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ORIGINAL ARTICLE

Efficacy of probiotics in outcome of acute watery diarrhea in children aged 06 months to 12 years admitted to the pediatrics department of Bacha Khan Medical Complex, Swabi

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ABSTRACT

Background: Acute watery diarrhea (AWD) affecting children contribute to high rates of morbidity and mortality in both developed and developing nations. Use of probiotics, especially *Lactobacillus acidophilus*, has been suggested as an additional therapeutic option in the management of childhood diarrhea. This study aimed to evaluate the effectiveness of probiotics in treating diarrhea in children aged 06 months to 2 years.

Methods: A total of 552 children, aged between 6 months and 12 years, who were diagnosed with severe watery diarrhea, participated in this study. Out of these, 300 children took daily doses of *L. acidophilus* for five consecutive days, while the remaining 252 children were given a placebo. Initial stool specimens were obtained from all participants to detect the presence of *Giardia lamblia*, *Entamoeba histolytica*, and *Ascaris lumbricoides*. The primary outcomes assessed included the duration of diarrhea, hospital stay length, stool consistency, frequency of bowel movements, electrolyte imbalances, and the time taken for symptom resolution. Statistical analysis was performed using t-tests for continuous variables, chi-square tests for categorical variables, and regression models to examine factors contributing to positive clinical outcomes.

Results: Children who received probiotics showed a marked improvement in duration of diarrhea (42.50 ± 11.80 hours vs. 58.40 ± 27.50 hours) and reduced hospital stay (66.10 ± 9.80 hours vs. 81.50 ± 27.00 hours), with p-values of < 0.001 and 0.008, respectively. They also showed quicker improvements in bowel movement frequency and stool consistency, along with fewer electrolyte disturbances ($p < 0.001$). The clinical efficacy of the probiotic was 91.0%, significantly higher than the control group's 79.9% ($p = 0.021$).

Conclusion: Our findings strongly advocate for the effectiveness of probiotics in treating diarrhea in children.

Keywords: Diarrheal Pathogens, Pediatric Diarrhea, Probiotics, Therapeutic Effectiveness

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Introduction

Acute gastroenteritis continues to be a significant global health concern, particularly among children aged less than five years (1). In Pakistan, it is a primary contributor to childhood illness and death, with approximately 40,000 child fatalities each year attributed to diarrhea (2). Diarrheal diseases are responsible for being the second leading cause of childhood death globally, as reported by the World Health Organization (WHO) (3).

The widespread occurrence of AWD in children is frequently linked to critical health issues, including malnutrition, hypokalemia, and acidosis, all of which can be life-threatening without proper treatment (4). Despite their effectiveness in preventing malnutrition and managing symptoms, oral rehydration therapy (ORT) and zinc supplementation do not significantly reduce the frequency of bowel movements or shorten the duration of diarrhea. (5). Given the need for more effective treatments, there is an urgent demand for therapies that not only reduce the duration of diarrhea but also alleviate its symptoms. Probiotics, especially *L. acidophilus*, have emerged as promising candidates for managing diarrhea. These probiotics work by decreasing stool frequency, enhancing stool consistency, and shortening diarrhea duration, all while posing minimal risk of significant side effects (6-8). Despite their promising potential, research on the effectiveness of probiotics in Pakistan is still limited (9). Most studies to date have been carried out in developed countries, where the conditions for microbial colonization and sanitation vary significantly from those found in Pakistan. (10, 11, 12). This gap highlights the need for more research to assess the effectiveness of probiotics within Pakistan's healthcare setting. Additionally, many studies have concentrated on viral or bacterial infections, leading to limited knowledge about the role of probiotics in treating diarrhea, especially those caused by bacterial pathogens (3).

The objective of this study was to assess the clinical effectiveness of *L. acidophilus* in treating childhood diarrhea in Pakistan. The study aims to provide valuable information to influence pediatric nursing practice in Pakistan and improve our understanding of probiotics as a treatment for diarrhea.

