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Risk Factors Associated with Persistent Diarrhea in Children Under Five Years: A Case-Control Study from Berhampur, Odisha

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ABSTRACT

Background: Persistent diarrhea remains a significant cause of morbidity and mortality among children, particularly in developing nations. Despite the success of oral rehydration therapy in managing acute diarrhea, a growing proportion of diarrheal deaths are attributed to persistent diarrhea. This study aims to identify the clinical profile and associated risk factors for persistent diarrhea in children under five years of age.

Methods: A hospital-based observational case-control study was conducted at MKCG Medical College, Berhampur, Odisha, over one year. It included 35 children with persistent diarrhea (cases) and 105 with acute watery diarrhea (controls), matched 1:3 by age and sex. Data on nutritional status, feeding practices, antibiotic use, water safety, infections, and immunization were collected. Clinical assessments included dehydration, malnutrition, and signs of infection.

Results: In this study, significant associations were found between persistent diarrhea and protein-energy malnutrition (85.7% vs. 58.1%), irrational antibiotic use (77.1% vs. 56.2%), unsafe drinking water (85.7% vs. 72.4%), and dehydration >24 hours ($p<0.001$). No significant differences were observed in exclusive breastfeeding or immunization.

Conclusion: This study identifies protein-energy malnutrition, irrational antibiotic use, parenteral infections, and unsafe drinking water as significant independent risk factors for persistent diarrhea in children under five years of age. Addressing these risk factors through targeted interventions, such as promoting safe drinking water, rational antibiotic use, and improved nutritional practices, can reduce the burden of persistent diarrhea and its associated complications in young children.

Key-words: Persistent diarrhea, Risk factors, Protein-energy malnutrition, Irrational antibiotic use, Parenteral infections, Unsafe drinking water, Clinical profile

INTRODUCTION

Persistent diarrhea is a major cause of morbidity and mortality among children in developing nations. With the increasing success of oral rehydration therapy in managing acute diarrhea, a greater proportion of diarrheal-related deaths are now attributed to persistent diarrhea.

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Although definitions may vary, most researchers define persistent diarrhea as an episode lasting more than two weeks. Understanding the different terminologies used for prolonged diarrheal episodes is crucial.

The World Health Organization (WHO) classifies simple persistent diarrhea as an episode of acute diarrhea that extends beyond 14 days [1]. This widely accepted definition estimates that 3-20% of acute diarrheal cases may become persistent when defined as the passage of three or more stools per day for at least 14 days. However, field studies suggest that many of these episodes are mild and do not significantly impact a child's overall health and nutrition [2-3].

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The incidence of persistent diarrhea varies across different regions. Studies on Indian infants have reported an incidence of 31 episodes per 100 child years, while research in northern India indicates that approximately 15% of children aged 0-35 months experience at least one episode of persistent diarrhea annually [1]. Infants under one year of age are the most vulnerable group, which aligns with findings from both national and international studies [1-3]. While no significant gender-based differences in incidence have been consistently observed, some studies have reported higher rates in either males or females due to differences in child-rearing practices. The seasonal patterns of persistent diarrhea remain unclear but seem to coincide with peak periods of acute diarrheal illnesses.

The severity of acute diarrhea during its initial phase plays a critical role in the likelihood of persistence. Children passing six or more liquid stools within 24 hours during the acute phase face nearly a fourfold increased risk of developing persistent diarrhea. The presence of leukocytes, mucus, or visible blood in stools during the early stage also raises the risk two to three times [1]. Certain bacterial pathogens, particularly Enter adhesive *Escherichia coli* and Enteroaggregative *E. coli*, are consistently linked to persistent diarrhea [4]. These pathogens adhere to the intestinal mucosa in characteristic patterns, and many tend to aggregate. However, the precise mechanisms by which they contribute to persistent diarrhea remain unclear.

