The Effect of Zinc Supplementation on The Duration of Acute Watery Diarrhea in Children Age 6 Months To 5 Years Old

Asma Jahan[1], Huma Mir[1], Jan Mohammad[1], Fatima Jahan[2]

[1]Department of Pediatrics, Khyber Teaching Hospital (KTH), Peshawar, Pakistan.
[2]Department of Zoology, Shaheed Benazir Bhutto Women University, Peshawar, Pakistan

ARTICLE INFO

ABSTRACT

Introduction: Health burden of acute watery diarrhea in children aged 6 months to 5 years is quite significant. Zinc supplementation could potentially be an effective, affordable intervention which is seldomly investigated locally. Hence the study was planned with aim to explore the potential impact of oral zinc supplementation on the duration of acute watery diarrhea in children aged 6 months to 5 years. Results of the study could benefit clinicians in providing better treatment plan and improve the outcomes in acute diarrheal illness in children. **Materials and methods:** This randomized controlled trial was carried out at the department of Pediatrics, Khyber Teaching Hospital, during the period from 5th August 2024 to 5th February 2025. A total of 212 (106 in each group) patients irrespective of gender, aged 6 months to 5 years presenting with acute diarrhoeal illness were assigned to group A (with zinc supplementation) and B (without zinc supplementation). Efficacy (time to acute diarrhea resolution) was compared in both groups. **Results:** The mean age of the participants in group A (with zinc) was 2.69±1.19 years compared to 2.75±1.21 years in group B (without zinc). Male participants were 64 (60.4%) in group A while 56 (52.8%) in group B. 64 patients (60.4%) patients reported passing loose stools in group A compared to 50 (47.2%) in group B. 36 patients (34.0%) were breast fed in group A compared to 40 (37.7%) in group B. The mean time to resolution of diarrhea (efficacy) in group A (with zinc) was 3.34±1.27 days and 4.74±1.56 days in group B (without zinc). The p value for mean difference in efficacy was 0.000. **Conclusion:** Mean time to resolution of diarrhea was significantly lower in patients receiving zinc compared to patients who did not receive it showing the potential beneficial role of zinc in acute diarrheal illness in children.

INTRODUCTION

One of the most common and upsetting medical disorders among children is acute diarrheal illness.1 Diarrhea carries a substantial risk to infant mortality in underdeveloped countries, with an anticipated yearly toll reaching half a million.2 Oral rehydration solution (ORS) supplementation and adequate dietary guidance are the cornerstones of treating acute dehydrating diarrhea.3 But it's important to emphasize that ORS is ineffective in reducing the amount and frequency of bowel movements, which emphasizes the requirement of all-encompassing therapeutic approaches.4,5 In this regard, oral zinc administration from the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) has been advised for children.6 It is important to recognize that zinc deficiency is major factor in particular circumstances of underdeveloped countries whereby poor nutritional status and other deficiencies are still widespread.7 Additionally, the incidence of diarrhea in malnourished kids makes this shortage worse, which emphasizes the need of zinc supplementation.8,9

Zinc is an essential component of many enzymes and its structural and catalytic functions are significant for membrane integrity and cytotoxic T cell responses.10 Mode of action of zinc in diarrheal illness in multipronged, including preserving the stability of intestinal brush border, promoting immunity against infections through modification in cellular membranes and functioning resulting in lower illness duration and reducing risk of complications.1 The length and frequency of diarrhea have been shown to be positively impacted by oral zinc supplementation in prior research, with a reduction of duration of recovery and stool frequency.10,11 Trivedia and colleagues found that the zinc group showed 62% decrease in daily stool frequency, compared to 26% decrease in the placebo

arm.12 In a research the proportion of kids with watery stool (42% vs 70%, p=0.05) and the frequency of diarrheal episodes (3.88±1.11 vs. 4.58±1.03, p=0.001) were significantly lower in zinc group compared to placebo group.13 This research aimed to ascertain the potential impact of oral zinc supplementation on the duration of acute watery diarrhea in children aged 6 months to 5 years. Given the substantial health burden of acute watery diarrhea in children, the study was crucial as no study has been carried out previously in local settings. Examining zinc supplementation might provide an efficient and cost-effective solution. The study's evidence-based recommendations will help legislators and healthcare professionals in better patient management.

