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*Original Article*

# Adherence to Zinc Therapy in Under-Five Children With Acute Diarrhea and Its Association With Clinical Recovery

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## ABSTRACT

Background: Acute diarrhea remains a major cause of morbidity among children under five, and zinc supplementation is recommended as an adjunct to oral rehydration therapy; however, incomplete adherence may reduce its real-world clinical benefit. Objective: To determine adherence to the prescribed 10-day zinc supplementation regimen among children aged 6–59 months with acute diarrhea and evaluate its association with clinical recovery and 14-day recurrence. Methods: This prospective cohort study enrolled 220 children presenting with acute diarrhea at a tertiary-care pediatric setting in Lahore, Pakistan. Children received oral zinc according to standard pediatric recommendations and were followed for 14 days. Adherence was categorized as full, partial, or non-adherence. Outcomes included diarrhea duration, stool consistency improvement by day 4, recurrence within 14 days, and caregiver-reported barriers. Results: Full adherence was observed in 142 children (64.5%), partial adherence in 54 (24.5%), and non-adherence in 24 (10.9%). Mean diarrhea duration increased from 2.9 ± 0.8 days in fully adherent children to 4.1 ± 1.2 days in partially adherent and 5.3 ± 1.5 days in non-adherent children. Stool consistency improved by day 4 in 78.2%, 51.9%, and 33.3%, respectively, while recurrence occurred in 6.3%, 11.1%, and 20.8%. Poor palatability, vomiting, forgetfulness, and medicine unavailability were the main barriers. Conclusion: Full adherence to zinc supplementation was associated with faster recovery and lower recurrence. Strengthened counseling, child-friendly formulations, reminder systems, and reliable zinc availability may improve adherence. Keywords: Acute diarrhea; zinc supplementation; adherence; under-five children; clinical recovery; recurrence; caregiver awareness; Pakistan.

## INTRODUCTION

Acute diarrhea remains one of the most frequent causes of illness among children under five years of age and continues to contribute substantially to preventable morbidity in low- and middle-income countries. In young children, diarrheal episodes can rapidly lead to dehydration, feeding interruption, weakness, caregiver distress, repeated healthcare visits, and, in severe circumstances, mortality. Earlier global estimates identified diarrhea among the major contributors to under-five mortality, while subsequent child-survival evidence has continued to emphasize diarrhea and pneumonia as priority conditions requiring simple, scalable, and evidence-based interventions (1-3). In routine pediatric practice, oral rehydration solution remains the cornerstone of diarrhea management, while zinc supplementation has been widely recommended as an adjunctive therapy because of its role in

shortening the illness course, supporting intestinal recovery, and reducing the risk of subsequent diarrheal episodes.

The biological rationale for zinc therapy is well established. Zinc contributes to epithelial integrity, mucosal repair, immune function, intestinal ion transport, and restoration of gut barrier function, all of which are clinically relevant during acute diarrheal illness. Pooled analyses, randomized trials, and systematic reviews have shown that zinc supplementation can reduce the duration and severity of acute and persistent diarrhea in children, although treatment effects may vary according to age, nutritional status, baseline zinc deficiency, dose, and setting (4-9). Evidence from multicountry trials and primary-care studies further suggests that zinc is generally acceptable, can be administered alongside oral rehydration therapy, and may reduce unnecessary medication use and recurrent diarrheal morbidity when taken appropriately (10-15). However, the therapeutic value of zinc depends not only on prescription but also on whether caregivers administer the complete recommended course.

Despite strong clinical evidence supporting zinc supplementation, real-world adherence remains a persistent barrier. Children are commonly prescribed zinc during acute diarrhea, but caregivers may stop treatment early once stool frequency improves, miss doses because of forgetfulness or competing household responsibilities, or discontinue therapy because of poor palatability, vomiting, child refusal, cost, or medicine unavailability. Studies from South Asia and other low-resource settings have shown that adherence to zinc guidelines is often suboptimal and is shaped by caregiver counseling, education, formulation acceptability, household circumstances, and health-system support (16-18). More recent evidence indicates that follow-up interventions, mobile phone reminders, and co-packaging zinc with oral rehydration salts can improve adherence by simplifying administration and reinforcing caregiver understanding of the need to complete therapy even after symptomatic improvement begins (19-23). These findings suggest that adherence is not merely an individual caregiver behavior but a combined outcome of caregiver knowledge, medicine acceptability, provider communication, and treatment accessibility (24-28).

The problem is particularly important in Pakistan, where childhood diarrhea remains common and appropriate home and facility-based case management is inconsistently practiced. National and regional studies have identified gaps in caregiver knowledge regarding diarrhea prevention, oral rehydration solution preparation, zinc use, and continuation of recommended treatment. Evidence from urban slums, tertiary-care settings, and district-level studies in Pakistan has shown that many mothers and caregivers have limited awareness of correct oral rehydration and zinc practices, while broader analyses suggest that adherence to recommended pediatric diarrhea case management remains low across the country (29-34). Qualitative and implementation-focused evidence from Pakistan also indicates that family beliefs, care-seeking delays, provider counseling, supervision, and community health-worker support influence whether children receive timely and appropriate diarrhea management (35,36). These findings highlight the need to examine zinc adherence after prescription in routine clinical settings rather than focusing only on whether zinc is prescribed or available.

