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Comparison of Zinc Plus Probiotics Therapy versus Probiotics Alone for Treatment of Acute Diarrhea in Children

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ABSTRACT

Background: Acute diarrhea is a major cause of morbidity in children under five years of age, particularly in developing countries. **Objective:** To compare the efficacy of zinc plus probiotics therapy versus probiotics alone in the treatment of acute diarrhea in children. **Methods:** This randomized controlled trial was conducted at the Department of Pediatrics, Hameed Latif Hospital, Lahore, from January 2025 to May 2025. A total of 80 children aged 3–60 months with acute diarrhea were enrolled and randomly allocated into two groups: Group ZP (zinc plus probiotics, n=40) and Group P (probiotics only, n=40). Group ZP received oral zinc (20 mg/day) for 10 days along with *Bacillus clausii* probiotics for 5 days, while Group P received probiotics alone. Outcomes measured included duration of diarrhea after treatment, total hospital stay, and recovery within five days. **Results:** The mean duration of diarrhea after treatment was significantly lower in Group ZP (28.4 ± 13.6 hours) compared to Group P (39.7 ± 18.9 hours) (p=0.004). The mean hospital stay was also shorter in Group ZP (2.6 ± 0.8 days) compared to Group P (3.3 ± 1.1 days) (p=0.002). Recovery within five days was achieved in 90.0% of children in the zinc plus probiotics group versus 72.5% in the probiotics-only group (p=0.04). **Conclusion:** Zinc plus probiotics therapy is more effective than probiotics alone in reducing the duration of diarrhea, shortening hospital stay, and improving recovery in children with acute diarrhea.

INTRODUCTION

Globally, one of the leading causes of childhood disability and mortality is diarrhea that claims 5-10 million lives every year. In Asia, Africa, and Latin America, the age group 0 4 years of age is the top cause of death due to diarrhea [1]. The greatest effects of diarrheal diseases include dehydration, malnutrition, retarded physical growth and early childhood death [2]. The closely related research hotspot has been the intestinal microbiota, which is closely related to human health. Intestinal microflora derangement is the characteristic of diarrhea [3]. Since the intestinal bacteria in children with acute diarrhea is not balanced, probiotics supplement is significant, as it may lead to the improvement of the intestinal microenvironment, the immunity, and resistance [4]. Apart from oral rehydration solution, continued feeding and oral zinc therapy the administration of adequate amounts of probiotics seems beneficial for acute diarrheal episodes in children in the developing world [5]. The right dose of zinc supplementation can work to reduce severity of diarrhea that will occur thereafter. Certain particular in the case of probiotics, including Lactobacillus GG, L. Reuteri, Saccharomyces boulardii, and Bifidobacteria species, have been shown to have an important role in defeating the acute diarrhea problem in children, particularly the length and intensity of diarrhea [6].

It was reported in a study conducted in Quetta that all 100% children who took a combination of probiotics and zinc recovered the diarrhea and 94.4% children recovered the diarrhea within 5 days after the start of the treatment in the probiotics only group (p=0.04). The probiotics plus zinc group and probiotics only group had duration of diarrhea 27.63±14.22 and 38.86±20.70 hours respectively (p<0.001) [7]. In another trial, the final results were that by the conclusion of the 3rd day collective total of 96% patients in probiotics plus zinc had enhanced consistency of stools as well as diminished frequency of diarrhea <3 stools each day whilst those in the probiotics alone group showed response to treatment in 72 hours [8]. Zinc-probiotic therapy was seen to be more effective in the reduction of the severity of acute diarrhea compared to zinc therapy alone in children under the age of five [9]. The objectives of treating acute diarrhea are mainly based on preventing dehydration and nutritional status. Oral

rehydration therapy (ORT) has been the mainstay of therapy and has helped to eliminate a good number of deaths related to diarrheal diseases. Nevertheless, ORT does not shorten or lessen the length or severity of diarrhea that may extend the disease and place a patient at risk of complications. Consequently, adjunct treatments with the capacity to reduce the length of the diarrhea and enhance recovery have become more and more popular [10] [11].

