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Bacteremia in Diarrheal Children With Severe Pneumonia

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Abstract

Objectives. Diarrhea and pneumonia are the leading causes of under-5 childhood mortality. However, there is limited information on bacterial etiology of severe pneumonia in children with diarrhea. We analyzed bacterial pathogens from the blood of children under the age of 5 years. *Methods*. In this retrospective cross-sectional study, we studied all children having severe pneumonia with or without diarrhea admitted to the icddr,b (International Centre for Diarrheal Disease Research, Bangladesh) who had their blood culture done during January 2014 to December 2014. *Results*. Among a total of 159 study children, 118 had diarrhea. There were 13 bacterial isolates, and predominant organisms were gram-negative bacteria (11/13, 85%). Children with diarrhea coexisting with severe pneumonia proportionately had higher bacteremia (12/141 [10.16%] vs 1/41 [2.43%]), but the difference was not statistically insignificant ($P = .186$). *Conclusion*. We recognized that the coexistence of diarrhea and severe pneumonia had proportionately higher bacteremia, especially gram-negative bacteria compared with those without diarrhea. The results emphasize the trend of bacterial etiology of pneumonia in children with diarrhea and may warrant revised antibiotics guideline for their management.

Keywords

pneumonia, diarrhea, bacteremia, pediatrics

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Introduction

To date, pneumonia and diarrhea are the leading infectious causes of deaths of children younger than 5 years of age, despite a large decline in deaths from 12.7 million in 1990 to 5.6 million in 2016.[1-3] Of the 5.6 million deaths in children younger than 5 years of age in 2016, 16% were due to pneumonia and 8% due to diarrhea.[1,2,4] In Bangladesh, the mortality from pneumonia and diarrhea is 16% and 6%, respectively, which is still high.[1,2] Comorbidity of severe pneumonia and diarrhea in children is common and often associated with high mortality.[5] The death rate is perceived to be higher when children presented with pneumonia coexisting diarrhea compared with those without diarrhea.[6] To our knowledge, there is very limited information on bacterial etiology of severe pneumonia in children younger than 5 years of age coexisting with diarrhea compared with those without diarrhea.

The Dhaka Hospital of International Centre for Diarrheal Disease Research, Bangladesh (icddr,b) treats a number of children younger than 5 years of age having severe pneumonia with and without diarrhea.[7] These children often require admission for critical care and experience high death rates.[8] It is imperative to understand whether there is any difference in bacterial etiology of severe pneumonia in children with and without diarrhea as that may help properly choose antibiotics in managing such children. Thus, we aimed to investigate bacterial pathogens causing pneumonia in

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children with diarrhea compared with those without diarrhea.

Materials and Methods

Ethical Approval and Informed Consent

In this retrospective chart analysis, anonymous and de-identified data were used from the hospital electronic system; thus, no parental consent was required. The study was approved by the Research Review Committee and Ethical Review Committee of icddr,b.

Study Design

This was a retrospective cross-sectional study. We studied children of either sex, aged 2 to 59 months, admitted with severe pneumonia to the longer stay ward and intensive care unit (ICU) of the Dhaka Hospital of icddr,b between January 2014 and December 2014. We evaluated children with severe pneumonia and diarrhea compared with those without diarrhea for the bacterial pathogens isolated from their blood. Pneumonia was initially defined clinically following the World Health Organization (WHO) classification[9] and confirmed by the WHO-recommended radiologic classifications.[10]

