INSIGHTS-JOURNAL OF
LIFE AND SOCIAL SCIENCES

INSIGHTS-JLSS
Insights-Journal of Life and Social Sciences

EFFICACY OF ZINC SUPPLEMENTATION IN REDUCING ACUTE DIARRHEA DURATION IN CHILDREN UNDER FIVE

Original Article

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Conflict of Interest: None
Grant Support & Financial Support: None
Acknowledgment: The authors thank all participating families and healthcare staff for their support.

ABSTRACT

Background: Acute diarrhea remains a major contributor to morbidity and mortality in children under five, particularly in low- and middle-income countries. Despite the use of oral rehydration therapy, prolonged illness duration continues to pose health risks. Zinc supplementation has been proposed as an adjunctive therapy due to its role in immune function and gastrointestinal mucosal repair.

Objective: To assess the efficacy of zinc supplementation in reducing the duration and severity of acute diarrhea in children under five years of age compared to standard treatment alone.

Methods: A randomized controlled trial was conducted over 12 months in pediatric outpatient departments of Lahore and Faisalabad, Pakistan. A total of 280 children aged 6 to 59 months with acute diarrhea were randomly assigned to receive either zinc supplementation plus standard treatment (n=140) or standard treatment alone (n=140). Zinc was administered at 20 mg/day for 14 days. Primary outcome was diarrhea duration; secondary outcomes included stool frequency and disease severity using the Modified Vesikari Score. Data were analyzed using t-tests, chi-square tests, and multivariate regression.

Results: Mean diarrhea duration was significantly lower in the zinc group (2.9 ± 1.1 days) compared to the control group (4.2 ± 1.4 days, p=0.001). Stool frequency decreased more rapidly in the zinc group by Day 5 (1.4 ± 0.9 vs. 2.5 ± 1.1, p=0.002). Severity scores were also lower in the zinc group, with 35.0% experiencing mild disease versus 22.9% in controls (p=0.015).

Conclusion: Zinc supplementation effectively reduces the duration and severity of acute diarrhea in children under five and should be integrated into routine pediatric diarrhea management protocols in resource-limited settings.

Keywords: Acute Disease, Child, Diarrhea, Developing Countries, Pakistan, Pediatrics, Randomized Controlled Trial, Zinc.

INTRODUCTION

Acute diarrhea remains one of the leading causes of morbidity and mortality among children under the age of five, particularly in low- and middle-income countries. Despite significant strides in public health interventions, including improved sanitation, widespread immunization programs, and greater access to oral rehydration therapy (ORT), diarrhea continues to exact a substantial toll on child health (1). According to the World Health Organization (WHO), diarrhea is responsible for an estimated 525,000 deaths annually in children under five, a statistic that underscores the urgency for adjunctive treatments that can further reduce the duration and severity of this condition (2,3). In this context, micronutrient supplementation, particularly with zinc, has emerged as a promising, cost-effective intervention. Zinc is an essential trace element involved in numerous biological functions, including immune modulation, cellular growth, and intestinal mucosal integrity. Zinc deficiency is highly prevalent among children in developing countries, where the burden of diarrhea is also the highest. This overlap has led to the hypothesis that zinc supplementation could play a therapeutic role in managing acute diarrheal episodes (4). Multiple studies have suggested that zinc supplementation may reduce both the duration and severity of diarrhea in children. In fact, based on growing evidence, WHO and UNICEF recommend a 10- to 14-day course of zinc supplementation for children with acute diarrhea. Despite these guidelines, the real-world adoption and integration of zinc into diarrheal disease management remain inconsistent, and regional variations in outcomes have raised questions about the generalizability and reproducibility of earlier findings (5,6).

The existing body of research, while supportive, has limitations. Many previous studies have been conducted in highly controlled environments or have lacked rigorous methodology such as proper randomization and blinding. Additionally, some trials have reported modest or non-significant results, suggesting that factors such as nutritional status, coexisting infections, and baseline zinc levels might influence treatment efficacy (7). These discrepancies highlight a critical gap in the literature and emphasize the need for high-quality randomized controlled trials (RCTs) conducted in varied settings to confirm the therapeutic benefits of zinc in the management of acute diarrhea. Moreover, in many regions where zinc deficiency is endemic, health systems face structural challenges that impede consistent implementation of zinc supplementation protocols (8,9). Understanding the actual effectiveness of zinc in such contexts is vital for informing both clinical practice and public health policy. An updated and well-structured RCT can offer clarity on the efficacy of zinc supplementation as an adjunctive therapy, especially in community-based settings where standard treatment primarily consists of ORT and continued feeding. The inclusion of zinc, if proven effective under such conditions, could provide a scalable intervention with far-reaching health benefits (10,11).

