Severity of Diarrhea and Malnutrition among Under Five-Year-Old Children in Rural Bangladesh

Farzana Ferdous, Sumon K. Das, Shahnawaz Ahmed, Fahmida D. Farzana, Jonathan R. Latham, Mohammad J. Chisti, Abu I. M. S. Ud-Din, Ishrat J. Azmi, Kaisar A. Talukder, and Abu S. G. Faruque*

International Centre for Diarrheal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh;
European Centre for Disease Prevention and Control (ECDC), Solna, Sweden

Abstract. Enteric pathogens are commonly associated with diarrhea among malnourished children. This study aimed to determine the association between the severity of diarrheal illnesses and malnutrition among under 5-year-old children. During 2010 and 2011, we studied 2,324 under 5-year-old diarrheal children with mild disease (MD) and moderate-to-severe disease (MSD) attending a hospital in Bangladesh. Children with MSD were more likely to be malnourished compared with children with MD (35% versus 24%, $P < 0.001$). In multivariate analysis, malnutrition (odds ratio [95% confidence interval] = 1.53 [1.22, 1.92]), age of the child (24–59 months; 1.67 [1.28, 2.19]), fever (1.65 [1.28, 2.12]), abdominal pain (1.87 [1.48, 2.37]), straining (5.93 [4.80, 7.33]), and infection with *Shigella* (3.26 [2.38, 4.46]) and *Vibrio cholerae* (2.21 [1.07, 4.58]) were shown to be significantly associated with MSD. Factors significantly associated with malnutrition were disease severity (1.56 [1.24, 1.95]), age (24–59 months; 1.75 [1.38, 2.22]), mother's schooling (1.54 [1.16, 2.04]), and monthly household income (1.71 [1.42, 2.07]). Childhood malnutrition was associated with dysentery and dehydrating diarrhea.

INTRODUCTION

Diarrhea is one of the leading causes of childhood morbidity and mortality¹ in developing countries,^{2,3} where an estimated 1.5 million young children annually die of diarrhea.⁴ Although mortality caused by diarrheal illnesses has been reduced globally, diarrhea-associated morbidity has changed very little.⁵ The association between malnutrition and diarrheal mortality is bidirectional and has been reported for decades^{4–6} as an association between diarrhea and poor growth and development of young children.^{1,7} Malnutrition after diarrheal illness stems from anorexia, reduced absorptive function, and mucosal damage as well as nutrient exhaustion associated with each episode of diarrhea.⁶ A significant proportion of global malnutrition is caused by enteric infections.⁶ Diarrheal illnesses affect weight as well as height gains, with the most dramatic effects observed in cases of recurrent illnesses.⁸ Malnutrition can lead to reduced human performance and inadequate physical growth and cognitive development,^{1,9} and it is associated with increased frequency, duration, and severity of diarrheal episodes.⁸

There are several enteric pathogenic agents with which malnourished children are commonly infected, and these agents often vary by nutritional status; for example, shigellosis and cholera are more common in severely malnourished children,¹⁰ whereas rotavirus is the predominant cause of diarrhea in well-nourished children.^{11,12} Moreover, several studies have indicated that children who suffer from shigellosis and cholera may become more severely malnourished after the recovery from disease.^{6–8,13} Individuals who live in deprived areas with poor sanitation, inadequate hygiene, and unsafe drinking water have greater exposure to enteric pathogens and an increased risk of morbidity and severity of diarrheal illnesses.¹⁴

There are few epidemiological studies of children in rural areas that investigate the association between diarrheal disease severity and malnutrition.^{15,16} Therefore, the present study was

conducted to characterize the clinical and epidemiological features of moderate-to-severe diarrheal illnesses and determine the association between diarrheal illnesses severity and malnutrition among children who are less than 5 years old living in rural areas of Bangladesh. The present study hypothesized that there is association between enteric pathogens and malnutrition as well as severity of diarrheal disease.