Methods

A comparative analytical study was conducted to evaluate the treatment, held at the Department of Pediatrics, MTI-GKMC/BKMC in Swabi, Pakistan, from April 15 to October 15, 2023. The Research Ethics Committee granted approval for the study (Approval No. 2444/PF/GKMC) on March 15, 2023 and written informed consent was acquired from the parents or legal guardians of all participants.

A total of 552 children diagnosed with acute watery diarrhea were included in the study. To be eligible, participants had to be between 6 months and 12 years of age, and their diarrhea had to last no longer than seven days, and they had no history of chronic gastrointestinal disorders or immune deficiencies. Acute watery diarrhea was diagnosed based on WHO criteria, which specify that it involves the occurrence of at least three loose stools per day for a duration of less than 14 days (13). Children were excluded from the study if they had taken antibiotics or probiotics within two weeks before participation or had severe comorbid conditions.

The study participants were randomly distributed into two groups: one group (n = 300) received probiotics, while the other (n = 252) was given a placebo. The randomization process was carried out through a computerized randomization table (14), and the assignment was kept concealed in sealed envelopes to ensure blinding and minimize any selection bias.

In the probiotic group, each child was given two daily oral doses of Lactobacillus acidophilus (Lacteol Fort), providing 2 × 10^8 CFU for a maximum of 5 days. The control group was administered a placebo that matched the probiotic treatment. Both groups received standard supportive care, including ORS to address dehydration, along with other symptomatic treatments as necessary. Stool samples were collected at the beginning of the study to screen for potential pathogens, including *E. histolytica*, *G. lamblia,* and *A. lumbricoides*.

The primary endpoints of this study were the duration of diarrhea, defined as the time from symptom onset to the disappearance of loose stools, and the length of hospital stay, measured in hours. Secondary outcomes measured included the daily frequency of stools, stool consistency (evaluated using the Bristol Stool Scale), electrolyte imbalances (such as hyponatremia and hypokalemia), and the time taken for symptoms to resolve, which was defined as the cessation of diarrhea, fever, and vomiting. Clinical efficacy was assessed based on the percentage of children who experienced complete symptom resolution, defined as the absence of symptoms for 48 hours.

Data analysis was performed using SPSS (version 17.0). Independent t-tests compared continuous variables, while chi-square tests assessed categorical data. A p-value < 0.05 was considered significant. Univariate regression analysis was conducted to evaluate prognostic factors, with odds ratios (ORs) and 95% confidence intervals (CIs) calculated.

Results

The demographic and clinical information for participants in both the probiotic and control groupswere assessed. The mean age of the children in the probiotic group was 3.50 ± 1.40 years, while those in the control group had a slightly older mean age of 3.87 ± 1.18 years (p = 0.002). Regarding weight, the average weight in the probiotic group was 15.02 ± 4.20 kg, whereas in the control group it was 16.01 ± 3.25 kg (p = 0.028). The gender distribution was similar across both groups, with 54% girls and 46% boys. A significant difference was found in the incidence of severe dehydration: 64% of children in the control group experienced severe dehydration, compared to just 18% in the probiotic group (p < 0.001). On the other hand, 82% of the probiotic group showed variable degrees of dehydration, while only 36% of the control group showed signs of dehydration (p < 0.001). These differences suggest a variation in baseline clinical severity between the two groups. **Figure 1** illustrates the prevalence of intestinal pathogens detected in the participants.

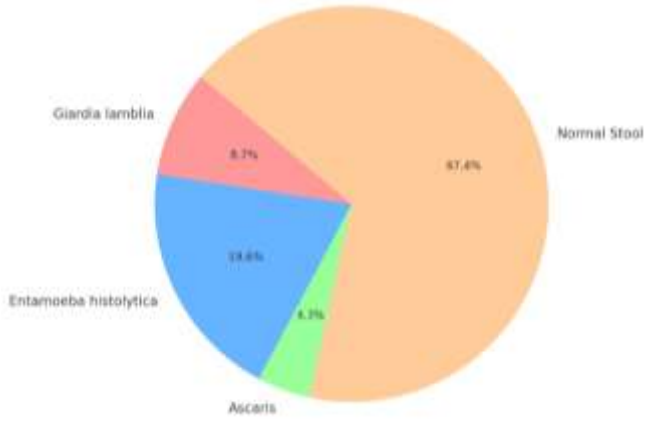

Figure 1: Prevalence of diarrhea pathogens among study participants.