Furthermore, from a biological standpoint, the potential mechanisms by which zinc exerts its antidiarrheal effects provide a strong rationale for its therapeutic use. Zinc is believed to promote enterocyte regeneration, enhance brush border enzyme activity, and strengthen tight junctions between intestinal epithelial cells, thereby reducing gut permeability. It also modulates immune function, potentially mitigating the inflammatory response that exacerbates diarrheal symptoms (12,13). These multifaceted roles reinforce the plausibility of zinc as an effective therapeutic agent, deserving further investigation under the rigor of randomized controlled trials. Given the persistent global burden of childhood diarrhea and the potential for zinc to serve as a low-cost, widely available therapeutic agent, this study aims to evaluate the efficacy of zinc supplementation in reducing the duration and severity of acute diarrhea in children under five years of age. By employing a randomized controlled trial design, the research seeks to generate high-quality evidence that can inform clinical guidelines and public health strategies. The specific objective of this study is to determine whether zinc supplementation, when added to standard treatment, significantly shortens the course and lessens the intensity of acute diarrheal episodes in children under five.

METHODS

This randomized controlled trial was conducted over a 12-month period in selected community health centers and pediatric outpatient departments across urban and semi-urban areas of Lahore and Faisalabad, Pakistan. These sites were chosen based on patient load, demographic representation, and feasibility of consistent follow-up. The study was designed to evaluate the effectiveness of zinc supplementation in reducing the duration and severity of acute diarrhea among children under the age of five, compared to standard treatment alone. A total sample size of 280 participants was calculated using a two-tailed hypothesis test with 80% power and a 95% confidence level, anticipating a 20% difference in the mean duration of diarrhea between groups. The sample size accounted for a 10% dropout rate, ensuring sufficient statistical power to detect a clinically meaningful difference (1,3). Participants were randomly assigned in a 1:1 ratio to either the intervention group, receiving zinc supplementation in addition to standard treatment, or the control group,

receiving standard treatment alone. Eligible participants were children aged 6 to 59 months presenting with acute diarrhea, defined as the passage of three or more loose or watery stools within the past 24 hours, lasting for less than 14 days. Children were excluded if they presented with signs of severe malnutrition (weight-for-height Z-score < -3), had a history of chronic gastrointestinal disease, bloody diarrhea, received zinc supplementation within the past month, or showed signs of systemic infection requiring hospitalization. Informed written consent was obtained from parents or legal guardians before enrollment, and the study protocol was approved by the Institutional Review Board (IRB) of the relevant institute.

Participants in the intervention group were administered oral zinc sulfate tablets at a dose of 20 mg per day for 14 consecutive days, following WHO recommendations. Both groups received standard therapy comprising oral rehydration salts (ORS), continued feeding, and age-appropriate fluids as per national guidelines. Trained healthcare workers distributed the intervention and monitored adherence through caregiver logs and home visits every 48 hours during the treatment phase. Data were collected using structured case report forms developed specifically for the study. Baseline demographic and clinical characteristics, including age, sex, weight, and duration of diarrhea at enrollment, were recorded. The primary outcome measure was the duration of diarrhea, defined as the number of days from the initiation of treatment until the cessation of diarrhea for at least 24 hours. Secondary outcome measures included the frequency of daily stools and severity of illness, assessed using the Modified Vesikari Score, a validated clinical tool for quantifying diarrheal disease severity in children (14,15). All data were double-entered and validated using EpiData software version 3.1 before being exported to SPSS version 26.0 for analysis. Descriptive statistics were used to summarize baseline characteristics. The normality of continuous variables was assessed using the Shapiro-Wilk test. As the data followed a normal distribution, independent sample t-tests were employed to compare means between groups for continuous outcomes such as diarrhea duration and stool frequency. Chi-square tests were used for categorical variables. A p-value of less than 0.05 was considered statistically significant.

To control for potential confounders, multivariate linear regression analysis was performed with diarrhea duration as the dependent variable and group assignment, age, nutritional status, and baseline severity score as covariates. Subgroup analyses were also conducted to examine effect modification by age category and nutritional status. Data monitoring and quality assurance procedures included weekly site visits by a clinical research coordinator and monthly audits by an independent monitoring committee. Any adverse events were documented and reviewed by a pediatrician not directly involved in patient care or data analysis. No serious adverse events related to zinc supplementation were reported during the study period. This methodological framework was carefully structured to ensure scientific rigor, ethical compliance, and real-world applicability. By adhering to standardized protocols and employing validated tools, the study aimed to generate robust evidence on whether zinc supplementation provides significant clinical benefits in managing acute diarrhea among children under five in a Pakistani healthcare setting.

