Original Article

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Clinical Efficacy of Use of Probiotics in Children with Acute Watery Diarrhea

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Author`s Contribution

[1]Conception and design, drafting of the manuscript
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[4]Material preparation and literature search.[5,6]Drafting the work or revising it critically for important intellectual content

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ABSTRACT

Objective To determine the clinical efficacy of probiotics in children with acute watery diarrhea in children aged 6 months to 5 years, at H.H Sheikh Khalifa Bin Zayed Al-Nahyan Hospital/Combined Military Hospital, Muzaffarabad.

Methodology: The Randomized Controlled Trial was done at Pediatric department, H.H Sheikh Khalifa Bin Zayed Al-Nahyan Hospital/CMH, Muzaffarabad from January 2020 to December 2021. All patients aged 6 months to 5 years with acute watery diarrhea who present with severe, minimal, or no dehydration within the first five days of illness were included. Children meeting the inclusion criteria were consecutively enrolled and randomly assigned to either the study group (ORS plus oral administration of Saccharomyces Boulardii) or the control group (ORS alone). From day 1 to day 5, the quantity and consistency of feces were counted. On day 5, clinical effectiveness was indicated by 3 stools or fewer per day. SPSS version 26 was used for data analysis.

Results: Of 252 patients, a significant mean difference of number of stools and consistency was observed on day 3, day 4, and day 5 (p:<0.005). A significant association of efficacy was observed with probiotic group (p: 0.021). After adjustment for other covariates, efficacy was 2.37 times higher among children who were in probiotic group as compared to control group (OR 2.37, 95% CI 1.07-5.24, p: 0.033). The efficacy was 3.23 times higher among children with age ≤3 years than children with age >3 years (aOR 3.23, 95% CI 1.32-7.91, p: 0.010). The efficacy was 94% lower among children without dehydration (aOR 0.06, 95% CI 0.01-0.52, p: 0.011) and 91% lower among children with some dehydration (aOR: 0.09, 95% CI 0.01-0.77, p: 0.028).

Conclusion: The efficacy of probiotics was observed to be higher in treatment of acute watery diarrhea in hospitalized children. Probiotics, when used as an adjunct to standard therapy, may be beneficial in reducing the severity and duration of diarrhea, potentially leading to improved clinical outcomes.

Key words: Effectiveness, Probiotics, Acute watery diarrhea.

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Introduction

Among the globe, diarrheal infections are regarded as one of the major fatal health concerns in children.[1,2] Due to the fact that every child in Pakistan experiences 5–6 episodes of acute watery diarrhea per year, it is also the major cause of both childhood death and morbidity in that nation.[3,4]

Moreover, with about 40,000 fatalities in children under the age of five, associated with diarrheal diseases, Pakistan ranks as the third country globally with the highest burden of mortality attributed to diarrhea.[5] Diarrheal illnesses in children can often be prevented and effectively treated. However, if left untreated, severe dehydration resulting from fluid loss can pose life-threatening risks and potentially lead to fatalities. Therefore, it is crucial to manage dehydration promptly and appropriately to ensure the well-being and safety of affected children.[6] The mainstay of care for acute watery diarrhea continues to be rehydration and realimentation.[6,7] Acute watery diarrhea in children has been treated with a variety of medications,

including antibiotics, antimotility medicines, anticholinergics, and oral rehydration salts, however these medications are now considered dangerous due to their negative effects. Recent studies and research have developed novel approaches for treating acute watery diarrhea, including the use of probiotics as a supplement to other treatments to reduce diarrhea frequency and length.[8,9] For the treatment of acute watery diarrhea, a variety of probiotics have been employed. Based on findings from published research, Saccharomyces boulardii has been shown to be a highly effective treatment for acute diarrhea, with the added benefit of causing no adverse side effects.[10,11] While numerous studies on probiotics have been conducted in international settings, there is a scarcity of reported outcomes from Pakistan despite the widespread use of probiotics in the country.

Recognizing this gap, our study aimed to investigate the efficacy of probiotics in managing acute watery diarrhea specifically within the pediatric population. By conducting this study, we sought to contribute valuable insights into the effectiveness of probiotic interventions in a Pakistani context, addressing a critical need for locally relevant research in this field.

