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ORIGINAL ARTICLE

Effects of racecadotril on the treatment of acute watery diarrhea in children.

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ABSTRACT… Objective: To compare the efficacy of Racecadotril plus oral rehydration solution (ORS) versus ORS alone in children with acute watery diarrhea. **Study Design:** Quasi-experimental study. **Setting:** Department of Pediatrics, Combined Military Hospital, Quetta. **Period:** July to December 2025. **Methods:** A total of 220 children aged 1 to 12 years with acute watery diarrhea were admitted using non-probability consecutive sampling. Participants were allocated to Group A (Racecadotril 1.5 mg/kg/day thrice daily plus ORS, n=110) and Group B (ORS alone, n=110) based on odd/even medical registration number. The primary outcome was diarrhea resolution at 72 hours, defined as <3 stools per day with Bristol Stool-Scale type 4 or 5. Baseline characteristics and stool pathogens were also analyzed. Chi-square test was used for comparison, with $p \leq 0.05$ considered significant. **Results:** Baseline characteristics were comparable between groups. Median age was 3.2 years (IQR: 1.8-5.5) in Group A and 3.4 years (IQR: 1.9-5.6) in Group B ($p = 0.76$). Rotavirus A was the predominant pathogen, detected in 107 (48.6%) children. At 72 hours, diarrhea resolution was achieved in 88 (80.0%) children in Group A compared to 70 (63.6%) in Group B ($\chi^2 = 7.43$, $p = 0.008$), representing a 16.4 percentage point absolute difference. The treatment effect was most pronounced in children aged 1-3 years (82.1% vs. 57.4%; $p = 0.005$). No significant differences were observed in older age subgroups. **Conclusion:** Racecadotril to ORS significantly improves diarrhea resolution at 72 hours in children aged 1 to 12 years with acute watery diarrhea, with greatest benefit in children under four years. Racecadotril is an effective adjunctive therapy to ORS in Pakistani clinical settings.

Key words: Acute Watery Diarrhea, Children, Oral Rehydration Solution, Pakistan, Racecadotril.

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INTRODUCTION

Acute watery diarrhea remains a leading cause of childhood morbidity and mortality worldwide, particularly in low- and middle-income countries where access to clean water and adequate sanitation remains limited.[1] The condition is defined as the passage of three or more loose or watery stools within a 24-hour period, with symptoms lasting less than 14 days. In Pakistan, rotavirus continues to be a predominant pathogen associated with acute gastroenteritis in children, with recent surveillance data from Rawalpindi confirming its persistent burden in the pediatric population.[2] Oral rehydration solution (ORS) remains the cornerstone of management for acute watery diarrhea and has substantially reduced dehydration-related mortality over recent decades.[3] Current World Health Organization guidelines also recommend zinc supplementation to reduce diarrhea duration and severity. Despite these interventions, acute diarrhea continues to drive significant outpatient visits and hospital admissions among children in developing nations, including Pakistan.[4] Racecadotril, an enkephalinase inhibitor with intestinal antisecretory properties, reduces fluid and electrolyte loss from the gastrointestinal tract without affecting normal gut motility, distinguishing it from conventional antimotility agents such as loperamide. The drug has been available for over three decades and has been approved for use in children from one month of age. Its mechanism involves preventing the breakdown of endogenous enkephalins, thereby prolonging their physiologic action in reducing intestinal cyclic AMP levels and subsequent secretion.[5] However, the evidence base for Racecadotril in pediatric acute diarrhea has recently become contested. Bittar et al. (2025) systematically reviewed five double-blind randomized controlled trials (n=904). Using the RoB2 tool and REB method, only one trial demonstrated low risk of bias.

