Risk Factors for Death in Bangladeshi Children Under 5 Years of Age Hospitalized for Diarrhea and Severe Respiratory Distress in an Urban Critical Care Ward

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Abstract

Children with diarrhea hospitalized for respiratory distress often have fatal outcome in resource-limited settings, although data are lacking on risk factors for death in such children. We sought to evaluate clinical predictors for death in such children. In this prospective cohort study, we enrolled under-5 children with diarrhea admitted with severe respiratory distress to the intensive care unit of Dhaka Hospital of International Centre for Diarhoeal Disease Research, Bangladesh, from September 2014 through September 2015. We compared clinical and laboratory characteristics between study children those who died (n = 29) and those who survived (n = 62). In logistic regression analysis, after adjusting for potential confounders, the independent predictors for death in children hospitalized for diarrhea and severe respiratory distress were severe sepsis and hypoglycemia ($P < .05$ for all). Thus, recognition of these simple parameters may help clinicians identify children with diarrhea at risk of deaths in order to initiate prompt management for the better outcome, especially in resource-poor settings.

Keywords

Bangladesh, children, death, diarrhea, hypoglycemia, severe respiratory distress, severe sepsis

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Introduction

Diarrhea is one of the leading infectious causes of death in children younger than 5 years. It accounted for 9% of 5.8 million global deaths and 6% of 0.119 million deaths in Bangladesh in 2015.[1] Among hospitalized children with diarrhea, most of the deaths result from diarrheal complication or associated problems.[2]

In a critical care ward, children with diarrhea also commonly present with respiratory distress either due to presence of pneumonia or complication of diarrheal illness.[3] They often experience fatal outcome resulting from the development of metabolic acidosis or respiratory acidosis from severe pneumonia or a combination of both.[4] There is lack of understanding about the role of respiratory acidosis or mixed metabolic and respiratory acidosis on fatal outcome in children with diarrhea.

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diarrheal disease hospital and every day a number of children present here with respiratory distress. A good number of them require admission in the critical care ward and often experience fatal outcome.[2] However, there is paucity of data on the risk factors of death in such children. Our aim was to evaluate the independent associated factors of fatal outcome in children with diarrhea under 5 years of age admitted to the critical care ward with severe respiratory distress.

Materials and Methods

Ethical Statement

In this prospective cohort study, caregivers were not asked for any interview.

Data were de-identified before analysis. This study was approved by the research review committee and ethical review committee of icddr,b.

Study Site

This study was done in Dhaka Hospital of icddr,b, which often treats around 150 000 patients annually. The intensive care unit (ICU) of this hospital manages around 1000 children under 5 years of age each year. The robust description of the study site has been provided elsewhere.[3]

Study Design

This is a prospective cohort study in which we enrolled all children with diarrhea, of either sex, aged 0 to 59 months, who were admitted to the ICU from September 2014 through September 2015 with severe respiratory distress. We had monitored and followed-up the study children during their stay at the ICU. The patients were monitored in the ICU up to the recovery from respiratory distress with the improvement of associated problems or until any fatal outcome was evident. Comparison was made between survivors and deaths.

Investigations

Complete blood count, blood culture, serum electrolytes, and arterial blood gas analysis were performed for all patients in a reference laboratory of icddr,b.[3] Chest X-rays were done in the Radiology Department of Dhaka Hospital of icddr,b.

Definition

Severe Pneumonia was defined based on World Health Organization (WHO) classification of pneumonia.[5] Respiratory distress was considered severe when there was increased breathing with use of accessory muscle and presence of tracheal tug and/or grunting respiration.[3]

Severe malnutrition was defined as the child having severe wasting (weight for height/length Z score < -3 of median of the WHO growth standard), severe underweight (weight for age Z score < -3 of median of the WHO growth standard), or nutritional edema.[5]

Respiratory alkalosis: pH >7.6 with $PCO_2 < 30$ mm Hg (OPTI CCA-TS, Blood Gas Analyzer).

Metabolic acidosis: pH <7.2 with $HCO_3 < 18$ mm Hg.