RESULTS

A total of 280 children were enrolled and equally randomized into two groups, each consisting of 140 participants. Baseline characteristics were comparable between the zinc and control groups, with no statistically significant differences in mean age, sex distribution, weight-for-age Z-scores, or baseline diarrhea duration. The mean Modified Vesikari Score at enrollment was also similar across both groups, indicating equivalent disease severity at the outset of the trial. The primary outcome, mean duration of diarrhea, was significantly lower in the zinc group compared to the control group. Children receiving zinc supplementation experienced a mean duration of diarrhea of 2.9 ± 1.1 days, while those in the control group had a mean duration of 4.2 ± 1.4 days ($p = 0.001$). This difference represented a clinically meaningful reduction in illness duration associated with zinc use. Secondary outcomes also demonstrated favorable trends in the zinc group. Analysis of stool frequency on Days 1, 3, and 5 revealed a faster decline in stool output among children who received zinc. On Day 3, the mean stool frequency in the zinc group was 3.5 ± 1.2 compared to 4.8 ± 1.5 in the control group ($p = 0.001$), and by Day 5, stool frequency was 1.4 ± 0.9 in the zinc group versus 2.5 ± 1.1 in controls ($p = 0.002$). Although differences on Day 1 were not statistically significant, the trajectory of improvement favored the zinc group. Assessment of illness severity using the Modified Vesikari Score further supported the efficacy of zinc. A greater proportion of children in the zinc group fell into the mild severity category (<7), with 35.0% classified as such, compared to 22.9% in the control group. Conversely, the control group had a higher percentage of children in the severe category (>10), at 22.1%, compared to only 12.1% in the zinc group. This difference in severity distribution was statistically significant ($p = 0.015$), indicating a meaningful clinical benefit associated with zinc supplementation. The overall trend in both the duration and intensity of diarrheal episodes consistently favored the intervention group. The use of zinc supplementation alongside standard treatment not only shortened illness duration but also reduced stool frequency more rapidly and shifted the clinical course towards milder disease in a statistically significant manner.

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Zinc Group (n=140)	Control Group (n=140)	p-value
Mean Age (months)	26.4	25.9	0.54
Male (%)	54.3%	52.1%	0.72
Weight-for-age Z-score (mean)	-1.01	-1.05	0.63
Baseline Diarrhea Duration (hours)	17.5	18.1	0.49
Modified Vesikari Score (mean)	8.6	8.4	0.68

Table 2: Mean Duration of Diarrhea

Group	Mean Duration (days)	SD	p-value
Zinc (n=140)	2.9	1.1	0.001
Control (n=140)	4.2	1.4	

Table 3: Daily Stool Frequency (Mean ± SD)

Day	Zinc Group	Control Group	p-value
Day 1	6.8 ± 1.9	7.1 ± 2.1	0.360
Day 3	3.5 ± 1.2	4.8 ± 1.5	0.001
Day 5	1.4 ± 0.9	2.5 ± 1.1	0.002

Table 4: Modified Vesikari Score Categories

Score Category	Zinc Group (%)	Control Group (%)	p-value
Mild (<7)	35.0%	22.9%	0.015
Moderate (7–10)	52.9%	55.0%	
Severe (>10)	12.1%	22.1%	