MATERIAL AND METHODS

This randomized controlled trial was carried out at the department of Pediatrics, Khyber Teaching Hospital, Peshawar during the period from 5th August, 2024 to 5th February, 2025. Approval for the conduct of the study was obtained from College of Physicians and Surgeons, Pakistan vide no: CPSP/ REU/ PED- 2021-020-6190, dated 4th August 2024. Male and female patients aged 6 months to 5 years with a history of acute diarrhea lasting fewer than 14 days, experiencing three or more loose within the preceding 24 hours were enrolled. Patients with congenital anatomical abnormalities, immunocompromised patients, syndromic babies and antibiotic induced diarrhea were excluded. Acute diarrheal illness was defined as 3 or more episodes of loose watery stools per day for less than 14 days. Efficacy was defined by time taken for resolution of diarrhea. Total sample size was 212 (106 in each group) calculated using Open Epi software taking the assumptions; anticipated efficacy of zinc as 14.0% and 2.0% efficacy of placebo, power of test 80% and 95% confidence level.13 participants were recruited using non- probability consecutive sampling technique and its was hypothesized that oral zinc supplementation is effective in quick resolution of acute diarrhea in children aged 6 month to 5 years as compared to no zinc supplementation.

Detailed clinical histories including demographic variables, number and consistency of stool, history regarding normal bowel habits, feeding and nutrition, any medical condition including malabsorption syndrome were taken. Comprehensive physical examinations were conducted. The established guidelines for rehydration, inclusive of ORS and intravenous Ringer's lactate solution for severe dehydration, were rigorously followed. Patients were randomly allocated, through block randomization, into parallel groups with a 1:1 allocation ratio. Parents remained blinded to the oral supplementation allocations. Patients in the intervention group received empirical first-line antibiotics, probiotics, low osmolar ORS and oral zinc supplementation in the form of zinc syrup at a dose of 1mg/kg/day. Patients in control arm received the same therapy as intervention group except oral zinc supplementation. Time to diarrhea resolution was noted in both groups. Data was analyzed using SPSS version 23 (IBM Inc. NY). Normality of data was checked by Shapiro wilk test. Means ± standard deviations and median (IQR) were calculated for quantitative variables like age, duration of diarrhea, number of stools etc. Frequencies & percentages were calculated for categorical variables like gender, socioeconomic status, mother education, and consistency of stool, type of diet and complete resolution of symptoms. Efficacy of zinc was stratified against age, gender, and other variables to control effect modifiers. Post stratification independent sample test was used to compare the differences between the groups. Probability values equal or less than 0.05 was considered significant.

RESULTS

The mean age of the participants in group A (with zinc) was 2.69±1.19 years compared to 2.75±1.21 years in group B (without zinc). Majority of the participants were aging 3 years or below in group A (n = 79, 74.5%) compared to 80 patients (75.5%) patients aging 3 years or below in group B. Male participants were 64 (60.4%) in group A while 56 (52.8%) in group B. Poor socioeconomic status was recorded in 58 participants (54.7%) in group A and 55 (51.9%) in group B. 64 patients (60.4%) patients reported passing loose stools in group A compared to 50 (47.2%) in group B. 36 patients (34.0%) were breast fed in group A compared to 40 (37.7%) in group B. (table 2).

