice for the second time. Conflicts were managed by group discussions. After

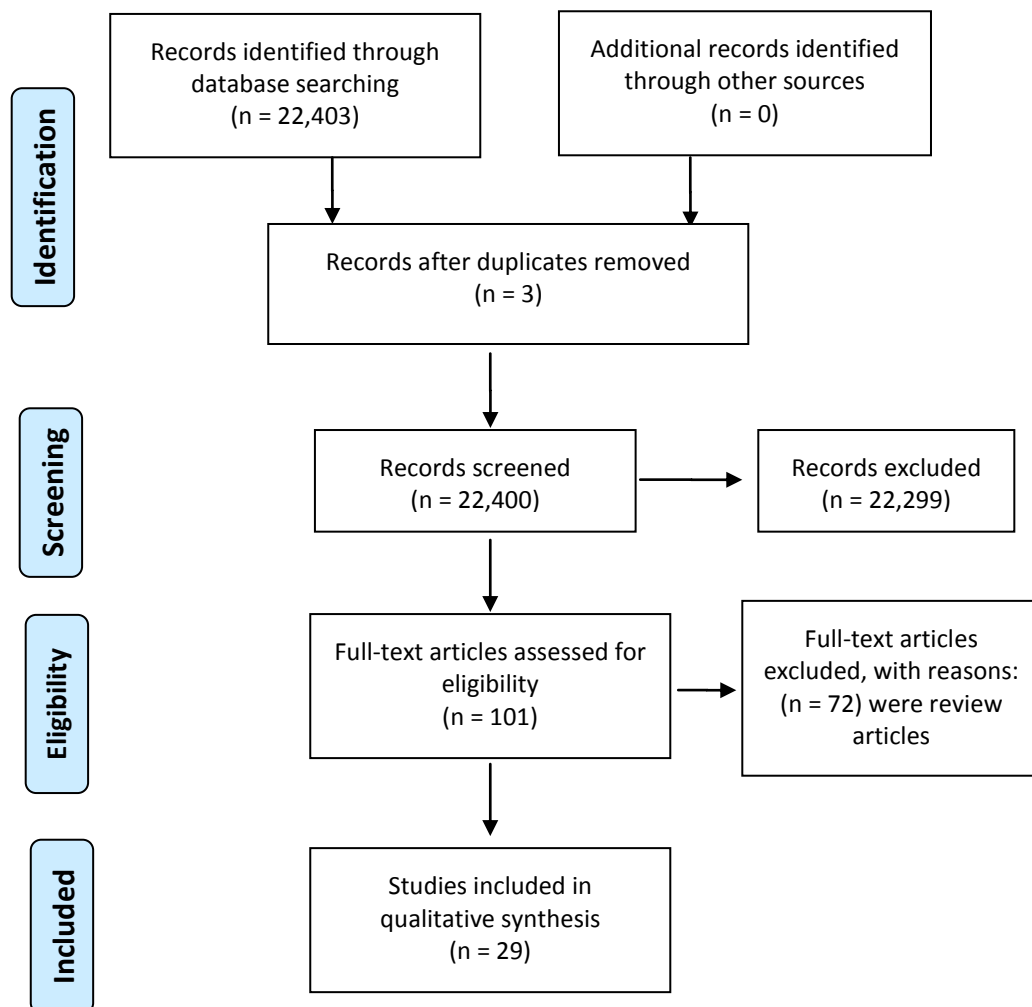


Figure-1: PRISMA flow chart showing inclusion and exclusion of studies [11]

discussion, 72 more articles were excluded because they were review articles, and 3 more articles were excluded because the articles were duplicated between the primary search engines and finally 29 articles were selected to be included in the systematic review. The PRISMA flow chart (Figure-1) depicts the search and inclusion process for the systematic review.

Quality Appraisal

Studies were appraised for quality using CADIMA. Through CADIMA, standards for critical appraisal and the rating scale were defined. We followed the critical appraisal tools for systematic reviews developed by the University of Adelaide, South Australia [12]. A rating scale from 0 to 3 was based on the following criteria: (1) Study design—cross-sectional, case-control, or cohort study = 1, otherwise = 0; (2) Sample size—large = 1, small = 0; (3) Selection of participants—random selection or lack of bias = 1, non-random sample or convenience sample or presence of bias = 0 points. Based on the above-mentioned criteria, the researchers rated each of the 29 studies independently from a range of 0 to 3. Due to having no major inter-observer variations in the evaluation of the quality of the studies, an average of the three scores was presented in Table-3 under the quality appraisal section.

