

Review

Efficacy of Zinc Supplements in Managing Acute Diarrhea in Children: Article Review

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Abstract

This review assesses the effectiveness of zinc supplementation in managing acute diarrhea among young children, focusing on randomized controlled trials conducted between 2010 and 2020. A systematic search of major databases identified 10 relevant publications for the study. The studies demonstrated a clear pattern supporting the beneficial effect of zinc supplementation on reducing the duration, frequency, and severity of sudden diarrhea episodes in children. Notable discoveries include the efficacy of therapeutic zinc supplementation in older children, the potential benefits of lower zinc doses in mitigating adverse effects, and the importance of combining oral rehydration salts with zinc to enhance absorption. While some studies yield inconsistent outcomes, the overall data support the cost-effective and influential role of zinc supplementation in resolving acute diarrhea in pediatric populations. The complex insights gathered contribute to refining healthcare treatments and informing public health measures to advance child well-being, particularly in regions facing substantial diarrheal disease burden. This review thoroughly examines the research on zinc supplementation for the treatment of acute diarrhea in children, assessing its antiviral, antibacterial, immune-enhancing, barrier-strengthening, and anti-inflammatory properties. Its main aim is to inform healthcare providers about the potential benefits of integrating zinc supplementation to improve the management and reduce acute diarrhea episodes in children.

Keywords: Zinc Supplementation, Acute Diarrhea, Pediatric Health, Randomized Controlled Trials, Child well-being

Introduction

Acute diarrhea in children is characterized by the rapid appearance of loose or watery stools, frequently accompanied by an increase in how often one passes the stool, abdominal pain, and occasionally vomiting [1]. The condition is frequently self-limiting and short-lived, typically lasting fewer than 14 days [2]. Acute diarrhea can result from a range of infectious agents, including bacteria, viruses, and parasites, as well as non-infectious causes such as dietary modifications, medications, and food intolerances [3].

Acute diarrhea, as defined by the World Health Organization (WHO), refers to the occurrence of 3 or more loose or watery bowel movements within 24 hours [1]. This terminology is widely accepted and used in clinical practice and research to describe severe diarrhea in children. Acute diarrhea continues to be a significant global health problem that impacts kids, particularly in poorer nations. It is a pri-

mary factor in both morbidity and death, contributing to approximately 1.3 million deaths annually among children under the age of five [4]. In recent years, the possible function of zinc supplementation in controlling severe diarrhea has attracted substantial interest. Zinc is an essential micronutrient that plays a key role in several physiological processes, including immunological function, growth, and development. It has been proven to have significant consequences for the treatment of acute diarrhea in children [5]. The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) have acknowledged the relevance of zinc supplementation as a cost-effective and safe intervention for controlling acute diarrhea [1].

Zinc supplementation in children with acute diarrhea exerts multiple beneficial mechanisms. Zinc exhibits antiviral and antibacterial effects, inhibiting viral and bacterial replication and reducing the severity and duration of diarrhea [6]. Zinc also en-

hances immune function by supporting the production and activation of immune cells [6]. In addition, zinc maintains intestinal barrier integrity by strengthening tight junctions between enterocytes, which limits fluid and electrolyte loss in the gut lumen. It also reduces intestinal inflammation linked to acute diarrhea. By supporting electrolyte balance, zinc lowers the risk of dehydration, a significant complication of diarrhea [7]. Together, these mechanisms explain the role of zinc supplementation in reducing the duration and severity of acute diarrhea episodes in children.

Several studies have demonstrated that zinc supplementation, when combined with oral rehydration therapy (ORT), can significantly reduce the duration and severity of diarrhea episodes [6-8]. Furthermore, zinc supplementation has been associated with a decreased risk of treatment failure, subsequent episodes of diarrhea, and mortality [9-10]. In addition to its direct effects on diarrhea management, zinc has been shown to enhance intestinal barrier integrity and function, thereby promoting gut health and reducing the risk of future infections [11]. This review also explores the impact of zinc supplementation on nutritional status, growth, and cognitive development in children with acute diarrhea. The purpose of this review is to critically evaluate research on zinc supplementation in treating acute diarrhea in children. It examines its antiviral, antibacterial, immune-enhancing, barrier-strengthening, and anti-inflammatory properties and their impact on reducing episodes of diarrhea.

