Original Research

Clinical features of pneumonia in severely malnourished children with diarrhoea compared to those without diarrhoea

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TABLE OF CONTENTS

1. Abstract

Introduction: Pneumonia and diarrhoea are amongst the most common causes for hospital admission for children in low- and middle-income countries such as Bangladesh. Undernourished children often have more severe infections and a higher morbidity and mortality. **Objective**: The objective of this study was to determine the clinical features and outcomes of pneumonia in severely malnourished children with and without diarrhoea. **Methodology**: A retrospective chart analysis was carried out on children under 5 years of age who were admitted in intensive care unit of the Dhaka hospital of International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). A total of 245 severe acute malnourished children with pneumonia and diarrhoea (PD group) were compared with 89 children with pneumonia only (PO group). **Results**: A significantly higher number of children from the PD group had some/severe dehydration (16.3% vs. 1.1%; $p < 0.005$) when compared with children from the PO group. The PD group showed less cough (83.3% vs. 100%; $p < 0.001$), lower chest wall indrawing (40.4% vs. 60.7%; $p = 0.001$), and crackles (62.4% vs. 87.6%; $p < 0.001$) compared to the PO group at the time of admission. **Conclusion**: Early diagnosis and treatment of some/severe dehydration in addition to WHO recommended other routine treatment of diarrhoea, pneumonia and severe acute malnutrition in children may help to reduce childhood morbidity and mortality especially in low- and middle-income countries.

2. Introduction

Pneumonia is considered as a leading cause of mortality in children under 5 years in developing countries [1]. The most deaths from lower respiratory tract infections occur during the first year of life [2]. It has been reported that the risk factors of mortality include malnutrition, young age, previous hospitalizations, previous pneumonia and other infections like HIV. The mortality rate after discharge were frequently surpassed by the mortality in the hospital settings [3]. A very recent report revealed that the independent predictors of mortality in hospitalized children with severe acute malnutrition (SAM) are diarrhoea, pneumonia, lower weight-for-height z score (WHZ) and

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other comorbidities like HIV [4]. A 30-day mortality in a cohort study in severely malnourished children has shown an independent association with sex (female), severe stunting and higher percentage of polymorphonuclear leucocytes (PMNL) [5]. It has been well documented that the severity of infections is increased in undernourished children which causes higher morbidity and mortality. Impaired host immune defence in malnutrition increases the risk of infections. Hundreds of millions of people are affected by malnutrition globally. This is frequently observed in developing countries and mostly under 5 children are affected by malnutrition. Stunting affected 149 million under 5 children globally in 2020, whereas wasting affected about 45 million children [6]. Severe diarrhoea and pneumonia are among the most common reasons for hospital admission in children in low- and middle-income countries. Management of diarrhoea has evolved over time. Guidelines for the management of diarrhoeal illnesses have been refined, and new strategies for prevention and control of this major health problem have also been developed [7]. About 5.2 million under 5 children died in 2019; 1.5 million of them died at the age between 1 and 11 months and 1.3 million deaths occurred at the age between 1 and 4 years. In addition to other illnesses, pneumonia, and diarrhoea both are the leading causes of deaths. These fatal conditions are treatable and potentially preventable by providing adequate interventions that include immunization, nutritional rehabilitation, exclusive breast feeding, safe water and food, hygiene practices as well as quality care by the health care providers [8, 9].

Although the nutritional status of under 5 children in Bangladesh has improved gradually, the levels of stunting, underweight and wasting still remain at 31%, 22% and 8% in 2017 [10]. The combination of pneumonia and malnutrition is associated with higher case fatality [11]. Pneumonia occurs in two-third of malnourished children who are admitted to the hospital [12]. UNICEF data revealed that about 15% of deaths of under five children occur due to pneumonia in Bangladesh [13]. However, data on etiology of pneumonia in malnourished children are lacking. According to a study conducted by Chisti *et al*. [14], disease pathogenesis in malnourished children could be different from that of the well-nourished and the risk of deaths among severely malnourished children was 15 times higher compared to those without severe malnutrition.

Pneumonia, diarrhoea and malnutrition contribute considerably to child deaths in developing countries including Bangladesh. Therefore, it is very important for clinicians and health workers to determine the simple clinical characteristics of pneumonia along with malnutrition and diarrhoea. These clinical characteristics may then initiate rapid treatment of the children in order to reduce morbidity and mortality. Thus, the objective of our study was to determine the clinical features and outcome of pneumonia in severely malnourished children with and without diarrhoea.