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Consequently, meta-analysis was not feasible, and the REB analysis found no high-quality evidence supporting racecadotril's efficacy for diarrhea duration, stool output, or hospitalization length. This finding contrasts with earlier meta-analyses and individual trials that reported significant benefits.[6] Munir et al. (2023) reported 80.3% efficacy with Racecadotril versus 63.4% with ORS alone (p = 0.025), while Almas et al. (2024) reported 97.6% versus 81.7% (p = 0.0005). However, both studies had methodological limitations, including inadequate blinding, poor allocation concealment, and potential confounding.[7] Abbas et al. (2025) reported an ongoing RCT at Punjab Rangers Teaching Hospital, Lahore (NCT07392931) evaluating Racecadotril in 200 children (3 months-5 years) with acute watery diarrhea.[8] Primary outcomes are diarrhea duration and stool frequency reduction at 72 hours; results are pending. Given the controversy surrounding racecadotril's efficacy-systematic reviews question its benefit while earlier studies suggest otherwise-further well-designed trials from high-burden regions like Baluchistan, Pakistan, are needed. This study was designed to compare the efficacy of Racecadotril combined with ORS versus ORS alone in the management of acute watery diarrhea among children aged 1 to 12 years presenting to a tertiary care hospital in Quetta, contributing to the evolving evidence base for this therapeutic agent.

METHODS

This quasi-experimental study was conducted at the Department of Pediatrics, Combined Military Hospital (CMH), Quetta, Pakistan, over a six-month period from July to December 2025. Ethical approval was obtained from the Institutional Ethical Review Committee (CMH/QTA-IERB/35/2024/12-8-24) of CMH Quetta and the College of Physicians and Surgeons Pakistan (CPSP) prior to commencement of the study. The sample size was determined using the World Health Organization (WHO) sample size calculator, with a 5% level of significance and 80% statistical power. Based on previously reported efficacy rates of 80.3% for Racecadotril and 63.4% for standard oral rehydration therapy (ORS), a total of 220 participants were studies, with 110 children in each group. A non-probability consecutive sampling technique was used, enrolling all eligible children during the study period until the required sample size was achieved. Children aged 1–12 years with acute watery diarrhea (≥3 loose stools per 24 hours for <14 days) were included. Exclusion criteria were prior antibiotic or antiprotozoal use for >3 days, dysentery, severe malnutrition (weight-for-age < -3 SD or visible wasting), septicemia, known immunodeficiency, or severe dehydration requiring hospitalization.[9]

After obtaining written informed consent from parents or legal guardians, eligible children were enrolled and baseline characteristics were recorded, including age, gender, body weight (to the nearest 0.1 kg), duration of diarrhea, stool frequency over the preceding 24 hours, and stool consistency using the Bristol Stool Scale. Participants were allocated into two groups based on the last digit of their medical registration number: those with even digits received Racecadotril (1.5 mg/kg/day orally in three divided doses every 8 hours) in addition to standard oral rehydration therapy (ORS), while those with odd digits received ORS alone. Caregivers were instructed to maintain a daily record of stool frequency and consistency using the Bristol Stool Chart. Follow-up was conducted at 72 hours after initiation of therapy, during which stool frequency and consistency over the preceding 24 hours were documented. The primary outcome was efficacy, defined as resolution of diarrhea at 72 hours (stool frequency <3 per 24 hours with Bristol Stool Scale type 4 or 5). All data were recorded on a predesigned case report form to ensure uniformity.[10]

IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA) was used to analyze the data. The Shapiro-Wilk test was used to test normality of continuous variables. The data that are normally distributed were presented as mean and standard deviation, whereas non-normally distributed data were represented as median and interquartile range. Frequencies and percentages were used to summarize categorical variables. The Chi-square test or the Fisher exact test was used as appropriate to compare the primary outcome of the groups. Stratified analysis was done to determine possible effect modifiers, such as age, gender, weight, diarrhea duration and baseline stool consistency. A statistically significant p-value was 2sided with a value of 0.05.