Table 1

Mean and standard deviations of patients according to various parameters (n = 212, 106 in each group)

Group	Parameters	Mean	Std. Deviation
With Zinc	Age (years)	2.69	1.190
	Diarrhea Duration (days)	9.19	2.183
	Resolution Duration (days)	3.34	1.279
Without Zinc	Age (years)	2.75	1.219
	Diarrhea Duration (days)	8.08	2.599
	Resolution Duration (days)	4.74	1.563

Figure 1

Mean and standard deviations of patients
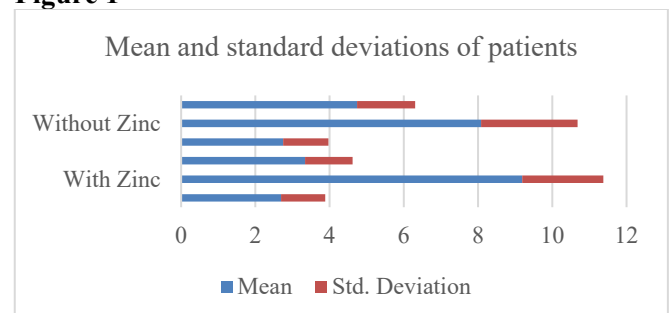
Table 2

Frequencies and percentages according to various parameters (n = 212, 106 in each group)

| Parameters	Group	Subgroups	Frequency	Percent
Age (years)	With Zinc	3 or below	79	74.5
		More than 3	27	25.5
	Without Zinc	3 or below	80	75.5
		More than 3	26	24.5
Gender	With Zinc	Male	64	60.4
		Female	42	39.6
	Without Zinc	Male	56	52.8
		Female	50	47.2
Mother education	With Zinc	Matric or below	49	46.2
		Above matric	57	53.8
	Without Zinc	Matric or below	52	49.1
		Above matric	54	50.9
Socioeconomic status	With Zinc	Poor	58	54.7
		Fair	48	45.3
	Without Zinc	Poor	55	51.9
		Fair	51	48.1
Stool consistency	With Zinc	Firm	42	39.6
		Loose	64	60.4
	Without Zinc	Firm	56	52.8
		Loose	50	47.2
Diet	With Zinc	Breast Fed	36	34.0
		Bottle Fed	37	34.9
		Regular Diet	33	31.1
	Without Zinc	Breast Fed	40	37.7
		Bottle Fed	43	40.6
		Regular Diet	23	21.7

Figure 2
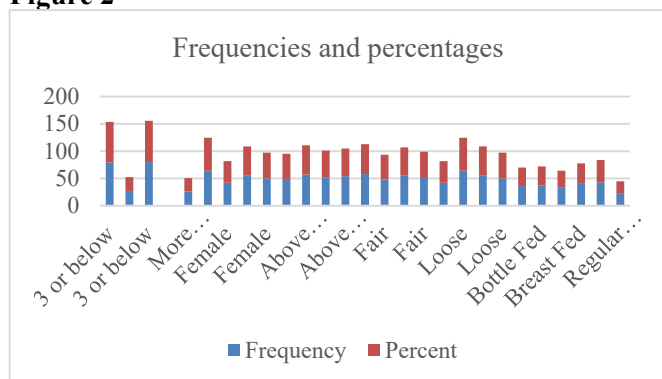
Frequencies and percentages

The mean time to resolution of diarrhea (efficacy) in group A (with zinc) was 3.34±1.27 days and 4.74±1.56 days in group B (without zinc). The p value for mean difference in efficacy was 0.000. (Table 3).

