

RESEARCH ARTICLE

Serum zinc level in children with acute lower respiratory tract infection: A hospital-based case-control study



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Abstract

Background: A few studies of Bangladeshi children have reported an independent association between severe zinc deficiency and acute lower respiratory tract infection (ALRTI) after adjusting for important confounders, although evidence to the contrary also exists. The current study was conducted to examine the relationship between low zinc levels in children with ALRTI and in those without respiratory disease who attended a tertiary hospital in Bangladesh.

Methods: This hospital-based case-control study was conducted among 36 children aged 2–60 months with ALRTI and 36 controls without respiratory illness. Clinical data were recorded, and serum zinc levels were measured within 24 hours of enrollment. Multivariate logistic regression was used to adjust for age, sex, family size, maternal education, breastfeeding, immunisation status, passive smoking exposure and anthropometric indices.

Results: The median (inter-quartile range) serum zinc level was significantly lower among cases than controls [82.5 (51.5–102.3) $\mu\text{g/dL}$ vs. 133.0 (100.8–171.0) $\mu\text{g/dL}$. Zinc deficiency (serum zinc ≤ 60 $\mu\text{g/dL}$) was more frequent among cases (41.7%) than controls (2.8%). After adjustment for age, sex, family size, breastfeeding, anthropometric indices, immunisation, maternal education, and passive smoking exposure, low serum zinc levels were independently associated with ALRTI (adjusted OR = 26.2; 95% CI: 2.8–248.6. Passive smoking exposure was also independently associated with ALRTI (adjusted OR = 5.6; 95% CI: 1.5–21.0).

Conclusion: Low serum zinc levels (≤ 60 $\mu\text{g/dL}$) were strongly associated with ALRTI among children, with affected children having approximately 26-fold higher odds of ALRTI than those with higher zinc levels. These findings suggest that zinc deficiency may be an important modifiable risk factor for ALRTI in this population.

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Key messages

This hospital-based case-control study provides a strong association between low serum zinc levels and acute lower respiratory tract infection among Bangladeshi children aged 2–60 months. The findings strengthen existing evidence from resource-limited settings and highlight the potential public health importance of early detection and preventive interventions for zinc deficiency to help reduce lower respiratory tract infections in children.

Introduction

Acute respiratory infections (ARI) are among the leading causes of pediatric hospital admission and death in low- and middle-income countries (LMICs) [1]. Children under five are particularly vulnerable to acute lower respiratory tract infections (ALRTI), including bronchiolitis and pneumonia. In Bangladesh, pneumonia accounted for 15% of all deaths among children under five in 2015. Globally, an estimated 156 million new episodes of ALRTI occur annually in this age group [2]. Previous studies have demonstrated that malnutrition significantly increases both the incidence and severity of ALRTIs [3, 4]. Overcrowding, poor nutrition, maternal education, early weaning, low immunisation coverage, and essential micronutrient deficiencies are the major contributing factors for the high burden of ALRTI in LMICs [5]. Malnourished children are susceptible to infections like ALRTI, probably due to impaired cellular immunity and possible deficiency of micronutrients like zinc [3].

Zinc is an essential trace element that participates in a broad spectrum of biological processes and is required for the activity of more than 300 enzymes in the human body [6]. Additionally, zinc contributes to immune regulation by supporting the function of immunomodulatory molecules and signalling pathways. Zinc also has anti-viral activity by enhancing interferon production and inhibiting intracellular replication of pathogens [7]. Therefore, zinc deficiency may increase susceptibility to ALRTIs by impairing host immune responses and compromising the integrity of the respiratory epithelium during inflammation.

Previous studies investigating the association between zinc deficiency and ALRTI have reported inconsistent findings, possibly due to differences in population characteristics, nutritional status, socioeconomic conditions, and study design [8, 9]. In Bangladesh, updated evidence on serum zinc status among children with ALRTI remains limited, and most studies are a decade old; they have made limited adjustments for potential confounding variables [10, 11]. Therefore, this study was conducted to evaluate the association between severe zinc deficiency and ALRTI among Bangladeshi children using multivariable logistic regression while adjusting for age, sex, maternal education, and passive smoking exposure. The study also aimed to quantify the magnitude of association between severe zinc deficiency and ALRTI. By comparing serum zinc levels in children with and without ALRTI, this study aims to provide updated local evidence on the role of zinc deficiency as a potentially modifiable risk factor for ALRTI. The findings may inform evidence-based nutritional and preventive strategies, including micronutrient-based interventions, to reduce childhood pneumonia in resource-limited settings.

Methods

Study design

This hospital-based case-control study was conducted from October 2022 to October 2023 in the in- and outpatient department of Paediatrics at Bangladesh Medical University, Dhaka, Bangladesh. The study was designed to compare serum zinc levels in children aged 2 to 60 months diagnosed with acute lower respiratory tract infections (ALRTIs) and controls.