Results

A summary of the methodology, characteristics of findings, the impact of probiotics on acute gastroenteritis outcomes in children, quality appraisal, and the countries of the studies are presented in Table-3. Of the 29 studies reviewed, 5 were conducted in the United States, and Iran, 3 were conducted in Europe, 2 were conducted in Canada, India and Poland, and 1 each in Belgium, Romania, Turkey, Bangladesh, China, Uganda, Botswana, Mexico, Korea, and Canada/United States. All 29 studies were clinical trials [13-41]. All of the selected studies were conducted among children, ranging from infancy to adolescents/teenagers.

The total sample size used in studies ranged from 29 to 1811, having a median sample size of 200 (Quartile-1 = 92 and Quartile-3 = 816); 3 out of 29 (10.3%) had sample sizes of more than 1000. In terms of standardized tools, all studies (100%) used standardized assessment tools. An average score of 3 out of 3, meant excellent in 3 studies (10.3%), 2 meant moderate/good in 25 studies (86.2%), and 0-1 meant poor in one study (3.4%).

Benefits of probiotics in the treatment of acute gastroenteritis in children

Of the 29 studies, 19 (65.5%) showed the benefits of probiotics in gastroenteritis treatment. Five studies supported the notion that probiotics improved acute gastroenteritis conditions in children [13-15, 26, 30]. Nocerino et al. found that probiotics lowered acute gastroenteritis in children [13]. Hesaraki et al. concluded that probiotics improved acute gastroenteritis conditions by improving recovery, reducing disease severity, and improving vital signs [14]. Lopetuso et al. have found probiotics to be effective in treating acute gastroenteritis [15]. Schnadower et al. showed the benefits of adherence to probiotic treatments when treating acute gastroenteritis in children, which resulted in better outcomes [26]. Mosaddek et al. also found improved outcomes for children with acute gastroenteritis after being prescribed probiotics [30].

Two studies by Schnadower et al. and Mosaddek et al. revealed that the use of probiotics in the treatment of gastroenteritis in children resulted in better outcomes in ambulatory settings and quicker recovery times [27, 30]. Eight studies also determined that probiotics reduced acute gastroenteritis in children [18, 25, 28-29, 32, 35, 37, 40]. Three studies have shown that the use of probiotics reduced hospitalization rates for children with acute gastroenteritis [29, 32, 33, 38]. One study reported that probiotics significantly reduced the duration of rotaviral diarrhoea [20]. Two studies also concluded that probiotics improved outcomes for children diagnosed with special conditions associated with acute gastroenteritis, such as nosocomial infections [39] and hyperbilirubinemia [36].

Lack of benefits of probiotics in the treatment of acute gastroenteritis in children

Of the 29 studies, 8 (27.6%) failed to validate the benefits of probiotics in gastroenteritis in children. Those studies found no benefit or improvement in treating acute gastroenteritis in children with probiotics [17,19,21-24,31,41,]. One study by Ahmadipour et al. [31] even emphasized that zinc supplementation was more effective than probiotics in treating acute diarrhea. Another study by Freedman et al. [22] revealed that probiotics had no effect on immunoglobulin A modulation, which is the antibody that helps the body to fight infections. A study by Olek et al. [41] determined

that probiotics had no impact on improving acute gastroenteritis symptoms, including diarrhea frequency or abdominal symptoms.

Mixed results in treatment of acute gastroenteritis in children

Of the 29 studies, 2 (6.9%) reported mixed results. One study by Szymanski and Szajewska [16] found that probiotics reduced hospitalizations from acute gastroenteritis but not the diarrheal symptoms. Another study by Bhat et al. [38] observed that probiotics reduced diarrheal output in patients receiving outpatient treatment for gastroenteritis but not in hospitalized patients.