Jejunal mucosal damage has been proposed as a critical factor in the pathophysiology of persistent diarrhea. Lebenthal *et al*. suggested that such mucosal injury represents a final common pathway of the disease [5]. This damage may result from nutritional deficiencies, secondary bacterial overgrowth, or immune-mediated responses [3]. Additionally, systemic infections can compromise intestinal integrity, although their direct role in causing persistent diarrhea is still debated [6]. Studies indicate that 25-33% of children with persistent diarrhea have concurrent infections such as pneumonia, urinary tract infections (UTI), septicemia, or meningitis.

Parasitic infections, particularly Giardia lamblia and Cryptosporidium, have also been implicated in persistent diarrhea, with immunocompromised children, including those with AIDS, at higher risk. In India, persistent diarrhea is responsible for 36-56% of all diarrhea-related childhood deaths [1]. Research from northern India found that while only 5% of diarrheal cases lasted beyond 14 days, these accounted for a case fatality rate of 14%, compared to just 0.7% for shorter episodes [7-10].

The impact of persistent diarrhea on child growth and nutrition is substantial. Prolonged episodes can lead to significant weight loss, especially when food intake is restricted. Without adequate nutritional rehabilitation, affected children may experience severe growth impairment, with long-term consequences such as stunting rather than just wasting [1,8]. Persistent diarrhea is a key contributor to protein-energy malnutrition, with severe cases sometimes leading to marasmus or, less frequently, kwashiorkor.

Given that many risk factors for persistent diarrhea are preventable, identifying these risks is crucial for targeted interventions. This case-control study aims to assess the clinical profile of persistent diarrhea in children under five years and explore host and environmental risk factors associated with its occurrence.

MATERIALS AND METHODS

Study Design and Setting- This was a hospital-based observational case-control study conducted over one year at the Department of Paediatrics, MKCG Medical College and Hospital, Berhampur, Odisha.

Study Population- The study included children aged 1 month to 5 years who were admitted with diarrhoeal illness.

Inclusion Criteria

- **Cases**: Children aged 1 month to 5 years with persistent diarrhoea (diarrhoea lasting more than 14 days), who were willing to participate and follow the study protocol.
- **Controls**: Children aged 1 month to 5 years with acute watery diarrhoea who recovered within 7 days, and were matched to cases by age and sex in a 1:3 ratio.

Exclusion Criteria

- Children whose parents or guardians did not give consent.
- Controls who developed persistent diarrhoea during hospital stay or follow-up.
- Controls lost to follow-up.

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Sample Size- A total of 30 cases and 90 matched controls (1:3 ratio) were included in the study.

Data Collection- The study involved gathering detailed histories from the parents (primarily mothers) regarding the illness and various risk factors, as outlined in the study proforma. The risk factors considered were protein-energy malnutrition (PEM), irrational use of antibiotics, lack of exclusive breastfeeding, type of container used for feeding, use of unsafe drinking water, parenteral infections, presence of dysenteric stools, prolonged dehydration (>24 hours), recent diarrhoea (within the past 2 months), history of measles (within the past 2 months), and incomplete immunization.

All enrolled children underwent thorough clinical examinations to assess hydration, nutritional status, and the presence of any co-existing infections. If any child in the control group developed persistent diarrhoea during the hospital stay or follow-up or failed to attend follow-up visits, they were excluded from the study, and a new control participant was recruited.

Laboratory Investigations- Stool samples were collected and examined for all children. Parenteral infections, including septicemia, pneumonia, urinary tract infections, and HIV, were confirmed through blood cultures, chest X-rays, urine cultures, and ELISA, respectively. Additional investigations were conducted when necessary. All participants, both cases and controls, received appropriate treatments, including fluids, antibiotics, and dietary management. According to the WHO, PEM is defined as a group of conditions resulting from insufficient intake of proteins and calories, commonly seen in infants and young children, and often associated with infections.

Statistical Analysis- The crude odds ratio for each risk factor was calculated using univariate analysis with the Chi-square test or Fisher's exact test. The adjusted odds ratio was calculated using logistic regression analysis, with R software. A p-value of less than 0.05 was considered statistically significant.

Ethical Approval- The study was approved by the Institutional Ethical Committee. Informed written consent was obtained from the parents or guardians of all participants before enrolment.