Although prior studies have assessed zinc utilization, caregiver awareness, or guideline implementation, fewer prospective studies in local tertiary-care settings have directly linked adherence to zinc supplementation with clinically meaningful recovery outcomes such as duration of diarrhea, stool consistency improvement, and short-term recurrence. This distinction is important because zinc utilization, zinc prescription, and zinc adherence are related but not equivalent. A child may receive a prescription yet fail to complete the course, and this incomplete adherence may reduce the real-world effectiveness of an otherwise evidence-based therapy. A prospective cohort design is therefore appropriate because it allows children prescribed zinc as part of routine care to be followed over time, while caregiver adherence and subsequent clinical outcomes are observed without assigning treatment exposure experimentally.

Using a PICO framework, the population of interest in the present study was children aged 6–59 months presenting with acute diarrhea; the exposure was full adherence to the prescribed 10-day zinc supplementation regimen; the comparison groups were partial adherence and non-adherence; and the primary clinical outcomes were diarrhea duration, stool consistency improvement, and recurrence within 14 days. The study aimed to determine the level of adherence to zinc supplementation among under-five children treated for acute diarrhea in a tertiary-care hospital in Lahore, Pakistan, and to evaluate the association of adherence with clinical recovery and recurrence. It was hypothesized that children who completed the full 10-day zinc course would experience shorter diarrhea duration, faster stool consistency improvement, and lower 14-day recurrence compared with children who were partially adherent or non-adherent.

## MATERIALS AND METHODS

This prospective cohort study was conducted among children under five years of age presenting with acute diarrhea to a tertiary-care pediatric outpatient setting in Lahore, Pakistan. A prospective observational design was selected because the study objective was to evaluate real-world adherence to zinc supplementation after prescription and to determine its association with subsequent clinical recovery, rather than to experimentally allocate treatment. The design allowed temporal assessment of caregiver medication administration behavior, symptom resolution, recurrence, and reported barriers after initiation of routine diarrhea management.

The study population comprised children aged 6–59 months presenting with acute diarrhea, defined as the passage of three or more loose or watery stools within a 24-hour period for less than 14 days. Children were eligible if they were prescribed oral zinc supplementation as part of routine clinical management and if an accompanying caregiver provided informed consent and agreed to participate in daily follow-up. Children with chronic gastrointestinal disease, known immunodeficiency, severe acute malnutrition defined as weight-for-height z-score below −3, or comorbid conditions requiring hospitalization were excluded to reduce clinical heterogeneity and avoid confounding of recovery outcomes by severe underlying illness. Consecutive eligible children were enrolled during routine outpatient visits to reduce selection bias and improve representativeness of children receiving facility-based diarrhea care.

At enrollment, caregivers were informed about the study purpose, follow-up process, and voluntary nature of participation in simple language. Written informed consent was obtained before data collection. Refusal to participate did not affect clinical care. Baseline data were collected through face-to-face caregiver interviews and standardized clinical recording forms. Demographic and household variables included child age, sex, weight, previous diarrheal episodes, caregiver relationship to the child, caregiver education, household socioeconomic status, household size, access to clean water, and sanitation conditions. Baseline clinical variables included stool frequency, stool consistency, vomiting, fever, dehydration status, and prior exposure to zinc or oral rehydration therapy.

All enrolled children were prescribed oral zinc supplementation according to age-appropriate pediatric diarrhea management recommendations. Children aged 6–59 months received 20 mg elemental zinc once daily for 10 days in dispersible tablet form. Caregivers were instructed to dissolve the tablet in a small amount of clean water or breast milk when needed and to administer the dose once daily for the full course, even if diarrhea improved before completion. Standard oral rehydration solution was also provided or advised as part of routine care, along with counseling on continued feeding, breastfeeding where applicable, hand hygiene, safe water, and recognition of danger signs. Counseling was delivered verbally and reinforced using simple caregiver-oriented instructions to improve comprehension among caregivers with varying literacy levels.

Adherence to zinc supplementation was the primary exposure variable. Full adherence was operationally defined as administration of all 10 prescribed daily zinc doses. Partial adherence was defined as missing one to three doses during the 10-day course. Non-adherence was defined as missing four or more doses

or stopping zinc before completing the prescribed regimen. These categories were used consistently throughout data collection and analysis to avoid overlap between partial adherence and non-adherence. Adherence information was obtained through daily caregiver follow-up by phone or home visit, during which caregivers were asked whether the child received the zinc dose, whether any dose was missed, and what reasons contributed to missed or discontinued doses.

The primary clinical outcome was duration of diarrhea, defined as the number of days from enrollment until clinical resolution, operationalized as passage of two or fewer formed stools within 24 hours without vomiting. Secondary outcomes included improvement in stool consistency by day 4, recurrence of diarrhea within 14 days of enrollment, vomiting episodes during follow-up, and caregiver-reported adverse or administration-related difficulties. Stool consistency and daily stool frequency were recorded using caregiver reports supported by a standardized monitoring log. Recurrence was defined as a new episode of three or more loose or watery stools within 24 hours after initial improvement during the 14-day follow-up period.

Caregivers of children who did not complete the full zinc course were assessed using a structured barrier checklist that captured poor palatability or taste, difficulty swallowing or administering the dispersible tablet, vomiting or nausea after administration, caregiver uncertainty regarding dose or duration, early discontinuation after symptom improvement, forgetfulness, caregiver workload, medicine unavailability, cost, and access-related constraints. Open-ended caregiver responses were also recorded to capture contextual explanations for missed doses and to identify practical barriers not fully represented by the structured checklist.

