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COMPARATIVE EFFICACY OF ORAL ZINC SUPPLEMENTATION VERSUS PROBIOTIC THERAPY IN REDUCING DURATION OF ACUTE DIARRHEA IN CHILDREN UNDER FIVE YEARS

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Abstract

Background: *Acute diarrhoea remains a leading cause of morbidity and mortality among children under five years of age worldwide. Zinc supplementation is recommended by WHO/UNICEF as part of standard therapy, while probiotics are increasingly recognized for their role in restoring gut microbiota and reducing diarrhoeal severity. However, direct comparisons between these two interventions are limited.*

Objectives: *To compare the efficacy of oral zinc supplementation versus probiotic therapy in reducing the duration of acute diarrhoea in children under five years of age.*

Study Design & Setting: *This comparative cross-sectional study was conducted in the pediatric outpatient and emergency departments of Shaikh Zayed Hospital, Lahore between January and June 2025.*

Methodology: *A total of 120 children aged 2 months to 59 months with acute watery diarrhoea of <72 hours' duration were enrolled. Participants were randomly allocated into two groups: zinc group (n=60) receiving oral zinc sulphate for 10 days, and probiotic group (n=60) receiving* Saccharomyces boulardii *for 5 days, along with standard care. The primary outcome was duration of diarrhoea in hours; secondary outcomes included total stool frequency, need for hospitalization, intravenous fluids, adverse events, and caregiver acceptability.*

Results: *The mean duration of diarrhoea was 64.3 ± 18.7 hours in the zinc group and 56.8 ± 16.5 hours in the probiotic group (p=0.01). Mean stool frequency was higher in the zinc group (11.4 ± 3.2 vs. 9.7 ± 2.8; p=0.004). Adverse events were more frequent in the zinc group (15.0% vs. 5.0%), while caregiver acceptability was high in both groups.*

Conclusion: *Probiotic therapy was more effective than zinc supplementation in reducing the duration and stool frequency of acute diarrhoea in children under five, with fewer adverse events and high acceptability.*

INTRODUCTION

Acute diarrhoea remains one of the leading causes of morbidity and mortality among children under five years worldwide, especially in low- and middle-income countries where access to prompt rehydration and supportive care is limited.+ Global estimates and WHO guidance continue to emphasise oral rehydration salts (ORS) and zinc supplementation as standard first-line therapies because of their documented ability to reduce stool output, reduce duration of illness and lower dehydration-related complications.[3] Zinc therapy was widely adopted after trials and meta-analyses demonstrated clinically meaningful reductions in duration and severity of acute diarrhoeal episodes; consequently, WHO/UNICEF recommend zinc (10–20 mg/day for 10–14 days depending on age) as part of routine management.[4] Recent guideline updates and large trials have focused on optimizing zinc dose to retain benefit while minimising side effects such as vomiting; notably, a randomized trial showed that lower zinc doses were non-inferior to the standard 20 mg dose with fewer adverse events, prompting renewed consideration of dose strategies in programmatic use.[5]

Parallel to the zinc evidence base, probiotics have emerged as promising adjuncts for acute childhood diarrhoea. Multiple randomized controlled trials and meta-analyses indicate that certain probiotic strains — particularly Saccharomyces boulardii and selected Lactobacillus and Bifidobacterium species — can shorten diarrhoeal duration and reduce the probability of prolonged illness, with Saccharomyces boulardii frequently ranking highest in network meta-analytic comparisons.[6,7] A multicentre randomized trial of S. boulardii reported reductions in both duration and severity of acute diarrhoea in pediatric patients, and subsequent 2024–2025 systematic reviews and strain-specific analyses have reinforced the yeast's favourable signal, while highlighting heterogeneity by pathogen, strain, dose and study setting.[8]

Despite independent evidence supporting both interventions, the clinical question of comparative efficacy — zinc supplementation versus probiotic therapy — has received limited direct head-to-head investigation. Systematic reviews emphasise heterogeneity across probiotic trials and note that certainty of evidence is often low to moderate due to differences in strains, dosing regimens and outcome definitions.[9] Meanwhile, zinc retains strong programmatic support because of low cost, ease of delivery and broad implementation, though implementation gaps and variable uptake persist across countries.[10]

This comparative assessment is therefore timely and relevant: a rigorously conducted trial or synthesis comparing oral zinc supplementation and probiotic therapy on duration of acute diarrhoea in children under five would clarify relative benefits, adverse events, and contextual applicability. Such evidence could inform national guideline decisions about whether probiotics should be recommended as an alternative or adjunct to zinc, and under what circumstances specific strains or dosing strategies are preferable.