Table 3
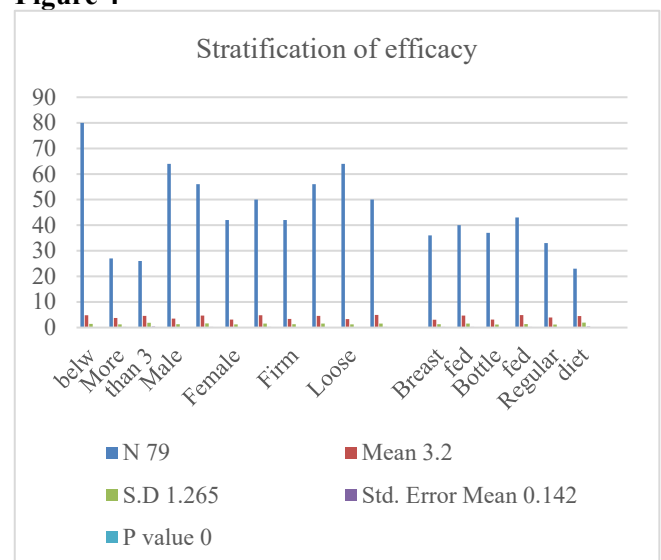
Comparison of Efficacy (diarrhea resolution duration) in both groups (n = 212, 106 in each group)

Efficacy	Group	N	Mean	S.D	Std. Error Mean	P value
Diarrhea Resolution Duration (days)	With Zinc	106	3.34	1.279	.124	0.000
	Without Zinc	106	4.74	1.563	.152	

Figure 3

Comparison of Efficacy
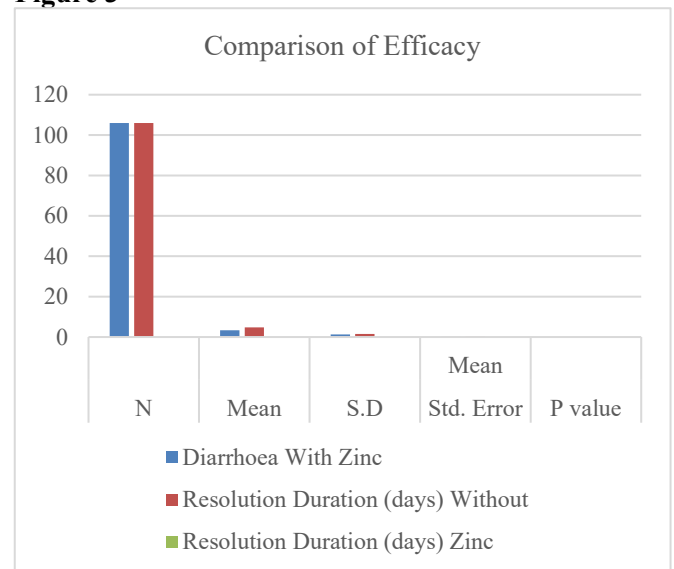
Subgroup analysis of efficacy with various clinical and demographic parameters is reported in table 4. Statistically significant association was observed between efficacy and parameters such as age, gender, stool consistency and pattern of diet (p value <0.05).

Figure 4

Stratification of efficacy

Table 4

Stratification of efficacy (diarrhea resolution duration) with various parameters (n = 212, 106 in each group)

Parameters			Group	N	Mean	S.D	Std. Error Mean	P-value
Age (years)	3 or below	Efficacy	With Zinc	79	3.20	1.265	.142	0.000
			Without Zinc	80	4.79	1.464	.164	
	More than 3	Efficacy	With Zinc	27	3.74	1.259	.242	0.060
			Without Zinc	26	4.58	1.858	.364	
Gender	Male	Efficacy	With Zinc	64	3.47	1.284	.161	0.000
			Without Zinc	56	4.70	1.606	.215	
	Female	Efficacy	With Zinc	42	3.14	1.260	.194	0.000
			Without Zinc	50	4.78	1.529	.216	
Stool consistency	Firm	Efficacy	With Zinc	42	3.38	1.306	.201	0.000
			Without Zinc	56	4.57	1.559	.208	
	Loose	Efficacy	With Zinc	64	3.31	1.271	.159	0.000
			Without Zinc	50	4.92	1.563	.221	
Diet	Breast fed	Efficacy	With Zinc	36	3.06	1.330	.222	0.000
			Without Zinc	40	4.70	1.539	.243	
	Bottle fed	Efficacy	With Zinc	37	3.11	1.173	.193	0.000
			Without Zinc	43	4.88	1.401	.214	
	Regular diet	Efficacy	With Zinc	33	3.91	1.182	.206	0.143
			Without Zinc	23	4.52	1.904	.397	