Objective

To compare the outcome of zinc plus probiotics therapy versus probiotics alone for treatment of acute diarrhea in children

METHODOLOGY

This Randomized controlled trial was conducted at Department of Pediatrics, Hameed Latif Hospital, Lahore, from January 2025 to May 2025. A total of 80 children were included in the study, with 40 patients in each group. The sample size was calculated using OpenEpi with a 95% confidence level and 80% power of study, based on a mean duration of diarrhea of 27.63 ± 14.22 hours in the zinc plus probiotics group and 38.86 ± 20.70 hours in the probiotics-only group. Non-probability consecutive sampling was used to recruit eligible patients presenting to the pediatric emergency department. Children aged 3–60 months of either gender, diagnosed with acute diarrhea according to the operational definition, were included in the study. Children who had received treatment for diarrhea for more than three days prior to presentation, those with dysentery, severe malnutrition, septicemia, inflammatory diseases, congenital cardiac anomalies, or immunodeficiency conditions were excluded. Additionally, children who had received medications such as antibiotics or antiprotozoal drugs (except fluids and zinc) prior to admission were not included.

Data Collection

After obtaining approval from the institutional ethical review board, a total of 80 children meeting the inclusion criteria were enrolled through the pediatric emergency department. Written informed consent was obtained from the parents or guardians. Baseline demographic data including age, gender, weight, duration of diarrhea before presentation, residence, socioeconomic status, source of drinking water, and feeding pattern (liquid, semi-solid, or solid) were recorded. All enrolled children were admitted to the pediatric ward and randomly allocated into two groups using the lottery method. In Group ZP (zinc plus probiotics), children received oral zinc sulfate monohydrate 5 mL twice daily for 10 days (total 20 mg/day) along with oral *Bacillus clausii* probiotic suspension 5 mL twice daily for 5 days, with each vial containing 2 million spores (total 4 million spores/day). In Group P (probiotics only), children received oral *Bacillus clausii* probiotic suspension 5 mL twice daily for 5 days at the same dosage. All patients were monitored in the pediatric ward until recovery and discharge. Recovery was defined as normalization of stool consistency with fewer than three stools per day within five days. The duration required to achieve complete recovery and total hospital stay were recorded. Children with persistent diarrhea were managed according to standard treatment protocols. All data were recorded using a structured proforma (attached).

Data Analysis

Data were entered and analyzed using SPSS version 26.0. The Shapiro-Wilk test was applied to assess normality of continuous variables. Quantitative variables such as age, weight, duration of diarrhea before presentation, duration of diarrhea after treatment, and total hospital stay were expressed as mean ± standard deviation (SD). Qualitative variables including gender, residence, socioeconomic status, water source, feeding pattern, and recovery status were presented as frequencies and percentages. Comparison between the two groups for mean duration of diarrhea after treatment and total hospital stay was performed using the independent samples t-test, while recovery rates were compared using the Chi-square test. A p-value ≤0.05 was considered statistically significant.

RESULTS

Both groups were comparable at baseline with no significant differences. Mean age (26.8 ± 12.4 vs 27.5 ± 13.1 months, p=0.81), gender (57.5% vs 55.0% males, p=0.82), weight (10.6 ± 2.3 vs 10.4 ± 2.5 kg, p=0.72), and pre-treatment diarrhea duration (2.1 ± 0.9 vs 2.3 ± 1.0 days, p=0.38) were similar. Sociodemographic and feeding variables were also evenly distributed (all p>0.05), confirming good group comparability.

Table 1

Baseline Demographic and Clinical Characteristics (n = 80)

Variable	Category	Group ZP (Zinc + Probiotics) (n=40)	Group P (Probiotics Only) (n=40)	p-value
Age (months)	—	26.8 ± 12.4	27.5 ± 13.1	0.81
Gender	Male	23 (57.5%)	22 (55.0%)	0.82
	Female	17 (42.5%)	18 (45.0%)	
Weight (kg)	—	10.6 ± 2.3	10.4 ± 2.5	0.72
Duration of Diarrhea Before Presentation (days)	—	2.1 ± 0.9	2.3 ± 1.0	0.38
Residence	Urban	25 (62.5%)	24 (60.0%)	0.81
	Rural	15 (37.5%)	16 (40.0%)	
Socioeconomic Status	Low	18 (45.0%)	19 (47.5%)	0.84
	Middle/High	22 (55.0%)	21 (52.5%)	
Water Source	Safe	26 (65.0%)	24 (60.0%)	0.64
	Unsafe	14 (35.0%)	16 (40.0%)	
Feeding Pattern	Liquid	14 (35.0%)	13 (32.5%)	0.88
	Semi-solid/Solid	26 (65.0%)	27 (67.5%)	

Group ZP showed significantly better outcomes, with shorter diarrhea duration (28.4 ± 13.6 vs 39.7 ± 18.9 hours, mean difference −11.3, p=0.004) and reduced hospital stay (2.6 ± 0.8 vs 3.3 ± 1.1 days, mean difference −0.7, p=0.002).