Methodology

The department of Paediatric medicine at H.H. Sheikh Khalifa Bin Zayed Al-Nahyan Hospital/Combined Military Hospital, Muzaffarabad, undertook this randomized controlled trial from January 2020 to December 2021. The ethics committee and relevant authorities were approached for administrative approval. Following the guidelines outlined in the Helsinki Declaration, parents were briefed about the potential risks and advantages of the study prior to granting written consent for their children's participation in the assessment and intervention. Additionally, parental consent was sought for the utilization of the data for research purposes and subsequent publication. All patients aged 6 months to 5 years with acute watery diarrhea who present with severe, minimal, or no dehydration within the first five days of illness. Children who were severely underweight, severely dehydrated, had chronic diarrhea, had received antibiotic treatment in the five days prior, had a known chronic, uncontrolled intestinal condition like celiac disease or pancreatic insufficiency, had co-morbid conditions like cardiac, respiratory, or renal disease, or had dysentery were all excluded.

By taking the standard deviation from previous study from probiotic and control group is 4.7 ±2.5 and 5.5 ±3.2 respectively.[12] Confidence interval 95%, power 75%, ratio of sample size 1, the sample size of 99 was required for each group. The sample size was raised to 126 children in each group while still considering the loss of follow-up as a concern. All of those children who met the requirements for participation were split into two groups at random. The control group received only oral rehydration supplement (ORS), while the study group received ORS plus oral administration of a probiotic Saccharomyces Boulardii (250 mg in two divided doses for infants under three months, and 250 mg twice a day for infants over three months) diluted in water to a concentration of about two teaspoons.

The age, gender, weight, maternal age, level of schooling, and degree of dehydration of the children, among other characteristics that may affect the result, were noted. Total duration of diarrhea, mean quantity of stools per day, consistency of feces, and length of stay in the hospital were the main end measures.

More than three loose stools per day were considered to be a sign of acute watery diarrhea. On the basis of clinical symptoms, dehydration was divided into three categories: nil, some, and severe. The clinical examination was conducted to determine whether a patient had some dehydration or no dehydration (two or more of the following indications, including restlessness, irritability, sunken eyes, drinking eagerly, and skin pinch returning slowly).[13]

The Bristol Criteria were used to define stools' consistency. Those who received types 5-7 were classified as having diarrhea. From day 1 to day 5, the quantity and consistency of feces were counted. On day 5, clinical effectiveness was indicated by 3 stools or fewer per day.

For statistical analysis, SPSS version 26 was employed. The Repeated Measure ANOVA test was used to investigate the mean difference between the quantity of stools and consistency of stools each day. While the independent t-test was used to investigate the mean difference in the amount and consistency of stools each day in the two groups. In order to investigate the relationship between efficacy and baseline and clinical features, the Chi-square/Fisher-Exact test was used. P-values lower than 0.05 were regarded as significant.

Results

Of 252 patients, the overall mean age and weight were 3.67 ±1.29 years and 15.43 ±3.74 kg respectively. Particularly mean age in probiotic group and control group was 3.42

Table I: Mean difference of demographic and clinical characteristics with respect to group. (n=252)

	Group	Mean ±SD	p-value	95% CI
Age (in years)	Probiotic	3.42 ±1.36	0.002	-0.80 to -0.18
	Control	3.91 ±1.16		
Weight (in Kg)	Probiotic	14.91 ±4.14	0.029	-1.94 to -0.10
	Control	15.94 ±3.22		
Mother's age, years	Probiotic	29.78 ±8.62	0.334	-3.49 to 1.19
	Control	30.94 ±10.19		
Duration of diarrhea (in days)	Probiotic	4.34 ±0.68	0.343	-0.09 to 0.27
	Control	4.26 ±0.77		
Duration of hospital stay (in days)	Probiotic	3.16 ±0.88	0.694	-0.16 to 0.24
	Control	3.12 ±0.71		
Number of stools (Day 1)	Probiotic	5.39 ±0.92	0.285	-0.11 to 0.36
	Control	5.27 ±0.96		
Number of stools (Day 2)	Probiotic	4.54 ±0.83	0.876	-0.22 to 0.18
	Control	4.56 ±0.78		
Number of stools (Day 3)	Probiotic	3.69 ±0.57	<0.001	-0.51 to -0.24
	Control	4.07 ±0.53		
Number of stools (Day 4)	Probiotic	2.68 ±0.77	<0.001	-0.56 to -0.19
	Control	3.06 ±0.75		
Number of stools (Day 5)	Probiotic	1.99 ±0.88	0.040	-0.48 to -0.01
	Control	2.24 ±1.01		
Consistency of stools (Day 1)	Probiotic	6.54 ±0.49	0.167	-0.03 to 0.21
	Control	6.46 ±0.50		
Consistency of stools (Day 2)	Probiotic	5.92 ±0.72	0.307	-0.25 to 0.08
	Control	6.01 ±0.63		
Consistency of stools (Day 3)	Probiotic	5.58 ±0.64	<0.001	-0.50 to -0.18
	Control	5.92 ±0.63		
Consistency of stools (Day 4)	Probiotic	5.16 ±0.91	0.045	-0.48 to -0.01
	Control	5.40 ±1.02		
Consistency of stools (Day 5)	Probiotic	4.37 ±1.42	<0.001	-1.06 to -0.38
	Control	5.09 ±1.34		