MATERIALS AND METHODS

This comparative cross-sectional was conducted at the pediatric outpatient and emergency departments of Shaikh Zayed Hospital, Lahore and was carried out between January and June 2025. Children aged 2 months to 59 months who presented with acute watery diarrhoea of less than 72 hours' duration and who were otherwise hemodynamically stable were eligible and were enrolled after their caregivers gave written informed consent; children with severe malnutrition (weight-for-height Z-score <-3), dysentery (gross blood in stool), known chronic gastrointestinal disease, recent use of zinc or probiotics within the past 7 days, or with severe systemic illness requiring immediate admission were excluded. A total sample of 120 patients was recruited and were allocated in a 1:1 ratio to receive either oral zinc supplementation or probiotic therapy. Randomization was performed using computer-generated blocks of variable size and allocations were concealed in sequentially numbered, opaque, sealed envelopes which were opened only

after enrolment. The zinc group was given oral zinc sulphate as per WHO recommendations (20 mg once daily for children ≥6 months; 10 mg once daily for infants <6 months) for 10 days, and the probiotic group was given Saccharomyces boulardii sachets (250 mg twice daily) for five days; both interventions were provided in addition to standard care including oral rehydration therapy and feeding advice. Baseline demographic and clinical data including age, sex, duration of diarrhoea prior to presentation, degree of dehydration, and recent antibiotic use were recorded on a predesigned pro forma. The primary outcome was duration of diarrhoea measured in hours from randomization until the last watery stool followed by 48 hours without watery stool; secondary outcomes were total number of stools from randomization to resolution, requirement for intravenous fluids or hospitalization, adverse events (vomiting, rash), and caregiver-reported acceptability. Caregivers were given a stool diary and were telephoned daily until resolution; in cases where caregivers brought the child for follow-up, diaries were cross-checked against clinical notes.

Data were entered into a secure database and were analysed using SPSS version 25. Continuous variables were tested for normality and were summarized as mean ± standard deviation or median (interquartile range) as appropriate; comparisons between groups were made using independent-samples t-test or Mann–Whitney U test, and categorical variables were compared using chi-square or Fisher's exact test. Time-to-resolution was also analysed using Kaplan–Meier survival curves and the log-rank test. A p value <0.05 was considered statistically significant..

RESULTS

The baseline characteristics of the study population were comparable between the two groups. The mean age of children in the zinc group was 28.6 ± 13.4 months, while in the probiotic group it was 29.1 ± 14.2 months. Male gender was predominant in both groups, accounting for 53.3% in the zinc group and 56.7% in the probiotic group. The mean duration of diarrhoea before enrollment was 36.4 ± 15.2 hours in the zinc group and 35.1 ± 14.8 hours in the probiotic group. The distribution of mild and moderate dehydration, as well as recent antibiotic use, was similar across groups, with no statistically significant difference. This shows that both groups were well matched at baseline, as given in table 1.

Regarding the primary outcome, the mean duration of diarrhoea after initiation of therapy was 64.3 ± 18.7 hours in the zinc group compared to 56.8 ± 16.5 hours in the probiotic group, and this difference was statistically significant (p = 0.01). The median duration of diarrhoea was also shorter in the probiotic group (55 hours) compared to the zinc group (62 hours), indicating that probiotics were associated with faster resolution of diarrhoeal episodes, as given in table 2. In terms of secondary outcomes, children in the zinc group passed a higher mean number of stools until resolution (11.4 ± 3.2) compared to the probiotic group (9.7 ± 2.8), and this difference reached statistical significance (p = 0.004). Hospitalization was required in 10% of children in the zinc group versus 5% in the probiotic group, while intravenous fluid administration was needed in 13.3% and 8.3% respectively; both differences were not statistically significant. Adverse events, particularly vomiting, were more frequent in the zinc group (15.0%) compared to the probiotic group (5.0%), though the difference did not reach statistical significance. Caregiver-reported acceptability of therapy was high in both groups, but was slightly higher in the probiotic group (93.3%) compared to the zinc group (86.7%), as given in table 3.

Time-to-resolution analysis using Kaplan–Meier curves showed that the median time to diarrhoea resolution was 63 hours in the zinc group and 54 hours in the probiotic group, and this difference was statistically significant (log-rank p = 0.02). By 72 hours of therapy, 85.0% of children in the probiotic group had recovered compared to 73.3% in the zinc group, and by 96 hours almost all children in both groups had complete resolution of diarrhoea. This demonstrates a faster clinical recovery with probiotics, as given in table 4.

Table 1. Baseline Characteristics of Study Participants (n = 120)

Variable	Zinc Group (n = 60)	Probiotic Group (n = 60)	p-value
Mean age	28.6 ± 13.4	29.1 ± 14.2	0.82
Gender	32 (53.3%)	34 (56.7%)	0.71
	28 (46.7%)	26 (43.3%)	
Mean duration of diarrhea before enrollment	36.4 ± 15.2	35.1 ± 14.8	0.63
Mild dehydration	21 (35.0%)	23 (38.3%)	0.71
Moderate dehydration	39 (65.0%)	37 (61.7%)	0.71
Recent antibiotic use	7 (11.7%)	8 (13.3%)	0.78

Table 2. Primary Outcome: Duration of Diarrhea (hours)

Outcome	Zinc Group (n = 60)	Probiotic Group (n = 60)	p-value
Mean duration ± SD	64.3 ± 18.7	56.8 ± 16.5	0.01
Median (IQR)	62 (52–74)	55 (46–66)	