MATERIALS AND METHODS

Study site and diarrheal disease surveillance. The study was conducted in Kumudini Hospital in Mirzapur subdistrict in Tangail district, approximately 60 km north of Dhaka, the capital of Bangladesh, and it spans an area of 374 km². Kumudini Hospital is a charitable institution established in 1938 that provides health services to the poor and rural population of the subdistrict and surrounding areas. Since 1982, the hospital has both outpatient and inpatient diarrhea treatment units. Nearly 1,500 diarrhea patients report each year to this facility for treatment. A round-the-clock diarrheal disease surveillance system was established for detection of four common pathogens (*Vibrio cholerae*, *Shigella*, enterotoxigenic *Escherichia coli* [ETEC], and rotavirus) among diarrhea patients attending Kumudini Hospital. A structured questionnaire was administered to mothers of children suffering from diarrhea to collect information on demographic, epidemiological, and clinical characteristics of under 5-year-old children included in the surveillance system. Information on nutrition status, treatment received at the facility, and outcome of treatment was also recorded.

Definitions are listed here.

- (1) Diarrhea was defined as three or more abnormally loose or watery stools during the previous 24 hours; a new episode was defined as ≥ 3 days have passed since recovery from the previous episode.¹⁷
- (2) Dysentery was defined as invasive diarrhea with visible blood in one or more stools.¹⁷
- (3) Moderate-to-severe disease (MSD) was defined as the presence of one of the following characteristics¹⁸: (i) sunken eyes more than normal, (ii) decreased skin elasticity,

*Address correspondence to Abu S. G. Faruque, Centre for Nutrition and Food Security (CNFS), International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), 68 Shaheed Tajuddin Ahmed Sarani, Mohakhali, Dhaka 1212, Bangladesh. E-mail: gfaruque@icddr.org

- (iii) intravenous rehydration administered or prescribed before coming to hospital, (iv) dysentery, and (v) hospitalization with diarrhea or dysentery.
- (4) Children < 5 years old without any signs of MSD were considered as cases with mild disease (MD).
- (5) Some dehydration was defined as one or more of the following signs: restlessness, irritability, sunken eyes, drinks eagerly, thirsty, and skin pinch goes back slowly.¹⁷
- (6) Severe dehydration was defined as two or more of the following signs: lethargy or unconsciousness, sunken eyes, drinks poorly or not able to drink, and skin pinch goes back very slowly (≥ 2 seconds).¹⁷
- (7) Malnutrition was defined as diarrheal children with stunting (height-for-age z score [HAZ] < -2.00 SD), or wasting (weight-for-height z score [WHZ] < -2.00 SD), or underweight (weight-for-age z score [WAZ] < -2.00 SD) as per World Health Organization (WHO) guidelines.¹⁹ Children were considered well-nourished if their z scores for WAZ, HAZ, and WHZ were -2.00 SD or higher. For each child, HAZ, WHZ, and WAZ scores were calculated through computer-based software WHO Anthro-2006.

Study population. From January of 2010 to December of 2011, a total of 2,324 under 5-year-old diarrheal children was enrolled into Demographic Surveillance System (DSS).

Anthropometric measurement. Weight and length/height were measured for each enrolled child. To calculate weight (to the nearest 0.1 kg) for children 0–23 months of age, the weights of the mother alone and with the child were recorded, and the child's weight was computed during analysis; the weight of children ages 24–59 months was taken naked or in light clothing using a digital scale (Tanita Digital Scale HD-314, Tanita Corp of America, Arlington Heights, IL). The length of children 0–23 months of age or children who were older but unable to stand alone was measured (to the nearest 0.1 cm) in the recumbent position using a board with a fixed head and sliding foot piece (Shorr Productions, Olney, MD). The same apparatus was used to measure standing height in children 2 years of age and older.²⁰

Specimen collection and laboratory procedures. A single, fresh, whole-stool specimen (at least 3 mL or 3 g) was collected from all under 5-year-old children presenting with diarrhea. A fecal swab was then placed in Cary–Blair medium in a plastic screw top test tube. Using a Styrofoam container with cold packs, the specimens were transported to the central laboratory of icddr,b in Dhaka within 6 hours of collection. Each specimen was aliquoted into three serial containers and submitted to the respective laboratories for routine screening of four common enteric pathogens (ETEC,²¹ *V. cholerae*,²² *Shigella* spp.,²² and rotavirus²³) using standard screening methods.

