

# Prospective hospital based study on persistent diarrhoea

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## Abstract

**A total of 383 children aged less than 5 years suffering from acute watery diarrhoea or dysentery were studied in hospital to determine the rate of persistent diarrhoea. Altogether 335 (87.5%) recovered within 13 days. Only in 48 (12.5%) did the diarrhoea continue for 14 days or more, and they were considered as having persistent diarrhoea. Children aged between 7 and 18 months had a significantly increased incidence of persistent diarrhoea. Children suffering from grade II-IV malnutrition constituted the majority (70.8%) of those with persistent diarrhoea. Higher rates of isolation of *Shigella flexneri*, *Shigella dysenteriae* 1, and *Salmonella typhimurium* were observed among patients with persistent diarrhoea than in those with diarrhoea of shorter duration. No positive correlations were observed between the clinical severity of disease at hospital admission and measles. Breast fed babies were not prone to persistent diarrhoea.**

Diarrhoeal diseases are a major cause of morbidity and mortality, particularly in children in developing countries, and have been extensively studied over the past three decades. Most of the research relates to acute or chronic diarrhoeal illness. Though persistent diarrhoea is an important problem, our understanding of it is still limited.

Persistent diarrhoea has been defined as a diarrhoeal episode of presumed infectious aetiology that begins suddenly and lasts more than 14 days.<sup>1</sup> It seems to be a separate clinical and epidemiological entity and a battery of risk factors may be associated with this condition. Accurate information regarding its incidence and risk factors should come from prospective community based studies but such studies are few.<sup>2-4</sup> However, it has been recommended by the Diarrhoeal Diseases Control Programme of the World Health Organisation that hospital based studies of this problem should also be carried out in developing countries.<sup>5</sup> The present study is an attempt to determine the incidence of persistent diarrhoea and to delineate some of the risk factors associated with it in hospitalised patients.

## Methods

Dr B C Roy Memorial Hospital for Children is the biggest paediatric hospital in Calcutta, providing free treatment to inpatients and outpatients. Patients come from all socioeconomic groups, either directly or after referral from other state hospitals. Approximately 6000 patients with acute watery diarrhoea or dysentery are admitted to the hospital annually and another

7000 to 8000 patients with acute diarrhoea or dysentery receive treatment as outpatients. Patients are treated throughout the year, but most are seen during the hot summer months (April to July) and during the monsoon (August to September). A surveillance system was set up by the National Institute of Cholera and Enteric Diseases to study a representative sample of diarrhoea patients at this hospital.

## SUBJECTS

Children of both sexes up to the age of 5 years, suffering from acute watery diarrhoea or dysentery (blood and mucus in stools) of less than three days' duration, irrespective of severity, and admitted between 8 am and 1 pm during the first four days of the week were studied. Patients with post measles diarrhoea were included.

Patients who had received antibiotics before admission, or those with a history of diarrhoea exceeding three days and those with diarrhoea complicated by systemic illness – for example respiratory tract infection or septicaemia – were excluded.

## DEFINITIONS

Diarrhoea was defined as the passage of three or more loose stools during the preceding 24 hours. In breast fed babies, the mother's perception was considered in defining diarrhoea. Cessation of diarrhoea was defined as the passage of the last loose stool followed by three consecutive days without diarrhoea. Persistent diarrhoea was defined as an episode of diarrhoea lasting for 14 days or more.

## CLINICAL EVALUATION

On hospital admission, a detailed clinical history was obtained and a thorough physical examination was performed. Findings were recorded on a proforma. The severity of watery diarrhoea was assessed by clinical signs and symptoms of dehydration,<sup>6</sup> whereas dysentery was assessed by frequency of stools per day together with associated symptoms like fever and tenesmus.<sup>7</sup> Patients were weighed naked, to the nearest 10 g, and were allocated to different 'weight for age' nutritional groups according to the Indian Academy of Paediatrics using Harvard standard weight.<sup>8</sup> Investigators recorded the following parameters daily: number of stools; consistency; presence of blood and mucus in stool; temperature; presence of abdominal pain; tenesmus; anorexia; vomiting; treatment with drugs or fluid (intravenous, oral or both); and the nature and amount of food given. Children were followed up daily until

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Accepted for publication  
24 September 1990

discharged. Usually, WHO guidelines<sup>6</sup> were followed for the management of diarrhoea in the hospital. Patients with mild to moderately dehydrated watery diarrhoea received standard oral glucose electrolyte solution (WHO formula). Those who were severely dehydrated were treated initially with Ringer's lactate solution followed by oral glucose electrolyte solution. Furazolidone was used in standard doses in selected patients only. Patients with dysentery received furazolidone, cotrimoxazole, or ampicillin and if there was no clinical improvement after 72 hours they were changed to nalidixic acid, in standard doses for five days. Feeding schedules of the children were continued and older children received the full hospital diet after correction of dehydration.

#### MICROBIOLOGICAL PROCEDURES

Faecal samples were collected on hospital admission and examined microscopically for the presence of blood and mucus and ova, cysts, and parasites. Samples were also cultured or tested for bacterial and viral enteropathogens using standard techniques.<sup>9</sup> Further samples were examined from children who suffered persistent diarrhoea.