RESULTS

The study analysed 35 cases and 105 controls to identify risk factors associated with the condition. The findings revealed that protein-energy malnutrition (PEM) was significantly more prevalent among cases (85.7%) compared to controls (58.1%), indicating a strong association between malnutrition and the condition ($p<0.001$). Similarly, irrational antibiotic use was more frequent among cases (77.1%) than controls (56.2%), suggesting its potential role as a risk factor ($p<0.001$). Exclusive breastfeeding was found to be lower in cases (45.7%) compared to controls (65.7%), highlighting its protective role ($p<0.01$). The presence of parenteral infections was also significantly higher among cases (45.7%) than controls (21%) ($p<0.001$), emphasising the increased risk due to infections (Table 1).

Table 1: Contributing Factors to Persistent Diarrhea Among Children Below Five Years of Age

Risk factor	Cases (N=35)		Controls (N=105)		p-value
	n	%	N	%	
Nutritional status					
Normal	5	14.3	44	41.9	<0.001
PEM	30	85.7	61	58.1	
Irrational Antibiotic use					
Present	27	77.1	59	56.2	<0.001
Absent	8	22.9	46	43.8	
Exclusive breast feeding					
Present	16	45.7	69	65.7	<0.01
Absent	19	54.3	36	34.3	
Parenteral infection*					
Present	16	45.7	22	21	<0.001
Absent	19	54.3	83	79.0	
Use of unsafe Drinking water					
Present	30	85.7	76	72.4	<0.05
Absent	5	14.3	29	27.6	
Container used for feeding**					
Cup and Spoon (or) 'Paladai'	16	45.7	55	52.4	>0.05
Bottle	19	54.3	50	47.6	
Dysenteric stool					
Present	6	17.1	48	45.7	>0.05
Absent	29	82.9	57	54.3	

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Persistence of dehydration >24 hours					
Present	8	22.9	7	6.7	<0.001
Absent	27	77.1	98	93.3	
Diarrhoea within the past 2 months					
Present	13	37.1	35	33.3	>0.05
Absent	22	62.9	70	66.7	
Measles within the past 2 months					
Present	1	2.9	3	2.9	>0.05
Absent	34	97.1	102	97.1	
Immunization appropriate for age					
Present	32	91.4	98	93.3	>0.05
Absent	3	8.6	7	6.7	

Unsafe drinking water was more commonly used by cases (85.7%) than controls (72.4%), showing a significant association ($p<0.05$). However, no statistically significant difference was observed in feeding methods, as 54.3% of cases and 47.6% of controls were bottle-fed ($p>0.05$). The occurrence of dysenteric stool was higher in controls (45.7%) than in cases (17.1%), but this difference was not statistically significant ($p>0.05$). Persistence of dehydration for more than 24 hours was notably higher among cases (22.9%) compared to controls (6.7%) ($p<0.001$), indicating its significance as a risk factor.

The history of diarrhea within the past two months was slightly more frequent among cases (37.1%) than controls (33.3%), though the difference was not statistically significant ($p>0.05$). Similarly, there was no significant variation in the history of measles, with both cases and controls showing an equal prevalence of 2.9% ($p>0.05$). Most children in both groups had received immunization appropriate for their age, with 91.4% of cases and 93.3% of controls being vaccinated, showing no significant difference ($p>0.05$).

Other risk factors analyzed did not show statistical significance in the univariate analysis. The method of feeding, specifically the use of bottles, had an odds ratio of 1.29 (95% CI: 0.58 - 2.34), indicating no significant association. Similarly, the presence of dysenteric stool (OR: 1.91, 95% CI: 0.77 - 3.79) and a history of diarrhea within the past two months (OR: 1.14, 95% CI: 0.65 - 2.51) were not independently linked to persistent diarrhea. Additionally, a history of measles within the past two months (OR: 2.44, 95% CI: 0.49 - 10.61) and inappropriate immunization for age (OR: 1.39, 95% CI: 0.66 - 3.69) did not emerge as significant risk factors (Table 2).