Management

Standard hospital guidelines were followed in the clinical management of these patients, which have been described elsewhere.[3]

Measurements

Case report forms were developed, pretested, and finalized for acquisition of relevant data. Data collection for these children included gender, age, poor socioeconomic status (socioeconomic condition was considered poor if caregivers were slum dwellers as monthly income was not recorded in the questionnaire), lack of exclusive breastfeeding, vaccination according to EPI schedule, prior antibiotic usage; presence of cough, fever, convulsion, hypoglycemia (random blood sugar <3 mmol/L), hypoxemia (SPO_2 <92%), grunting, lethargy, fast breathing, dehydrating diarrhea (some and severe dehydration), severe malnutrition, adventitious breath sound, severe pneumonia, severe sepsis[3]; use of inotropes, mechanical ventilation; hospital acquired infection, required change of antibiotics, bacteremia, pathogen in urine and stool, total leucocyte count, immature neutrophil, hypocalcemia (serum calcium <2.12 mmol/L), hyponatremia (serum sodium <130 mmol/L), hypokalemia (serum potassium <3.5 mmol/L), hyperkalemia (serum potassium >5.3 mmol/L), hypernatremia (serum sodium >150 mmol/L), raised creatinine, metabolic acidosis, respiratory alkalosis.

Statistical Methods

All data were entered into a personal computer and edited before analysis using SPSS Statistics for Windows (Version 20.0; IBM, Armonk, NY) and Epi Info (version 7.0; USD, Stone Mountain, GA). Differences in proportions were compared by the χ^2 test or Fisher exact test when applicable, and differences of means were compared by Student's t test or Mann-Whitney test, as appropriate. A probability of less than .05 was considered statistically significant. Strength of association was determined by calculating odds ratio

Table 1. Factors Present on Admission That Were Associated With Deaths of Children With Diarrhea Under 5 Years of Age Having Severe Respiratory Distress[a].

Characteristics	Deaths (n = 29), n (%)	Survivors (n = 62), n (%)	OR	95% CI	P
Female sex	20 (69)	26 (41.9)	3.07	1.20-7.83	.029
Age (months), median (IQR)	9 (6, 14)	7.5 (4, 13)	—	—	.226
Poor socioeconomic condition	18 (78.3)	47 (87)	0.53	0.15-1.90	.529
Lack of exclusive breastfeeding up to 6 months of age	21 (80.8)	41 (74.5)	1.43	0.45-4.52	.736
Vaccination following EPI schedule	23 (79.3)	45 (72.6)	1.4	0.40-4.90	.763
Got antibiotic prior to admission	17 (73.9)	29 (54.7)	2.34	0.79-6.88	.187
Presence of cough	24 (82.8)	46 (75.4)	1.56	0.50-4.822	.608
Presence of fever (>38°C)	13 (44.8)	32 (51.6)	0.76	0.31-1.84	.705
Presence of convulsion	12 (41.4)	29 (46.8)	0.83	0.32-1.95	.798
Hypoglycemia	12 (41.4)	4 (6.5)	10.23	2.92-35.87	<.001
Hypoxemia (SPO_2 < 92%)	22 (75.9)	32 (51.6)	2.94	1.09-7.89	.049
Grunting respiration	8 (27.6)	14 (22.6)	1.3	0.47-3.58	.797
Lethargy	14 (48.3)	18 (29)	2.28	0.91-5.67	.119
Presence of fast breathing	25 (86.2)	55 (88.7)	0.79	0.21-2.96	.738
Dehydrating diarrhea	6 (20.7)	19 (31.1)	0.57	0.20-1.64	.433
Severe malnutrition	24 (82.8)	36 (58)	3.46	1.16-10.28	.037
Adventitious breath sound	20 (69)	44 (72)	0.85	0.32-2.25	.951
Severe pneumonia	28 (96.6)	56 (90.3)	3	0.34-26.1	.423
Progression to severe sepsis	24 (82.8)	21 (33.9)	9.37	3.12-28.08	<.001
Required inotrope(s)	20 (69)	9 (14.5)	13.08	4.54-37.67	<.001
Mechanical ventilation	13 (46.4)	5 (8)	9.88	3.04-32.08	<.001
Developed HAI	3 (10.3)	4 (6.5)	1.67	0.34-8.01	.675
Required change of antibiotics	29 (100)	43 (70.5)	Undefined	Undefined	.000
Bacteremia	6 (21. 4)	5 (8.2)	3.05	0.84-11.04	.159
Organism isolation from urine	1 (25)	4 (33.3)	0.66	0.05-8.63	1.00
Organism isolated from stool	9 (32)	11 (21.2)	1.76	0.62-4.97	.416
Total leucocyte count (cmm), median (IQR)	17 770 (11 610, 32 350)	18 060 (11 990, 29 700)	—	—	.943
Immature neutrophil	8.0 (5.50, 21.75)	10.0 (5.0, 14.25)	—	—	.774
Hypocalcemia	20 (69)	36 (58)	1.6	0.63-4.08	.444
Hyponatremia	9 (31)	8 (12.9)	3.03	1.02-8.96	.075
Hypokalemia	12 (41.4)	18 (29)	1.72	0.68-4.33	.353
Hyperkalemia	9 (31)	10 (16)	2.34	0.82-6.60	.175
Hypernatremia	10 (34.5)	27 (43.5)	0.68	0.27-1.70	.554
Raised creatinine	19 (65.5)	35 (56.5)	1.46	0.58-3.66	.554
Metabolic acidosis	14 (48.3)	22 (35.5)	1.69	0.69-4.15	.35
Respiratory alkalosis	1 (3.4)	6 (9.7)	0.33	0.03-2.90	.423

Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range.
Data are presented as n (%), unless otherwise noted.

