Malnutrition is a determining factor in diarrheal duration, but not incidence, among young children in a longitudinal study in rural Bangladesh¹⁻³

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ABSTRACT Diarrhea and malnutrition are common in young children in developing countries and a reciprocal relationship has been postulated with diarrhea leading to malnutrition and malnutrition predisposing to diarrhea. To investigate the importance of malnutrition as a determining factor in diarrheal illnesses, data were analyzed from a longitudinal communitybased study done in rural Bangladesh. Children classified by nutritional status according to a variety of anthropometric indicators were prospectively evaluated for incidence, duration, and etiology of diarrhea. Children with low weight for length had longer durations of diarrhea than better nourished children; however, children of differing nutritional status had similar diarrheal incidences. The duration of diarrhea, including that associated with enterotoxigenic Escherichia coli and Shigella, increased progressively as nutritional status indicators worsened. These results suggest that nutritional interventions alone are unlikely to reduce the high incidence of diarrhea, but that efforts to improve nutritional status may have a beneficial effect on the duration of diarrhea and its unfavorable nutritional consequences. Am J Clin Nutr 1984;39:87-94.

KEY WORDS Infantile diarrhea, Escherichia coli, malnutrition, nutritional status, Shigella

Introduction

Diarrheal diseases and malnutrition are common in children of developing countries and an interaction between them has been postulated (1, 2). Diarrhea has been found to have an adverse effect on growth and to be an important cause of malnutrition (3-5). At the same time, malnourished children have a greater severity of diarrhea (6) and an increased risk of death from a variety of infectious diseases, including diarrhea (7, 8).

Several field studies have suggested that nutritional status is a determinant of the prevalence of diarrhea (9-11). An increased prevalence of diarrhea could be due either to an increased incidence of diarrheal episodes or to a longer average duration of illness, but few previous studies have examined these factors separately. Furthermore, the limited reported results are not consistent. One study in Guatemala (12) found an increased incidence of diarrhea in underweight (lower weight for age) children 1 to 4

yr old, but three other studies did not find a

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relationship between young children's relative weight and their diarrheal incidence (9, 13, 14). A study in Nigeria (9), but not one in Bangladesh (14), found an increased diarrheal incidence in wasted (low weight for length) children. Although several field studies have suggested that malnourished children may have diarrheal episodes of longer duration, the use in most of these studies of a recall period for diarrheal occurrence of 1 wk (or more) and the lack of precise criteria for the beginning and end of diarrhea render the data on diarrheal duration of questionable value. Several hospital based studies indicated that cholera had a longer duration in both children and adults with poorer nutritional status than in better nourished patients (15-17).

Since previous field studies of nutritional status as a risk factor for diarrhea have not determined the etiological agents associated with the illnesses, it is also possible that the increased prevalence of diarrhea in malnourished children is due to their greater propensity to have specific types of diarrhea (eg, shigellosis or giardiasis) that are associated with a longer illness. Alternatively, intestinal malabsorption, frequently associated with severe malnutrition, may be responsible for noninfectious diarrhea in the more undernourished children. Thus, studies to determine if malnourished children have an increased incidence or duration of diarrhea need to consider illnesses due to specific enteropathogens. We assessed the incidence and duration of diarrhea associated with bacterial, viral and parasitic pathogens in a longitudinal study in rural Bangladesh (18). Two agents, enterotoxigenic Escherichia coli (ETEC) and Shigella, accounted for more than 40% of diarrheal episodes in children less than 5 vr old in the study communities (19).

Since classification of children's nutritional status based on weight as a percentage of the expected weight for a child of that age does not permit a differentiation between acute and chronic undernutrition, we classified children according to a wider variety of indicators. Relative weight for age, length for age, and weight for length were used, as was a cross-classification of these indicators to establish categories of children who were

normal, wasted, stunted, or concurrently wasted and stunted as proposed by Waterlow et al (20). Children so classified were prospectively evaluated for the etiology, incidence, and duration of diarrhea occurring in subsequent 60-day periods.

Methods

The study was conducted in two villages in the Matlab field research area of the International Centre for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B) between March 30, 1978 and March 28, 1979. The study was approved by the ethical review committee of the ICDDR, B and by the Bangladesh Medical Research Council. Informed consent was obtained to include 177 (94%) of the 188 available children between 2 and 48 months of age in the villages. Twenty additional children joined the study group during the year, for a total of 197 children participating in the study. One hundred twenty-five children were less than 24 months old (18). Descriptions of the villages, study population, surveillance methodology, and laboratory procedures have been published (18, 19, 21, 22). An episode of diarrhea was defined when four or more liquid stools were passed on at least 1 day; the episode was considered to be resolved on the 1st day with fewer than three liquid stools. However, if a child had three or more liquid stools on any day within 3 days after an episode of diarrhea, that day and intervening days were included in the same episode. Enteropathogens were considered to be associated with a diarrheal episode if they were identified from a specimen obtained during or 1 day before or after the episode.