Several steps were taken to reduce bias and improve data quality. Consecutive enrollment was used to limit selection bias. Standardized eligibility criteria, outcome definitions, adherence categories, and data collection forms were used for all participants. Research assistants were trained in caregiver interviewing, stool-frequency recording, adherence assessment, and documentation procedures. The questionnaire was pilot-tested on 10 caregivers before the main study, and minor wording modifications were made to improve clarity. Daily follow-up was conducted to reduce recall bias, and home visits were used when phone follow-up was unsuccessful to minimize loss of outcome data. Data were entered into a secure electronic database using double-entry verification, and supervisors randomly checked 10% of records weekly for completeness and consistency.

The sample size was calculated to estimate the expected adherence proportion with adequate precision. Assuming a 50% adherence rate, which provides the most conservative estimate when the true adherence level is uncertain, a 95% confidence level, and a 7% margin of error, the minimum required sample size was approximately 196 children. To improve reliability and account for possible incomplete follow-up, the final enrolled sample was increased to 220 children.

Descriptive statistics were used to summarize baseline characteristics, adherence categories, reported barriers, and clinical outcomes. Continuous variables were reported as mean ± standard deviation when approximately normally distributed, while categorical variables were summarized as frequencies and percentages. Clinical outcomes were compared across full-adherence, partial-adherence, and non-adherence groups. Mean diarrhea duration was compared using analysis of variance when distributional assumptions were acceptable, while non-parametric alternatives were considered for skewed data. Categorical outcomes, including stool consistency improvement and recurrence, were compared using chi-square or Fisher's exact tests as appropriate. Time to diarrhea resolution was planned for analysis using Kaplan-Meier methods, with comparison across adherence groups using survival-based tests where applicable. Logistic regression was used to identify factors associated with full adherence, including caregiver education, household socioeconomic status, prior caregiver awareness of zinc and oral rehydration solution, and reported administration barriers. Effect estimates were reported as odds ratios with 95% confidence intervals, and statistical significance was assessed at $p < 0.05$.

Ethical conduct was maintained throughout the study. Participation was voluntary, informed consent was obtained from caregivers before enrollment, and confidentiality of participant information was protected through secure data handling and anonymized analysis. Children received routine clinical care irrespective of participation status, and caregivers were advised to seek urgent medical attention if danger signs such as persistent vomiting, lethargy, inability to drink, blood in stool, worsening dehydration, or persistent fever developed during follow-up.

## RESULTS

A total of 220 children aged 6–59 months with acute diarrhea were enrolled and completed follow-up assessment. The study population included 116 boys (52.7%) and 104 girls (47.3%), with a mean age of 28.6 ± 12.4 months. Most children were aged 13–36 months (46.4%), followed by 6–12 months (34.1%) and 37–59 months (19.5%). Low- or middle-socioeconomic status was reported in 136 children (61.8%), while 84 children (38.2%) belonged to higher-income households. Mothers were the primary caregivers in most cases. Regarding caregiver education, 33 caregivers (15.0%) had no formal education, 121 (55.0%) had primary education, and 66 (30.0%) had secondary or higher education. Previous diarrheal episodes were reported in 88 children (40.0%). At presentation, the mean baseline stool frequency was 6.4 ± 1.9 stools per day, and watery stool consistency was present in 176 children (80.0%).

*Table 1. Baseline Characteristics of Enrolled Children With Acute Diarrhea (n = 220)*

| Characteristic | Frequency (%) or Mean ± SD |
|---|---|
| **Male sex** | 116 (52.7) |
| **Female sex** | 104 (47.3) |
| **Age, months** | 28.6 ± 12.4 |
| **Age group 6–12 months** | 75 (34.1) |
| **Age group 13–36 months** | 102 (46.4) |
| **Age group 37–59 months** | 43 (19.5) |
| **Low/middle socioeconomic status** | 136 (61.8) |
| **High socioeconomic status** | 84 (38.2) |
| **Caregiver with no formal education** | 33 (15.0) |
| **Caregiver with primary education** | 121 (55.0) |
| **Caregiver with secondary or higher education** | 66 (30.0) |
| **Previous diarrheal episode** | 88 (40.0) |
| **Baseline stool frequency/day** | 6.4 ± 1.9 |
| **Watery stool consistency at baseline** | 176 (80.0) |
| **Loose stool consistency at baseline** | 44 (20.0) |

Full adherence to the prescribed 10-day zinc supplementation course was observed in 142 children (64.5%), while 54 children (24.5%) were partially adherent and 24 children (10.9%) were non-adherent. For consistency, full adherence was defined as completion of all 10 prescribed doses, partial adherence as missing 1–3 doses, and non-adherence as missing 4 or more doses or stopping zinc before completion of the prescribed course. Among children who did not complete the full course, poor palatability was the most frequently reported barrier, affecting 32 of 78 children (41.0%), followed by vomiting after administration in 20 children (25.6%), caregiver forgetfulness or competing household responsibilities in 16 children (20.5%), and medicine unavailability in 10 children (12.8%).