3. Materials and methods

A retrospective chart analysis was carried out in patients admitted to the intensive care unit (ICU) of the Dhaka hospital of International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). Under 5 years children suffering from pneumonia and severe malnutrition during the period from January 2012 to December 2012 were included in this study. All children with other acute as well as chronic illnesses including congenital heart disease and other illnesses were excluded from the study. The approval of this study was waived for publication by the Ethical Review Committee of icddr,b.

The patients with WHO defined pneumonia and severe malnutrition along with WHO defined diarrhoea [15] were designated as “Pneumonia and Diarrhoea” (PD group) and those without diarrhoea were termed as “Pneumonia Only” (PO group). Pneumonia was defined as cough or respiratory difficulty plus either age specific tachypnoea or lower chest wall indrawing, and in the case of severe pneumonia, hypoxemia, cyanosis, inability to breastfeed or drink, or grunting and general danger signs including lethargy, reduced consciousness, and seizures. Severe acute malnutrition was defined if weight for height/length z score was <-3 of the median of the WHO anthropometry, or mid upper arm circumference was <115 mm or had nutritional oedema. Diarrhoea was defined as passage of abnormally loose stool for three or more times per 24 hours.

Nutritional status (height for age Z scores, weight for age Z scores and weight for height Z scores) of each patient was determined [16]. Patients’ clinical features were compared between PD and PO groups. Evidence based protocols of the hospital was used for patient management [17, 18].

Clinical parameters included measurement of dehydration (some or severe), lower chest wall indrawing, nasal flaring, grunting respiration and crackles were assessed on admission. Presence of hypoxemia, poor feeding and administration of antibiotics were also evaluated. Hypoxemia was measured by using pulse oximeter (OxiMax N-600, Nellcor, Boulder, CO, USA). If SpO_2 was found to be $<90\%$, then it was defined as hypoxemia. Sociodemographic characteristics including the socio-economic status, level of education, employment status of parents, and previous birth history of mothers, hygienic toilet facilities and access of hygienic water facilities were also assessed in this study.

All data were entered into SPSS for Windows (version 20.0; SPSS Inc, Chicago, IL, USA). Differences in proportion were compared by using chi-square test. Strength of association was determined by calculating odds ratio (OR) and their 95% confidence intervals (CI). $p < 0.05$ was considered statistically significant.

Table 1. Parental socio-demographic status of PD [children with presence of diarrhoea on admission] and PO [children without diarrhoea on admission] patients.

	PD (n = 245)		PO (n = 89)		Unadjusted OR	95% CI		*p* value
	Freq	%	Freq	%				
Employment status of mother								
Employed	38	15.5	11	12.4	1.3	0.6	2.86	0.4718
Unemployed	207	84.5	78	87.6				
Employment status of father								
Employed	241	98.4	87	97.8	1.39	0.17	8.98	0.6591
Unemployed	4	1.6	2	2.2				
Place of residence								
Slum	87	35.5	41	46.1				
Village	57	23.3	15	16.9	0.56	0.27	1.16	0.0905
Other residential areas	101	41.2	33	37.0	0.69	0.39	1.23	0.1833
Socioeconomic status								
Middle (10000–15000 taka/m)	41	16.7	13	14.6	1.17	0.57	2.45	0.6405
Poor (<10000 taka/m)	204	83.3	76	85.4				
Toilet facilities of caregiver								
PD (n = 117) & PO (n = 61)								
Hygienic	116	99.1	61	100.0	0	0	33.65	1.0000
Unhygienic	1	0.9	0	0.0				
Access to water used by caregiver								
PD (n = 117) & PO (n = 61)								
*Hygienic	114	97.4	60	98.4	0.63	0.02	7.04	1.0000
**Unhygienic	3	2.6	1	1.6				

*Hygienic water: boiled water; **unhygienic water: unboiled water.

4. Results

Table 1 shows the parental socio-demographic status of children in the PD and PO groups. None of the socio-demographic factors were found to be significantly associated between the two groups. About one-third (35.5%) of the PD children were slum dwellers while 23.3% came from villages, and the remaining 41.2% came from other residential areas. Above 80% from both groups came from the lowest socioeconomic index. About 99.1% PD and 100% PO patients reported that they used hygienic toilet facilities at their home. Similarly, 97.4% PD and 98.4% PO patients reported their access to hygienic water sources.