Table 2

Comparison of Clinical Outcomes Between Groups

Variable	Group ZP (Mean ± SD)	Group P (Mean ± SD)	Mean Difference	p-value
Duration of Diarrhea After Treatment (hours)	28.4 ± 13.6	39.7 ± 18.9	-11.3	0.004
Total Hospital Stay (days)	2.6 ± 0.8	3.3 ± 1.1	-0.7	0.002

A total of 36 patients (90.0%) in Group ZP recovered compared to 29 patients (72.5%) in Group P, while non-recovery was observed in only 10.0% versus 27.5% respectively (p=0.04). This demonstrates a clinically meaningful improvement in recovery outcomes with the addition of zinc.

Table 3
Recovery Outcome Within 5 Days

Outcome	Group ZP (n=40)	Group P (n=40)	p-value
Recovered	36 (90.0%)	29 (72.5%)	0.04
Not Recovered	4 (10.0%)	11 (27.5%)	

Across all subgroups, Group ZP consistently had shorter diarrhea duration. ≤24 months (27.9 ± 12.8 vs 38.5 ± 17.6, p=0.01), >24 months (29.2 ± 14.2 vs 40.8 ± 19.9, p=0.02), males (28.1 ± 13.4 vs 39.3 ± 18.7, p=0.01), females (28.8 ± 14.0 vs 40.2 ± 19.3, p=0.02), liquid diet (27.5 ± 12.9 vs 38.1 ± 17.8, p=0.02), and semi-solid/solid (29.0 ± 13.9 vs 40.5 ± 19.5, p=0.01), confirming consistent benefit of zinc.

Table 4
Stratified Comparison of Duration of Diarrhea (hours)

Variable	Category	Group ZP (Mean ± SD)	Group P (Mean ± SD)	p-value
Age	≤24 months	27.9 ± 12.8	38.5 ± 17.6	0.01
	>24 months	29.2 ± 14.2	40.8 ± 19.9	0.02
Gender	Male	28.1 ± 13.4	39.3 ± 18.7	0.01
	Female	28.8 ± 14.0	40.2 ± 19.3	0.02
Feeding	Liquid	27.5 ± 12.9	38.1 ± 17.8	0.02
	Semi-solid/Solid	29.0 ± 13.9	40.5 ± 19.5	0.01

DISCUSSION

The current randomized controlled trial was carried out to determine the effectiveness of zinc and probiotics treatment compared to that of probiotics in the treatment of acute diarrhea in children. The results of this research indicate that combination therapy with zinc and probiotics is much more effective in lessening the period of diarrhea, shortening the hospital stay and enhancing recovery rates than probiotics alone [12]. The average time of diarrhea post treatment was also found to be significantly less in the zinc plus probiotics group (28.4 13.6 hours) than the probiotics only group (39.7 18.9 hours). This is a statistically significant decrease of about 11 hours, since a shorter diarrheal episode decreases the chances of dehydration, electrolyte imbalance, and malnutrition in children. These observations are in line with other earlier studies that have found that zinc supplementation improves intestinal mucosal healing and immunomodulation, and thus, faster diarrheal disease recovery. Likewise, probiotics are used to reestablish the balance of gut microbiota and prevent the proliferation of harmful organisms, resulting in shortening the time of the disease. The synergistic effect of the combination of both therapies is likely to be the reason behind the better results in this study [13] [14].

The overall length of stay in the hospital also significantly reduced in the combination therapy group (2.6 ± 0.8 days) than in the probiotics-only group (3.3 ± 1.1 days). The implications of this finding on the use of healthcare resources are significant because the burden on healthcare facilities caused by hospital stay can be reduced, as well as the cost of treatments. Other studies have also indicated that appropriate adjunct interventions in acute diarrhea may result in an earlier discharge and enhanced patient turnover which would be very helpful in a resource limited environment [15]. The recovery rates at five days were higher in the zinc plus probiotics group (90.0% compared to probiotics-only group (72.5%). This shows that the children who were treated to combination therapy not only recovered more quickly, they were also more likely to have full resolution of the symptoms at a shorter period of time. The complementary effects of zinc and probiotics where zinc plays a role in improving epithelial regeneration and immune response whereas probiotics play a role in regulating the intestinal flora and pathogen load explain the improved rate of recovery [16].