Materials and Methods

This literature review focuses explicitly on the effectiveness of zinc supplementation for the treatment of acute diarrhea in children, supported by randomized controlled trials [RCTs] conducted between 2010 and 2020. To identify relevant studies, an extensive search was conducted across major databases, including PubMed, ScienceDirect, Web of Science, and Google Scholar. The search terms used included "zinc," "zinc supplement," "acute diarrhea," "pediatric acute diarrhea," "treatment of acute diarrhea," and "effect of zinc supplement in children."

Initially, 1,566 articles were identified through systematic database searches. However, to ensure the inclusion of high-quality evidence, strict inclusion criteria were applied, focusing exclusively on randomized clinical trials. As a result, 1,328 articles were excluded as they did not meet these criteria. After using the inclusion criteria, 238 articles remained for further evaluation. Subsequently, a

thorough assessment was conducted on the remaining articles. Among them, 132 articles were excluded due to limited access or lack of relevance to the review's specific focus. This left a subset of 106 articles that specifically addressed the treatment of acute diarrhea in children for closer examination. Within this subset, an additional 96 articles were excluded from the review. These articles either failed to demonstrate significant changes in response to zinc supplementation or lacked direct relevance to the relationship between diarrhea and zinc. Ultimately, 10 articles were included in the review, forming the foundation for a comprehensive analysis of the effects and mechanisms of zinc supplementation in the management of acute diarrhea in children. To ensure the selection of appropriate RCTs that match the inclusion criteria, the search technique employed relevant keywords and filters. The studies considered for inclusion were those published within the designated time frame and explored the impact of zinc supplementation on acute diarrhea in pediatric populations. The chosen RCTs were carefully assessed for their methodology, sample size, interventions, outcomes, and findings. By combining and examining the results of the selected RCTs, this review aims to provide a thorough analysis of the relevant literature and shed light on the effectiveness of zinc supplementation in the management of acute diarrhea in children. The details of the search are explained in Figure 1.

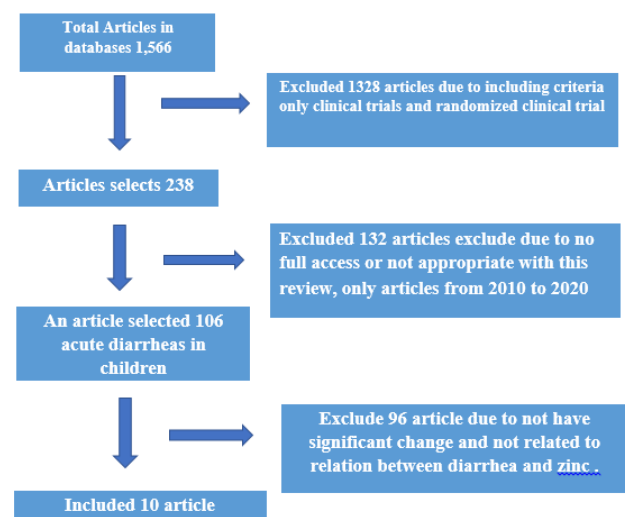


Figure 1: The process of searching

Cases Review

After an extensive review of 10 articles, it is evident that 7 provide substantiated evidence supporting the beneficial effect of zinc in reducing the duration, frequency, and severity of acute diarrhea in young people. These findings indicate that zinc supplementation plays a crucial role in effectively

addressing this prevalent condition in pediatric populations. And some of them have little effect.