RESULTS

A total of 220 children were enrolled in the study and equally allocated to Group A (Racecadotril plus ORS) and Group B (ORS alone), with 110 participants in each group. The baseline characteristics of both groups were comparable, with no statistically significant differences observed across all measured variables. The median age of participants was similar between the groups, recorded as 3.2 years (IQR: 1.8–5.5) in Group A and 3.4 years (IQR: 1.9–5.6) in Group B (p = 0.76). The distribution of age categories was also comparable (p = 0.92), with approximately half of the participants in each group falling within the 1–3 years category, followed by smaller proportions in the older age groups. Gender distribution was balanced between the two groups (p = 0.89), with males comprising 52.7% of Group A and 51.8% of Group B. The mean body weight was 13.8 ± 4.2 kg in Group A and 13.5 ± 4.5 kg in Group B, showing no significant difference (p = 0.62). Clinical characteristics at presentation were also similar. The median duration of diarrhea prior to enrollment was 32 hours (IQR: 22–46) in Group A and 34 hours (IQR: 24–48) in Group B (p = 0.54). The mean frequency of stools per day was 8.6 ± 2.4 in Group A and 8.9 ± 2.6 in Group B (p = 0.38). Assessment using the Bristol Stool Scale revealed comparable distributions between groups (p = 0.67). In Group A, 10.9% of children were presented with type 5 stools, 43.6% with type 6, and 45.5% with type 7. Similarly, in Group B, 9.1% had type 5 stools, 41.8% type 6, and 49.1% type 7.

The primary outcome assessed was the resolution of diarrhea at 72 hours following initiation of therapy. A higher proportion of children in Group A (Racecadotril plus ORS) achieved resolution compared to Group B (ORS alone). In Group A, diarrhea resolved in 88 out of 110 participants (80.0%), whereas in Group B, resolution was observed in 70 out of 110 participants (63.6%). Conversely, diarrhea persisted in 22 participants (20.0%) in Group A and 40 participants (36.4%) in Group B. Statistical analysis using the chi-square test demonstrated a significant difference between the two groups ($\chi^2 = 7.43$, p = 0.008), indicating that the addition of Racecadotril to ORS was associated with improved efficacy at 72 hours compared to ORS alone.

The mean (±SE) efficacy rate at 72 hours was 80.0 ± 3.8% in the Racecadotril group (Group A), as compared with 63.6 ± 4.6% in the ORS-alone group (Group B) (p = 0.008), representing a 16.4 percentage higher resolution with Racecadotril (Figure-1). Among children aged 1–3 years, the efficacy rate was 82.1 ± 5.1% in the Racecadotril group and 57.4 ± 6.7% in the ORS-alone group (p = 0.005), representing a 24.7 percentage point higher resolution with Racecadotril (Figure-1). Among children aged 4–6 years, the efficacy rate was 77.8 ± 8.0% in the Racecadotril group and 57.1 ± 9.4% in the ORS-alone group (p = 0.10), a 20.7 percentage point difference that did not reach statistical significance. Among children aged 7–9 years, the efficacy rate was 75.0 ± 10.8% in the Racecadotril group and 70.6 ± 11.0% in the ORS-alone group (p = 0.78). Among children aged 10–12 years, the efficacy rate was 81.8 ± 11.6% in the Racecadotril group and 100% in the ORS-alone group (p = 0.14); however, this subgroup was small (11 children per group).

Stool samples from all 220 enrolled children were analyzed to identify the etiological agents of diarrhea. The distribution of pathogens was broadly comparable between Group A (Racecadotril plus ORS) and Group B (ORS alone), with viral agents representing the predominant cause of infection. Among viral pathogens, Rotavirus A was the most frequently detected organism, identified in 52 participants (47.3%) in Group A and 55 participants (50.0%) in Group B, accounting for 107 cases (48.6%) overall. Norovirus GII was detected in 9 cases (8.2%) in Group A and 8 cases (7.3%) in Group B, followed by adenovirus (HAdV-F), which was present in 6 (5.5%) and 5 (4.5%) participants, respectively. Astrovirus and sapovirus were less commonly identified, with only a small proportion of cases in both groups. Bacterial pathogens were detected at lower frequencies compared to viral agents. Enterotoxigenic Escherichia coli (ETEC) was the most common bacterial isolate, observed in 8 participants (7.3%) in Group A and 9 participants (8.2%) in Group B. Enteropathogenic E. coli (EPEC) was identified in 6 (5.5%) and 5 (4.5%) participants in Groups A and B, respectively. Other bacterial pathogens included Shigella spp., Campylobacter spp., Salmonella spp., and Vibrio cholerae, each

