ORIGINAL ARTICLE

Deaths Following Acute Diarrhoeal Diseases Among Hospitalised Infants in Kuala Lumpur

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Abstract

The risk factors and modes of death following acute diarrhoeal illness in children admitted to University Hospital, Kuala Lumpur between 1982 and 1997 were studied retrospectively. Among 4,689 cases of acute gastroenteritis admitted, ten deaths were noted. The case mortality rate was 2.1/1000 admissions. All deaths were infants below one year, with eight females and two males. Acute renal failure and acute pulmonary oedema were common preceding events. Female sex, infants less than twelve months, the presence of hyper or hyponatraemia and moderate to severe dehydration on admission were risk factors for deaths.

Key Words: Deaths, Acute diarrhoea, Risk factors

Introduction

The use of oral rehydration solution has led to a significant reduction in the mortality of diarrhoeal diseases[1]. In developing countries, however, it remains an important cause of childhood mortality, where it was estimated to cause 2.9 million deaths in 1992[2]. The risk factors for mortality following diarrhoeal illness in developing countries were young age, severe malnutrition, severe dehydration, lack of breast feeding, presence of concomitant bacteraemia and lack of immunisation[3-7]. In developed countries, however, the risk factors were quite different. Very low birth weight, prematurity, low Apgar scores, poor maternal education were the notable risk factors in the US[8-10]. It had been shown that identification of risk factors of mortality following acute diarrhoeal illness would lead to the formulation of better prevention strategies and the eventual reduction of mortality rate[1,11].

Malaysia is a newly industrialised country, with approximately 40% of the population in the urban area[12]. Basic health care is free and is readily available to the general population. According to official statistics, intestinal infections including cholera, enteric fevers, food poisoning and other infections accounted for 155 deaths in Malaysia in 1995[12]. Of these, 69 were children below 14 years of age. These data did not provide any insight into the risk factors that lead to mortality following intestinal infections. Alternatively, hospital-based records might give useful information when national figures are lacking.

The aims of the present study were to identify the risk factors and the circumstances that lead to death following acute diarrhoeal illness among hospitalised children from a large urban teaching hospital in Malaysia. Better prevention strategies can then be formulated by the relevant health authorities to reduce future mortality.

Materials and Methods

The University of Malaya Medical Centre is a large teaching hospital situated in Kuala Lumpur. It serves mainly the middle and lower social classes of the population of the federal capital of Malaysia. Each year approximately 350 - 400 admissions to the paediatric unit of the hospital were due to acute gastroentetitis[13].

A retrospective review was carried out of all deaths in children under 16 years of age secondary to acute gastroenteritis, defined as the presence of three or more episodes of loose stools per day for less than 14 days' duration, from January 1982 to December 1997. Deaths associated with acute gastroenteritis were defined as deaths occurred as a direct result of acute gastroenteritis or its immediate complications.

The collection of data was divided in three parts. First,data on deaths from the paediatric unit during the study period were obtained from the medical record department of the hospital. Case records of all deaths that had been encoded as acute gastroenteritis, diarrhoea or severe dehydration were retrieved and reviewed. All deaths that fulfilled the above criteria were included. The demographic data, feeding practices, pre-admission treatment, growth parameters, physical and laboratory findings on admission; and the terminal events that lead to deaths were noted.

A database was then compiled of age, sex, ethnicity and months of admission of all children admitted with a diagnosis of acute gastroenteritis to the paediatric unit during the same period were obtained from the central data processing unit of the hospital. These data were compared with similar data of the index cases to identify risk factors in the demography of patients that might lead to increased risk of dying from acute diarrhoeal diseases.

Finally, to gain further insight into the risk factors and the preceding events that lead to death, a matched case control study was designed. Each diarrhoeal death was matched three historical controls, that had the same age, sex and ethnicity, and were admitted during the same year and same month with the index cases. One of the index case (Case 10) was an infant whose parents were immigrant from Indonesia. Since the lifestyle of Indonesians immigrants were very similar to the urban Malays in Malaysia, three Malays patients were used as matched historical controls. If three matched historical controls were unavailable from admissions during the same month, then admissions within the preceding or subsequent months were used.

The following data were obtained from the index cases and the historical controls: social class (as determined by the occupation of the father of the patient); presence of and the degree of dehydration on admission; mean duration of diarrhoea before admission (in days); presence of hyponatraemia (serum sodium <130mmol/L) or hypernatraemia (serum sodium >150mmol/L); and the presence of stool pathogen(s). Fisher Exact test was used for statistical analysis. A risk factor was considered significant if the p-value was <0.05.

Results

During the study period, a total of 4,689 children with a diagnosis of acute gastroenteritis were admitted to the paediatric unit of the hospital (Table I). Ten deaths were caused by acute gastroenteritis or its immediate complications. The overall case mortality rate was

Table I
Risk Factors for Death Following Acute Gastroenteritis

No of Admissions		Deaths	p-value*
Total	4689	10	
Male	2763	2	
Female	1926	8	0.015
< 1 year	1292	10	
>1 year	3397	0	0.0000003
Malays	1914	2	0.44[a]
Chinese	1047	2	0.17[a]
Indians	1631	5	
Others	97	1	

** : Fisher's Exact Test*

[a]: Malays vs Indians and Chinese vs Indians.