±1.36 years and 3.91 ±1.16 years respectively (p- 0.002). (Mean weight in probiotics 14.91 ±4.14 vs. control 15.94 ±3.22 p- 0.029). There were 134 (53.2%) females and 118 (46.8%) males. The mean duration of diarrhea was 4.31 ±0.73 days whereas duration of hospital stay was 3.14 ±0.79 days. Most of the children 151 (59.9%) were presented with some dehydration, followed by no dehydration 72 (28.6%) and severe dehydration in 29 (11.5%) children. Table I

With respect to time, there was a discernible decrease in the frequency of stools (p: 0.001). A non-significant difference of mean number of stools was observed between groups on day 1 (p: 0.285) and day 2 (p: 0.876). Similarly, a non-significant difference of mean consistency of stools was observed between groups on day 1 (p: 0.167) and day 2 (p: 0.307). However, the Probiotic group showed a significantly lower average of stools on days 3, 4, and 5 compared to the Control group, with statistically significant differences (p-<0.05). Additionally, the consistency of stools was notably different between the groups on days 3, 4, and 5, with significant variations observed (p-<0.05). These findings suggest potential effects of the probiotic intervention on

Table II: Comparison of efficacy with demographics and clinical characteristics. (n=252)

Group	Efficacy		p-value
	Yes (n=215)	No (n=37)	
Group			
Probiotic	114 (90.5)	12 (9.5)	0.021
Control	101 (80.2)	25 (19.8)	
Age			
>3 years	187 (87.8)	26 (12.2)	0.009
≤3years	28 (71.8)	11 (28.2)	
Gender			
Male	99 (83.9)	19 (16.1)	0.595
Female	116 (86.6)	18 (13.4)	
Weight			
≤15 kg	48 (88.9)	6 (11.1)	0.517
>15 kg	167 (84.3)	31 (15.7)	
Maternal age			
≤30years	137 (85.1)	24 (14.9)	0.894
>30 years	78 (85.7)	13 (14.3)	
Duration of diarrhea			
≤4 days	113 (83.7)	22 (16.3)	0.437
>4 days	102 (87.2)	15 (12.8)	
Mother's educational status			
Less than matric	102 (79.1)	27 (20.9)	0.004
More than equal to intermediate	113 (91.9)	10 (8.1)	
Degree of dehydration			
No Dehydration	60 (83.3)	12 (16.7)	0.190
Some dehydration	127 (84.1)	24 (15.9)	
Moderate/severe dehydration	28 (96.6)	1 (3.4)	

Table III: Regression analysis for factors associated with efficacy. (n=252)

Group	Efficacy			
	OR (95% CI)	p-value	aOR (95% CI)	p-value
Group				
Probiotic	2.35 (1.12-4.92)	0.023	2.37 (1.07-5.24)	0.033
Control	Ref		Ref	
Age				
>3 years	2.83 (1.26-6.35)	0.012	3.23 (1.32-7.91)	0.010
≤3years	Ref		Ref	
Mother's educational status				
More than equal to intermediate	2.99 (1.38-6.48)	0.005	2.84 (1.24-6.48)	0.013
Less than matric	Ref		Ref	
Degree of dehydration				
No Dehydration	0.17 (0.02-1.44)	0.106	0.06 (0.01-0.52)	0.011
Some dehydration	0.18 (0.03-1.45)	0.110	0.09 (0.01-0.77)	0.028
Moderate/severe dehydration	Ref		Ref	

stool frequency and consistency over the observed period. Table I

The overall efficacy was found to be 215 (85.3%). A significant association of efficacy was observed with probiotic group (p: 0.021), age of the children (p: 0.009), and mother's educational status (p: 0.004). Table II