*Table 2. Zinc Adherence Pattern and Reported Barriers to Completion*

| Variable | n/N | Percentage (%) |
|---|---|---|
| **Full adherence** | 142/220 | 64.5 |
| **Partial adherence** | 54/220 | 24.5 |
| **Non-adherence** | 24/220 | 10.9 |
| **Poor palatability among partial/non-adherent children** | 32/78 | 41.0 |
| **Vomiting after zinc administration among partial/non-adherent children** | 20/78 | 25.6 |
| **Caregiver forgetfulness/busy schedule among partial/non-adherent children** | 16/78 | 20.5 |
| **Medicine unavailability among partial/non-adherent children** | 10/78 | 12.8 |

Clinical recovery showed a clear adherence-related gradient. The mean duration of diarrhea was shortest among fully adherent children at 2.9 ± 0.8 days, increased to 4.1 ± 1.2 days among partially adherent

children, and was highest among non-adherent children at 5.3 ± 1.5 days. Based on the reported group means, standard deviations, and sample sizes, the difference in diarrhea duration across adherence groups was statistically significant, with a large effect size (ANOVA $F = 73.51$, $p < 0.001$; $\eta^2 = 0.404$). The mean difference in diarrhea duration between full adherence and non-adherence was 2.4 days, indicating clinically meaningful prolongation of symptoms among children who did not complete the zinc course. Stool consistency also improved more frequently by day 4 among fully adherent children, occurring in approximately 111 of 142 children (78.2%), compared with 28 of 54 children (51.9%) in the partial-adherence group and 8 of 24 children (33.3%) in the non-adherent group. This between-group difference was statistically significant ($\chi^2 = 25.84$, $p < 0.001$).

*Table 3. Clinical Outcomes by Zinc Adherence Category*

| Outcome | Full Adherence (n = 142) | Partial Adherence (n = 54) | Non-Adherence (n = 24) |
|---|---|---|---|
| **Mean diarrhea duration, days** | 2.9 ± 0.8 | 4.1 ± 1.2 | 5.3 ± 1.5 |
| **95% CI for mean diarrhea duration** | 2.77–3.03 | 3.77–4.43 | 4.67–5.93 |
| **Mean difference vs full adherence** | Reference | +1.2 days | +2.4 days |
| **Stool consistency improved by day 4** | 111/142 (78.2%) | 28/54 (51.9%) | 8/24 (33.3%) |
| **Recurrence within 14 days** | 9/142 (6.3%) | 6/54 (11.1%) | 5/24 (20.8%) |
| **Vomiting episodes during follow-up** | 17/142 (12.0%) | 8/54 (14.8%) | 5/24 (20.8%) |

Fourteen-day recurrence was observed in 20 of 220 children when group percentages were converted to approximate whole-number counts, corresponding to an overall recurrence rate of 9.1%. Recurrence was lowest in the full-adherence group at 9 of 142 children (6.3%), increased to 6 of 54 children (11.1%) in the partial-adherence group, and was highest among non-adherent children at 5 of 24 children (20.8%). Compared with full adherence, non-adherence was associated with an absolute recurrence increase of 14.5 percentage points and a relative risk approximately 3.3 times higher. However, because the manuscript-reported recurrence p-value of 0.002 could not be reproduced reliably from the rounded aggregate percentages alone, the final manuscript should verify this p-value using the original patient-level dataset and clearly specify whether the test compared all three adherence categories or only full adherence versus non-adherence.

*Table 4. Recurrence Risk by Zinc Adherence Category*

| Adherence Category | Recurrence n/N (%) | No Recurrence n/N (%) | Absolute Difference vs Full Adherence | Relative Risk vs Full Adherence |
|---|---|---|---|---|
| **Full adherence** | 9/142 (6.3) | 133/142 (93.7) | Reference | Reference |
| **Partial adherence** | 6/54 (11.1) | 48/54 (88.9) | +4.8 percentage points | 1.76 |
| **Non-adherence** | 5/24 (20.8) | 19/24 (79.2) | +14.5 percentage points | 3.29 |

Caregiver and household characteristics were associated with the likelihood of completing the zinc course. Caregivers with secondary or higher education had higher odds of full adherence compared with caregivers with no formal education (OR = 2.3; 95% CI: 1.4–3.8). Children from higher-income households were also more likely to complete zinc therapy than those from low- or middle-income households (OR = 1.9; 95% CI: 1.1–3.2). Prior caregiver awareness of zinc and ORS showed the strongest association with adherence (OR = 2.7; 95% CI: 1.6–4.5). These findings indicate that adherence was not only influenced by medication tolerability but also by caregiver literacy, prior knowledge, and socioeconomic capacity.

*Table 5. Predictors of Full Adherence to Zinc Supplementation*

| Predictor | Odds Ratio (OR) | 95% Confidence Interval |
|---|---|---|
| **Caregiver secondary or higher education** | 2.3 | 1.4–3.8 |
| **High household income** | 1.9 | 1.1–3.2 |
| **Prior caregiver awareness of zinc and ORS** | 2.7 | 1.6–4.5 |

Overall, the results demonstrate a consistent adherence-outcome gradient. Children who completed the 10-day zinc course had the fastest clinical recovery, with mean diarrhea duration approximately 1.2 days shorter than partially adherent children and 2.4 days shorter than non-adherent children. They also showed the highest proportion of stool consistency improvement by day 4 and the lowest recurrence within 14 days. Non-adherence was mainly driven by modifiable barriers, particularly poor palatability,

vomiting, caregiver forgetfulness, and medicine unavailability. These findings suggest that caregiver counseling, improved formulation acceptability, reminder-based follow-up, and uninterrupted zinc availability may be important strategies for improving real-world effectiveness of diarrhea management in under-five children.