Table-3: Impact of Probiotics on Acute Gastroenteritis Outcomes in Children

Author [Ref]	Major Findings	Treatment Impact of Probiotics on Acute GE in Children	Quality Appraisal (Out of 3)	Country of Study
Nocerino et al. [13]	n = 377; The proportion of children with acute gastroenteritis was lower in group A (13%) for children given daily cow's milk and for group B (19.5%), who were given a probiotic (<i>Lactobacillus paracasei</i>)	Positive	2-good	Europe
Hesaraki et al. [14]	n = 84; Probiotic (kidilact) improved recovery, reduced disease severity, and improved vital signs in children with acute gastroenteritis	Positive	2-good	Iran
Lopetuso et al. [15]	n = 1811; Gelatin tannate and tyndallized probiotics were highly effective in the treatment of acute gastroenteritis	Positive	3-excellent	Europe
Szymanski and Szajewska [16]	n = 91; Probiotic (<i>L. reuteri</i>) did not reduce the duration of diarrhea, but it did reduce hospitalizations associated with acute gastroenteritis	Positive/ No	2-good	Poland
Freedman et al. [17]	n = 1565; In Canada and the U.S., probiotics did not benefit children with acute gastroenteritis	No	3-excellent	Canada & United States
Refeey et al. [18]	n = 160; Probiotic (<i>L. acidophilus</i>) reduced the severity of acute diarrhea associated with acute gastroenteritis in children	Positive	2-good	Iran

Freedman et al. [19]	n = 886; Probiotics (<i>Lactobacilli</i>) did not prevent the development of moderate to severe acute gastroenteritis within the 14 days of the study's enrollment	No	2-good	Canada
Lee et al. [20]	n = 29; Probiotic (<i>L. acidophilus</i>) was an effective treatment for acute rotaviral gastroenteritis	Positive	2-good	Korea
Freedman et al. [21]	n = 816; No evidence supported the benefits of routine probiotic administration to children with acute gastroenteritis regardless of infecting virus	No	2-good	United States
Freedman et al. [22]	n = 133; Probiotic had no effect on immunoglobulin A modulation in children with acute gastroenteritis	No	2-good	Canada
Schnadower et al. [23]	n = 813; Probiotic <i>L. rhamnosis</i> GG (LGG) did not improve outcomes in children with acute gastroenteritis	No	2-good	United States
Schnadower et al. [24]	n = 971; a 5-day course of <i>L. rhamnosis</i> GG did not lead to better outcomes among preschool children with acute gastroenteritis	No	2-good	United States
Kluijfhout et al. [25]	n = 46; Use of probiotics normalized stool consistency significantly or improved diarrhea-related acute gastroenteritis symptoms	Positive	2-good	Belgium
Schnadower et al. [26]	n = 971; Adherence to probiotic treatment for acute gastroenteritis resulted in better outcomes	Positive	2-good	United States
Schnadower et al. [27]	n = 970; there were benefits associated with probiotic (LGG) administration in ambulatory children presented to the emergency department with acute gastroenteritis	Positive	2-good	United States
Condratovici et al. [28]	n = 36; The use of xyloglucan (probiotic) resulted in faster onset of action and improvement of diarrheal symptoms associated with acute gastroenteritis	Positive	2-good	Romania
Dinleyici et al. [29]	n = 1200; Probiotics led to reduced rates of hospitalization and reduced diarrhea for children with acute gastroenteritis	Positive	3-excellent	Turkey
Mosaddek et al. [30]	n = 166; The use of probiotics resulted in quicker recovery from acute gastroenteritis (due to rotavirus, <i>E. coli</i> , multiorganisms, <i>Campylobacter</i> , <i>Vibrio cholerae</i> , <i>Salmonella</i> , <i>Shigella</i> , and <i>Klebsiella</i>)	Positive	1-poor	Bangladesh

Ahmadipour et al. [31]	n = 146; Zinc was more effective than probiotics in treating viral diarrhea associated with acute gastroenteritis in children	No	2-good	Iran
Sudha et al. [32]	n = 200; Probiotic (<i>B. clausii</i>) reduced diarrhea associated with acute gastroenteritis in children	Positive	2-good	India
Chen et al. [33]	n = 194; 3 probiotic strains (<i>Bifidobacterium lactis</i> Bi07, <i>Lactobacillus rhamnosus</i> HN001, and <i>Lactobacillus acidophilus</i> NCFM) resulted in shorter durations of diarrhea, hospitalizations, and improved health outcomes among children with acute gastroenteritis	Positive	2-good	China
Grenov et al. [34]	n = 400; Probiotics had no effect on diarrhea in children with acute gastroenteritis conditions that were associated with severe acute malnourishment during hospitalization, but probiotics did reduce the number of days with diarrhea in children receiving outpatient treatment	Positive/No	2-good	Uganda
Gutierrez-Castrellon et al. [35]	n = 336; Probiotic reduced the frequency and duration of episodic diarrhea in children with acute gastroenteritis conditions	Positive	2-good	Mexico
Torkamen et al. [36]	n = 92; Probiotics were beneficial in the treatment of infants with hyperbilirubinemia associated with acute gastroenteritis	Positive	2-good	Iran
Sharif et al. [37]	n=200; Probiotics resulted in significantly lower days of diarrhea among children with acute gastroenteritis outcomes	Positive	2-good	Iran
Bhat et al. [38]	n = 120; The probiotic was effective in the reduction of diarrhea and hospitalizations in children with acute gastroenteritis	Positive	2-good	India
Bruzzese et al. [39]	n = 90; Probiotic (<i>Lactobacillus</i> GG) reduced the incidence of nosocomial infections associated with acute gastroenteritis in children	Positive	2-good	Europe
Pernica et al. [40]	n = 76; Probiotic resulted in lower odds of diarrhea from acute gastroenteritis conditions	Positive	2-good	Botswana
Olek et al. [41]	n = 438; Probiotic (<i>Lactobacillus plantarum</i>) did not reduce the incidence of diarrhea, the frequency of diarrhea, or the incidence of abdominal symptoms associated with acute gastroenteritis in children	No	2-good	Poland