The findings of the univariate regression analysis revealed the efficacy was 2.35 times higher among children who were in probiotic group than those who were in control group (OR: 2.35, 95% CI 1.12-4.92). Furthermore, efficacy in accordance to age, maternal educational status and degree of dehydration was done by univariate regression analysis as shown in Table III

Discussion

In terms of probiotic utilization, acute diarrhea is the condition that has been the most thoroughly studied, particularly in children. Probiotics showed an excellent safety profile, a substantial reduction in the length of diarrhea, a decrease in bowel frequency, and a shortening of hospital stays.[8,14,15] In this study, the overall mean age was 3.67 ±1.29 years, with 134 (53.2%) females and 118 (46.8%) males. Consistently, Ali R et al,[16] reported that the children had an average age of 24.3 months, with a variability of approximately ±18.65 months. Among them, 47 (58.8%) were boys, and 33 (41.3%) were girls. This aligns with Farhat A et al,[17] findings, which stated that the patients' mean age was 21.73 months, with a standard deviation of ±13.14 months. Among all cases, there were 94 (49%) males and 98 (51%) females.

According to the current study findings, the efficacy was 2 times higher among children who were in probiotic group as compared to the children who were in control group. The efficacy was 3 times higher among children with ≤3 years of age as compared to the children with >3 years of age. The efficacy was 2 times higher among children with less than equal to matric mother's education as compared to those with more than equal to matric mother's education. The efficacy was 94% lower among children with no dehydration and 91% lower among children with some dehydration. In the comparison of this study the treatment demonstrated significantly higher effectiveness in probiotics along with antibiotic group compared to antibiotic alone group (90.6% vs. 78.1%; p = 0.017). In accordance with this study, previous by Ali R et al,[16] indicated that the average stool count was significantly lower in patients treated with a combination of probiotics and ORS (3.25 ± 1.13) compared to those treated with ORS alone (4.13 ± 0.79) for acute diarrhea (p < 0.001). However inconsistently Grenov B et al[18] reported that the during inpatient treatment, there was no distinction in the duration of diarrhea between the probiotic and placebo cohorts (P = 0.69). However, our findings were supported by the KHAN NA et al[19] as probiotics have demonstrated significantly greater efficacy in reducing stool frequency in cases of acute diarrhea. Specifically, 92 out of 100 patients (92%) in the probiotic group showed improvement, whereas in Group B, 71 out of 100 patients (71%) exhibited improvement.[19] Probiotics are commonly used to treat diarrhea because they alter the intestinal ecology and have been shown to be effective against enteric infections. Probiotics appear to have positive effects in acute diarrhea that are strain-specific, dose-dependent, highly effective in viral gastroenteritis, and more pronounced when probiotic therapy is started early in the course of the illness.[14]

According to the results of the present investigation, there was no discernible relationship between the mean duration of diarrhea and the length of hospitalization. On days 3, 4, and 5, a substantial mean variation in the number of stools was further seen. On days 3, 4, and 5, a significant mean difference in the quantity of stools was noted. Probiotics'

clinical applications may be understood through studies and trials, but in order to fully reap the health advantages of probiotics, it is crucial to understand how they work.[8,20,21] Probiotics have been extensively researched during the past several years for the treatment of diarrheal illnesses in pediatric populations.[15-18,21] Thus, intestinal flora existing in the intestinal mucosal barrier interacts with immune cells to promote the health and welfare of the host when probiotic is delivered. Less invasiveness and improved effectiveness are its benefits.[22] The results of the study might be highlighted in light of limitation that it was done at a single center with a small sample size.

Additionally, certain crucial factors including long-term results, dietary condition, laboratory features, prior treatment, and culture results were not examined. In a research, children who received probiotic treatment also saw weight growth.[23] Probiotics have been found in certain trials to enhance the nutritional condition of malnourished children, but further research is necessary.[23-25] The current study did not observe blinding, despite the fact that it was a randomized controlled experiment.

Conclusion

The efficacy was considerably higher among children who were in probiotic group as compared to the children who were in control group. In addition, efficacy was found higher among children in larger age group and more than equal to matric mother's education.

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