The first article of a randomized controlled study that examined the effects of various zinc supplementation regimens on the frequency and course of acute respiratory tract infections and diarrhea in children aged 6-23 months [12]. The trial was carried out in remote regions of Laos. Three thousand four hundred seven children participated in the trial. They were randomized into four groups: daily zinc tablets for prevention, daily zinc supplements for diarrhea treatment, daily multiple-micronutrient powder, or daily placebo powder. Overall, the data demonstrated that the various supplementation regimens had little or no impact on acute lower respiratory tract infections (ALRI), acute upper respiratory tract infections (AURI), or diarrhea. On the other hand, compared with placebo, therapeutic zinc supplementation significantly reduced the duration of diarrhea episodes and the likelihood of further episodes in children older than 18 months. The study emphasizes that zinc supplementation may reduce the number of diarrheal illness episodes among older children. The results also suggest that preventive zinc supplementation, which targets all children at risk of zinc insufficiency, may be a more effective strategy than limiting supplementation to the treatment of diarrhea alone.

Another study aimed to assess the effectiveness and potential drawbacks of using lower doses of zinc in treating diarrhea in children [13]. The randomized multicenter trial involved 4,500 children aged 6 to 59 months from Tanzania and India. The WHO and the United Nations Children's Fund (UNICEF) recommend 20 mg of zinc daily for 10 to 14 days. However, concerns about increased vomiting prompted this study to investigate the safety and efficacy of reduced dosages (5, 10, and 20 mg). Key outcomes measured included the duration of diarrhea, fecal quantity, and the incidence of vomiting within 30 minutes of zinc administration. Results indicated that the standard 20 mg dose was as effective as the lower doses (5 mg and 10 mg) for treating diarrhea, with lower doses associated with significantly reduced vomiting. These findings are significant for the treatment of pediatric diarrhea, suggesting that lower zinc doses can maintain efficacy while minimizing vomiting and potentially improving treatment adherence. The study suggests reevaluating current zinc dosage recommendations to optimize diarrhea management in children.

The effectiveness of giving zinc supplements to treat children's acute diarrhea is examined in the paper "Efficacy of zinc supplementation in the

management of acute diarrhea: a randomized controlled trial" [14]. The study was conducted at the pediatric department of Srinakharinwirot University Hospital in Thailand. In this double-blind study involving 86 children with acute diarrhea, participants were randomly assigned to receive zinc supplements or a placebo. The research findings suggest that treatment outcomes for children with acute diarrhea improved significantly when zinc supplements were administered. The median duration of diarrhea in the zinc group was 44 hours, compared with 52 hours in the control group. Additionally, the zinc group had a median of 5 stools, whereas the control group had a median of 7 stools. In addition, compared with the control group, the children in the zinc group required less hospitalization time and fewer days of IV fluid therapy. These findings suggest that zinc supplementation may help children with acute diarrhea recover more quickly, have fewer stools overall, and spend less time in the hospital.

A 2016 study investigated the impact of bundling zinc and oral rehydration salts (ORS) on adherence to diarrhea treatment among Ethiopian patients [15]. Conducted through a cluster-randomized controlled experiment across 32 health facilities in eight national districts, the research revealed that packaging zinc and ORS in a pouch with educational messaging significantly improved treatment adherence compared with standard methods. Both central bundling and health center (HC) level bundling approaches were associated with increased adherence. However, bundling without educational messaging did not show a notable difference in adherence. The study found that the HC-level bundling approach was more cost-effective than central bundling. Despite a higher cost per episode in central bundling, combining zinc with ORS in a pouch with instructional guidance increased adherence to diarrhea treatment. The research suggests implementing the HC-level bundling approach to improve cost-effectiveness and provides valuable insights for decision-making in similar contexts, particularly in Ethiopia.

In a randomized clinical trial, researchers investigated the efficacy of zinc supplementation for severe diarrhea in children from developed countries, focusing on Swiss children aged 2 months to 5 years [16]. The study involved 87 participants: 42 received zinc, and 45 received a placebo. The results indicated a significant reduction in diarrhea duration in the zinc-treated group compared with the placebo group (median 47.5 hours vs 76.3 hours; $p=0.03$). Additionally, the zinc group showed a lower incidence of diarrhea ($p=0.02$),

with only 5% still experiencing diarrhea after 120 hours of therapy, compared to 20% in the placebo group ($p=0.05$). The study concludes that zinc supplementation can effectively reduce the frequency and severity of diarrhea in Swiss children aged 2 months to 5 years, underscoring the potential benefits of zinc supplementation in affluent nations. However, challenges related to noncompliance raise questions about optimal treatment courses and medication selection.