DISCUSSION

The results showed that the mean diarrhea resolution duration was shortened with zinc supplementation at 3.34 ± 1.27 days compared with the group without zinc supplementation at 4.74 ± 1.56 days, p = 0.000. These outcomes provided robust evidence to demonstrate the utility of zinc for the control of diarrheal conditions, as also demonstrated in other investigation by Brown et al., (2013).[14]

The subgroup analysis also suggested that the improvement in the duration of diarrhea in the current study was more prominent in the children of three years or below where the mean number of days to resolution was 3.20 ± 1.27 in the zinc group and 4.79 ± 1.46 in the non-zinc group. Other studies conducted by Patel et al., (2016) were also done and comparable results found whereby zinc intervention considerably minimized diarrhea duration among the younger group hence the rationale that zinc has a more potent dose dependent therapeutic intervention during the early ages.[15]

Results for the efficacy of zinc among male children were slightly higher (3.47 ± 1.28 days) than females (3.14 ± 1.26 days). This trend is in concordance with other studies like Bhandari et al., (2013) but the biological reason behind these gender differences is still uncertain and should be studied further.[16]

The resolution duration was shorter among children with firm stools than those with loose stools (3.38 ± 1.31 in the zinc group, 4.57 ± 1.56 in the non-zinc group for firm stoolers; 3.31 ± 1.27 in the zinc group, 4.92 ± 1.56 in the non-zinc group for loose stoolers). These results are align with the study by Walker et al. (2010) who observed that zinc supplementation was most beneficial in the improvement of stool frequency and the reduction of the severity of diarrheal attacks.[17]

The duration of diarrhea until resolution, among children who received zinc if breast fed was 3.06 ± 1.33 as compared to 4.70 ± 1.54 among children who did not receive zinc. Also, children who received zinc supplementation through the operation had an improved mean days of resolution that was 3.11 ± 1.17 than the mean days of resolution in children who did not receive zinc, that is 4.88 ± 1.40. These outcomes align with other studies by Lazzerini et al. (2013) on how zinc is effective generally in feeding but slightly superior in breastfed kids due to the immune-modulatory effects of breast milk.[18]

Socioeconomic and the maternal educational status of the groups also did not reveal statistically significant difference in the efficacy. This implies that zinc supplementation does not depend on these variables, which is in aligning with other research, such as Bhutta et al. (2000), which pointed out a general use of zinc in controlling diarrhea.[19]

CONCLUSION

In this study, zinc supplement shortens the duration of diarrheal episodes in children under five years irrespective of their gender, nature of stool and their diet preference. These results support the call for integrating zinc into the strategies for the treatment of diarrhea, which is consistent with current international policies on health.

REFERENCES

1. Laghari GS, Hussain Z, Shahzad H. Effect of zinc supplementation on the frequency and consistency of stool in children with acute diarrhea. Cureus. 2019; 11(3):e4217.World Health Organization. Readings on diarrhea: student manual. World Health Organization; 1992. https://doi.org/10.7759/cureus.4217

2. Liu L, Black RE, Cousens S, Mathers C, Lawn JE, Hogan DR. Causes of child death: comparison of MCEE and GBD 2013 estimates. The Lancet. 2015;385(9986):2461-2. https://doi.org/10.1016/s0140-6736(15)61132-1

3. World Health Organization. Department of Child, Adolescent Health. Handbook IMCI: integrated management of childhood illness. World Health Organization; 2005.

4. Snyder JD, Merson MH. The magnitude of the global problem of acute diarrhoeal disease: a review of active surveillance data. Bulletin of the world health organization.1982;60(4):605.