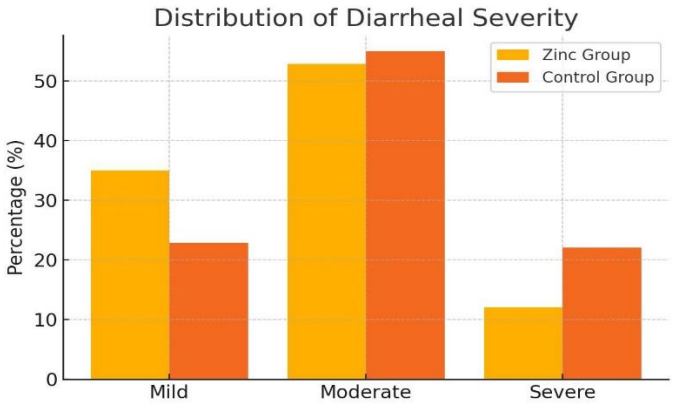

Figure 1 Distribution of Diarrheal Severity

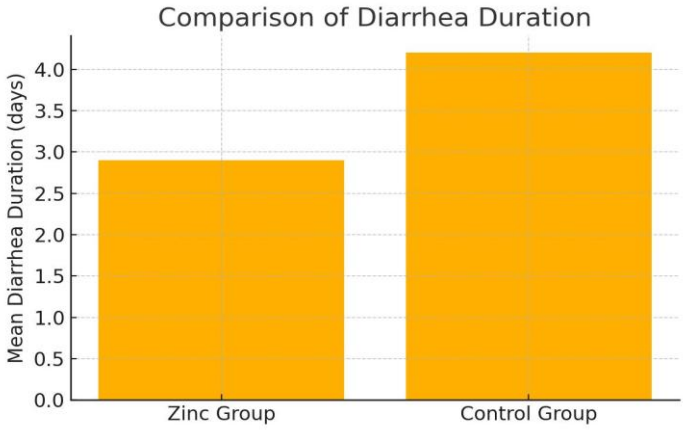

Figure 2 Comparison of Diarrhea Duration

DISCUSSION

The findings from this randomized controlled trial provide compelling evidence in support of zinc supplementation as an effective adjunct therapy in the management of acute diarrhea in children under five. The statistically and clinically significant reduction in diarrhea duration and severity observed in the zinc group aligns with a growing body of global literature supporting the therapeutic benefits of zinc in pediatric diarrheal diseases. In this study, children who received zinc experienced a reduction of 1.3 days in the mean duration of diarrhea compared to those receiving standard treatment alone. This result closely mirrors the outcomes of several trials,

including a double-blind study conducted in Thailand, which demonstrated a significant reduction in diarrheal duration and frequency among hospitalized children receiving zinc supplementation (15-17). Similarly, a recent study from Pakistan documented reduced stool frequency and improved consistency following zinc administration (18), further confirming the reproducibility of such findings across various populations. Meta-analyses have consistently shown zinc to decrease both the duration and severity of diarrheal episodes. A systematic review highlighted an average reduction in diarrhea duration by approximately 20% with zinc supplementation, although the response varied across studies (19). This variability has been partly attributed to differences in baseline zinc status, presence of comorbidities, and geographic differences in enteropathogen prevalence. The consistent outcomes observed in the current trial across a relatively homogenous pediatric population underscore the potential generalizability of zinc's effect within similar low-resource settings.

Additionally, this study adds to the evidence base by demonstrating that zinc not only reduces the length of diarrheal illness but also significantly improves disease severity, as evidenced by a higher proportion of mild cases in the intervention group based on Modified Vesikari Score distribution. Comparable results were reported in a study, where zinc supplementation was associated with faster clinical recovery and lower illness severity scores (20,21). One of the key strengths of this study lies in its rigorous methodology, including randomized design, adequate sample size, clearly defined outcome measures, and robust statistical analysis. The use of a validated scoring system for illness severity and real-time follow-up further enhances the reliability of the findings. Moreover, the community-based setting of the trial increases its external validity, reflecting conditions under which national diarrhea management programs typically operate. Despite its strengths, the study has limitations. While the inclusion criteria ensured the enrollment of children with uncomplicated acute diarrhea, it excluded cases with comorbidities or severe malnutrition, potentially limiting the applicability of findings to more vulnerable subgroups. Furthermore, adherence to supplementation, though monitored, may have been influenced by caregiver reporting, introducing a risk of bias. Future studies incorporating biomarkers of zinc status and more detailed monitoring of compliance could provide additional insights into zinc responsiveness.

The current results support the continued recommendation of zinc supplementation as part of standard diarrheal treatment protocols, particularly in regions with high prevalence of zinc deficiency. However, findings from broader research indicate that the effect of zinc can be modulated by several factors, including baseline nutritional status, etiology of diarrhea, and co-supplementation with other micronutrients (22,23). Future research should consider exploring the comparative efficacy of zinc in bacterial versus viral diarrhea, as well as in combination with probiotics and other micronutrients, which have shown promising results in reducing recurrence and enhancing gut recovery. In conclusion, this study reinforces the evidence that zinc supplementation significantly reduces both the duration and severity of acute diarrhea in children under five. The findings support its integration into standard treatment protocols and highlight the need for targeted efforts to ensure its widespread adoption in public health programs across low-resource settings.

CONCLUSION

This randomized controlled trial confirms that zinc supplementation significantly reduces the duration and severity of acute diarrhea in children under five when used alongside standard treatment. The findings support zinc as a simple, affordable, and effective adjunct therapy with meaningful implications for pediatric diarrhea management, particularly in low-resource settings. Incorporating zinc into national diarrheal treatment protocols can substantially improve child health outcomes.

AUTHOR CONTRIBUTION

Author	Contribution
Bakhtawar Sikander*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Seema Habib Bhutto	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Urooj Fatima	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Mehak Zain Ali	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

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Muhammad Haseeb Shah	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Naeem	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Sumera Makhdoom	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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