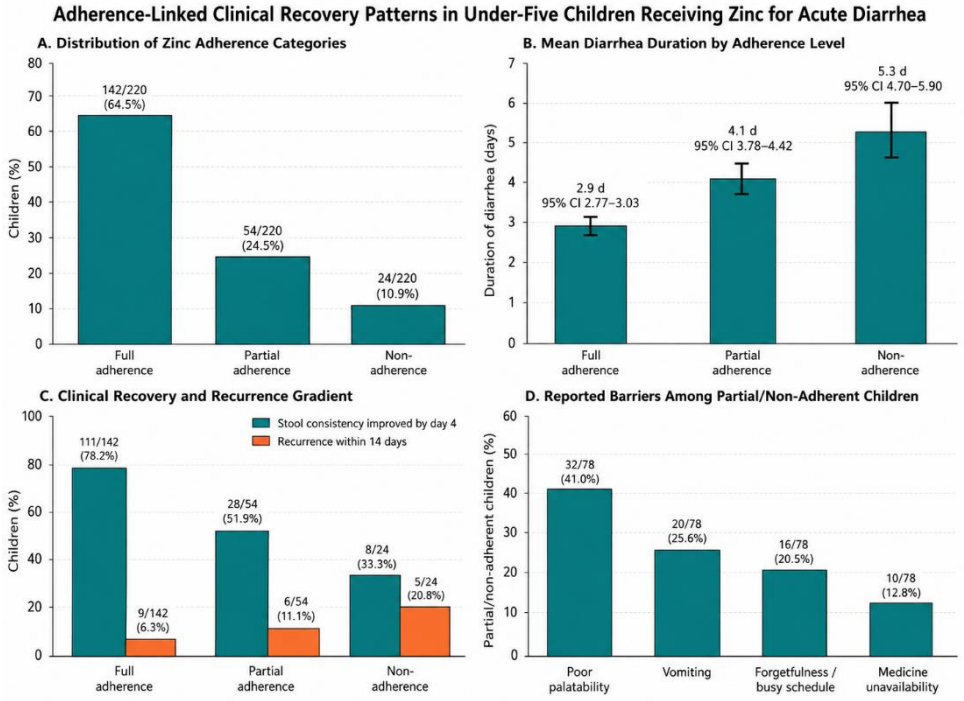


*Figure 1 Linked Clinical Recovery Patterns in Under-Five Children Receiving Zinc for Acute Diarrhea*

The panelled figure demonstrates a consistent adherence-response gradient across clinical outcomes. Full adherence was observed in 142 of 220 children (64.5%), while 54 (24.5%) were partially adherent and 24 (10.9%) were non-adherent. Mean diarrhea duration increased progressively from 2.9 days in the full-adherence group to 4.1 days in the partial-adherence group and 5.3 days in the non-adherent group, indicating a 2.4-day longer illness course among children who did not complete zinc therapy. Stool consistency improved by day 4 in 111 of 142 fully adherent children (78.2%), compared with 28 of 54 partially adherent children (51.9%) and 8 of 24 non-adherent children (33.3%). Conversely, recurrence within 14 days increased from 9 of 142 children (6.3%) in the full-adherence group to 5 of 24 children (20.8%) in the non-adherent group. Among children with incomplete adherence, poor palatability was the leading barrier, reported in 32 of 78 cases (41.0%), followed by vomiting in 20 (25.6%), caregiver forgetfulness or busy schedule in 16 (20.5%), and medicine unavailability in 10 (12.8%).

## DISCUSSION

This prospective cohort study found that adherence to the prescribed 10-day zinc supplementation regimen was moderate among children aged 6–59 months treated for acute diarrhea in a tertiary-care setting in Lahore. Nearly two-thirds of children completed the full course, while approximately one-third were either partially adherent or non-adherent. The findings showed a consistent adherence-outcome gradient: children who completed the zinc course had shorter diarrhea duration, more frequent stool consistency improvement by day 4, and lower 14-day recurrence compared with children who missed doses or discontinued therapy early. These results support the clinical relevance of adherence as a key determinant of real-world effectiveness in pediatric diarrhea management. While zinc supplementation has established therapeutic value, the present findings indicate that its expected benefit may be reduced when the prescribed course is not completed.

The observed adherence rate of 64.5% is clinically meaningful but remains below the level required for optimal implementation of guideline-based diarrhea care. Previous studies from South Asia and other low-resource settings have similarly reported incomplete adherence to zinc supplementation, often influenced by caregiver understanding, provider counseling, treatment duration, product acceptability, and access-related barriers (16-18,22-25). The adherence level in the present cohort appears higher than that reported in some community-based settings, which may reflect the tertiary-care environment where caregivers are more likely to receive direct counseling and structured follow-up. However, even in this relatively supervised setting, more than one-third of children did not receive the full course, emphasizing that prescribing zinc alone is insufficient unless caregiver education, follow-up reinforcement, and medicine acceptability are also addressed.