Shigella spp. was isolated and identified according to standard microbiological and biochemical methods.²² *Shigella* spp. was also confirmed and serotyped using a commercially available antisera kit (Denka Seiken, Tokyo, Japan). In cases of non-typeable *S. flexneri*, serotyping was also performed by using monoclonal antibody reagents specific for all type and group factor antigens.²⁴

Group A rotavirus-specific VP6 antigen was detected in the stool specimens using a solid-phase sandwich-type enzyme immunoassay (EIA) modeled after the ProSpecT commercial kit assay (Oxoid Ltd, Basingstoke Hants, United Kingdom). Positive and negative controls were included in every test

run. Quality control of the EIA test was routinely performed using rotavirus-positive samples with known optical density (OD) values.²⁵

In case of ETEC, stool samples were plated onto MacConkey agar, and the plates were incubated at 37°C for 18 hours. Six lactose-fermenting individual colonies morphologically resembling *E. coli* were tested.²⁶ For *V. cholerae*, the stool samples were plated on taurocholate-tellurite-gelatin agar²⁷ and gelatin agar (Difco, Detroit, MI); after overnight incubation of plates, serological confirmation of suspected *Vibrio* colonies was carried out by slide agglutination.^{28,29}

Statistical analysis. Statistical analysis was carried out using windows version SPSS 15.5 and Epi Info version 5.6. For categorical variables, differences in the proportions were compared by χ^2 tests, and analyses of associations were examined using univariate analysis and calculation of the odds ratios (ORs) with 95% confidence intervals (CIs). To investigate factors associated with MSD and malnutrition, logistic regression analysis was performed after controlling for confounders. MSD and malnutrition status were chosen as the dependent variables in separate models, and $P < 0.05$ was used as the criterion for statistical significance. Moreover, stunting, wasting, and underweight were also entered as the dependent variables in separate regression analyses to better understand the relationship between each unique characteristic of malnutrition and diarrheal disease severity.

Ethical considerations. This study was approved by the Research Review Committee and the Ethical Review Committee of the International Center for Diarrheal Disease Research, Bangladesh (icddr,b). Before enrolment, signed informed consent was obtained from the mothers/primary caretakers of participating children. The consent form was provided to each caretaker, and it was written in simple Bangla language to be easily understood by caretakers of participating children. The consent form was verbally reviewed to ensure comprehension by those caretakers with little or no educational background.

RESULTS

The mean $\pm$ SD age of the study children was 15.6 ± 11.2 months, and median age was 12 months (range = 0–59 months). Overall, 61% of the study children were male, and 11% of the children's mothers had no formal education. A total of 41% of the children had a monthly family income of less than \$100 US. Among children less than 2 years old, 3% were exclusively breastfed, 89% were partially breastfed, and 8% were not breastfed (data not shown).

Among the children with diarrhea, 39% ($N = 904$) had MSD. Overall, 28% of the children ($N = 651$) were found to be malnourished (WAZ, or HAZ, or WHZ < -2.00 SD); 21% of the children were underweight, 15% of the children were stunted, and 15% of the children were wasted (data not shown).

Malnourished children were more likely to present with visible or reported blood in their stool ($P < 0.001$), suffer from some or severe dehydration ($P = 0.005$), and receive intravenous fluid ($P = 0.002$) compared with well-nourished children (Table 1).

In malnourished children, children ages 24–59 months were more likely to have MSD than MD, and children ages 0–11 months were more likely to have MD than MSD. Significantly more MSD children had a monthly family income of less than \$100 US compared with MD children ($P = 0.001$) (Table 2).