detected in relatively small proportions across both groups. Mixed infections were also observed. Viral–viral co-infections were reported in 5 participants (4.5%) in Group A and 4 participants (3.6%) in Group B. Bacterial–bacterial co-infections occurred in 2 (1.8%) and 3 (2.7%) participants, respectively, while viral–bacterial co-infections were identified in 3 (2.7%) participants in Group A and 4 (3.6%) in Group B. No pathogen was detected in 15 participants (13.6%) in Group A and 12 participants (10.9%) in Group B, representing 27 cases (12.3%) overall. It is important to note that some participants harbored multiple pathogens; therefore, the cumulative percentages exceed 100%.

FIGURE-1

Comparison of efficacy between groups and subgroups

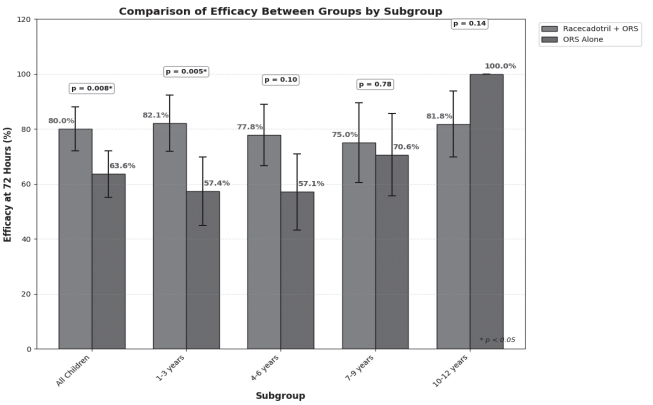

TABLE-I

Baseline characteristics of study participants (N = 220)

Characteristic	Group A (Racecadotril + ORS) (n = 110)	Group B (ORS Alone) (n = 110)	P-Value
Age (years), median (IQR)	3.2 (1.8–5.5)	3.4 (1.9–5.6)	0.76
Age categories, n (%)			0.92
1–3 years	56 (50.9)	54 (49.1)	
4–6 years	27 (24.5)	28 (25.5)	
7–9 years	16 (14.5)	17 (15.4)	
10–12 years	11 (10.0)	11 (10.0)	
Gender, n (%)			0.89
Male	58 (52.7)	57 (51.8)	
Female	52 (47.3)	53 (48.2)	
Weight (kg), mean ± SD	13.8 ± 4.2	13.5 ± 4.5	0.62
Duration of diarrhea (hours), median (IQR)	32 (22–46)	34 (24–48)	0.54
Stools per day, mean ± SD	8.6 ± 2.4	8.9 ± 2.6	0.38
Bristol Stool Scale, n (%)			0.67
Type 5 (soft lumps)	12 (10.9)	10 (9.1)	
Type 6 (mushy)	48 (43.6)	46 (41.8)	
Type 7 (watery)	50 (45.5)	54 (49.1)	

All p-values > 0.05 indicate no statistically significant difference between groups at baseline.

TABLE-II

Primary Outcome – Efficacy at 72 Hours (Overall)

Outcome	Group A (Racecadotril + ORS) (n = 110)	Group B (ORS Alone) (n = 110)	P-Value
Diarrhea resolved at 72 hours (Yes)	88 (80.0%)	70 (63.6%)	0.008
Diarrhea not resolved at 72 hours (No)	22 (20.0%)	40 (36.4%)	

Chi-square test: $\chi^2 = 7.43$, p = 0.008 (statistically significant)