Table II
Details of the Ten Cases of Deaths Following Acute Gastroenteritis

Case	Age (month)	Sex	Race	Associated Medical Conditions	Body wt[1]	Month of Admission	Duration of diarrhoea (d)	Degree of dehydration	Serum Na+ (mmol/L)	Stool Pathogen	Terminal Events
1.	7	F	Mal	-	-	Apr	2	Shock	149	-	Acute renal failure SVT
2.	5	F	Chi	-	0.87	Apr	2	Shock	135	-	Pulmonary oedema
3.	1.5	F	Ind	-	0.71	Sep	2	Shock	141	-	Metabolic acidosis
4.	1.5	F	Ind	-	0.71	Oct	2	<5%	127	-	Aspiration
5.	11	F	Chi	Down's syndrome heart failure	0.36	Aug	2	10%	151	-	Acute pulmonary oedema acute renal failure
6.	3	F	Ind	Down's syndrome	0.59	May	1	7%	139	*Nontyphoid Salmonella*	Aspiration
7.	5	F	Ind	-	0.44	Feb	7	10%	123	-	Sepsis
8.	4	F	Mal	Chronic Renal failure	-	Mar	1	7%	-	-	Died soon after admission
9.	1	M	Ind	-	0.46	Jan	1	<5%	129	*E.coli*	Hypothermia aspiration, severe marasmus
10.	2	M	Imm	-	1.0	Jul	2	Shock	169	-	Acute renal failure seizures, DIVC

Note: M: male, F: female, Mal: Malaya, Chi: Chinese, Ind: Indian, Imm: Immigrant. SVT: supraventricular tachycardia
Jan: January, Feb: February, Mar: March, Apr: April, Jul: July, Aug: August, Sep: September;
[1]:Percentage of 50th centile body weight of Malaysian children at the same age.

2.1/1000 admissions. All deaths were infants below one year of age (median 3.5 months; mean 4.1 months). There were two males and eight females. Although more males than females were admitted with acute gastroenteritis during the study period, the case mortality rate for males was 0.7/1000 admissions while that for females 4.1/1000 admissions (p-value <0.015). More Indian children died than Malay and Chinese, but this was not statistically significant (Table I).

Table II shows the details of the ten index cases. Seven infants were previously healthy before the onset of their illness. One female infant had agenesis of the right kidney, congenital pelvi-ureteric junction obstruction and hydronephrosis of the left kidney. She was in stable chronic renal failure after pyeloplasty. One female infant who had Down's syndrome, annular pancreas and atrio-ventricular defect was being treated for heart failure. Another female infant had Down's syndrome, but no significant abnormality noted.

Two infants were given inappropriately prepared artificial feeds. One female Indian infant was given diluted infant formula alternating with sugar water by her grandmother, in the believe that this would quench her excessive thirst. She had had diarrhoea for seven days and was severely marasmic when admitted. An Indonesian infant was given feeds that were twice the recommended concentration in the believe that this would make the child grow faster. His serum sodium was 169mmol/L on admission. Four infants were seen by their general practitioners 24 hours before admission. One child was prescribed oral rehydrating solution, while another child was given an antidiarrhoeal drug. Information on pre-admission treatment on the remaining two cases were not available.

Weights on admission were available in eight infants. Two infants who died within half an hour and 3.5 hours after admission were not weighed. The remaining eight cases had a median body weight of less than 3rd centile for age. Eight cases were moderately to severely dehydrated on admission, four were in shock. Hypo and hypernatraemia were common.

Terminal events that preceded death were studied. Two cases died shortly after admission to hospital. Acute renal failure and acute pulmonary oedema were present in three and two infants respectively. Three deaths were attributed to aspiration pneumonia, possibly as a result of impaired swallowing reflex in severe malnutrition.

Table III
Risk Factors for Deaths as Compared with Matched Historical Controls

	Deaths	Control	p-value[a]
Ethnic group (M:C:I)	2:2:5	9:6:15[b]	
Sex (male:female)	2:8	6:24	
Social class IV or V	7/10	12/26[c]	0.18
Body weight on admission (≤ 2 S.D. from the mean for age)	6/8	7/16[c]	0.25
Presence of moderate to severe dehydration	7/10	3/30	0.001
Mean duration of diarrhoea before admission	2.8	2.0	0.70
Disturbances of serum sodium (<130 or >150 mmol/L)	5/9	2/27[c]	0.005
Presence of stool pathogens	2/10	5/30	0.57

[a]: *Fisher's Exact Test*
[b]: *3 Malays were used as controls for one Indonesian infant who died*
[c]: *Information on the remaining controls not available*

Septicaemia was the terminal event in one child, although blood culture was negative. No postmortem were carried out in any of the deaths.