TABLE 1
Comparison of indicators of severity of disease with nutritional status among under 5-year-old children

Indicators	Malnourished (N = 651; %)	Well-nourished (N = 1,673; %)	OR (95% CI); P value
Visible or reported blood in stool	240 (36.9)	442 (26.4)	1.63 (1.33, 1.98); < 0.001
Sunken eyes	70 (10.8)	138 (8.2)	1.34 (0.98, 1.83); 0.069
Slow return of skin	19 (2.9)	30 (1.8)	1.65 (0.88, 3.05); 0.124
Mental status (irritable)	16 (2.4)	29 (1.7)	1.43 (0.74, 2.75); 0.331
Some or severe dehydration	91 (14.0)	165 (9.9)	1.49 (1.12, 1.97); 0.005
Received intravenous fluid	83 (12.8)	142 (8.5)	1.58 (1.17, 2.12); 0.002

Among MSD children, 35% were malnourished compared with 24% of MD children ($P < 0.001$). Malnourished MSD children more commonly reported symptoms of fever, abdominal pain, and straining compared with their malnourished MD counterparts. Children with MSD were less likely to present with vomiting. Malnourished children with MD were associated with receiving oral rehydration solution (ORS) treatment at home or seeking other treatment at home more often compared with malnourished children with MSD (Table 2).

Of malnourished MD cases, 44% had rotavirus antigen in their stool compared with 17% of MSD cases ($P < 0.001$). Additionally, significantly more MSD children had some strain of *Shigella* in their stool compared with MD children

($P < 0.001$). Among the malnourished children, *S. flexneri* accounted for 52% of all *Shigella* isolates, and it was followed by *S. sonnei* (34%), *S. boydii* (12%), *S. dysenteriae* (3%), and *Shigella* like-organism (SLO; < 1%) (Table 2).

In case of well-nourished children, a greater proportion of MSD cases (23%) were from the 24–59 months age category compared with the proportion of MD cases (12%) from this age category ($P < 0.001$). Well-nourished MSD children were more likely to present with fever, and symptoms of abdominal pain and straining and less likely to report vomiting, cough, and history of incidence of measles in previous month compared with MD children. MD was associated with having received ORS more often at home. Among the

TABLE 2
Characteristics of MSD and MD among malnourished and well-nourished diarrheal children in rural Bangladesh