Study cases

Children aged 2 to 60 months presenting to the inpatient and outpatient departments of Paediatrics during the study period were screened for eligibility. Children diagnosed with acute lower respiratory tract infection (ALRTI) were assessed for the inclusion and exclusion criteria. Those with chronic illnesses, metabolic disorders, overt malnutrition, acute gastroenteritis, other concurrent infections, or a history of zinc supplementation within the preceding three months were excluded. Eligible caregivers were approached for informed consent. A total of 36 children who met all eligibility criteria and had guardians who provided written informed consent were enrolled as cases. ALRTI was diagnosed according to WHO criteria, defined as cough or difficulty breathing accompanied by tachypnoea (respiratory rate ≥ 50 breaths/minute in children aged 2–12 months and ≥ 40 breaths/minute in children aged 12–60 months), with or without chest indrawing.

Study controls

Controls were recruited from children attending for non-respiratory, non-inflammatory conditions (e.g., minor trauma, elective surgical evaluations, well-child visits). All potential controls were screened to ensure they had no respiratory symptoms within the last 14 days. Children were excluded if they had acute gastroenteritis, chronic illnesses, overt malnutrition, metabolic disorders, or had a history of taking zinc supplements within the last three months. A total of 36 children who fulfilled all eligibility criteria were enrolled as controls.

Data collection

Clinico-demographic information, including age, sex, family size, breastfeeding, immunisation, maternal education, and passive smoking exposure, was collected using a predesigned questionnaire. Anthropometric measurements were obtained using standardised techniques. Weight was measured with a calibrated digital scale, and height with an infantometer or stadiometer, as appropriate. Weight-for-age (WAZ) and height-for-age (HAZ) Z-scores were calculated by the WHO Anthro software and categorised as $> +2$ SD, between $+2$ SD and -2 SD, and < -2 SD. Anthropometric variables were included in the analysis as potential confounders.

Laboratory assessments

To measure serum zinc levels, around 2 mL of venous blood was collected from each participant on the first day of enrollment. Serum zinc estimation was

performed in the Department of Biochemistry, Bangladesh Medical University (former BSMMU), using a standardised colourimetric method with commercially available kits (Centromic GmbH, Germany). All samples were analysed using the same spectrophotometer in the same laboratory throughout the study.

For the assay, 1000 μL of reagent was added to two Eppendorf tubes: one containing 50 μL of serum and the other containing the standard solution. After incubation at 37°C for 5 minutes, absorbance was measured at 560 nm using a spectrophotometer, and the serum zinc concentration was calculated accordingly. Internal laboratory quality control procedures were routinely maintained throughout the analysis. Because the assay was instrument-based with automated absorbance measurement, observer-related variation was considered minimal; formal assessment of inter- and intra-observer variation and the coefficient of variation was not performed. Zinc deficiency was defined as serum zinc <60 $\mu\text{g}/\text{dL}$, and marginal deficiency as 60–100 $\mu\text{g}/\text{dL}$ [12]. Chest X-rays were documented where available.

Statistical analysis

Data were entered into Microsoft Excel and analysed using Epi Info version 7.2. Categorical variables were compared by using χ^2 tests. Continuous variables were compared using an independent t-test or Mann-Whitney U test, as appropriate, and are presented as mean \pm standard deviation (SD) or median (interquartile range [IQR]). Univariable and multivariable logistic regression analyses were performed to identify factors independently associated with ALRTI. Variables included age, sex, family size, maternal education, breastfeeding, immunisation status, passive smoking exposure, anthropometric indices, and serum zinc level. Odds ratios (ORs) and adjusted odds ratios (AORs) with 95% confidence intervals were calculated. A $P < 0.05$ was considered statistically significant.

Table 1 Comparison of demographic characteristics, anthropometric indices and serum zinc levels between acute lower respiratory tract infection cases and controls

Factors	Cases (n=36)	Control (n=36)	P
Median (interquartile range)			
Age (months)	43.0 (12.0–51.3)	25.5 (12.0–44.5)	0.19
Serum Zinc ($\mu\text{g}/\text{dL}$)	82.5 (51.5–102.3)	133. (100.8–171)	<0.00
Family size (persons)	5.0 (4.0–6.0)	5.0 (4.0–6.0)	0.65
Number (percent)			
Height for age z-score			
>2SD	8 (22.2)	6 (16.6)	
+2SD to -2SD	24 (66.8)	23 (63.8)	0.17
< -2SD	4 (11.1)	7 (19.4)	
Weight for age z-score			
>2SD	3 (8.33)	1 (2.8)	
+2SD to -2SD	30 (83.3)	33 (91.6)	0.51
<-2SD	3 (8.33)	2 (5.56)	

Ethical consideration

The study was done after obtaining ethical approval. Confidentiality was maintained throughout the study. Each child was assigned a unique identification number to ensure anonymity during sample collection, transportation, and reporting. Privacy protection was also emphasised when obtaining informed written consent from parents or guardians.

