Risk factors of persistent diarrhea in children below five years of age

A S M Bazlul Karim, Shaheen Akhter, Md Atiar Rahman, M F H Nazir

Department of Pediatric Nutrition and Gastroenterology,
Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000, Bangladesh

Background/ Objective: Persistent diarrhea is a known cause of childhood mortality, morbidity and malnutrition in developing countries. This study was conducted to find out the host and environmental risk factors associated with persistent diarrhea in Bangladeshi children below 5 years of age. Design: Prospective analytic case-control study. Setting: Tertiary hospital in Dhaka, Bangladesh. Methods: Fifty children with persistent diarrhea and 50 controls with acute diarrhea (matched for age and sex) comprised the study subjects. Results: Most of the children (82%) were aged below 2 years. Among the risk factors, Grade III malnutrition (p<0.008), irrational antibiotic use during acute diarrheal episode (p<0.0000005), use of unsafe drinking water (p<0.004) and lack of exclusive breast-feeding up to the first four months of life (p<0.004) were significantly associated with persistent diarrhea. Logistic analysis showed irrational antibiotic use (p<0.0001) during an episode of acute diarrhea and lack of exclusive breast-feeding (p<0.05) during the first four months of life as independent risk factors associated with persistent diarrhea. Conclusion: Improvement of nutritional status, encouraging exclusive breast-feeding during the first four months of life, discouraging the irrational use of antibiotic for the treatment of acute diarrhea, and provision of safe drinking water may be important for the prevention of persistent diarrheal disease as these have been identified as risk factors in Bangladeshi children below five years of age. [Indian J Gastroenterol 2001;20:59-61]

Key words: Diarrhea, epidemiology, prevention

Persistent diarrhea, defined as acute episode of diarrhea that lasts for 14 days or more with or without growth faltering, is a known cause of childhood mortality, morbidity and malnutrition in developing countries. It usually accounts for less than 10% of all diarrheal episodes but is associated with 30%-50% of death due to diarrhea. Although the clinical characteristics of persistent diarrhea are known, its exact pathogenesis is still unclear and is probably multifactorial. Malnutrition, infection, mucosal injury, delayed repair of mucosal injury, host susceptibility and various environmental factors may predispose a child to develop persistent diarrhea.

Bangladesh is a country with nearly 15.1 million under-5 population, with an under-5 mortality rate of 89 per 1000 live births and annual under-5 death of 312,000. Several studies have been done in Bangladesh and in other developing countries to find out the possible environmental and host risk factors for the development of persistent diarrhea in children. But data from these studies are inconclusive.

We, therefore, conducted this prospective case-control study to find out the possible host and environmental risk factors associated with persistent diarrhea in Bangladeshi children below 5 years of age who attended a tertiary care hospital in Dhaka city.

Methods

Fifty consecutive cases of persistent diarrhea and 50 age- and sex-matched controls with acute diarrhea who attended the Oral Rehydration Therapy corner or were admitted to the Pediatric in-patient department during January 1998 through July 1999 were enrolled in this prospective case-control analytic study. Sample size was chosen by computerized statistical analysis (Epi Info, version 6; Centers for Disease Control, Atlanta, GA) with confidence interval of 95%, power of 90 and ratio of cases vs. controls as 1:1. The assumption was that 57% of children in the persistent diarrhea group were not exclusively breast-fed, versus 25% in the control group, with an odds ratio of 4.0.

Children, both male and female, below 5 years of age with history of an apparent episode of acute watery diarrhea persisting for 14 days or more were included as cases of persistent diarrhea. Children below 5 years of age with an episode of acute watery diarrhea of less than 5 days' duration were included as acute diarrheal controls. The controls were matched for age and sex. They were followed up for 14 days from the onset of diarrhea; those whose diarrhea persisted for 14 days from the onset of diarrhea or who did not turn up for follow up for 14 days from the onset of diarrhea were excluded from the study. All the cases and controls were offered routine management. Verbal informed consent was taken from their parents before enrollment.

The investigators filled up a pre-structured questionnaire by interviewing the parents, usually mothers. The questions were on duration of diarrhea, treatment...
history during the present diarrhoeal period, history of diarrhoea in the previous 3 months, use of pre-lacteal food (i.e., food given before breast-milk, e.g., sweet water, honey), exclusive breast-feeding up to 4 months of age, bottle-feeding history, early weaning (before 5 months of age), use of animal milk (raw cow's or goat's milk), vaccine appropriate for age, use of safe (boiled or tube-well) drinking water, sanitation, history of measles in the previous 3 months, history of parental loss, high-potency vitamin A capsule intake appropriate for age in the previous 6 months, literacy status of mother, employment of mother, and type of housing. Weight of the children was taken using both bathroom and baby-weighing scale and nutritional status was determined by Gomez's classification of weight for age.¹⁴

**Statistical analysis**

All data are expressed in frequencies. Statistical analysis was done using the SPSS program (version 7.5 for Windows). Comparison between groups was done by χ² test and risk factors by Fisher's exact test for frequencies. Predictive capacity of individual risk factors over persistent diarrhoea was analyzed in logistic regression model. A p value less than or equal to 0.05 was considered significant.