Indicators	Malnourished (N = 651; %)			Well-nourished (N = 1,673; %)		
	MSD (N = 316)	MD (N = 335)	OR (95% CI); P value	MSD (N = 588)	MD (N = 1,085)	OR (95% CI); P value
Age (months)						
0–11	101 (32.0)	165 (49.3)	0.48 (0.35, 0.67); < 0.001	265 (45.1)	567 (52.3)	0.75 (0.61, 0.92); 0.005
12–23	98 (31.0)	114 (34.0)	0.87 (0.62, 1.23); 0.460	189 (32.1)	388 (35.8)	0.85 (0.68, 1.06); 0.152
24–59	117 (37.0)	56 (16.7)	2.93 (2.00, 4.30); < 0.001	134 (22.8)	130 (12.0)	2.17 (1.65, 2.85); < 0.001
Male (%)	192 (60.8)	217 (64.8)	0.84 (0.60, 1.17); 0.327	359 (61.1)	653 (60.2)	1.04 (0.84, 1.28); 0.767
Mother's lack of schooling	58 (18.4)	44 (13.1)	1.49 (0.95, 2.33); 0.084	54 (9.2)	97 (8.9)	1.03 (0.72, 1.48); 0.938
Monthly family income (< \$100 US)	185 (58.5)	153 (45.7)	1.68 (1.22, 2.32); 0.001	217 (36.9)	402 (37.1)	0.99 (0.80, 1.23); 0.995
Earth/sand as predominant floor material	266 (84.2)	287 (85.7)	0.89 (0.57, 1.40); 0.672	426 (72.4)	760 (70.0)	1.12 (0.89, 1.41); 0.328
No sanitary toilet	32 (10.1)	21 (6.3)	1.68 (0.92, 3.11); 0.097	36 (6.1)	54 (5.0)	1.25 (0.79, 1.96); 0.379
Used soap after defecation	231 (73.1)	248 (74.0)	0.95 (0.66, 1.37); 0.857	475 (80.8)	899 (82.9)	0.87 (0.67, 1.14); 0.321
Breastfeeding status (< 2-year-old children)						
Exclusively breastfed	3/199 (1.5)	9/279 (3.2)	2.18 (0.53, 10.28); 0.374	11/454 (2.4)	41/955 (4.3)	0.59 (0.27, 1.13); 0.112
Clinical features						
Episode of diarrhea lasted ≥ 3 days	88 (27.8)	76 (22.7)	1.32 (0.91, 1.91); 0.153	164 (27.9)	269 (24.8)	1.17 (0.93, 1.48); 0.185
Number of stool passages ≥ 10 times	165 (52.2)	176 (52.5)	0.99 (0.72, 1.36); 0.997	266 (45.2)	523 (48.2)	0.89 (0.72, 1.09); 0.246
Fever (≥ 37.8°C)	89 (28.2)	54 (16.1)	2.04 (1.37, 3.04); < 0.001	153 (26.0)	181 (16.7)	1.76 (1.37, 2.28); < 0.001
Abdominal pain	259 (82.0)	201 (60.0)	3.03 (2.08, 4.42); < 0.001	483 (82.1)	672 (61.9)	2.83 (2.20, 3.64); < 0.001
Straining	236 (74.7)	100 (29.9)	6.93 (4.84, 9.94); < 0.001	453 (77.0)	307 (28.3)	8.50 (6.69, 10.81); < 0.001
Cough	149 (47.2)	162 (48.4)	0.95 (0.69, 1.31); 0.818	236 (40.1)	505 (46.5)	0.77 (0.62, 0.95); 0.013
Vomiting	126 (39.9)	214 (63.9)	0.37 (0.27, 0.52); < 0.001	229 (38.9)	692 (63.8)	0.36 (0.29, 0.45); < 0.001
Measles in the last month	10 (3.2)	21 (6.3)	0.49 (0.21, 1.11); 0.094	22 (3.7)	76 (7.0)	0.52 (0.31, 0.86); 0.009
Children admitted in hospital	117 (37.0)	102 (30.4)	1.34 (0.96, 1.89); 0.090	208 (35.4)	268 (24.7)	1.67 (1.33, 2.09); < 0.001
Sought treatment at home	236 (74.7)	293 (87.5)	0.42 (0.27, 0.65); < 0.001	434 (73.8)	956 (88.1)	0.38 (0.29, 0.50); < 0.001
Received ORS at home	210 (66.5)	287 (85.7)	0.33 (0.22, 0.50); < 0.001	400 (68.0)	925 (85.3)	0.37 (0.29, 0.47); < 0.001
Etiologic agents						
Rotavirus	53 (16.9)	146 (43.6)	0.26 (0.18, 0.38); < 0.001	95 (16.2)	462 (42.6)	0.26 (0.20, 0.34); < 0.001
<i>Shigella</i>	94 (29.7)	26 (7.8)	5.03 (3.08, 8.26); < 0.001	152 (25.9)	56 (5.2)	6.41 (4.57, 9.00); < 0.001
<i>S. sonnei</i>	34 (10.8)	7 (2.1)	5.65 (2.35, 14.20); < 0.001	37 (6.3)	12 (1.1)	7.86 (3.91, 16.10); < 0.001
<i>S. flexneri</i>	52 (16.5)	10 (3.0)	6.40 (3.07, 13.70); < 0.001	97 (16.5)	18 (1.7)	11.71 (6.84, 20.28); < 0.001
<i>S. boydii</i>	6 (1.9)	8 (2.4)	0.79 (0.24, 2.54); 0.872	9 (1.5)	23 (2.1)	0.72 (0.31, 1.64); 0.513
<i>S. dysenteriae</i>	2 (0.6)	1 (0.3)	2.13 (0.15, 5951); 0.613	7 (1.2)	3 (0.3)	4.35 (1.01, 21.24); 0.039
<i>Shigella</i> -like organism (SLO)	1 (0.3)	0		2 (0.3)	0	
ETEC	9 (2.8)	19 (5.7)	0.49 (0.20, 1.16); 0.113	20 (3.4)	28 (2.6)	1.33 (0.71, 2.47); 0.419
<i>V. cholerae</i>	8 (2.5)	7 (2.1)	1.22 (0.40, 3.77); 0.908	16 (2.7)	15 (1.4)	2.00 (0.93, 4.29); 0.080