#### LACTOSE INTOLERANCE

Stool samples from the symptomatic children were also screened for lactose intolerance on the 14th day by heating a measured quantity of centrifuged liquid portion of stool with Benedict's reagent and by estimation of acidic pH by narrow range pH paper.

#### STATISTICAL ANALYSIS

The  $\chi^2$  test for significance was used for statistical analysis. Relative risk (RR) was calculated by Mantel and Haenszel method.<sup>10</sup>

### Results

A total of 383 children were studied. Of these, 315 (82.2%) had watery diarrhoea and 68 (17.8%) had dysentery. A total of 335 (87.5%) recovered within 13 days. In 33 (8.6%) children the diarrhoea continued for 14–20 days and in a further 15 (3.9%) it persisted for over 20 days. In all, 48 (12.5%) children were considered to have persistent diarrhoea.

#### HOST FACTORS

##### Age

Children aged 7 to 18 months had a significantly greater incidence of persistent diarrhoea (Table I). Relative risks (RR) of the two groups of children aged between 7 and 12 months and 13 and 18 months were 2.6 and 3.3, respectively.

##### Nutritional status

All children with persistent diarrhoea had some degree of malnutrition (Table II). Children with grades II-IV malnutrition constituted the majority (70.8%). Correlation of persistent diarrhoea

and malnutrition was highly statistically significant ( $\chi^2=61.3678$ ,  $p<0.000001$ ).

#### Character of stool, severity of the disease, and agents

When duration of diarrhoea was compared with either of the stool characters it was observed that out of 315 patients with watery diarrhoea only 25 (7.9%) developed persistent diarrhoea compared with 23 of 68 (33.8%) children with dysentery. The difference in the incidences of persistent diarrhoea among those with watery diarrhoea and dysentery was statistically significant ( $\chi^2=31.869$ ,  $p<0.0001$ ; RR=5.9). The clinical severity on hospital admission of patients with watery diarrhoea and those with dysentery had no correlation with the development of persistent diarrhoea (Table III). Table IV shows the detection of enteropathogens on admission to hospital. Enteropathogens were isolated from 81.2% of prospective persistent diarrhoea cases and from 57.9% patients who did not develop persistent diarrhoea. *Shigella flexneri*, *Shigella dysenteriae* 1, and *Salmonella typhimurium* were isolated statistically more often from patients who went on to develop persistent diarrhoea.

#### Seasonal distribution

The rate of hospital admission for acute diarrhoea or dysentery patients, particularly for disease caused by bacterial enteropathogens, was higher during hot summer months (April to July), and 38 (75%) patients with persistent diarrhoea were observed during that period.

#### Food habits

Investigation of the relation between different feeding patterns and the duration of diarrhoea showed that there were no breast fed babies among the 48 who developed persistent diarrhoea. Of those who developed persistent diarrhoea, 10.4% were bottle fed, 22.9% were cereal fed, and 66% were eating a mixed diet, whereas

TABLE I Distribution of age in relation to duration of diarrhoea

Age group (mths)	No (%)		
	Non-PD (n=335)	PD (n=48)	RR
0-6	64 (19.1)	0	-
7-12	82 (24.5)	22 (45.8)	2.6*
13-18	60 (17.9)	20 (41.7)	3.3†
19-24	40 (11.9)	5 (10.4)	0.9
25-59	89 (26.6)	1 (2.1)	0.06

PD=persistent diarrhoea; RR=relative risk.  
\* $\chi^2=8.6305$ ;  $p=0.003$ ; † $\chi^2=12.937$ ;  $p=0.0003$ .

TABLE II Duration of diarrhoea in relation to nutritional status

Nutritional status (% Harvard standard weight for age)	No (%)	
	Non-PD (n=335)	PD (n=48)
Normal (>80)	78 (23.3)	0 (0)
Group I malnutrition (71-80)	193 (57.6)	14 (29.2)
Groups II-IV malnutrition (<70)	64 (19.1)	34 (70.8)

$\chi^2=61.3678$ ;  $p<0.000001$ . PD=persistent diarrhoea.

TABLE III Duration of diarrhoea in relation to severity of the diseases

Severity	Watery diarrhoea* (No (%))		Dysentery† (No (%))	
	Non-PD (n=290)	PD (n=25)	Non-PD (n=45)	PD (n=23)
Mild	207 (71.4)	17 (68.0)	6 (13.8)	3 (13.0)
Moderate	62 (21.4)	6 (24.0)	30 (66.7)	15 (65.2)
Severe	21 (7.2)	2 (8.0)	9 (20.0)	5 (21.7)

\* $\chi^2=0.1283$ ;  $p=0.94$ ; † $\chi^2=0.028$ ;  $p=0.99$ . PD=persistent diarrhoea.