As presented in Table 2, the probiotic group experienced a significantly shorter duration of diarrhea and hospital stay compared to the control group. The mean duration of diarrhea in the probiotic group was 42.50 ± 11.80 hours, notably shorter than the control group's 58.40 ± 27.50 hours ($p < 0.001$). Likewise, the average hospital stay in the probiotic group was 66.10 ± 9.80 hours, significantly less than the 81.50 ± 27.00 hours observed in the control group ($p = 0.008$). Additionally, a much higher percentage (100%) of children in the probiotic group were discharged within 72 hours, compared to just 32.10% in the control group ($p < 0.001$). In contrast, 67.90% of children in the control group required hospitalization for more than 72 hours.

Table 2: Length of Diarrhea and Hospitalization in the Study Groups

Outcome	Probiotics Group	Control Group	p-value
Duration of Diarrhea (hours)	42.50 ± 11.80	58.40 ± 27.50	<0.001
Hospital Stay (hours)	66.10 ± 9.80	81.50 ± 27.00	0.008
Discharged ≤ 72 hours (%)	100%	32.10%	<0.001
Discharged > 72 hours (%)	0%	67.90%	<0.001
Hospital Stay ≤ 48 hours (%)	92%	44.70%	<0.001
Hospital Stay > 48 hours (%)	8%	55.30%	<0.001

The data presented in Table 3 illustrates the stool frequency and texture for both the probiotic and control groups across 1 to 5 days. Throughout the study, the probiotic group consistently demonstrated a notably larger decrease in stool frequency compared to the control group. On day 3, the average stool frequency in the probiotic group was 3.60 ± 0.60, which was considerably lower than the control group's 4.00 ± 0.55, with a p-value less than 0.001, indicating statistical significance. On day 4, the probiotic group showed an even more significant reduction in stool frequency, with a mean of 2.55 ± 0.75, while the control group had a mean of 3.10 ± 0.75 ($p < 0.001$).

Regarding stool texture, the probiotic group showed a more significant improvement on day 3, with a mean stool texture score of 5.50 ± 0.65 compared to 5.90 ± 0.60 in the control group ($p < 0.001$). This pattern continued throughout the study, with the probiotic group consistently showing better stool texture scores than the control group.

Table 3: Stool Frequency and Consistency in the Study Groups

Outcome	Probiotics Group	Control Group	p-value
Stool Frequency Day 1	5.30 ± 0.90	5.20 ± 0.95	0.300
Stool Frequency Day 2	4.50 ± 0.80	4.55 ± 0.75	0.880
Stool Frequency Day 3	3.60 ± 0.60	4.00 ± 0.55	<0.001
Stool Frequency Day 4	2.55 ± 0.75	3.10 ± 0.75	<0.001
Stool Frequency Day 5	2.00 ± 0.90	2.30 ± 1.00	0.038
Stool Consistency Day 1	6.40 ± 0.50	6.30 ± 0.55	0.225
Stool Consistency Day 2	5.80 ± 0.70	5.95 ± 0.60	0.295

Stool Consistency Day 3	5.50 ± 0.65	5.90 ± 0.60	<0.001
Stool Consistency Day 4	5.10 ± 0.90	5.35 ± 1.00	0.045
Stool Consistency Day 5	4.30 ± 1.40	5.00 ± 1.30	<0.001

Table 4 demonstrates that the probiotic group experienced a significantly lower incidence of electrolyte imbalances compared to the control group. Hyponatremia and hypokalemia were found in 7.3% of patients in the probiotic group, while 37.7% of patients in the control group were affected ($p < 0.001$). Specifically, hypokalemia occurred in 9.3% of the probiotic group versus 16.3% in the control group ($p = 0.045$). Additionally, calcium imbalances were less common in the probiotic group, with only 1.0% of patients affected, compared to 4.0% in the control group ($p = 0.004$).