Thirty historical controls matched for age, sex, and ethnicity were obtained for comparisons of the risk factors (Table III). In three of the control cases, serum sodium levels on admission were not obtained, while social class status of another four control cases was not available. The presence of moderate to severe dehydration on admission, and the presence of hyper or hyponatraemia were significantly associated with increased risk for death following acute diarrhoeal illness (Table III). Not surprisingly the social class of the index cases was not different from the controls as the hospital serves mainly middle and lower social classes.

Although body weight on admission was not significantly associated with an increased risk of dying from acute diarrhoeal diseases, six of the eight index cases had a body weight of at least two standard deviations from the mean for age. The median body weight of the eight index cases was 59% of the mean for age. The isolation rate of stool pathogens was generally low among the index cases and the controls. Two of the index cases had positive stool cultures: non-typhoid *Salmonella* and *E. coli* respectively, and none cases had a positive blood culture. Five of the control cases had a positive stool pathogen: rotavirus in two, and *Shigella*, non-typhoid *Salmonella*, and adenovirus in one case each.

Discussions

In a longitudinal, prospective, community-based studies from the developing world, Snyder et al estimated that the case-fatality rate of diarrhoeal illness in children under five years of age was 0.6 deaths per 100 illnesses[14]. Glass *et al* estimated that the mortality rate of diarrhoeal diseases among American children was one per every 500 hospitalised cases[15]. In this study based on hospitalised children, the case-mortality rate was 2.1 deaths/1000 admissions (0.21%), or approximately one deaths for every 500 admissions. This figure is very much lower than that of Snyder *et al* but similar to that of Glass *et al*. It is also much lower than the rates reported from the Indian subcontinent, where the mortality rate among hospitalised children was 4.9%[5].

Although the mortality rate was similar to that from a developed country, the risk factors that lead to death following acute diarrhoeal diseases; young age (<12 months of age), presence of significant dehydration and disturbances of serum sodium on admission were very similar to those observed in other developing countries[3-7]. A body weight of 2 S.D. from the mean for age was not statistically significant, the infants who died as a result of acute gastroenteritis were nevertheless generally malnourished. This has been observed previously in the developing world[5-7].

All the deaths in this study were in infants below twelve months of age, similar to other published observations[16,17]. The mortality rate among female infants was significantly higher than that of the male infants ($p<0.015$), in contrary to the findings of other authors[4,16]. The mean duration between the onset of illness and hospital admission was relatively short in all the ten index cases. Therefore socio-cultural bias, where ill female infants are brought to medical attention later than male infants, seems unlikely.

Two deaths observed had Down syndrome while another was in chronic renal failure. One infant with Down syndrome was receiving therapy for heart failure. Children with mental retardation are at higher risk of developing dehydration following acute gastroenteritis, possibly because of inadequate oral intake during a period of increased intestinal fluid loss[17]. The infant with chronic renal failure was more vulnerable to the adverse effects of fluid and electrolytes disturbances that occurred during acute gastroenteritis.

The presence of moderate to severe dehydration and disturbances of serum sodium were other risk factors associated with a fatal outcome following acute diarrhoeal illness. Significant dehydration were present in eight of the ten cases while four cases were in shock on admission. Timely fluid and electrolyte therapy is the main means of prevention of severe dehydration currently available. Programs promoted by the World Health Organisation for the use of oral rehydration therapy have reduced the mortality from diarrhoea-associated deaths in many developing countries[1]. However, the use of oral rehydration therapy may still be suboptimal, especially among the primary care physisians[18]. Disturbances of serum electrolytes,

especially hypernatraemia, were common occurrences in children who died of acute gastroenteritis in the 60's and 70's[16,17]. Recently, other authors had observed that hypernatraemic dehydration has become an uncommon complications following acute gastroenteritis[19,20]. Only one child in this study who developed severe hypernatraemia as a result of inappropriate preparation of feeds. Disturbances of serum sodium concentration were generally not severe in the remaining cases.

Based on autopsie findings of 140 children who died of diarrhoeal diseases, Butler *et al* found that the most frequent underlying causes of death (besides dehydration) were colitis and pneumonia, while the most frequent immediate causes of death were septicaemia, hypoglycaemia and hypokalaemia[21]. In the present study, the leading immediate causes of death were acute renal failure, aspiration pneumonia and acute pulmonary oedema. However, postmortem studies were not carried out for socio-cultural reasons. Therefore, other modes of underlying and immediate causes of deaths could be present but not identified.

This study showed that young age (below twelve months old), the presence of moderate to severe dehydration and hypo or hypernatraemia on admission were risk factors of death from acute diarrhoea. Presence of malnutrition and an underlying medical disorder that could contribute to rapid and severe imbalances of fluid and electrolyte were other important factors to consider whether a child with gastroenteritis should be referred for hospital admission. The low mortality rate following acute gastroenteritis observed over a period of 15 years in this hospital was similar to those from developed countries, but the risk factors that predisposed to death were similar to those from developing countries.

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