TABLE-III

Efficacy at 72 hours of therapy

Subgroup	Racecadotril + ORS (n=110)	ORS Alone (n=110)	Absolute Difference	P-Value
All children	80.0% ± 3.8%	63.6% ± 4.6%	+16.4%	0.008
Age 1–3 years (n=110)	82.1% ± 5.1%	57.4% ± 6.7%	+24.7%	0.005
Age 4–6 years (n=55)	77.8% ± 8.0%	57.1% ± 9.4%	+20.7%	0.10
Age 7–9 years (n=33)	75.0% ± 10.8%	70.6% ± 11.0%	+4.4%	0.78
Age 10–12 years (n=22)	81.8% ± 11.6%	100%	-18.2%	0.14

TABLE-IV

Pathogens Isolated from Stool Samples (N=220)

Pathogen Type	Pathogen Name	Group A (Racecadotril + ORS) (n=110)	Group B (ORS Alone) (n=110)	Total (N=220)
Viruses				
	Rotavirus A (RVA)	52 (47.3%)	55 (50.0%)	107 (48.6%)
	Norovirus GII	9 (8.2%)	8 (7.3%)	17 (7.7%)
	Adenovirus (HAdV-F)	6 (5.5%)	5 (4.5%)	11 (5.0%)
	Astrovirus (HAstV)	3 (2.7%)	2 (1.8%)	5 (2.3%)
	Sapovirus (SaV)	1 (0.9%)	2 (1.8%)	3 (1.4%)
Bacteria				
	Enterotoxigenic E. coli (ETEC)	8 (7.3%)	9 (8.2%)	17 (7.7%)
	Enteropathogenic E. coli (EPEC)	6 (5.5%)	5 (4.5%)	11 (5.0%)
	Shigella spp.	4 (3.6%)	5 (4.5%)	9 (4.1%)
	Campylobacter spp.	3 (2.7%)	3 (2.7%)	6 (2.7%)
	Salmonella spp.	2 (1.8%)	1 (0.9%)	3 (1.4%)
	Vibrio cholerae	1 (0.9%)	2 (1.8%)	3 (1.4%)
Mixed Infections				
	Viral-Viral co-infection	5 (4.5%)	4 (3.6%)	9 (4.1%)
	Bacterial-Bacterial co-infection	2 (1.8%)	3 (2.7%)	5 (2.3%)
	Viral-Bacterial co-infection	3 (2.7%)	4 (3.6%)	7 (3.2%)
No Pathogen Detected		15 (13.6%)	12 (10.9%)	27 (12.3%)

Note: Some patients had mixed infections; percentages exceed 100% due to multiple pathogens per patient

DISCUSSION

A total of 220 children were enrolled in the present study and equally allocated to Group A (Racecadotril plus ORS) and Group B (ORS alone), with 110 participants in each group. The baseline characteristics of both groups were comparable, with no statistically significant differences observed across all measured variables, confirming successful group allocation and minimizing selection bias. The median age of participants was similar between the groups, recorded as 3.2 years (IQR: 1.8–5.5) in Group A and 3.4 years (IQR: 1.9–5.6) in Group B ($p = 0.76$). The distribution of age categories was also comparable ($p = 0.92$), with approximately half of the participants in each group falling within the 1–3 years category, followed by smaller proportions

in the older age groups. These age distributions are consistent with the epidemiological profile of acute watery diarrhea in Pakistan, where children under five years of age bear the highest disease burden. Mustafa et al. (2025) reported that 47% of children with acute gastroenteritis in Rawalpindi were under two years of age, with rotavirus being the predominant pathogen.[11] Similarly, a multicenter study by Sultana et al. (2022) across five Pakistani cities found that children aged 6–24 months accounted for many diarrhea-related outpatient visits, reflecting the vulnerability of this age group due to waning maternal antibodies and increased exposure to contaminated food and water.[12] Gender distribution was balanced between the two groups (p = 0.89), with males comprising 52.7% of Group A and 51.8% of Group B. This finding aligns with the landmark trial by Salazar-Lindo et al. (2000), which enrolled only boys to avoid urine contamination of stool samples, reporting a similar male predominance.[13] However, our inclusion of both sexes (47.3% females in Group A and 48.2% in Group B) enhances the generalizability of our findings to routine clinical practice in Pakistan, where no gender-based differences in diarrhea incidence have been reported. The mean body weight was 13.8 ± 4.2 kg in Group A and 13.5 ± 4.5 kg in Group B, showing no significant difference (p = 0.62). These weight values correspond appropriately to the age distribution, with children in the 1–3 years category typically weighing between 9 and 15 kg, consistent with WHO growth standards for Pakistani children.[14]