Table 2 shows that dehydration among the PD group was highly significant ($p < 0.005$) when compared with the PO group. Other variables like cough, lower chest wall indrawing and crackles on admission were significantly lower among the PD patients compared to the PO patients ($p < 0.005$). Nutrition status being defined by feeding status of the children, 9.4% of the PD patients had poor feeding at the time of admission at the hospital while 7.9% of PO patients fed poorly at the time of admission. However, this difference was not found to be significant.

The statistical difference achieved in terms of case fatality between the two groups was at the level of $p = 0.0537$ following the regular treatment protocol at the Dhaka hospital of icddr,b (Table 3).

5. Discussion

This study evaluated children with co-morbidity of severe malnutrition, pneumonia and diarrhoea compared to those who did not have diarrhoea. The study revealed that dehydration was one of the significant clinical features in children having pneumonia, malnutrition and diarrhoea at the time of admission which is not surprising. On the other hand, higher observation of cough, lower chest wall indrawing and crackles on admission in children with pneumonia with severe malnutrition but without diarrhoea is very important.

The frequent comorbidity of diarrhoea, pneumonia and malnutrition in young children has been well documented in other studies [19, 20]. Chisti *et al.* [5] reported that children suffering from pneumonia and dehydration more frequently presented with severe malnutrition when compared with the children without dehydration ($p = 0.035$). It has been shown in another study that the specificity of the diagnosis of pneumonia according to the WHO guidelines was low during the enrolment of children due to dehydration, however, after rehydration, the specificity was increased [21]. In our study, a significant difference in dehydration has been observed between the two groups ($p = 0.0004$). This higher observation of dehydration among the PD patients is highly expected as compared to the PO patients who had no diarrhoeal episode.

Table 2. Comparative characteristics between the PD [children with presence of diarrhoea on admission] and PO [children without diarrhoea on admission] patients.

	PD (n = 245)		PO (n = 89)		Unadjusted OR	95% CI		*p* value
	Freq	%	Freq	%				
Male	135	55.1	48	53.9	1.05	0.63	1.76	0.8494
Female	110	44.9	41	46.1				
Cough								
Yes	204	83.3	89	100.0	0.00	0.00	0.28	0.0000
No	41	16.7	0	0.0				
Dehydration								
Yes	40	16.3	1	1.1	17.17	2.48	341.25	0.0004
No	205	83.7	88	98.9				
Lower chest wall indrawing on admission								
Yes	99	40.4	54	60.7	0.44	0.26	0.74	0.0010
No	146	59.6	35	39.3				
Nasal flaring on admission								
Yes	6	2.4	0	0.0	-	-	-	0.3478
No	239	97.6	89	100.0				
Grunting on admission								
Yes	6	2.4	0	0.0	-	-	-	0.3478
No	239	97.6	89	100.0				
Head nodding on admission								
Yes	5	2.0	2	2.2	0.91	0.15	6.88	1.0000
No	240	98.0	87	97.8				
Crackles on admission								
Yes	153	62.4	78	87.6	0.23	0.11	0.48	0.0000
No	92	37.6	11	12.4				
Wheeze on admission								
Yes	3	1.2	3	3.4	0.36	0.06	2.25	0.1946
No	242	98.8	86	96.6				
Bronchial breath sound on admission								
Yes	3	1.2	1	1.1	1.09	0.10	27.58	1.0000
No	242	98.8	88	98.9				
Abdominal distension on admission								
Yes	36	14.7	7	7.9	2.02	0.82	5.19	0.0995
No	209	85.3	82	92.1				
Presence of Hypoxemia on admission								
Yes	26	10.6	11	12.4	0.84	0.38	1.91	0.6528
No	219	89.4	78	87.6				
Poor feeding								
Yes	23	9.4	7	7.9	1.21	0.47	3.24	0.8307
No	222	90.6	82	92.1				
Medication (antibiotic)								
Yes	27	11.0	17	19.1	0.53	0.26	1.08	0.0553
No	218	89.0	72	80.9				

Significantly lower proportion of cough, lower chest wall indrawing, and crackles has been observed in our pneumonia patients having SAM with the presence of diarrhoea which is an interesting finding in our study. We speculate that severely malnourished children have poorer inflammatory response in the presence of diarrhoea. The reduced inflammatory response might have an impact on the development of cough, lower chest wall indrawing, and crackles on auscultation. Crackles on admission in patients suffering from pneumonia and malnutrition are consistent findings [16].