A clinical trial conducted in Tanzania investigated the impact of daily multivitamin (MV) and zinc supplementation on infectious illnesses in infants [17]. The randomized, double-masked, placebo-controlled study involved 2,400 children born to HIV-negative mothers in a low-malaria area, divided into four groups: MVs, zinc, zinc + MVs, and placebo. Over eighteen months, infants received their assigned supplements orally. The study revealed that daily zinc supplementation from six weeks of age significantly reduced the incidence of acute upper respiratory infections and diarrhea in Tanzanian infants compared to those without zinc supplementation. Despite a slight, non-significant increase in overall mortality among infants taking zinc, there was no additional reduction in morbidity or death with multivitamin treatment. The study suggests that providing daily zinc supplements to newborns in Tanzania from 6 weeks of age can significantly reduce the incidence of severe upper respiratory infections and diarrhea, but adding multivitamins does not confer additional benefits.

In a single-blind, prospective, controlled trial, researchers aimed to assess the efficacy of a novel hypotonic oral rehydration solution (ORS) containing zinc and prebiotics for the treatment of acute diarrhea in children aged 3 to 6 months [18]. The study randomly assigned participants to two groups: one receiving a standard hypotonic ORS and the other receiving a novel formulation with prebiotics and zinc. The primary endpoint was the rate of diarrhea remission within 72 hours. Results showed that the novel ORS formulation (group 2) led to a significantly higher proportion of resolved diarrhea within 72 hours (72.9%) compared to the regular ORS group (50%). Group 2 also consumed more ORS in the first 24 hours and reported fewer missed workdays for parents. Additionally, fewer patients in group 2 required supplemental medication for diarrhea. The study suggests that incorporating zinc and prebiotics into a hypotonic ORS can reduce the duration of severe diarrhea in children, providing evidence for improved treatment outcomes.

The randomized, double-blind, placebo-controlled study investigated the effectiveness of an oral rehydration solution (ORS) enriched with *Lactobacillus reuteri* DSM 17938 and zinc (ORS+Lr&Z) for the treatment of acute diarrhea in healthy infants aged 6 to 36 months [19]. Compared to a standard ORS without *Lactobacillus reuteri* DSM 17938 and zinc (ORS-Lr&Z), both groups exhibited reduced diarrhea severity by the second treatment day. Although the ORS+Lr&Z group showed a trend towards better outcomes, the differences were not statistically significant, likely due to the limited number of participants. The study, which was ethically approved and obtained parental consent, concluded that both ORS formulations effectively managed acute diarrhea in healthy infants. The ORS enriched with *Lactobacillus* DSM 17938 and zinc was well-tolerated with no reported adverse effects, highlighting its potential as a safe treatment option.

A clinical trial in Kolkata, India, evaluated various supplementation strategies for the treatment of acute diarrhea in children aged 6 to 24 months [20]. Participants were randomized into four groups: placebo vitamin A, a mixture of vitamins and micronutrients, vitamin A alone, or placebo with oral rehydration solution. All supplemented groups demonstrated a significant reduction in diarrhea outcomes compared with placebo, with the combination of zinc and micronutrients group recovering faster than the zinc plus vitamin A group. The study suggests that supplementing with a combination of minerals and vitamins did not exceed the effectiveness of zinc alone, underscoring the importance of zinc supplementation in managing childhood diarrhea and its implications for public health programs in developing nations.