Study Setting and Enrollment of the Participant

The study children were admitted and treated at the Dhaka Hospital of icddr,b. The Dhaka Hospital of icddr,b provides free treatment to around 152 000 patient annually. Of them, around 62% are under the age of 5 years. Most of them live in the poor communities from urban and peri-urban Dhaka.[11] More detail description of this hospital has been provided elsewhere.[7] Children with severe pneumonia with hypoxemia who did not have the features of respiratory failure (such as gasping respiration or requiring cardiopulmonary resuscitation) on arrival at the ICU of Dhaka Hospital in icddr,b are usually treated with oxygen through bubble continuous positive airway pressure and those who had features of respiratory failure on arrival at ICU required mechanical ventilation. Severe pneumonia was diagnosed following WHO criteria, which was cough or difficulty in breathing plus presence of any one of the general danger signs (unable to feed or drink/lethargy or unconsciousness/convulsion) or sign of severe respiratory distress (severe chest wall in-drawing/grunting or central cyanosis/hypoxemia).[9] We included children with severe pneumonia in our study following this classification. Additionally, all our study children had hypoxemia (percentage of oxygen saturation <90 detected by pulse oxymeter[9]) and later were confirmed by radiology (primary end point consolidation/pleural effusion or other consolidation and infiltrate[10]). A total of 165 children with severe pneumonia having hypoxemia were identified, and among them, 119 (72.12%) had diarrhea and 46 (27.88%) had no diarrhea. Thus, a total of 165 young children constituted the analyzable sample for this analysis.

Patient Management and Measurements

The study children received antibiotics; oxygen therapy by using bubble continuous positive airway pressure for hypoxemia, except those having congenital heart diseases wherein they received WHO standard low-flow oxygen therapy through nasal cannula; and routine supportive care following the hospital's standard guidelines that have been described elsewhere.

Case report forms were developed for this study for data acquisition. Characteristics of those analyzed mainly included bacterial isolates from the bloodstream. Other analyses were demographics (age, gender), nutritional status, dehydration, severe sepsis, mental status, convulsion at admission, respiratory rate, and temperature.

Data were collected retrospectively from a computer-based patient management system. On admission to the Dhaka Hospital, every patient receives a unique identifying number against which all the data were recorded. The data include history, clinical examination findings, laboratory reports, treatment provided, dietary management, daily follow-up, and clinical outcomes.

Analysis

Data analysis was done by using SPSS (version 17.0; SPSS Inc, Chicago, IL) and Epi Info (version 7.0; USD, Stone Mountain, GA). Differences in proportions were compared by χ^2 test. In normally distributed data, differences in means were compared by Student's t test, and the Mann-Whitney U test was used for comparing data that were not normally distributed. A probability of less than .05 was considered statistically significant. The strength of association was determined by calculating the odds ratio and their 95% confidence intervals.

Results

One hundred fifty-nine children with severe pneumonia were identified for whom blood culture was done, and among them, 118 (74%) had severe pneumonia and diarrhea and only 41 (26%) had severe pneumonia

Table 1. Bacterial Isolates From Blood Culture Among Study Patients.

Isolates	Under-5 Children Having Both Severe Pneumonia and Diarrhea (N = 12), n (%)	Under-5 Children Having Severe Pneumonia Only (N = 1), n (%)
Escherichia coli	2 (16.66)	0
Pseudomonas spp	2 (16.66)	0
Acinetobacter spp	2 (16.66)	0
Enterococcus spp	1 (8.33)	0
Staphylococcus aureus	1 (8.33)	0
Streptococcus pneumoniae	1 (8.33)	0
Haemophilus influenzae (type b)	1 (8.33)	0
Serratia spp	1 (8.33)	0
Campylobacter spp	1 (8.33)	0
Klebsiella spp	0	1 (100)

Table 2. Comparison of Clinical Characteristics Among Under-5 Diarrheal Children Having Severe Pneumonia With Non-Diarrheal Group[a].

Characteristics	Diarrhea (N = 119)	Non-Diarrhea (N = 46)	OR	95% CI	*P*
Male sex	67 (56.3)	29 (63.0)	0.76	0.35-1.61	.541
Age in months median (IQR)	7 (5.0-12.0)	9 (4-13.25)			.526
Presence of fever	97 (81.5)	38 (82.6)	0.93	0.35-2.44	.951
Vomiting	48 (40.3)	13 (28.3)	1.72	0.77-3.85	.207
SAM	55 (46.2)	5 (10.9)	7.05	2.44-21.88	.000
Convulsion	26 (21.8)	4 (8.7)	2.94	0.94-10.63	.082
Abnormal mental status	86 (72.2)	38 (82.6)	0.55	0.21-1.39	.239
Reluctant to feed	89 (74.8)	21 (45.7)	3.53	1.63-7.68	.000
Severe sepsis	29 (24.4)	2 (4.5)	6.77	1.47-43.07	.008
Not vaccinated	17 (14.3)	6 (13.0)	1.28	0.43-3.98	.807

Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range; SAM, severe acute malnutrition.
[a]Data represent n (total number), unless specified.

without diarrhea. In children with severe pneumonia and diarrhea, blood culture was positive in 10.16% cases, whereas in children having no diarrhea, the culture was positive in 2.43% cases. The distribution of bacterial pathogens is shown in Table 1.

Study children with diarrhea more often presented with severe acute malnutrition (SAM), severe sepsis, and reluctant to feed than those without diarrhea (Table 2). The distribution of other variables in Table 2 was comparable among the groups. Among the blood culture–positive cases (n = 13; diarrheal group 12 and non-diarrheal group 1), median, interquartile range, age of the patient was 7 months (range = 4.5-10.5 months). Of them, 77% had SAM. Mean temperature of these children was 38°C, and on admission, white blood cell count (median, interquartile range) was 18 740/mm^3 (range = 10 630-31 210/mm^3). Among study children having bacteremia and diarrhea, only 2 had rectal swab culture positive (one *Campylobacter* and another non-typhoidal salmonella).

Discussion

We found a higher trend of bacteremia in children with severe pneumonia having diarrhea. However, the difference was not statistically significant and this might be due to the small sample size. Still, it was an important observation of this study and essentially deserves to have potential explanation. Among the bacterial isolates from blood, 85% were gram-negative bacteria and this is also another important observation for the study. The predominant gram-negative bacteria in children with severe pneumonia and diarrhea were *Escherichia coli, Acinetobacter* spp, and *Pseudomonas* spp. On the other hand, *Klebsiella* spp was the only bacterial pathogen isolated from blood in children with severe pneumonia in absence of diarrhea. However, *Streptococcus pneumoniae* and *Haemophilus influenzae*, 2 main bacterial pathogens causing pneumonia in the pre-vaccination era, constituted only 8.3% of all bacterial pathogens isolated from blood in children with diarrhea. This might be due to the fact that the spectrum of the bacterial

pathogens causing pneumonia is potentially changing with the introduction of vaccines against *Streptococcus pneumoniae* and *Haemophilus infulenzae*.

The observation of higher incidence of bacteremia with a predominance of gram-negative bacteria in our study population with diarrhea compared with those without diarrhea is understandable. In this study, we observed that the children with severe pneumonia and diarrhea more often had SAM and severe sepsis compared with those without diarrhea. A number of previous studies revealed the predominance of gram-negative bacteria isolated from the blood in children with SAM and severe pneumonia. Of them, *Klebsiella* spp was reported by 3 studies in South Africa and Ethiopia and *Escherichia coli* was identified as another common isolate in one study in Ethiopia.[12-14] Children with diarrhea having severe sepsis had shown to have high incidence of bacteremia with a predominance of gram-negative bacteria in Bangladesh.[15] Additionally, the role of potential translocation of bacteria through gut due to a potential breach of continuation of gut in children with diarrhea cannot be ruled out.

The main limitation of the study was the small sample size, and this limited our ability to have adequate information on bacterial etiology of our study population. For these reasons, it was difficult to understand whether these isolated pathogens from blood caused diarrhea or was it more of a "sepsis syndrome" or "multiorgan involvement" with the infection that led to the diarrhea in this population.

In conclusion, the results of our study suggest that children younger than 5 years of age with severe pneumonia and diarrhea had a trend of higher rates of bacteremia with a predominance of gram-negative bacteria compared with those without diarrhea. The results indicate the changing trend of bacterial etiology of pneumonia in diarrheal children that may warrant policy change in antibiotics guideline for their management especially in resource-poor settings. However, prospective research with a larger sample is imperative to accept or refute our observation.

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Author Contributions

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

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

TA: Contributed to conception; 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, analysis, and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

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