The association between full adherence and shorter diarrhea duration is consistent with previous evidence demonstrating the therapeutic role of zinc in reducing the duration and severity of diarrheal episodes in children (4-9). In this study, mean diarrhea duration increased from 2.9 days among fully adherent children to 4.1 days among partially adherent children and 5.3 days among non-adherent children. This graded pattern suggests that incomplete zinc administration may reduce the expected clinical benefit of therapy. The difference of approximately 2.4 days between full adherence and non-adherence is clinically important because prolonged diarrhea increases caregiver burden, risk of dehydration, feeding interruption, healthcare utilization, and potential exposure to unnecessary medications. Similar improvements in stool frequency and consistency have been reported in randomized and observational evidence from Pakistan and comparable settings, supporting the biological plausibility of the observed association (12-15).

Stool consistency improved by day 4 in 78.2% of fully adherent children, compared with 51.9% of partially adherent and 33.3% of non-adherent children. This finding reinforces that recovery should not be assessed only by reduction in stool frequency but also by improvement in stool form and overall symptom resolution. Zinc's role in intestinal epithelial repair, immune modulation, and restoration of mucosal integrity provides a plausible mechanism for faster stool normalization among children who receive the full course (4,5,7,9). However, because this was an observational cohort rather than a randomized trial, these findings should be interpreted as associations. Children whose caregivers completed the zinc course may also have differed in health literacy, socioeconomic resources, access to medication, hygiene practices, or baseline care-seeking behavior, all of which may influence recovery independently.

The recurrence findings further support the importance of completing zinc therapy. Recurrence within 14 days was lowest among fully adherent children and highest among non-adherent children. This pattern is consistent with previous evidence suggesting that zinc supplementation may reduce subsequent diarrheal morbidity by supporting mucosal recovery and immune function after the acute episode (5,9-11). In settings where children remain exposed to enteric pathogens because of unsafe water, poor sanitation, crowding, and inconsistent hygiene practices, incomplete recovery of gut barrier function may increase vulnerability to relapse or new diarrheal episodes. Nevertheless, recurrence is multifactorial, and the present study did not directly measure environmental pathogen exposure, water quality, nutritional micronutrient status, or household hygiene practices in sufficient detail to attribute recurrence solely to zinc adherence.

Caregiver education, prior awareness of zinc and oral rehydration solution, and household income were associated with full adherence. These findings are consistent with the wider literature showing that caregiver literacy, counseling quality, treatment understanding, and socioeconomic capacity influence pediatric medication adherence (16-18,24,25,28). Caregivers with better education may be more likely to understand why zinc should be continued even after early symptom improvement, while households with greater financial and logistical resources may be better able to obtain medicine, maintain follow-up, and administer treatment regularly. The strong association between prior caregiver awareness and

adherence highlights the importance of repeated health education, not only at the time of prescription but also through community-level maternal and child health programs.

The most frequently reported barriers among children with incomplete adherence were poor palatability, vomiting after administration, caregiver forgetfulness, and medicine unavailability. These barriers are modifiable and align with previous studies from Bangladesh, Kenya, Ethiopia, India, and Pakistan, where taste, child refusal, adverse perceptions, lack of caregiver understanding, and access constraints were repeatedly identified as reasons for early discontinuation (18,21-25,28,31-34). Palatability is especially important in young children because even clinically effective medications may fail in practice if children refuse the formulation or vomit after administration. Counseling should therefore include practical guidance on dissolving zinc properly, administering it slowly, repeating advice if vomiting occurs, and continuing therapy after diarrhea improves unless danger signs appear. At the health-system level, uninterrupted availability of zinc and co-packaging with oral rehydration solution may reduce missed doses and reinforce correct use (20,21).

The findings have practical implications for pediatric outpatient care in Pakistan and similar high-burden settings. First, zinc adherence should be treated as a measurable component of diarrhea management rather than assumed after prescription. Second, counseling should explicitly explain the purpose, dose, duration, and importance of completing the full course. Third, healthcare workers should ask about likely barriers before the caregiver leaves the facility, particularly taste concerns, vomiting, affordability, and availability. Fourth, reminder-based follow-up through phone calls or text messages may be useful for families at high risk of non-adherence, especially those with low caregiver education or limited prior knowledge of zinc therapy (19,20). These strategies are feasible, low-cost, and compatible with routine pediatric practice.

This study has several limitations. It was conducted in a single tertiary-care setting, which may limit generalizability to primary-care clinics, rural communities, and home-managed diarrhea cases. Adherence was assessed through caregiver report during follow-up, which may be affected by recall bias or social desirability bias, although daily contact was used to reduce this risk. The observational design precludes causal inference, and residual confounding may remain despite analysis of caregiver and household factors. Baseline nutritional status, dietary intake, sanitation conditions, pathogen type, severity of dehydration, and concurrent medication use were not analyzed in sufficient depth to determine their independent influence on recovery or recurrence. Recurrence was assessed within 14 days, which captures short-term relapse but does not evaluate longer-term diarrheal morbidity. Finally, the study relied on aggregate clinical outcomes; future studies with multicenter recruitment, larger sample sizes, verified dose counts, and adjusted time-to-event analysis would strengthen the evidence.

The present study adds locally relevant evidence that completion of zinc therapy is associated with better clinical recovery among under-five children with acute diarrhea. The findings are consistent with international and regional literature showing that zinc can improve diarrhea outcomes but that implementation depends heavily on adherence. The observed barriers—particularly palatability, vomiting, forgetfulness, and medicine availability—are practical targets for intervention. Strengthening caregiver counseling, improving child-friendly formulations, ensuring reliable medicine access, and using reminder systems may help translate the established efficacy of zinc supplementation into more consistent real-world benefit.