Monthly measurements of each child's physical growth were obtained by standard techniques (23, 24). Briefly, nude or lightly clothed children were weighed to the nearest 0.1 kg on a Salter scale, which was frequently standardized against known weights. Recumbent length was measured to the nearest 0.1 cm on a wooden platform with a sliding footboard. Sex-specific data for weight and length for age and weight for length were compared with the data from the National Center for Health Statistics (NCHS) population (25). Statistics for recumbent length were available from the NCHS sample only for children up to 36 months of age, so the Stuart and Meredith (26) reference population was used for children over 36 months of age. Measurements were expressed as a percentage of the NCHS (or Stuart and Meredith) median or as multiples of the standard deviation (Z score)⁴ of the reference population. Finally, measurements for weight and length, expressed simply as more or less than 2 SD below the NCHS median weight for length and length for age, were used for a cross-tabulation. Children with weights more than 2 SD below the reference median weight for length were considered wasted and those more than 2 SD below the reference median length for age were defined as stunted. Other children were considered "normal."

observed weight for lengthreference weight for length SD of reference weight for length

Since the children's nutritional status demonstrated marked seasonal changes (24), children were classified into nutritional status groups at the beginning of consecutive, nonoverlapping 60-day periods. Six such periods (1 yr) were usually available for each child. Periods in which the child was less than or at least 24 months old at the beginning of the period were analyzed separately. When episodes of diarrhea began in one 60-day period but continued into the subsequent period, all contiguous days of illness were used to determine the total duration but the episode was only counted in the first period. The incidence and average duration of all diarrheas and of diarrheas associated with ETEC and Shigella were calculated for specific groups and compared using t tests, Z tests for differences in proportions and analyses of variance (27).

Results

For children less than 24 months old, the mean duration of diarrhea in the lowest weight for length group (less than 80% of the NCHS standard) was 56% longer than the duration for children who were at least 90% of the standard (**Table 1**). Considering etiology, there was an increase of more than 150% in the duration of ETEC and Shigella diarrheal episodes (both p < 0.05). The incidence of all diarrhea or of diarrhea associated with ETEC or Shigella did not differ among the groups.

With weight for age and length for age groupings, trends toward longer durations in less well-nourished children were also apparent; however, the durations were significantly different only for ETEC diarrhea (Table 1). Again, the groups did not differ in diarrheal incidence.

Children were classified by their Z score of weight for length, weight for age, and length for age to determine more precisely how diarrheal duration varied as a function of nutritional status. As shown in Figure 1, the duration of ETEC diarrhea declined progressively as the Z score increased for each of the anthropometric measures. Compared with the best nourished group, the average duration of ETEC diarrhea was significantly longer for weight for length groups of less than -1 Z score, for length for age groups of less than -2 Z scores, and for weight for age groups of less than -3 Z scores. Between the highest and the lowest weight for length Z score groups, the average duration of ETEC diarrhea increased from 4.8 to 17.2 days. Similarly, the average duration of all diarrhea increased from 7.1 to 10.3 days and of Shigella diarrhea from 6.5 to 21.3 days.

When children were grouped by both their weight for length and length for age, those with wasting or concurrent wasting and stunting had the longest durations of diarrhea (Table 2). Those who were stunted but not wasted had a slight increase in diarrheal duration compared with normal children. The groups did not differ in their diarrheal incidence.

The diarrheal duration and incidence for children more than 24 months of age did

TABLE 1

Duration (days) and incidence (episodes per 1000 days) of all diarrhea and of diarrhea associated with enterotoxigenic *Escherichia coli* or Shigella in 60-day periods after classification of children <24 mo old by nutritional status