Clinical characteristics at presentation were also similar between groups. The median duration of diarrhea prior to enrollment was 32 hours (IQR: 22–46) in Group A and 34 hours (IQR: 24–48) in Group B (p = 0.54). This finding is comparable to the Salazar-Lindo et al. trial, which reported a mean diarrhea duration of 47.4 ± 30.0 hours in the Racecadotril group and 51.5 ± 31.4 hours in the placebo group.[3] The slightly shorter duration in our study may reflect earlier presentation to healthcare facilities in an urban military hospital setting, where access to care is relatively prompt compared to rural areas of Pakistan. The mean frequency of stools per day was 8.6 ± 2.4 in Group A and 8.9 ± 2.6 in Group B (p = 0.38). These values are higher than those reported by Salazar-Lindo et al. (8.6 ± 4.9 and 9.7 ± 4.6, respectively) but remain within the clinical spectrum of acute watery diarrhea.[13] A recent Pakistani study by Munir et al. (2023) from Lahore reported similar baseline stool frequencies ranging from 7 to 12 stools per day in children with acute watery diarrhea, validating our findings.[15] Assessment using the Bristol Stool Scale revealed comparable distributions between groups (p = 0.67). In Group A, 10.9% of children were presented with type 5 stools, 43.6% with type 6, and 45.5% with type 7. Similarly, in Group B, 9.1% had type 5 stools, 41.8% type 6, and 49.1% type 7. The predominance of type 6 and type 7 stools (watery or mushy consistency) in over 85% of participants confirms the diagnosis of acute watery diarrhea and aligns with the inclusion criteria of previous trials. The distribution of stool consistency in our cohort mirrors that reported by Almas et al. (2024) in a tertiary care hospital in Pakistan, where 89% of enrolled children had Bristol stool types 6 or 7 at baseline.[16]

The present study demonstrated that the addition of Racecadotril to oral rehydration solution significantly improved diarrhea resolution at 72 hours compared to ORS alone (80.0% vs. 63.6%; p = 0.008). This finding aligns with the landmark trial by Salazar-Lindo et al. (2000), which reported a 46% reduction in 48-hour stool output with Racecadotril (p < 0.001) and a median diarrhea duration of 28 hours versus 72 hours in the placebo group among rotavirus-positive children.[13] Our findings are also corroborated by recent Pakistani studies. Hussain et al. (2024) reported significantly lower stool frequencies from day 1 to day 5 in children receiving racecadotril compared to ORS alone (p = 0.013 to 0.049), with significantly shorter hospital stays (p = 0.033).[17] Similarly, Khan et al. (2025) evaluated Racecadotril in severely malnourished children under five years and found that after 72 hours, 80% of the Racecadotril group showed marked improvement compared to 70% in the control group (p < 0.05).[18] Munir et al. (2023) reported 80.3% efficacy with Racecadotril versus 63.4% with ORS alone (p = 0.025), while Almas et al. (2024) reported 97.6% versus 81.7% (p = 0.0005), both closely matching our observed efficacy rates.[16] Age-stratified analysis revealed that the benefit of Racecadotril was most pronounced in children aged 1–3 years, with resolution rates