Table 4: Imbalances of Electrolytes in the Study Groups

Electrolyte Imbalance	Probiotics	Control	p-value
Hyponatremia +Hypokalemia	22 (7.3%)	95 (37.7%)	<0.001
Hypokalemia Alone	28 (9.3%)	41 (16.3%)	0.045
Hyponatremia Alone	7 (2.3%)	17 (6.7%)	0.031
Hyperkalemia	2 (0.7%)	5 (2.0%)	0.205
Calcium Imbalance	3 (1.0%)	10 (4.0%)	0.004

As shown in Table 5, the probiotics group experienced a significantly faster time to symptom resolution. A greater proportion of children in the probiotics group achieved complete symptom resolution (defined as no symptoms for 48 hours) compared to the control group (86% vs. 63%, $p < 0.001$). Moreover, the probiotics group had a higher rate of resolution for both loose stools and fever, with 23.7% of children resolving these symptoms, compared to 19.8% in the control group ($p = 0.03$). For vomiting, symptom resolution was observed in 9.7% of children in the probiotics group, compared to 19.0% in the control group ($p = 0.01$).

Table 5: Symptom Resolution in the Study Groups

Symptom	Probiotics Group	Control Group	p-value
Loose motions + Vomiting + Fever	179 (59.7%)	130 (51.6%)	0.15
Loose motions + Fever	71 (23.7%)	50 (19.8%)	0.03
Vomiting Alone	29 (9.7%)	48 (19.0%)	0.01
Fever Alone	47 (15.7%)	60 (23.8%)	0.045
No Symptoms After 48 hrs	86%	63%	<0.001

The probiotic group showed significantly higher clinical efficacy (91.0%) compared to the control group (79.9%) ($p = 0.021$). Univariate regression analysis (Table 6) identified probiotics as a strong predictor of success, with children receiving

probiotics being 2.4 times more likely to succeed than those on placebo (OR: 2.40; 95% CI: 1.15–5.10; p = 0.020).

Efficacy was also influenced by demographic and clinical factors. Children aged 3 years or older were more likely to succeed than those younger than 3 (OR: 2.90; 95% CI: 1.28–6.59; p = 0.009). Children with mothers who had ≤ 10th grade education were 3.1 times more likely to succeed (OR: 3.10; 95% CI: 1.40–6.77; p = 0.003). Additionally, children with severe dehydration had a higher likelihood of success than those with mild dehydration (OR: 3.80; 95% CI: 1.60–9.10; p = 0.001).

Table 6: Factors Associated with Clinical Efficacy: Univariate Analysis

Factor	Category	Efficacy, % (n/N)	Odds Ratio (95% CI)	p-value
Intervention Group				
	Probiotics	91.0% (273/300)	2.40 (1.15 - 5.10)	0.020
	Control	79.9% (201/252)	Reference	-
Age Group				
	≤ 3 years	72.5% (196/270)	2.90 (1.28 - 6.59)	0.009
	> 3 years	88.2% (248/282)	Reference	-
Maternal Education				
	≤ Matric	92.5% (222/240)	3.10 (1.40 - 6.77)	0.003
	> Matric	78.4% (244/312)	Reference	-
Dehydration Status				
	Severe	97.0% (189/195)	3.80 (1.60 - 9.10)	0.001
	Some	85.0% (303/357)	1.80 (0.85 - 3.80)	0.120
	None*	-	Reference	-

Note: The "None" dehydration category was not included in the original dataset. Therefore, it is used as the reference category for calculating the odds ratio (OR), but no efficacy value is provided for this category. CI = Confidence Interval.