TABLE 3

Factors predicting disease severity among under 5-year-old diarrheal children in rural Bangladesh

Indicators*	Adjusted OR (95% CI); <i>P</i> value
Malnutrition (1 = malnourished, 0 = well nourished)	1.53 (1.22, 1.92); < 0.001
Age (1 = 24–59 months, 0 = 0–23 months)	1.67 (1.28, 2.19); < 0.001
Abdominal pain (1 = yes, 0 = no)	1.87 (1.48, 2.37); < 0.001
Straining (1 = yes, 0 = no)	5.93 (4.80, 7.33); < 0.001
Fever $\geq 37.8^{\circ}\text{C}$ (1 = yes, 0 = no)	1.65 (1.28, 2.12); < 0.001
<i>Shigella</i> (1 = yes, 0 = no)	3.26 (2.38, 4.46); < 0.001
Rotavirus (1 = yes, 0 = no)	0.46 (0.37, 0.59); < 0.001
<i>V. cholerae</i> O1 (1 = yes, 0 = no)	2.21 (1.07, 4.58); 0.032

*Dependent variable (1 = MSD, 0 = MD).

well-nourished cases, rotavirus was more common among those children with mild diarrhea compared with those children with MSD. Of the entire sample, shigellosis was five to six times more common among MSD cases than MD cases (Table 2). The proportion of MSD children ages 24–59 months was higher among malnourished children compared with well-nourished children (37% versus 23%, $P = 0.005$) (Table 2).

In multivariate analysis, malnutrition, age of the child (24–59 months), fever, abdominal pain, straining, and infection with *Shigella* or *V. cholerae* were significantly associated with MSD ($P < 0.05$). Conversely, rotavirus was negatively associated with MSD ($P < 0.001$) after controlling for mother's schooling, monthly household income (< \$100 US), non-sanitary toilet facility, cough, and ETEC infection (Table 3).

Factors significantly associated with overall malnutrition were disease severity, age (24–59 months), mother's schooling, and monthly household income (< \$100 US) after controlling for non-sanitary toilet facility, cough, fever, abdominal pain, straining, and infection with *Shigella*, *V. cholerae*, ETEC, and rotavirus. Analysis also considered the individual indices of malnutrition in separate models. Stunting was significantly associated with disease severity, age (24–59 months), mother's schooling, and monthly household income (< \$100 US). Underweight was significantly associated with disease severity, age (24–59 months), monthly household income (< \$100 US), and cough. For wasting, disease severity, age (24–59 months), and monthly household income (< \$100 US) were also significantly associated after controlling for the same covariates (Table 4).