**Results**

The 50 children with persistent diarrhoea (24 male) were aged 45 days to 5 years (mean 1.4 [SD 1.1] years); 10 (20%) cases were below 5 months, 26 (52%) below 1 year and 41 (82%) were below 2 years of age.

Risk factors that were found significantly associated with persistent diarrhoea are shown in the Table. Grade III malnutrition (weight for age 60% or less), antibiotic use during an episode of diarrhoea, unsafe drinking water use, and lack of exclusive breast-feeding up to 4 months of age were seen significantly (p < 0.0000005) more among children suffering from persistent diarrhoea. On logistic regression analysis antibiotic use (p < 0.0001) and lack of exclusive breast-feeding (p < 0.05) were found as independent risk factors associated with persistent diarrhoea.

**Discussion**

The risk factors that promote the occurrence of persistent diarrhoea in children are not well understood and data from different studies are conflicting, inconclusive and insufficient. A majority (82%) of the children with persistent diarrhoea in our study presented before 24 months of age. Other studies also found that a majority of episodes occur either in infancy or in children below 2 years of age.¹⁰,¹¹,¹²,¹³,¹⁴ We and others¹⁶,¹⁷ observed no sex-related difference in the incidence of persistent diarrhoea. One possible reason for the higher incidence observed in male children in some studies¹⁵,¹⁸ might be that in some societies male children are more cared for and so are referred earlier to hospital for treatment.

Several community-based longitudinal studies¹⁹,²⁰,²¹ have confirmed that protein-energy malnutrition (PEM) is a major risk factor for the occurrence of persistent diarrhoea in children. About ninety percent of children in each group in our series were suffering from various grades of malnutrition at presentation, but Grade III malnutrition was found more among children suffering from persistent diarrhoea. Since we did not measure the nutritional status of each child before the onset of diarrhoea, it is difficult to determine whether the PEM was a cause or effect of persistent diarrhoea. By using weight-for-height Z-score²² as a measure of nutritional status, Baqui et al.²³ observed that the lower decline in weight-for-height status was associated with 87% excess risk of persistent diarrhoea. However, low weight-for-age and low height-for-age, as measures of nutritional status, were not found as risk factors in their study. On the contrary, Bhandari et al.²⁴ reported from India that prior malnutrition, defined as weight-for-age <70%, was associated with a more than 3-fold increased risk of persistent diarrhoea.

Indiscriminate use of antibiotics during an episode of acute diarrhoea may suppress the growth of useful gut flora and may lead to persistent diarrhoea due to super-infection. In one study, only 15% of children with persistent diarrhoea were found to have the same pathogenic organisms in the stool samples of days 1-3 and 15-17.²⁵ In our study and in earlier ones,¹⁰,¹² antibiotic use during an episode of diarrhoea was found more frequently among children suffering from persistent diarrhoea compared to their acute diarrhoea controls. These observations should discourage the unnecessary use of antibiotics during an episode of acute diarrhoea, except in cases of systemic infection associated with PEM.
Bardhan et al. [11] found that enteraggregative E. coli, Aeromonas spp., and Klebsiella spp. were significantly associated with persistent diarrhea in Bangladeshi children. These infections could be acquired through unsafe drinking water or use of dirty bottles with unclean teat. In our study, although unsafe drinking water use was seen more often among children suffering from persistent diarrhea, no significant difference was observed in bottle use between the two groups. Breast milk is safe and protects children from diarrhea due to its anti-infective, immunologic, and anti-allergic properties. Only 24% of children in our series suffering from persistent diarrhea were found exclusively breast-fed up to 4 months of age. Other studies from different developing countries confirm this observation. [10,12,20]

Antibiotic use during an episode of acute diarrhea and lack of exclusive breast-feeding up to 4 months of life were the two independent predictors for the occurrence of persistent diarrhea in the children we studied. Some factors shown by other investigators to be significantly associated with persistent diarrhea were not found significant in our study. Small size of the sample and different socio-cultural factors may be related to these different observations.

We conclude that preventable factors like PEM, indiscriminate antibiotic use during an episode of acute diarrhea, unsafe drinking water and lack of exclusive breast-feeding are risk factors for the occurrence of persistent diarrhea in children.

References

Correspondence to: Dr. Baziul Karim, Associate Professor, Fax: 880 (2) 361 3794, E-mail: karimb@bangla.net

Acknowledgement: The authors would like to thank Dr MA Hasanat, Assistant Professor of Medicine, for statistical help.

Received April 13, 2000. Received in final revised form January 29, 2001. Accepted February 5, 2001

Indian Journal of Gastroenterology 2001 Vol 20 March - April 61