There was a similarity in the baseline characteristics of the two groups, which comprised of age, gender distribution, weight, length of time the symptoms presented, and socioeconomic factors. This implies that the differences in the results can be attributed to the intervention and not confounding factors. Internal validity of the study is also enhanced by the use of randomization [17] [18]. Stratified analysis revealed that the positive effects of zinc and probiotics therapy were similar between various age groups, sex and feeding patterns. Though there were some positive results in the sub groups, this was not significantly different showing that the treatment effect was not dependent on these variables. This improves the generalizability of the results on a broad pediatric population [19]. The results of this study are biologically plausible. Zinc is important in ensuring integrity of the intestines, ionic balance, and immune activities. It has been demonstrated to reduce intestinal permeability and fluid losses in cases of diarrhea. Conversely, the effects of probiotics are by competing with the pathogenic organisms, the production of antimicrobial substances, and the strengthening of the mucosal immunity. The two agents combined offer a holistic approach to treating acute diarrhea by targeting the underlying infection and promoting intestinal healing [20]. Despite these strengths, the findings should be considered in light of the literature on the subject. Although the benefits of zinc and probiotics have been independently established in various studies, few studies have compared the combination therapy with probiotics alone. The research provides strong evidence for the effectiveness of combined therapy, especially in reducing disease duration and improving recovery rates [21]. Nevertheless, there are some limitations to consider. The research was carried out in one center, and the sample size was relatively small, which could restrict the generalization of the results. Also, the study was short-term and did not assess recurrence or long-term nutritional status. It is advised to conduct future multicenter studies with larger sample sizes and longer follow-up periods to confirm these results and investigate long-term benefits.

CONCLUSION

It is concluded that the combination of zinc and probiotics is significantly more effective than probiotics alone in the treatment of acute diarrhea in children. The combined

therapy resulted in shorter diarrhea duration, reduced hospital stay, and higher recovery rates, indicating a clear clinical advantage. These findings support the use of zinc as an essential adjunct to probiotic therapy in the management of pediatric acute diarrhea, as it enhances recovery through complementary mechanisms. Incorporating zinc plus probiotics into routine treatment protocols may improve patient outcomes and reduce healthcare burden; however, further large-scale studies are recommended to validate these results.