Discussion

The primary goal of this study was to assess the clinical effectiveness of *L. acidophilus* in managing diarrhea among 552 children in Pakistan. Our results indicate that probiotics are effective in shortening the duration of diarrhea, reducing the frequency of hospitalizations, and improving stool consistency and frequency. These findings align with previous research that supports the beneficial role of probiotics in treating acute diarrhea in children. For instance, Minaz et al. (15) demonstrated a significant reduction of 15.9 hours in the duration of diarrhea in children receiving probiotics, compared to the control group. Similarly, Shah et al. (16) reported the efficacy of probiotics in reducing the incidence of acute diarrhea and enhancing clinical outcomes.

Our study also revealed that probiotics were particularly effective in children under the age of 3, with their efficacy being three times greater than in older children. This suggests that younger infants, who may have a more dynamic and sensitive gut microbiota, might derive more significant benefits from probiotic treatment (17). Additionally, maternal education was found to influence treatment outcomes, as children whose mothers had lower educational levels exhibited better results. This may reflect disparities in access to healthcare and early intervention.

The results also emphasize the role of probiotics in managing dehydration linked to

diarrhea. Children with mild or no dehydration demonstrated better outcomes than those with severe dehydration, where the effectiveness of probiotics was considerably diminished. This underscores the importance of integrating probiotics into a comprehensive treatment plan that includes proper hydration, in line with existing pediatric diarrhea management guidelines (18, 3). As a secondary outcome, the study showed significant improvements in stool frequency and consistency in the probiotic group. On days 1 and 4, children in the probiotic group had greater reductions in stool frequency and increased stool consistency compared to the control group. These results are consistent with findings by Kelisidis et al. (19), who observed similar improvements with Saccharomyces boulardii and other probiotic strains. The positive effects of probiotics may be attributed to their ability to restore balance in the gut microbiota, reduce bowel frequency, enhance stool consistency, and improve intestinal motility and absorption (20).

One of the most noteworthy findings was the reduction in hospital stay for the probiotic group. Children in this group had a mean hospital stay of 66.1 hours, compared to 81.5 hours in the control group. This finding mirrors those of studies like Bhat et al. (10), who reported shorter hospital stays for children treated with Saccharomyces boulardii for acute diarrhea. Shorter hospital stays not only minimize the risk of hospital-acquired infections but also ease the burden on healthcare systems, making probiotics a cost-effective treatment option for infants.

Limitations of the Study

Despite the support for probiotics in managing pediatric diarrhea, there are several limitations to this study that should be acknowledged. First, the research was conducted at a single center with a relatively small sample size, which may restrict the applicability of the results. Future research should involve multicenter trials with larger and more diverse populations to validate and broaden these findings. Additionally, the study did not differentiate between infectious and non-infectious causes of diarrhea, as microbiological testing was limited to parasitic infections (Giardia lamblia, Entamoeba histolytica, and Ascaris). The lack of testing for common viral (e.g., rotavirus, norovirus) or bacterial (e.g., Escherichia coli, Salmonella, Campylobacter) pathogens limits our ability to determine whether the effectiveness of probiotics differs based on the underlying causative pathogen. Future studies should incorporate stool cultures and advanced molecular diagnostic techniques to better understand the microbiological factors contributing to pediatric diarrhea and the role of probiotics in these different contexts.

Lastly, while this study focused on short-term outcomes, it did not evaluate the long-term effects of probiotic therapy or its potential in preventing recurrent episodes of diarrhea. Future research should explore these aspects to gain a deeper understanding of the sustained benefits and potential preventive role of probiotics in pediatric populations.

Conclusion

With the observed safety and positive outcomes associated with Lactobacillus acidophilus, probiotics can be considered a valuable adjunct in the management of pediatric diarrhea. However, further research is required to explore the long-term effects and to identify which specific probiotic strains are most effective for different causes of diarrhea.

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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.