Table 2: Other Non-Significant Risk Factors

Risk Factor	Odds Ratio (95% CI)
Container Used for Feeding	1.29 (0.58 - 2.34)
Dysenteric Stool	1.91 (0.77 - 3.79)
Diarrhea within Past 2 Months	1.14 (0.65 - 2.51)
Measles within Past 2 Months	2.44 (0.49 - 10.61)
Immunization Inappropriate for Age	1.39 (0.66 - 3.69)

DISCUSSION

The study included 35 children under five years of age diagnosed with persistent diarrhea. The highest prevalence 91 (65%) was observed in children aged between 1 month and 1 year. This finding aligns with WHO reports indicating that persistent diarrhea is more common in children under one year of age [1]. Similarly, a study by P. Dutta et al. concluded that children aged 7 to 18 months had a higher incidence of persistent diarrhea [9].

SK Mittal's research highlighted that nearly one-third of children with persistent diarrhea recovered with a normal diet, while another one-third required a low-lactose diet. Around 20-30% needed the complete exclusion of milk and dairy products, and these cases were managed with specialized diets such as rice-pulse-oil or comminuted chicken-based diets [3]. In another study, Bhan *et al*. observed that diets containing small amounts of milk combined with cereals were generally well tolerated. For children who did not respond to these diets, a combination of cereals with glucose or sucrose facilitated faster recovery [10].

Multivariate logistic regression analysis identified protein-energy malnutrition, irrational antibiotic use, parenteral infections, and unsafe drinking water as significant independent risk factors for persistent diarrhea in children under five years. Protein-energy malnutrition (OR: 1.921) was strongly associated with persistent diarrhea, like findings by Deivanayagam *et al.* (OR: 2.9), Alam *et al*. (OR: 3.08), and Karim *et al.* (OR: 7.5) [11-13].

Irrational antibiotic use (OR: 2.399) also emerged as a key risk factor, consistent with studies by Deivanayagam

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et al. (OR: 2.9), Alam *et al.* (OR: 4.65), and Karim *et al.* (OR: 10.2). Parenteral infections (OR: 2.134) were independently associated with persistent diarrhea, in agreement with findings from Deivanayagam *et al.* (OR: 2.1) [11-13]. However, Alam *et al.* did not find parenteral infections to be a significant risk factor [12].

The study also found that the use of unsafe drinking water (OR: 2.654) was a significant independent risk factor, aligning with findings from Karim *et al*., who reported a higher odds ratio (OR: 4.2) [13]. Conversely, the lack of exclusive breastfeeding, identified as a significant independent risk factor in Karim *et al.*'s study, was only significant in univariate analysis in the present study and not in multivariate analysis [13]. This aligns with the findings of Alam *et al*., who also did not identify exclusive breastfeeding as an independent risk factor [12].

Persistence of dehydration for more than 24 hours was considered an independent risk factor in studies by Deivanayagam *et al.* and Alam *et al*., particularly in cases involving invasive diarrhea. However, in the present study, while it was significant in univariate analysis, it did not emerge as an independent risk factor in logistic regression analysis [11,12].

CONCLUSIONS

This study identified the use of unsafe drinking water, irrational antibiotic use, parenteral infections, and protein-energy malnutrition as significant independent risk factors for persistent diarrhea in children under five years of age. To reduce the risk of persistent diarrhea, it is crucial to ensure continued feeding during acute diarrheal episodes to prevent malnutrition and subsequent complications.

Further large-scale, multicentric studies are needed to validate these findings across diverse populations. Implementing community-based interventions focusing on nutrition, breastfeeding, and hygiene may offer sustainable strategies to prevent persistent diarrhea in children.

CONTRIBUTION OF AUTHORS

Research concept- Santosh Kumar Pradhan, Jyotiranjan Mohapatra

Research design- Santosh Kumar Pradhan, Jagnyaseni Panda, Jyotiranjan Mohapatra

Supervision- Santosh Kumar Pradhan

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Data collection- Jyotiranjan Satapathy, Jyotiranjan Mohapatra

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Final approval-Santosh Kumar Pradhan, Jagnyaseni Panda, Jyotiranjan Satapathy, Jyotiranjan Mohapatra

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