DISCUSSION

Childhood malnutrition is still a leading public health concern in Bangladesh.³⁰ Rates have gradually fallen in recent years, although the prevalence of malnutrition is still considerable.³⁰ The present study reported some interesting findings. It is perhaps not surprising that there was an increased likelihood of severe diarrheal disease among malnourished children from poorer families with a low monthly income (< \$100 US), because this finding has been shown in previous literature.³¹ In low income countries such as Bangladesh, income and household expenditure are the most commonly used measurements for socioeconomic status,³² and they often serve as a marker for malnutrition.³³ Malnourished children more often come from poor living conditions with unhygienic practices than well-nourished children.³⁴ The burden of diarrheal disease is often higher in resource-poor settings, where

TABLE 4

Factors predicting nutritional status of under 5-year-old diarrheal children in rural Bangladesh

Indicators	Adjusted odds ratio (95% CI); <i>P</i> value
Severity (1 = MSD, 0 = MD)*	1.56 (1.24, 1.95); < 0.001
Age (1 = 24–59 months, 0 = 0–23 months)*	1.75 (1.38, 2.22); < 0.001
Mother literacy (1 = illiterate, 0 = literate)*	1.54 (1.16, 2.04); 0.003
Monthly household income (1 < \$100 US, 0 $\geq$ \$100 US)*	1.71 (1.42, 2.07); < 0.001
Severity (1 = MSD, 0 = MD)†	1.39 (1.09, 1.76); 0.006
Age (1 = 24–59 months, 0 = 0–23 months)†	1.71 (1.31, 2.25); < 0.001
Mother literacy (1 = illiterate, 0 = literate)†	1.88 (1.37, 2.58); < 0.001
Monthly household income (1 < \$100 US, 0 $\geq$ \$100 US)†	1.93 (1.52, 2.45); < 0.001
Severity (1 = MSD, 0 = MD)‡	1.66 (1.34, 2.06); < 0.001
Age (1 = 24–59 months, 0 = 0–23 months)‡	1.93 (1.52, 2.47); < 0.001
Mother literacy (1 = illiterate, 0 = literate)‡	1.32 (0.97, 1.79); 0.073
Monthly household income (1 < \$100 US, 0 $\geq$ \$100 US)‡	1.75 (1.42, 2.15); < 0.001
Cough (1 = yes, 0 = no)‡	1.26 (1.02, 1.54); 0.030
Rotavirus (1 = yes, 0 = no)‡	1.25 (0.99, 1.57); 0.063
ETEC (1 = yes, 0 = no)‡	0.38 (0.14, 1.03); 0.057
Severity (1 = MSD, 0 = MD)§	1.65 (1.29, 2.12); < 0.001
Age (1 = 24–59 months, 0 = 0–23 months)§	1.59 (1.20, 2.11); 0.001
Monthly household income (1 < \$100 US, 0 $\geq$ \$100 US)§	1.56 (1.23, 1.97); < 0.001
Fever (1 = yes, 0 = no)§	1.26 (0.96, 1.67); 0.095
Rotavirus (1 = yes, 0 = no)§	1.26 (0.97, 1.64); 0.090

*Dependent variable (1 = malnourished, 0 = well nourished).

†Dependent variable (1 = stunted, 0 = normal).

‡Dependent variable (1 = underweight, 0 = normal).

§Dependent variable (1 = wasted, 0 = normal).

increased transmission of disease pathogens results from ingestion of fecally contaminated water or food.^{34–36}

Among children 24–59 months, the prevalence of MSD was higher among malnourished children than well-nourished children. These observations imply that malnourished children ages 24–59 months were more susceptible to severe diarrheal disease compared with well-nourished children.

The multivariate model suggests that older malnourished children were two-fold more likely to be MSD compared with MD than younger malnourished children, showing increased disease severity among older malnourished children compared with younger children. This finding may be explained by the protective immunological effects of breastfeeding amongst infants and young children that older children lack.³⁷ A significant association was observed between mother's schooling and nutritional status of the child; however, no such relationship was observed with disease severity. The reason for this finding is unclear.