5. Shah Bb, Inam Ku, Shakoor S. Role of Oral Zinc Supplementation in treatment of Acute Dehydrating Diarrhea in children aged 6 months to 5 years. PJMHS 2021; 15(11):3002-3. https://doi.org/10.53350/pjmhs2115113002

6. Mahalanabis D, World Health Organization. Development of an improved formulation of oral rehydration salts (ORS with antidiarrhoeal and nutritional properties: a" super ORS"). World Health Organization; 1985.

7. Tielsch JM, Khatry SK, Stoltzfus RJ, Katz J, LeClerq SC et al. Effect of daily zinc supplementation on child mortality in southern Nepal: a community-based, cluster randomised, placebo-controlled trial. The Lancet. 2007;370(9594):1230-9. https://doi.org/10.1016/s0140-6736(07)61539-6

8. Mayo Wilson E, Junior JA, Imdad A, Dean S, Chan XH et al. Zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years of age. Cochrane Database of Systematic Reviews. 2014 ;(5):CD009384. https://doi.org/10.1002/14651858.cd009384.pub2

9. Al-Sonboli NA, Gurgel RQ, Shenkin A, Hart CA, Cuevas LE. Zinc supplementation in Brazilian children with acute diarrhoea. Ann Trop Paediatr. 2003;23(1):3-8.Sazawal S, Black RE, Bhan MK, Bhandari N, Sinha A, Jalla S. Zinc supplementation in young children with acute diarrhoea in India. N Engl J Med. 1995; 333:839–44. https://doi.org/10.1179/000349803125002797

10. Trivedi SS, Chudasama RK, Patel N. Effect of zinc supplementation in children with acute diarrhea: randomized double blind controlled trial. Gastroenterology research. 2009;2(3):168. https://doi.org/10.4021/gr2009.06.1298

11. Sadiq F, Jan MS, Tariq M, Ullah I, Khan AA, Suleman M. Effect of zinc supplement on duration of acute watery diarrhea from 6 months to 5 year aged children. Professional Med J. 2023 Oct 5;30(10):1328-33. https://doi.org/10.29309/tpmj/2023.30.10.7705

12. Brown, K. H., Hess, S. Y., Vosti, S. A., et al. (2013). Zinc supplementation and its impact on growth and diarrhea morbidity in children: A systematic review and meta-analysis. Nutrition Reviews, 71(2), 127–144. https://doi.org/10.1111/nure.12010

13. Patel, A., Mamtani, M., Dibley, M. J., & Badhoniya, N. (2016). Therapeutic zinc supplementation for managing acute diarrhea in children under five: A systematic review. Public Health Nutrition, 19(6), 1032-1040. https://doi.org/10.1017/S1368980015002715

14. Bhandari, N., Mazumder, S., Taneja, S., Dube, B., Agarwal, R. C., Mahalanabis, D., & Fontaine, O. (2013). Zinc supplementation during acute diarrhea reduces diarrheal morbidity in preschool children: A randomized controlled trial. The Journal of Nutrition, 143(5), 836-842. https://doi.org/10.3945/jn.112.174615

15. Walker, C. L. F., Bhutta, Z. A., Bhandari, N., Teka, T., Shahid, F., & Black, R. E. (2010). Zinc supplementation for the treatment of diarrhea in infants in developing countries: A meta-analysis. The Lancet Infectious Diseases, 10(10), 751-762. https://doi.org/10.1016/S1473- 3099(10)70142-3

16. Lazzerini, M., & Wanzira, H. (2013). Oral zinc for treating diarrhoea in children. Cochrane Database of Systematic Reviews, 2013(12), CD005436. https://doi.org/10.1002/14651858. CD005436.pub5

17. Bhutta, Z. A., Bird, S. M., Black, R. E., Brown, K. H., Gardner, J. M., Hidayat, A., ... & Scherpbier, R. W. (2000). Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: Pooled analysis of randomized controlled trials. The American Journal of Clinical Nutrition, 72(6), 1516-1522. https://doi.org/10.1093/ajcn/72.6.1516