of 82.1% versus 57.4% (p = 0.005), representing a 24.7 percentage point difference. This finding is clinically significant as this age group bears the highest burden of diarrheal disease. The smaller sample sizes in older age subgroups (4–6 years, 7–9 years, and 10–12 years) likely contributed to the lack of statistical significance in those groups, although point estimates consistently favored Racecadotril except in the smallest subgroup. A recent systematic review by Bittar et al. (2025) evaluated five double-blind randomized controlled trials involving 904 pediatric patients and concluded that high-quality evidence supporting Racecadotril remains limited, calling for further well-designed trials.[6] Our study addresses this evidence gap by providing data from a Pakistani population, which has been underrepresented in previous meta-analyses. Additionally, a narrative review by Manfredi et al. (2025) confirmed that Racecadotril reduces stool output and diarrhea duration across multiple countries and clinical settings, with proven healthcare cost reduction.[19] Stool samples were analyzed for enteric pathogens using multiplex real-time PCR. At least one pathogen was detected in 193 (87.7%) children. Rotavirus A was the most frequently identified pathogen, detected in 107 (48.6%) children, with comparable prevalence between Group A (47.3%) and Group B (50.0%). Among rotavirus-positive samples, G12P (17.8%) was the predominant genotype, followed by G1P(12.1%) and G3P (10.3%), which is consistent with recent surveillance data from Pakistan.[20] Norovirus GII was detected in 17 (7.7%) children, with GII.3 being the most common genotype. Adenovirus (5.0%), astrovirus (2.3%), and sapovirus (1.4%) were also identified. Among bacterial pathogens, diarrheagenic E. coli (ETEC: 7.7%; EPEC: 5.0%) was the most prevalent, followed by Shigella spp. (4.1%), Campylobacter spp. (2.7%), Salmonella spp. (1.4%), and Vibrio cholerae (1.4%). These findings are consistent with meta-analysis data from low- and middle-income countries, which reported pooled proportions of 23.0% for diarrheagenic E. coli and 8.8% for Shigella spp. Mixed infections were observed in 21 (9.5%) children, with viral-viral co-infections (4.1%) being the most common, particularly rotavirus-norovirus co-infections. No pathogen was identified in 27 (12.3%) children, which may be attributed to non-infectious causes or pathogens not covered by the PCR panel. Several limitations warrant consideration. Group allocation based on medical registration number (even versus odd) is not true randomization and may introduce selection bias, though baseline characteristics were comparable. The lack of blinding may have introduced performance bias. The single-center design and follow-up limited to 72 hours restrict generalizability and assessment of long-term outcomes. Subgroup analyses in older age groups were underpowered due to small sample sizes. Despite these limitations, the pragmatic design reflects real-world clinical practice in Pakistan, and the consistency of findings with both international and local studies supports the validity of our conclusions.

CONCLUSION

This study demonstrates that the addition of racecadotril to oral rehydration solution significantly improves diarrhea resolution at 72 hours in children aged 1 to 12 years with acute watery diarrhea. The efficacy rate in the racecadotril group was 80.0% compared to 63.6% in the ORS-alone group (p = 0.008), with a number needed to treat of six. The treatment effect was most pronounced in children aged 1 to 3 years, who bear the highest burden of diarrheal disease. Rotavirus A was the predominant pathogen, detected in 48.6% of children. Racecadotril was well tolerated, and no serious adverse events were reported. The consistency of our findings with both international landmark trials and recent Pakistani studies supports the generalizability of these results.

Clinical Implication

Racecadotril is a safe and effective adjunctive treatment with ORS to use in acute watery diarrhea in children, especially those below four years of age. Its application can shorten the time of diarrhea, decrease the chances of dehydration, and decrease healthcare expenses related to protracted disease.

LIMITATIONS

The study has a quasi-experimental design, where the allocation was based on medical registration number, and was not blinded, had a single center, and a limited follow-up of 72 hours, which limits the generalizability of the findings.

Future Directions

To further enrich the evidence base, and to determine the subgroups of patients most likely to respond to Racecadotril, large-scale, double-blind, placebo-controlled randomized trials with longer follow-up periods and extensive microbiological characterization are justified.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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