The primary outcome of the study, which examined the effectiveness of oral zinc supplementation in treating acute gastroenteritis in Polish children, found no significant difference in diarrhea duration between the zinc and placebo groups [21]. The trial, conducted on well-nourished, healthy children aged 3 to 48 months, used a randomized, double-blind design in which participants received either zinc sulfate or a placebo for 10 days. Additional measures, including stool frequency, vomiting frequency, intravenous fluid intake, and the proportion of children with prolonged diarrhea, did not differ significantly between the two groups. These findings imply that zinc supplementation may not confer additional advantages in the treatment of acute gastroenteritis in regions where zinc deficiency is uncommon.

Discussion

This review of ten studies examining zinc supplementation for acute pediatric diarrhea reveals variable efficacy across different populations. Seven studies demonstrated beneficial effects, while three showed minimal or no significant impact, highlighting the importance of contextual factors in treatment outcomes. The effectiveness of zinc supplementation appears strongly linked to baseline nutritional status and geographic location. Studies from resource-limited settings showed consistent benefits. In Laos, therapeutic zinc significantly reduced the duration and incidence of diarrhea among children older than 18 months, with 3,407 participants [12]. A Thai study involving 86 patients reported reduced median diarrhea duration from 52 to 44 hours, decreased stool frequency from 7 to 5, and shorter hospitalization time [14]. The Tanzanian trial with 2,400 infants demonstrated that daily zinc supplementation significantly reduced both diarrhea and acute upper respiratory infections over 18 months [17]. In India, zinc-containing regimens proved effective in reducing diarrhea outcomes among 167 children [20]. Conversely, the Polish study found no significant difference in diarrhea duration, stool frequency, or vomiting between zinc and placebo groups among 141 well-nourished children [21]. The Swiss study is an exception, showing significant efficacy, with a median reduction in diarrhea duration from 76.3 to 47.5 hours ($p=0.03$) among 87 children in a developed-country setting, despite notable noncompliance [16]. These findings suggest zinc supplementation primarily benefits populations with existing zinc deficiency [12, 21].

The multicenter trial involving 4,500 children found that lower doses of 5 mg and 10 mg were as effective as the WHO-recommended 20 mg dose while substantially reducing the incidence of vomiting, with important implications for treatment adherence [13]. The Laotian study found therapeutic zinc particularly effective in children older than 18 months, suggesting age-dependent responses require consideration in supplementation strategies [12].

Combination approaches showed variable results across four studies. In a study of 60 children receiving hypotonic ORS with zinc and prebiotics, 72.9% achieved remission within 72 hours, compared with 50% with standard ORS, suggesting synergistic effects through enhanced gut microbiota [18]. However, ORS supplemented with *Lactobacillus reuteri* and zinc showed no statistically significant benefit over standard ORS in 51 infants, likely due to the small sample size [19]. The Indian trial found

that combining zinc with multiple micronutrients did not exceed the effectiveness of zinc alone; the zinc-micronutrient group recovered only marginally faster than the zinc-vitamin A group, suggesting that zinc is the critical therapeutic component [20].

The Ethiopian cluster-randomized trial involving 176 children across 32 health facilities demonstrated that packaging zinc with ORS plus educational messaging significantly improved treatment adherence over twelve days, with health center-level bundling proving more cost-effective than central bundling [15]. This highlights that delivery mechanisms and patient education are critical determinants of real-world effectiveness beyond clinical efficacy alone. The Swiss study similarly noted significant nonadherence despite demonstrated efficacy, underscoring the need to understand barriers related to taste, treatment duration, and cultural factors [16]. The Tanzanian trial showed that zinc's benefits extend beyond diarrhea to include reduced acute upper respiratory infections, supporting its broad immunomodulatory role in maintaining epithelial barrier integrity and immune function [17]. However, a non-significant, albeit slight, increase in overall mortality in the zinc group warrants cautious interpretation and continued safety monitoring in large-scale supplementation programs.