Note: GE = Gastroenteritis

Discussion

Gastrointestinal benefits of probiotics

In this systematic review, there was strong evidence to support probiotics' potential to improve acute gastroenteritis in children. Probiotics have been shown to improve acute gastroenteritis outcomes in children by reducing the severity of the conditions and improving recovery times [14,18,30]. Probiotics have also been shown to significantly reduce diarrheal symptoms associated with acute gastroenteritis [25,28,29,32]. Probiotics as an effective therapy for acute gastroenteritis illnesses in children lead to improved outcomes. This includes reductions in severe dehydration and death. This finding has been supported by two other studies, Hania et al. [42] and Guarino et al. [43]. These authors found significant relationships between probiotic use and improved outcomes for acute gastrointestinal symptoms in children.

Hospitalizations and the use of probiotic therapies

The duration and frequency of hospitalizations for children using probiotics as a treatment for gastroenteritis were further evaluated in this review. Findings have revealed that the use of probiotics as a treatment therapy for children with acute gastroenteritis conditions has also resulted in reduced hospitalization rates [16,29, 33]. The reduction of hospitalizations in children with acute gastroenteritis illnesses not only benefits the health of the affected children but also supports their emotional well-being. Children who are hospitalized have higher rates of psychological distress, resulting in trauma or stress [44]. This is a further example of how probiotic therapies can be beneficial. According to Dinleyici et al. and Guandalini et al., probiotic treatment for acute gastroenteritis conditions in children reduced hospitalizations, duration, and frequency [45,46].

No substantial benefits associated with the use of probiotics

While the majority of the studies in the review revealed the benefits of using probiotics for treating childhood gastroenteritis, there are still some studies that found no benefits of probiotics.

In this review, 8 studies found no benefits to probiotics for gastroenteric illnesses in children. Three studies found that probiotics did not reduce gastroenteritis severity, or yield better outcomes [17,19,24]. Two studies found no clinical benefit, relief in clinical symptoms, or viral clearance when using probiotics to treat gastroenteritis conditions [21,23]. Two studies also found no reduction in the incidence of watery stool, the mean number of loose stools, or abdominal symptoms [22,41]. Finally, one study compared the use of probiotics to zinc supplementation for the treatment of gastroenteritis conditions. The study found that zinc supplementation improved outcomes in terms of reducing hospitalization or duration and causing fewer complications [31]. These findings could have differed from the majority of studies due to the type of probiotics used, the type of gastroenteritis condition being treated, the treatment course, and adherence to treatment by patients.

Conclusions

Globally, probiotics have played a significant role in improving acute gastroenteritis in children. Probiotics have improved recovery, reduced severity, reduced diarrheal-related symptoms, and reduced hospitalizations in children with acute gastroenteritis conditions. Revealing that children could benefit from probiotic therapies, it is very important to support the use of probiotic therapies in the treatment of acute gastroenteritis in children. Further research is needed to study the roles of innovative probiotic therapies in treating acute and chronic gastroenteritis of multiple etiologies in children.

Author's contribution

AKM conceptualized the study. EAKJ extracted the data. AKM validated the study. EAKJ, AB, PPE, FI, and EO prepared the original draft. EAKJ and AKM reviewed and edited the manuscript. All authors have read and agreed to the published version of the manuscript.

Competing interest

No competing interest/conflict of interest.

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