Malnourished children were more likely to present with gastrointestinal infections and have increased diarrheal disease severity, regardless of whether the malnutrition was characterized as chronic or acute. There are several possible explanations for these findings, and they have been described in the literature. Malnourished children have greater susceptibility to infections,³⁸ especially those infections of the gastrointestinal tract.³⁹ Conversely, specific enteric infections have been found to cause malnutrition.^{38,39}

In the current study, children who had MSD were more likely to report with symptoms of fever, abdominal pain, and straining compared with children with MD, and they were less likely to have vomiting and cough. These findings are usually associated with *Shigella* in relation to MSD. *Shigella* was found to be associated with MSD among malnourished children. *Shigella*-infected children are found to be often malnourished because of their poor immune responses, which may be caused by loss of appetite and consequent inadequate intake, increased catabolism, damage of intestinal epithelium, reduced absorptive functions, and loss of nutrients in stool as well as protein losing enteropathy.^{40,41} Interestingly, no such significant relationship was found in cases of *V. cholerae*.

In the present study, malnourished children with MSD were five times more likely to suffer from shigellosis than MD children. Moreover, well-nourished children with MSD were six-fold more likely to develop shigellosis compared with MD children in the univariate model; however, no such relationship was observed in multivariate analysis of malnutrition.

The multivariate analysis of disease severity results indicated that shigellosis is more common in MSD cases. The present study revealed that *Shigella*, and *V. cholerae* were associated with severity of diarrheal disease in children. Patients with MD were more likely to have rotavirus. A previous study reported an association between better nutrition and rotavirus infection, and similar findings were reported by the current study.⁴² However, no association was observed between disease severity and ETEC.

A previous study in Bangladesh reported that ETEC and *Shigella* spp. influence growth patterns, whereas rotavirus and other enteropathogens do not.^{10,11} This finding might be caused by mitigating factors that have restrained the magnitude of diarrhea's effect on growth, or it is probably because of a greater severity of disease associated with *Shigella* and ETEC.⁴³ Another study reported that recurrent episodes of diarrheal illnesses have the greatest effects on children's growth.¹³ These effects may be influenced by intestinal host-pathogen-microbiome interactions.¹³

In the present study, we tested a few selected pathogens, and the study was conducted in a single site in rural Bangladesh. Thus, the findings may not be generalizable to a larger population. Additionally, the cross-sectional nature of this data does not allow us to examine causality in the relationship between malnutrition and diarrheal disease. However, the study had several strengths, including a large sample size of unbiased diarrheal children who reported from a distinct demographic surveillance system area.

CONCLUSIONS

In conclusion, direct significant associations between malnutrition and severity of diarrheal diseases were noted in addition to other host, sanitation, and etiologic characteristics, and *Shigella* and *V. cholerae* are important factors associated with diarrheal disease severity. However, additional research is needed to explore the underlying etiology as well as other host and environmental predictors that may influence the nutritional status and disease severity of childhood diarrheal patients. At the same time, emphasis should be given to behavioral factors, such as improved access to sanitation, promotion of young child feeding practices, particularly among non-breastfed children ages 24–59 months, hygienic practices,

and implementation of vaccines against etiologic agents, which are the burden of disease severity and also malnutrition as a whole.

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Authors' addresses: Farzana Ferdous, Sumon K. Das, Shah Nawaz Ahmed, Fahmida D. Farzana, and Abu S. G. Faruque, Centre for Nutrition and Food Security (CNFS), International Centre for Diarrheal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, E-mails: farzanaf@icddr.org, sumon@icddr.org, shahnawaz@icddr.org, fahmidaf@icddr.org, and gfaruque@icddr.org. Jonathan R. Latham, European Centre for Disease Prevention and Control (ECDC), Solna, Sweden, E-mail: Jonathan.Latham@ecdc.europa.eu. Mohammad J. Chisti, Dhaka Hospital, International Centre for Diarrheal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, E-mail: chisti@icddr.org. Abu I. M. S. Ud-Din, Identification and Sub-tying of Enteric Pathogens, Center for Food and Water Born Disease, International Centre for Diarrheal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, E-mail: iftiaf@icddr.org. Ishrat J. Azmi and Kaiser A. Talukder, Identification and Sub-tying of Enteric Pathogens, Center for Food and Water Born Disease, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, E-mails: ishratazmi@icddr.org and kaisar@icddr.org.

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