TABLE IV Enteropathogens detected initially in persistent diarrhoea (PD) and non-PD cases

Enteropathogen detected	No (%)	
	Non-PD (n=335)	Prospective PD (n=48)
Enteropathogenic <i>Escherichia coli</i>	33 (9.9)	4 (8.3)
Rotavirus	31 (9.3)	0 (0)
<i>Vibrio cholerae</i>	28 (8.4)	0 (0)
<i>Shigella flexneri</i>	16 (4.8)	13 (27.1)
<i>Campylobacter jejuni</i>	14 (4.2)	0 (0)
<i>Aeromonas</i> sp	13 (3.9)	3 (6.3)
<i>Salmonella typhimurium</i>	8 (2.4)	8 (16.7)
<i>S dysenteriae</i> 1	7 (2.1)	10 (20.8)
Cryptosporidium	5 (1.5)	0 (0)
<i>Clostridium difficile</i>	1 (0.3)	0 (0)
<i>Entamoeba histolytica</i>	1 (0.3)	0 (0)
<i>Giardia lamblia</i>	1 (0.3)	0 (0)
Enteropathogens in combination	36 (10.7)	1 (2.1)
Total	194 (57.9)	39 (81.3)

in children without persistent diarrhoea, 17.3% were bottle fed, 17.7% were cereal fed, 40.6% had mixed feeding, and 23.5% were breast fed. It was clear that breast fed babies were not prone to persistent diarrhoea compared with the others. No significant differences were observed, however, among the persistent and non-persistent diarrhoea babies who were bottle fed, cereal fed, or had mixed feeding.

#### Measles

Fourteen children with post measles diarrhoea and 64 with a history of measles within six months of admission were included in the study but all recovered within 13 days. No significant association between persistent diarrhoea and measles was observed.

Stool samples of 48 children with persistent diarrhoea were re-examined on the 14th day, but none was found to be either positive for any known enteropathogen or showed any evidence of lactose intolerance.

#### Discussion

The present study showed an incidence of persistent diarrhoea of 12.5% in children admitted to hospital. In this study most (87.5%) children suffering from persistent diarrhoea were aged between 7 and 18 months. This is in contrast to the progressive rise in incidence with increasing age observed in a community based study in Bangladesh.<sup>2</sup> In another study in rural India, however, the peak incidence of persistent diarrhoea occurred in children aged between 3 and 5 months.<sup>4</sup> In the present study, persistent diarrhoea was conspicuously absent in children below 6 months of age, which may reflect the universal practice of breast feeding in this age group.<sup>11, 12</sup>

As in previous reports,<sup>13, 14</sup> our study also indicated that malnutrition may be one of the precipitating factors in persistent diarrhoea. The higher incidence of persistent diarrhoea among malnourished children may possibly be the result of depressed immunity<sup>15</sup> and delayed recovery of intestinal mucosal injury after acute infection,<sup>16</sup> especially infection caused by enteroinvasive pathogens. In developing countries many children become malnourished just after weaning, because of a lack of an adequate or balanced diet. Furthermore, this is also the age when the risk of infection, particularly diarrhoea, is highest because of greater exposure via contaminated food, drinks, or even environment and lack of the protection probably provided by the breast milk.<sup>12</sup> It is also quite clear that frequent infections lead to malnutrition<sup>17</sup> and the high incidence of persistent diarrhoea among children older than 6 months of age could be a reflection of this.

It is well known that certain bacterial and viral infections, including measles, can depress the systemic cell mediated immunity, at least for a time. Some workers<sup>18</sup> have observed prolonged diarrhoea as a result of this but no such association was observed in the present study.

Regarding aetiological agents, it has been shown that most of the enteropathogens can cause acute as well as persistent diarrhoea except *Vibrio cholerae*. Increased rates of isolation of enteroinvasive organisms like *S dysenteriae* type 1, *S flexneri*, and *S typhimurium* were noticed during the initial period of illness of the children with persistent diarrhoea in our study, which confirm the findings of a study from Bangladesh.<sup>2</sup> It has also been reported that aggregative *Escherichia coli* may be responsible for persistent diarrhoea.<sup>19</sup> In our study, the severity of both watery diarrhoea and dysentery did not correlate with subsequent delayed recovery, which corroborates other studies.<sup>20, 21</sup> Diet has been proposed as a risk factor for persistent diarrhoea<sup>22</sup> because of changes it can cause to the intestinal microenvironment. None of the breast fed babies in our study suffered from persistent diarrhoea, although other dietary habits (bottle, cereal, and mixed feeding) did not seem to correlate significantly with the occurrence of persistent diarrhoea.

The authors thank the superintendent and visiting physicians of Dr B C Roy Memorial Hospital for Children, Calcutta for allowing us to study patients admitted under them. The authors also thank Drs S K Bhattacharya, D Dutta, U Mitra, M K Bhattacharya, R Rasaily, S P De, M R Saha, G B Nair, P Das, S K Niyogi, and Mr S N Sikdar for their valuable help during the study. The secretarial help of Mr S Karmakar is also acknowledged.

The paper was presented in the Indo-UK Workshop on Diarrhoeal Diseases and an abstract of the paper was published in the proceedings of the workshop.

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