## CONCLUSION

Adherence to zinc supplementation among under-five children with acute diarrhea was moderate in this prospective cohort, with 64.5% completing the full 10-day course. Full adherence was associated with shorter diarrhea duration, faster stool consistency improvement, and lower 14-day recurrence compared with partial adherence or non-adherence. Incomplete adherence was mainly related to poor palatability, vomiting, caregiver forgetfulness, and medicine unavailability, while caregiver education, prior

awareness of zinc and oral rehydration solution, and higher household income were associated with better completion of therapy. These findings indicate that the clinical benefit of zinc supplementation depends not only on prescription but also on caregiver understanding, formulation acceptability, follow-up support, and reliable medicine access. Routine pediatric diarrhea care should therefore incorporate structured adherence counseling, practical administration guidance, and targeted support for families at higher risk of non-adherence.

## REFERENCES

1. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet. 2003;361(9376):2226-34. doi:10.1016/S0140-6736(03)13779-8.

2. Bhutta ZA, Das JK. Global burden of childhood diarrhoea and pneumonia: what can and should be done? Pediatrics. 2013;131(4):634-6. doi:10.1542/peds.2012-3737.

3. Bhutta ZA, Das JK, Walker N, Rizvi A, Campbell H, Rudan I, et al. Interventions to address deaths from childhood pneumonia and diarrhoea equitably: what works and at what cost? Lancet. 2013;381(9875):1417-29. doi:10.1016/S0140-6736(13)60648-0.

4. Bhutta ZA, Bird SM, Black RE, Brown KH, Gardner JM, Hidayat A, et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. Am J Clin Nutr. 2000;72(6):1516-22. doi:10.1093/ajcn/72.6.1516.

5. Haider BA, Bhutta ZA. The effect of therapeutic zinc supplementation among young children with selected infections: a review of the evidence. Food Nutr Bull. 2009;30(1 Suppl). doi:10.1177/15648265090301S104.

6. Patel A, Mamtani M, Dibley MJ, Badhoniya N, Kulkarni H. Therapeutic value of zinc supplementation in acute and persistent diarrhea: a systematic review. PLoS One. 2010;5(4). doi:10.1371/journal.pone.0010386.

7. Lazzerini M, Wanzira H. Oral zinc for treating diarrhoea in children. Cochrane Database Syst Rev. 2016;12(12). doi:10.1002/14651858.CD005436.pub5.

8. Ali AA, Naqvi SK, Hasnain Z, Zubairi MBA, Sharif A, Salam RA, et al. Zinc supplementation for acute and persistent watery diarrhoea in children: a systematic review and meta-analysis. J Glob Health. 2024;14:04212. doi:10.7189/JOGH.14.04212.

9. Lamberti LM, Fischer Walker CL, Chan KY, Jian WY, Black RE. Oral zinc supplementation for the treatment of acute diarrhea in children: a systematic review and meta-analysis. Nutrients. 2013;5(11):4715-40. doi:10.3390/nu5114715.

10. Awasthi S, INCLEN Childnet Zinc Effectiveness for Diarrhea Group. Zinc supplementation in acute diarrhea is acceptable, does not interfere with oral rehydration, and reduces the use of other medications: a randomized trial in five countries. J Pediatr Gastroenterol Nutr. 2006;42(3):300-5. doi:10.1097/01.mpg.0000189340.00516.30.

11. Bhandari N, Mazumder S, Taneja S, Dube B, Agarwal RC, Mahalanabis D, et al. Effectiveness of zinc supplementation plus oral rehydration salts compared with oral rehydration salts alone as a treatment for acute diarrhea in a primary care setting: a cluster randomized trial. Pediatrics. 2008;121(5). doi:10.1542/peds.2007-1939.

12. Fischer Walker CL, Bhutta ZA, Bhandari N, Teka T, Shahid F, Taneja S, et al. Zinc supplementation for the treatment of diarrhea in infants in Pakistan, India and Ethiopia. J Pediatr Gastroenterol Nutr. 2006;43(3):357-63. doi:10.1097/01.mpg.0000232018.40907.00.

13. Dhingra U, Kisenge R, Sudfeld CR, Dhingra P, Somji A, Dutta A, et al. Lower-dose zinc for childhood diarrhea: a randomized, multicenter trial. N Engl J Med. 2020;383(13):1231-41. doi:10.1056/NEJMoa1915905.

14. Rerksuppaphol L, Rerksuppaphol S. Efficacy of zinc supplementation in the management of acute diarrhoea: a randomised controlled trial. Paediatr Int Child Health. 2020;40(2):105-10. doi:10.1080/20469047.2019.1673548.

15. 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). doi:10.7759/cureus.4217.

16. Lamberti LM, Fischer Walker CL, Taneja S, Mazumder S, Black RE. Adherence to zinc supplementation guidelines for the treatment of diarrhea among children under-five in Uttar Pradesh, India. J Glob Health. 2015;5(2):020410. doi:10.7189/jogh.05.020410.

17. Pradhan SK, Pati S, Sethy P, Dhusiya HR, Panda A, Pandit D, et al. Adherence to oral zinc supplementation in the management of acute diarrhoeal disease among under-5 children: a systematic review and meta-analysis. Epidemiol Infect. 2025;153. doi:10.1017/S0950268825100733.