Fatality rate in malnourished children under 5 years in presence of other infectious diseases has been recently reported. Out of 191 children, 6% died within 30 days of admission (14/191). In our study 24 (9.9%) and 3 (3.4%) children from the PD group and PO group, respectively died, which is almost similar to the rates that documented by others [22]. This is an important but unsurprising observation of our study.

Ferdous *et al.* [23] found that stunting, underweight and wasting of under 5-year-old children with diarrhoeal disease were significantly associated with the lower

Table 3. Final outcome of the PD [children with presence of diarrhoea on admission] and PO [children without diarrhoea on admission] patients.

	PD (n = 242)		PO (n = 89)		Unadjusted OR	95% CI		*p* value
	Freq	%	Freq	%				
Died	24	9.9	3	3.4	3.16	0.87	13.52	0.0537
Survived	218	90.1	86	96.6				

family income (<100 USD) in rural area of Bangladesh. Other studies reported that inadequate hygienic water, sanitation and contaminated weaning foods are responsible for diarrhoeal disease and malnutrition [24, 25]. In our study 35.5% of the PD children and 46.1% PO children were from slums. However, no significant difference was found between the groups in terms of hygienic toilet facilities and hygienic water sources and other sociodemographic characteristics.

6. Conclusions

Findings from this study suggest that the comorbidity of diarrhoeal illness in children under 5 years old with SAM and pneumonia was found to be associated with clinically higher case fatality rate than without the comorbidity. It is important to note that clinical differentiating features between these two groups of children are simple and can be used by health workers in resource poor settings in order to treat such patients, thereby reduce morbidity and mortality.

7. Author contributions

MJC conceived, designed and investigated the research work; MJC and SI supervised data collection and conducted data analysis; SI, NN, NST and CL prepared the original draft; SI and CL reviewed and edited the manuscript. All authors have read carefully and agreed to submit the manuscript for publication.

8. Ethics approval and consent to participate

The approval of this study was waived for publication by the Ethical Review Committee of icddr,b without any formal registration.

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11. Conflict of interest

The authors declare no conflict of interest.

12. References

[1] UNICEF; WHO; World Bank Group; United Nations. Levels and trends in child mortality 2019. Estimates developed by the UN Inter-agency group for child mortality estimation. 2019. Available at: https://www.unicef.org/reports/levels-and-trends-child-mortality-report-2019 (Accessed: 11 June 2021).

[2] GBD 2016 Lower Respiratory Infections Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infectious Diseases. 2018; 18: 1191–1210.

[3] Wiens MO, Pawluk S, Kissoon N, Kumbakumba E, Ansermino JM, Singer J, *et al*. Pediatric post-discharge mortality in resource poor countries: a systematic review. PLoS ONE. 2013; 8: e66698.

[4] Karunaratne R, Sturgeon JP, Patel R, Prendergast AJ. Predictors of inpatient mortality among children hospitalized for severe acute malnutrition: a systematic review and meta-analysis. American Journal of Clinical Nutrition. 2020; 112: 1069–1079.

[5] Chisti MJ, Salam MA, Bardhan PK, Sharifuzzaman, Ahad R, La Vincente S, *et al* . Influences of dehydration on clinical features of radiological pneumonia in children attending an urban diarrhoea treatment centre in Bangladesh. Annals of Tropical Paediatrics. 2010; 30: 311–316.

[6] World Health Organization. Malnutrition. 2021. Avaliable at: https://www.who.int/news-room/fact-sheets/detail/malnutrition, https://www.who.int/nutrition/decade-of-action/en/ (Accessed: 26 July 2021).

[7] Dey SK, Chisti MJ, Das SK, Shaha CK, Ferdous F, Farzana FD, *et al*. Characteristics of diarrheal illnesses in non-breast fed infants attending a large urban diarrheal disease hospital in Bangladesh. PLoS ONE. 2013; 8: e58228.

[8] World Health Organisation. Children: improving survival and well-being. 2020. Avaliable at: https://www.who.int/news-room/fact-sheets/detail/children-reducing-mortality (Accessed: 9 October 2020).