Study heterogeneity limits direct comparability. Sample sizes ranged from 51 participants in the *Lactobacillus* study [19] to 4,500 children in the dose-comparison trial [13], directly impacting statistical power. Follow-up duration varied from 72 hours in the prebiotic-ORS survey [18] to 18 months in the Tanzanian trial [17], capturing different aspects of zinc's impact. Outcome definitions differed substantially, with some measuring diarrhea duration, others focusing on stool frequency, hospitalization time, or adherence. The Ethiopian study focused primarily on adherence rather than clinical outcomes [15], while others examined multiple endpoints. Etiological variability in diarrhea across settings may also influence the effectiveness of zinc, as mechanisms may be more relevant to specific pathogens. However, none of the reviewed studies systematically examined treatment effects by diarrheal etiology.

The cumulative evidence supports zinc supplementation as effective adjunct therapy for acute childhood diarrhea in populations at risk of zinc deficiency, substantiating WHO recommendations, particularly for low- and middle-income countries [12-14, 17-18, 20]. However, in well-nourished populations with low prevalence of zinc defi-

ciency, such as Poland [21], routine supplementation may not yield substantial benefits and could represent inefficient resource allocation. Targeted supplementation based on geographic location, nutritional status, or clinical indicators appears more appropriate and cost-effective. Lower doses of 5-10 mg could improve treatment acceptance while maintaining efficacy [13], supporting guideline revision to optimize adherence and population-level effectiveness. Implementation strategies demonstrated in Ethiopia [15] offer scalable approaches for improving uptake in resource-limited settings through bundling with educational messaging. Key research priorities include identifying biomarkers or clinical indicators that predict which children will benefit most from zinc supplementation, thereby enabling more targeted interventions. The divergent results between developed and developing nations suggest baseline zinc status may be critical, but practical point-of-care assessment methods are needed. Optimal formulation, dose, and duration require refinement through additional studies across diverse populations. The finding that 5-10 mg doses are equally effective as 20 mg [13] suggests even lower doses might be sufficient. Long-term effects on growth, neurodevelopment, and immune function deserve longitudinal investigation, particularly given the mortality signal in Tanzania [17]. Research into combination therapies should continue, with particular attention to genuinely synergistic agents such as prebiotics [18], which require larger trials to confirm initial promising results. Implementation research examining real-world effectiveness, cost-effectiveness, and strategies for maximizing adherence is essential for translating trial findings into sustainable public health programs, building on the Ethiopian model [15].

Zinc supplementation effectively reduces duration, severity, and frequency of acute diarrhea in children at risk of zinc deficiency, particularly in resource-limited settings [12, 14, 17, 20]. Benefits are less consistent in well-nourished populations [21], though specific subgroups in developed nations may benefit [16]. Lower doses appear equally effective with fewer adverse effects [13]. Combination approaches show variable results, with zinc-prebiotics demonstrating promise [18] while multiple micronutrient combinations [20] and probiotic additions [19] showed limited additional benefit. Implementation strategies emphasizing bundling with educational messaging effectively improve adherence [15]. Zinc supplementation should be targeted to populations where evidence of benefit

is most substantial, with continued safety monitoring given the non-significant mortality signal in one large trial [17].

Conclusions

This review assessed published evidence on zinc supplementation for acute diarrhea in children. The body of evidence supports the use of zinc as a meaningful component of diarrhea management. Most findings support clinical benefit and improved recovery when zinc is administered alongside standard care. We believe that zinc supplementation should be routinely included in pediatric diarrhea treatment protocols, particularly in settings with high disease burden and limited resources. The approach aligns with public health priorities focused on low-cost and scalable interventions. Inconsistent findings across some studies likely reflect differences in age, dose, and program delivery rather than a lack of effect.

Based on this work, zinc supplementation should form part of standard diarrhea management alongside oral rehydration therapy. Health authorities should strengthen caregiver education to improve correct use and adherence. National child health programs should formally adopt zinc distribution as a component of their programs. Future research should focus on age-specific dosing, optimal treatment duration, and effective delivery models to strengthen impact at the community level.

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Conceptualized and designed, M.O.H. and H.H.R.; performed the literature and data analysis, B.Z.M.; Writing, P.O.H.; supervise, M.O.H. and H.H.R.

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