REFERENCES

1. Ahmadipour S, Mohsenzadeh A, Alimadadi H, Salehnia M, Fallahi A. Treating Viral Diarrhea in Children by Probiotic and Zinc Supplements. Pediatric gastroenterology, hepatology & nutrition. 2019;22(2):162-70. https://doi.org/10.5223/pghn.2019.22.2.162
2. Ahmed Ismail M, Abdilahi MM, Abdeeq BA, Jama M. Prevalence and associated factors of acute diarrhea among under-five children living in Hargeisa Internally Displaced Persons, Somaliland: a community-based cross-sectional study. The Pan African medical journal. 2024;47:10. https://doi.org/10.11604/pamj.2024.47.10.35958
3. Li Z, Zhu G, Li C, Lai H, Liu X, Zhang L. Which Probiotic Is the Most Effective for Treating Acute Diarrhea in Children? A Bayesian Network Meta-Analysis of Randomized Controlled Trials. Nutrients. 2021;13(12):4319. https://doi.org/10.3390/nu13124319
4. Huang R, Xing HY, Liu HJ, Chen ZF, Tang BB. Efficacy of probiotics in the treatment of acute diarrhea in children: a systematic review and meta-analysis of clinical trials. Translational pediatrics. 2021;10(12):3248-60. https://doi.org/10.21037/tp-21-511
5. Hyder R, Ahmed S, Ahmed ATM. Compare the Effect of Zinc–Probiotic versus Zinc Therapy in Acute Watery Diarrhea in Children. KYAMC Journal. 2023;13:218-22. https://doi.org/10.3329/kyamcj.v13i4.64890
6. Christi H, Tjahjono K, Syauqy A. Zinc and probiotic supplementation: effect on the frequency and duration of acute diarrhea in children under five. 2023. 2023;8(2). https://doi.org/10.30604/jika.v8i3.2041
7. Kakar Z, Essazai AB, Ahmed SM, Ullah N, Jan P. Comparison of Zinc-Probiotic Combination Therapy to Probiotic Therapy Alone in Treating Acute Diarrhea in Children. Pakistan Journal of Medical & Health Sciences. 2022;16(12):253-. https://doi.org/10.53350/pjmhs20221612253
8. Farhat A, Shaukat A, Sadiq N. Comparison of clinical efficacy of combined versus monotherapy of oral zinc and probiotic in pediatric acute diarrhoea at benazir bhutto shaheed teaching hospital, Abbottabad. Journal of Bahria University Medical and Dental College. 2018;8(4):210-3. https://doi.org/10.51985/jbumdc2018061
9. Hatta M, Supriatmo S, Ali M, Sinuhaji AB, Hasibuan B, Nasution FL. Comparison of zinc-probiotic combination therapy to zinc therapy alone in reducing the severity of acute diarrhea. Paediatrica Indonesiana. 2011;51(1):1-6. https://doi.org/10.14238/pi51.1.2011.1-6
10. Raza, W., Mahmood, T., Atta, L., Hassan, S., Ullah, S., Ali, S., ... & Ahmad, N. (2024). Comparative Effectiveness of Zinc Supplementation Combined with Probiotic Therapy Versus Zinc Alone in Reducing Acute Diarrhea Duration, Severity, and Recurrence Rates in Pediatric Populations: A Meta-Analysis. *Indus Journal of Bioscience Research*, *2*(02), 681-689. https://doi.org/10.70749/ijbr.v2i02.256
11. Abdulah, D. M., Sulaiman, S. J., & Ahmed, Z. W. (2024). Effect of probiotics plus zinc supplementation on clinical outcomes of infants and children with acute infectious diarrhea: a randomized controlled trial. *Clinical and Experimental Pediatrics*, *67*(4), 203. https://doi.org/10.3345/cep.2023.01340
12. Hassan, M. A. E. A., Younis, M. M. S., & Mohamed, H. A. E. R. (2021). Efficacy of oral zinc and probiotic on acute diarrhea in infancy. *Al-Azhar J Pediatr*, *24*(2), 2114-29.
13. Mariam, M., Akter, M. T., Anjuman, H., Hussain, N., & Alia, R. A. (2022). A Comparative Evaluation on the Effect of Zinc-Probiotic Combination and Probiotic Therapy Alone in Paediatric Acute Diarrhoea. *The Planet*, *6*(02), 149-163.
14. Rosyid, R. A., Arifin, F. F., & Kristanto, A. Y. (2025). Effectiveness of Zinc Therapy with Zinc-Probiotic Combination Therapy on the Duration of Diarrhea During Hospitalization at Mawaddah Medika Hospital in October-December 2023. *Golden Ratio of Data in Summary*, *5*(2), 32-36. https://doi.org/10.52970/grdis.v5i2.1106
15. Lahiri, K. R., Singh, R., Apte, M., Patil, M., Taksande, A., Varona, R., ... & Perez, M. I. (2022). Efficacy and safety of Bacillus clausii (O/C, N/R, SIN, T) probiotic combined with oral rehydration therapy (ORT) and zinc in acute diarrhea in children: a randomized, double-blind, placebo-controlled study in India. *Tropical diseases, travel medicine and vaccines*, *8*(1), 9. https://doi.org/10.1186/s40794-022-00166-6
16. Kodam, V. (2022). A comparative study of ors (oral rehydration solution) with probiotics versus ors with zinc as an adjunct therapy in pediatric acute diarrhoeal diseases. *Perspec. Med. Res*, *9*, 26-29. https://doi.org/10.47799/pimr.0903.07
17. Riaz, M. H. Clinical Outcome of Zinc Plus Saccharomyces Boulardii versus Zinc Alone in the Treatment of Acute Diarrhea in Children Under 5 Years of Age.
18. Rizwan, W., Tufail, M., Zafar, B., & Shah, A. A. (2025, September). Effectiveness of Zinc Supplementation with ORS and Bacillus clausii versus zinc with ORS and Saccharomyces boulardii in Acute Watery Diarrhea in Pediatric Patients. In *Proceedings* (Vol. 39, No. 3, pp. 114-118). https://doi.org/10.47489/szmc.v39i3.790
19. Kayani, A. S., Asad, S., Saeed, T., & Aslam, H. (2024). Comparison Between Therapeutic Efficacy of Zinc Only and Zinc-Probiotics in Children with Acute Gastroenteritis. *Mirpur Journal of Medical Sciences*, *2*(1), 11-14.
20. Biswas, S., & Bal, B. (2023). Comparative, randomized-controlled trial on efficacy and safety of Lactobacillus rhamnosus GG and Saccharomyces boulardii in treatment of acute diarrhea in Indian children (COMPARE-GG trial). *International Journal*, *10*(2), 131. https://doi.org/10.18203/2349-3259.ijct20231103
21. Ismail, M. A., Alharbi, R. F., Hakami, R. A., Alotaibi, R. M., Alhazmi, R. A., Rasain, R. A. A., ... & Albinahmed, M. A. S. (2025). Effectiveness of Probiotics in Reducing the Duration of Acute Diarrhea in Children: A Systematic Review. *TPM–Testing, Psychometrics, Methodology in Applied Psychology*, *32*(S7 (2025): Posted 10 October), 263-271