Table 3. Secondary Outcomes

Outcome	Zinc Group (n = 60)	Probiotic Group (n = 60)	p-value
Mean total stools until resolution	11.4 ± 3.2	9.7 ± 2.8	0.004
Hospitalization required	6 (10.0%)	3 (5.0%)	0.30
IV fluids required	8 (13.3%)	5 (8.3%)	0.38
Adverse events (vomiting)	9 (15.0%)	3 (5.0%)	0.07
Caregiver acceptability	52 (86.7%)	56 (93.3%)	0.23

Table 4. Kaplan–Meier Analysis of Time to Diarrhea Resolution

Variable	Zinc Group (n = 60)	Probiotic Group (n = 60)	Log-rank p-value
Median time to resolution (hours)	63	54	0.02
Resolution at 72 hours, n (%)	44 (73.3%)	51 (85.0%)	
Resolution at 96 hours, n (%)	59 (98.3%)	60 (100%)	

DISCUSSION

Acute diarrhoea remains a major cause of morbidity and mortality in children under five, especially in low- and middle-income countries. Zinc supplementation has been recommended by WHO/UNICEF as part of standard therapy due to its role in reducing stool output and illness duration.[11,12] Probiotics, particularly Saccharomyces boulardii and Lactobacillus species, have shown promise in restoring gut microbiota balance and decreasing diarrhoeal severity.[13,14] Despite evidence supporting both interventions, direct head-to-head comparisons remain limited. Understanding their relative efficacy is crucial for guiding clinical decision-making and policy recommendations. This study was therefore designed to compare the efficacy of oral zinc supplementation versus probiotic therapy in reducing the duration of acute diarrhoea in children under five. Our study found that children receiving probiotic therapy had a significantly shorter mean duration of diarrhoea compared with those receiving zinc supplementation (56.8 ± 16.5 hours vs 64.3 ± 18.7 hours; p = 0.01), a lower mean total stool count until resolution (9.7 ± 2.8 vs 11.4 ± 3.2; p = 0.004), and a higher proportion resolving by 72 hours (85.0% vs 73.3%); vomiting was more frequent in the zinc group (15.0% vs 5.0%). These results are concordant with reports that favour probiotics for more rapid clinical recovery: Arif et al. observed a mean duration of 2.4 days in the probiotic arm versus 3.3 days in controls

(p < 0.001), supporting a probiotic-associated reduction of roughly 0.9 days, which is similar in magnitude to our observed difference of ~7.5 hours (0.31 days) (18). Mateen et al. reported a large and highly significant between-group difference in duration (31.35 ± 2.34 hours vs 24.08 ± 2.50 hours; p = 0.0001), which parallels our finding of shorter duration in one treatment arm and underscores that effect sizes can be substantial when trials use specific strains, dosing and early enrollment criteria.[16] Kakar et al. found that combination therapy (probiotics plus zinc) produced a mean duration of 27.63 ± 14.22 hours compared to 38.86 ± 20.70 hours with probiotics alone (p < 0.001), suggesting additive or synergistic benefits when both agents are used, a consideration relevant to our head-to-head design where we observed benefit with probiotics alone but cannot assess combination effects.[20]

By contrast, Arshad et al. reported shorter mean diarrhoea duration in the zinc group (3.1 ± 1.2 days) than in the probiotic group (3.8 ± 1.4 days; p = 0.008) and lower stool frequency with zinc (4.7 ± 1.1 vs 5.2 ± 1.3; p = 0.021), findings that differ from our results.[15] Similarly, Abbas et al. found that zinc produced a significant reduction in stool frequency at 72 hours (mean 3.94 ± 2.84 vs 5.50 ± 2.77; p = 0.025) and a larger mean change in stool frequency (3.76 ± 0.89 vs 2.29 ± 0.63; p < 0.001), indicating that zinc's benefit on stool output may be pronounced in some populations or dosing regimens.[17] These discrepancies may reflect differences in study populations, baseline severity (our cohort had 65% vs 61.7% with moderate dehydration), timing of intervention (we enrolled within 72 hours), zinc dosing (we used WHO-recommended 20 mg/10 mg), probiotic strain and dose (we used S. boulardii 250 mg twice daily for five days), concomitant antibiotic use (11.7% vs 13.3% in our groups), and single-centre versus multicentre designs. Qamar et al. reported demographic comparability across groups and significant treatment effects on duration and length of stay, consistent with our randomized design which produced comparable baseline characteristics and allowed detection of significant time-to-resolution differences.[19] Regarding safety and resource use, our rates of hospitalization (10.0% vs 5.0%; p = 0.30) and IV fluid use (13.3% vs 8.3%; p = 0.38) did not differ significantly between arms, echoing Arif et al.'s observation of non-significant trends toward reduced hospital stay and IV fluids with probiotics.[18] The higher vomiting rate with zinc in our sample (15.0%) aligns with prior reports of gastrointestinal side effects associated with zinc, which can affect acceptability and adherence.

A key strength of this study was its randomized design, which minimized selection bias. Both groups were well-matched at baseline, ensuring comparability of results.

CONCLUSION

This study demonstrated that probiotic therapy was associated with faster resolution of acute diarrhoea compared to zinc supplementation in children under five. Both interventions were safe and well tolerated, with high caregiver acceptability..

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