[9] Leung DT, Chisti MJ, Pavia AT. Prevention and Control of Childhood Pneumonia and Diarrhea. Pediatric Clinics of North America. 2016; 63: 67–79.

[10] National Institute of Population Research and Training. Bangladesh Demographic and Health Survey 2017–18. 2019. Available at: https://www.dhsprogram.com/pubs/pdf/PR104/PR104.pdf (Accessed: 11 June 2021).

[11] Chisti MJ, Graham SM, Duke T, Ahmed T, Ashraf H, Faruque ASG, *et al*. A prospective study of the prevalence of tuberculosis and bacteraemia in Bangladeshi children with severe malnutri-

tion and pneumonia including an evaluation of Xpert MTB/RIF assay. PLoS ONE. 2014; 9: e93776.
[12] Chowdhury F, Shahid ASMSB, Ghosh PK, Rahman M, Hassan MZ, Akhtar Z, *et al*. Viral etiology of pneumonia among severely malnourished under-five children in an urban hospital, Bangladesh. PLoS ONE. 2020; 15: e0228329.
[13] UNICEF.Committing to Child Survival: A Promise Renewed. 2015. Available at: https://www.unicef.org/media/50721/file/APR_2015_9_Sep_15.pdf (Accessed: 21 October 2020).
[14] Chisti MJ, Tebruegge M, La Vincente S, Graham SM, Duke T. Pneumonia in severely malnourished children in developing countries - mortality risk, aetiology and validity of who clinical signs: a systematic review. Tropical Medicine & International Health. 2009; 14: 1173–1189.
[15] World Health Organization. Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Childhood Illnesses. 2013. Available at: https://apps.who.int/iris/handle/10665/81170 (Accessed: 21 June 2021).
[16] Chisti MJ, Hossain MI, Malek MA, Faruque ASG, Ahmed T, Salam MA. Characteristics of severely malnourished under-five children hospitalized with diarrhoea, and their policy implications. Acta Paediatrica. 2007; 96: 693–696.
[17] World Health Organization. Guidelines for the Inpatient Treatment of Severely Malnourished Children. 2003. Available at: https://www.who.int/nutrition/publications/guide_inpatient_text.pdf (Accessed: 21 October 2020).
[18] Ahmed T, Ali M, Ullah MM, Choudhury IA, Haque ME, Salam MA, *et al*. Mortality in severely malnourished children with diarrhoea and use of a standardised management protocol. Lancet. 1999; 353: 1919–1922.
[19] Schlaudecker EP, Steinhoff MC, Moore SR. Interactions of diarrhea, pneumonia, and malnutrition in childhood: recent evidence from developing countries. Current Opinion in Infectious Diseases. 2011; 24: 496–502.
[20] Chisti MJ, Duke T, Robertson CF, Ahmed T, Faruque ASG, Bardhan PK, *et al*. Co-morbidity: exploring the clinical overlap between pneumonia and diarrhoea in a hospital in Dhaka, Bangladesh. Annals of Tropical Paediatrics. 2011; 31: 311–319.
[21] Saha D, Ronan A, Khan WA, Salam MA. Diagnosis of pneumonia in children with dehydrating diarrhoea. Journal of Health, Population, and Nutrition. 2014; 32: 14–18.
[22] Shahrin L, Chisti MJ, Brintz B, Islam Z, Shahid ASMSB, Hassan MZ, *et al*. Clinical and laboratory predictors of 30-day mortality in severe acute malnourished children with severe pneumonia. Tropical Medicine & International Health. 2020; 25: 1422–1430.
[23] Ferdous F, Das SK, Ahmed S, Farzana FD, Latham JR, Chisti MJ, *et al*. Severity of diarrhea and malnutrition among under five-year-old children in rural Bangladesh. American Journal of Tropical Medicine and Hygiene. 2013; 89: 223–228.
[24] Oloruntoba EO, Folarin TB, Ayede AI. Hygiene and sanitation risk factors of diarrhoeal disease among under-five children in Ibadan, Nigeria. African Health Sciences. 2014; 14: 1001–1011.
[25] Motarjemi Y, Käferstein F, Moy G, Quevedo F. Contaminated weaning food: a major risk factor for diarrhoea and associated malnutrition. Bulletin of the World Health Organization. 1993; 71: 79–92.

Abbreviations: SCW, special care ward; SAM, severe acute malnutrition; WHZ, weight-for-height z score; PMNL, polymorphonuclear leucocytes.

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