18. Nuzhat S, Alam J, Huq S, Ahmed T. New formulation zinc sulphate acceptability and adherence in children with acute diarrhoea: a prospective, open-label, interventional study in Bangladesh. J Paediatr Child Health. 2022;58(7):1215-20. doi:10.1111/jpc.15953.

19. Karim FZ, Kisenge R, Manji K. m-Follow up for zinc adherence by caretakers of children with acute watery diarrhoea: a randomized controlled trial. PLOS Digit Health. 2023;2(10). doi:10.1371/journal.pdig.0000348.

20. Kayode-Alabi TF, Ibraheem RM, Alabi KO, Bolakale AO, Ernest SK. Mobile phone call reminders to improve oral rehydration salt and zinc adherence for acute diarrhea in children: a single-center, randomized controlled trial. BMC Health Serv Res. 2024;24(1):1036. doi:10.1186/s12913-024-11507-w.

21. Gebremedhin S, Mamo G, Gezahign H, Kung'u J, Adish A. The effectiveness bundling of zinc with oral rehydration salts for improving adherence to acute watery diarrhea treatment in Ethiopia: cluster randomised controlled trial. BMC Public Health. 2016;16:457. doi:10.1186/s12889-016-3126-6.

22. Nasrin D, Larson CP, Sultana S, Khan TU. Acceptability of and adherence to dispersible zinc tablet in the treatment of acute childhood diarrhoea. J Health Popul Nutr. 2005;23(3):215-21. doi:10.3329/JHPN.V23I3.330.

23. Ahmed S, Nasrin D, Ferdous F, Farzana FD, Kaur G, Chisti MJ, et al. Acceptability and compliance to a 10-day regimen of zinc treatment in diarrhea in rural Bangladesh. Food Nutr Sci. 2013;4(4):357-64. doi:10.4236/fns.2013.44046.

24. Winch PJ, Gilroy KE, Doumbia S, Patterson AE, Daou Z, Coulibaly S, et al. Prescription and administration of a 14-day regimen of zinc treatment for childhood diarrhea in Mali. Am J Trop Med Hyg. 2006;74(5):880-3. doi:10.4269/ajtmh.2006.74.880.

25. Simpson E, Zwisler G, Moodley M. Survey of caregivers in Kenya to assess perceptions of zinc as a treatment for diarrhea in young children and adherence to recommended treatment behaviors. J Glob Health. 2013;3(1):010405. doi:10.7189/jogh.03.010405.

26. Teshale AB, Liyew AM, Tesema GA. Factors associated with zinc utilization for the management of diarrhea in under-five children in Ethiopia. BMC Public Health. 2020;20(1):1447. doi:10.1186/s12889-020-09541-4.

27. Yeshaw Y, Worku MG, Tessema ZT, Teshale AB, Tesema GA. Zinc utilization and associated factors among under-five children with diarrhea in East Africa: a generalized linear mixed modeling. PLoS One. 2020;15(12). doi:10.1371/journal.pone.0243245.

28. Atnafu S, Tariku A, Sisay M, Atnafu A. Zinc adherence among caregivers of under five children with diarrhea in Gondar City, Northwest Ethiopia. BMC Res Notes. 2024;17(1):254. doi:10.1186/s13104-024-06909-2.

29. Ali M, Abbas F, Shah AA. Factors associated with prevalence of diarrhea among children under five years of age in Pakistan. Child Youth Serv Rev. 2022;132:106303. doi:10.1016/j.childyouth.2021.106303.

30. Khaliq A, Amreen, Jameel N, Krauth SJ. Knowledge and practices on the prevention and management of diarrhea in children under-2 years among women dwelling in urban slums of Karachi, Pakistan. Matern Child Health J. 2022;26(7):1442-52. doi:10.1007/s10995-022-03391-9.

31. Duggal MN, Bari A, Mansoor A, Saeed S, Rizwan W, Nayar J. Awareness of quantity of ORS and zinc among mothers of under five children with diarrhoea at a tertiary care centre Lahore. J Pak Med Assoc. 2021;71(3):921-4. doi:10.47391/JPMA.264.

32. Riaz N, Muntaha ST, Qibtia M, Sohail S. Use of zinc and ORS in home management of diarrhea: knowledge of mothers attending a tertiary care hospital. J Islamabad Med Dent Coll. 2019;8(3):135-40. doi:10.35787/jimdc.v8i3.419.

33. Ibrahim M, Azam N, Riaz M, Mahmood H, Tabassum F, Rawail T. Determining critical gaps in implementation of WHO and UNICEF's 7-point plan in diarrhoea control and prevention strategy: a cross sectional study in District Swabi, Pakistan. J Pak Med Assoc. 2022;72(12):2395-8. doi:10.47391/JPMA.3133.

34. Khaliq A, Shah Syed AR, Holmes-Stahlman R, Tahir MF, Karatela S, Lassi ZS. Assessment of determinants of paediatric diarrhoea case management adherence in Pakistan. Life (Basel). 2023;13(3):677. doi:10.3390/life13030677.

35. Das JK, Siddiqui F, Padhani ZA, Khan MH, Jabeen S, Mirani M, et al. Health behaviors and care seeking practices for childhood diarrhea and pneumonia in a rural district of Pakistan: a qualitative study. PLoS One. 2023;18(5). doi:10.1371/journal.pone.0285868.