Nutritional status	No. of 60-day periods	Days of Observation	All diarrhea		E coli diarrhea		Shigella diarrhea	
			Duration	Incidence	Duration	Incidence	Duration	Incidence
Wt for length*	_							
≥90%	138	8,385	6.8 ± 0.9†	16.9	4.2 ± 0.7	6.3	8.8 ± 2.3	1.8
80-89%	244	13,860	8.5 ± 0.8	16.2	10.1 ± 1.7	5.1	14.9 ± 3.1	2.1
≤79%	87	4,946	10.6 ± 1.7	16.4	10.8 ± 2.5	6.3	22.2 ± 5.0	2.6
Wt for age *								
≥75%	135	7,793	6.9 ± 0.8	15.5	4.5 ± 0.8	4.5	11.5 ± 2.4	1.5
60-74%	257	14,742	8.6 ± 0.8	17.9	8.2 ± 1.1	6.6	16.1 ± 2.9	2.4
<60%	77	4,476	10.2 ± 1.7	14.1	14.0 ± 4.0	5.1	15.1 ± 5.5	2.0
Length for age*								
≥95%	31	3.001	7.2 ± 1.5	14.0	4.2 ± 1.6	3.0		
90-94%	172	9.435	7.7 ± 0.9	18.4	7.1 ± 1.4	6.6	13.9 ± 3.0	1.8
85-89%	194	11.402	8.8 ± 1.0	17.2	8.8 ± 1.3	6.3	16.8 ± 3.5	2.5
<85%	72	4,173	9.1 ± 1.9	12.0	11.7 ± 5.0	3.6	11.2 ± 3.4	2.4

* Percentage of NCHS reference population median.

† Mean ± SEM.

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FIG 1. Duration of diarrhea associated with enterotoxigenic E coli by indicated anthropometric Z scores (NCHS/Center for Disease Control reference) in children less than 24 months old.

TABLE 2

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Duration of all diarrhea and of diarrhea associated with enterotoxigenic $E \ coli$ or Shigella in 60-day periods after anthropometric cross-classification of children <24 mo old by wt for length and length for age Z scores

Anthropometric classification	All diarrhea	E coli diarrhea	Shigella diarrhea
Normal	7.3 ± 1.0	$4.4 \pm 1.1^*$	12.0 ± 3.1
Stunted	8.0 ± 0.9	8.0 ± 1.3	13.8 ± 2.9
Wasted	10.9 ± 4.6	10.8 ± 7.3	
Wasted and stunted	9.5 ± 1.3	10.7 ± 2.1	15.4 ± 4.0
	Anthropometric classification Normal Stunted Wasted Wasted and stunted	Anthropometric classificationAll diarrheaNormal 7.3 ± 1.0 Stunted 8.0 ± 0.9 Wasted 10.9 ± 4.6 Wasted and stunted 9.5 ± 1.3	Anthropometric classificationAll diarrheaE coli diarrheaNormal 7.3 ± 1.0 $4.4 \pm 1.1^*$ Stunted 8.0 ± 0.9 8.0 ± 1.3 Wasted 10.9 ± 4.6 10.8 ± 7.3 Wasted and stunted 9.5 ± 1.3 10.7 ± 2.1

* Significant differences (p < 0.05) found for duration of *E coli* diarrhea in normal vs wasted children and vs stunted children.

not vary according to their nutritional status. The best nutritional status groups for weight for length had average durations of all diarrhea, ETEC diarrhea and Shigella diarrhea of 9.7, 9.2, and 12.3 days, respectively. Compared with younger children, these durations were 2 to 4 days longer than the average durations of the corresponding best nourished groups of children, but similar to the moderately malnourished groups.

Discussion

Anthropometry is often used to evaluate the nutritional status of children in a community (28, 29). Of the wide variety of measurements that can be taken, weight and length (or height) are the most frequently used (20). The child's weight is often compared with an international reference population and expressed as a percentage of the reference median weight for age as described by Gomez et al (30) or as a Z score (20). The use of the child's relative weight for age is limited because it does not discriminate between acute and chronic malnutrition. Thus, the use of weight for length, a measure that could reflect a more recent nutritional insult, has been recommended (20). A further refinement is the cross-classification of children based on their relative length for age (to assess stunting) and weight for length

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(to assess wasting) (20). It has been assumed that children with wasting or concurrent wasting and stunting would be at the highest risk for the adverse consequences of acute malnutrition. Indeed, it has been demonstrated that wasted children have higher rates of mortality (7, 8).

Among children in the first 2 yr of life in this study, the child's relative weight for length, ie, degree of wasting, was the strongest anthropometic predictor of diarrheal duration. Even children between -1 and -2SD below the reference median had a longer duration of ETEC diarrhea than better nourished village children. Furthermore, mean durations increased progressively as the Z score declined. Our study was unable to determine if there is a threshold level of wasting below which there is a substantial increase in diarrheal duration. The determination of such a threshold would be of use to establish a cutoff value for anthropometric screening programs. At this point, it would appear that children more than 2 Z scores below the median weight for length can be identified as being at increased risk of prolonged diarrhea after an acute enteric illness.