(OR) and its 95% confidence intervals (CIs). We have these statistics both in our univariate analysis and logistic regression. Initially, we performed univariate analyses of these characteristics to identify the factors that were significantly associated with death, and finally, we put them in a logistic regression model to identify the independent risk factors for death in children with diarrhea having severe respiratory distress after adjusting for potential confounders.

Result

A total of 91 children with diarrhea under 5 years of age with severe respiratory distress were enrolled in this study, and among them, 29 (32%) died. In univariate analysis, death was significantly higher in children who were female, and had hypoxemia, hypoglycemia, hyponatremia, severe malnutrition, and severe sepsis, compared to the survivors (Table 1).

Table 2. Result of Logistic Regression to Explore Independent Predictors for Death in Children With Diarrhea Under 5 Years of Age With Severe Respiratory Distress.

Characteristics	OR	95% CI	P
Female sex	3.22	0.91-11.39	.069
Severe malnutrition	2.22	0.58-8.59	.244
Hypoglycemia	8.01	1.86-34.53	.005
Hypoxemia	2.99	0.83-10.84	.095
Severe sepsis	4.97	1.42-17.45	.012
Hyponatremia	3.64	0.86-15.33	.078

Abbreviations: OR, odds ratio; CI, confidence interval.

In logistic regression analysis, after adjusting for potential confounders, such as hypoxemia, metabolic acidosis, hyponatremia, severe malnutrition, and female sex, the independent predictors for death in children with diarrhea under 5 years of age hospitalized with severe respiratory distress were severe sepsis and hypoglycemia (Table 2). Other variables were comparable between the groups (Table 1).

Discussion

The main observation of this study is the independent association of severe sepsis and hypoglycemia with death in children with diarrhea under 5 years of age presenting with severe respiratory distress. Children with severe sepsis usually present with compromised circulation leading to poor peripheral perfusion due to vasodilation, capillary leakage, and increased metabolic demand. Simultaneously, tissue hypoxemia develops when oxygen delivery is insufficient to meet metabolic demand and there is lactate production as a by-product of anaerobic cellular respiration resulting in metabolic acidosis, which is often associated with death, as frequently observed in our study children.[4]

Association of hypoglycemia with death in critical care medicine is not surprising[6,7] and might be due to failure of gluconeogenesis[7] in our sick children. Hypoglycemia appears to identify patients at particularly high risk for death who are critically ill[6,8] and is probably a marker of severe underlying disease process.

In univariate analysis, though, hypoxemia and severe malnutrition were found to have association with deaths in children with diarrhea under 5 years of age having severe respiratory distress compared to those who survived; they did not remain significant in logistic regression analysis after adjusting for potential confounders. However, a number of previous studies reported strong association of death with severe malnutrition,[9-11] hypoxemia,[3,12] hyponatremia,[13,14] and female sex.[14,15]

The main limitation of the study is the small sample size, which might have had an impact on the few predicting factors of death in our study children.

In conclusion, the results of our analyses suggest that bedside hypoglycemia or severe sepsis may be used as independent predicting factors for death in children with diarrhea under 5 years of age presenting with severe respiratory distress. Moreover, severe malnutrition, hypoxemia, and hyponatremia may also be used as the predicting factors for death in such children and it may help initiate early resuscitative measure for better outcome, especially in resource-limited settings. Future study with a larger sample might be carried out to accept or refute our clinical observation.

Author Contributions

T Alam: Contributed to conception and design; contributed to acquisition and analysis; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

T Ahmed: Contributed to conception and design; contributed to acquisition and analysis; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

MS: Contributed to conception and design; contributed to acquisition and analysis; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

LS: Contributed to conception and design; contributed to acquisition and analysis; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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PKB: Contributed to conception and design; contributed to acquisition and analysis; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

MJC: Contributed to conception and design; contributed to acquisition and analysis; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Authors' Note

Declaration of Conflicting Interests

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