No relationship was found between nutritional status and the incidence of diarrhea in general or of ETEC or Shigella diarrhea. The incidence of diarrhea is determined by the number of pathogens ingested (31) and by host factors, such as by the level of gastric acidity (32) and the state of intestinal immunity (31). One might expect that malnourished children would have greater exposure to enteric pathogens because of the unsanitary conditions of poor communities compared with the residences of better nourished and wealthier children. However, all children in this study lived in the same villages and were exposed to the same vehicles of infection, such as fecally contaminated food and water (22). Although hypochlorhydria has been reported in children with severe protein-energy malnutrition (33), there is little evidence that moderately wasted children, such as we studied, have sufficiently reduced gastric acid to increase their risk of diarrheal diseases. It is also unlikely that immunological factors substantially influence the risk of diarrhea in these young children. There are many different bacterial, viral, and parasitic agents responsible for diarrhea and the ETEC and Shigella identified in this study were of many different serotypes (Black RE, unpublished data). Since the natural immunity that does develop is probably pathogen and even serotype specific (34, 35), it is unlikely that young children have sufficient immunity to prevent many illnesses from occurring (19, 36).

The fact that wasted children have longer durations of diarrhea has several possible explanations. The duration of diarrhea may be a function of the number of bacteria that enter the small intestine (which probably did not differ according to nutritional status in these study children) and certain host factors, such as the rates of immune response and intestinal repair. Severely malnourished children have been shown to have defects in cell-mediated immune function (37-40), a reduced secretory IgA response of the respiratory tract (41, 42), and a decrease in IgAcontaining cells in the jejunal mucosa (43). Since even the best nourished groups of older children have diarrheal durations similar to moderately wasted younger children, immunity, which should be better developed in older children, is not a likely explanation for the nutrition-related differences in diarrheal duration.

A possible explanation is that malnourished children may have delayed recovery of the intestinal mucosa after infection. Brunser et al (44) noted a decreased mitotic index of mucosal cells in marasmic children. A slower turnover rate for intestinal cells would be expected to cause a delay in replacement of damaged enterocytes and correction of functional abnormalities that result from tissue invasion during Shigella or viral diarrheas or from the effects of cellbound toxin during ETEC diarrhea or cholera. Such a delay in mucosal recovery could result in a more prolonged diarrhea.

Another possible explanation for the longer diarrhea in relatively malnourished young children is persistent lactose malabsorption (45, 46) which has been identified in one study as the most common reason for prolonged diarrhea after an acute enteric illness (47). In an earlier study from the same

area of rural Bangladesh, it has been observed that diarrhea-free young children with a lower weight for length had a higher frequency of lactose malabsorption than better nourished children of the same age (48). After 36 months of age, a high proportion of all children regardless of nutritional status, had lactose malabsorption. Thus, the effect of diarrhea on lactose absorption should be most pronounced in young children, who usually have normal lactose absorption if they are well nourished, but reduced absorption if they are wasted. The predominant source of dietary lactose was breast milk, which was consumed by nearly all children younger than 24 months old, both when they were free from illness (49), as well as during diarrhea (Brown KH, unpublished data). Since breast-feeding was universal in young study children, the possible roles of breast milk either in prolonging diarrhea (because of lactose malabsorption) or in shortening diarrhea (due to transfer of passive immunity to the infant) could not be investigated.

It is said that a reciprocal relationship exists in which diarrhea leads to malnutrition and malnutrition predisposes to diarrhea (2). It is clear that diarrhea has adverse effects on growth (3-5). ETEC diarrhea had the most pronounced effect on short-term weight gain and Shigella diarrhea had the largest effect on annual linear growth in these study children (5). The previous evidence that malnutrition increased the incidence of diarrhea was mixed and we did not observe such an effect vis-à-vis all diarrhea or the two most frequent types of diarrhea affecting the study children. Malnourished children did, however, have diarrhea of longer duration. This longer duration could also explain the increased prevalence of diarrhea that has been noted previously in malnourished children. More prevalent diarrhea, especially if associated with malabsorption of lactose and possibly other nutrients would in turn be expected to exacerbate malnutrition.

These findings have implications for public health programs seeking to control morbidity and mortality of children in developing countries. Nutritional interventions alone are not likely to reduce the high incidence of diarrhea. However, efforts to improve nutritional status may be successful in limiting the duration of diarrhea and its negative nutritional consequences. Furthermore, these results suggest that more individualized nutritional and fluid and electrolyte management of diarrhea may be indicated for malnourished children.

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