Results

A total of 72 children were enrolled, including 36 ALRTI cases and 36 controls. The median (IQR) age of ALRTI cases was 43 (12.0–51.3) months compared with 25.5 (12.0–44.5) months among controls. Approximately one-third of the participants were aged ≤ 12 months. The proportion of boys in cases and controls were 72.2% and 58.3%, respectively. Anthropometric characteristics were nearly comparable between the two groups. No statistically significant differences were observed in height-for-age (HAZ) or weight-for-age Z-score (WAZ) categories between ALRTI cases and controls (Table 1). Among ALRTI cases, the mean (SD) duration of illness was 9.1 (3.1) days. Bronchopneumonia was the most frequent clinical diagnosis (55%), followed by lobar pneumonia (39%) and bronchiolitis (5%). Pulmonary infiltrates were the most common chest X-ray finding.

The median (IQR) serum zinc level was significantly lower among children with ALRTI [82.5 (51.5–102.3) $\mu\text{g}/\text{dL}$] than among controls [133.0 (100.8–171.0) $\mu\text{g}/\text{dL}$]. This finding supports an association between lower serum zinc levels and increased susceptibility to respiratory infections. Zinc deficiency (≤ 60 $\mu\text{g}/\text{dL}$) was present in 41.7% of ALRTI cases compared with only 2.8% of controls. In contrast, 75% of controls had serum zinc concentrations above 100 $\mu\text{g}/\text{dL}$, whereas only 30.6% of ALRTI cases did. Passive smoking exposure was more common among ALRTI cases than controls (66.7% vs. 27.8%).

Logistic regression analysis was performed to determine factors associated with ALRTI. In univariable analysis, passive smoking exposure (OR 5.2, 95% CI: 1.9–14.2; $P = 0.001$) and low serum zinc levels (OR 25.0, 95% CI: 3.1–203.2; $P = 0.003$) were significantly associated with ALRTI. After adjustment for age, sex, family size, maternal education, breastfeeding status, immunisation status, anthropometric indices, passive smoking exposure, and serum zinc level, children with low serum zinc levels (≤ 60 $\mu\text{g}/\text{dL}$) had significantly higher odds of ALRTI than those with higher zinc levels (AOR 26.2, 95% CI: 2.8–248.6). Anthropometric indices were not significantly associated with ALRTI in either univariable or multivariable logistic regression analyses. Passive smoking exposure also remained independently associated with ALRTI (AOR 5.6, 95% CI: 1.5–21.0 (Table 2).

Table 2 Univariable and multivariable logistic regression analysis of factors associated with acute lower respiratory tract infection

Factors	Case (n=36)	Control (n=36)	OR (95% CI)	AOR (95% CI)
Age				
≤12 months	11 (30.6)	12 (33.3)	Ref.	Ref.
>12 months	25 (69.4)	24 (66.7)	1.1 (0.4–3.1)	0.9 (0.3–3.2)
Sex				
Female	10 (27.8)	15 (41.7)	Ref.	Ref.
Male	26 (72.2)	21 (58.3)	1.9 (0.7–5.0)	2.3 (0.6–8.2)
Family members				
≤6 members	11 (30.6)	12 (33.3)	Ref.	Ref.
>6 members	25 (69.4)	24 (66.7)	1.1 (0.4–3.1)	1.6 (0.4–6.5)
Passive smoking				
No	12 (33.3)	26 (72.2)	Ref.	Ref.
Yes	24 (66.7)	10 (27.8)	5.2 (1.9 - 14.2) ^b	5.6 (1.5 - 21.0) ^b
Maternal education				
>Primary	22 (61.1)	23 (63.9)	Ref.	Ref.
≤Primary	14 (38.9)	13 (36.1)	1.1 (0.4–2.9)	1.0 (0.3–3.3)
Serum zinc				
High (>60 µg/dL)	21 (58.3)	35 (97.2)	Ref.	Ref.
Low (≤60 µg/dL)	15 (41.5)	1 (2.8)	25.0 (3.1–203.2) ^b	26.2 (2.8–248.6) ^b
Exclusive breastfeeding				
Yes	19 (46.3)	22 (53.7)	Ref.	Ref.
No	17 (54.8)	14 (45.1)	0.7 (0.3–1.8)	0.5 (0.1–1.9)
Immunization				
Partial	16 (55.5)	13 (63.9)	Ref.	Ref.
Complete	20 (44.4)	23 (36.1)	1.4 (0.6–1.7)	1.6 (0.5–5.4)
Height for age z-score				
>2SD	8 (22.2)	6 (16.6)	0.3 (0.05–1.3)	0.3 (0.01–8.9)
+2SD to -2SD	24 (66.8)	23 (63.8)	Ref.	Ref.
<-2SD	4 (11.1)	7 (19.4)	0.7 (0.2–2.5)	0.1 (0.01–1.3)
Weight for age z-score				
>2SD	3 (8.33)	1 (2.8)	0.5 (0.03–8.9)	0.3 (0.01–8.9)
+2SD to -2SD	30 (83.3)	33 (91.6)	Ref.	Ref.
<-2SD	3 (8.33)	2 (5.56)	0.3 (0.3-3.1)	0.1 (.008–1.3)

OR indicates odds ratio; AOR indicates adjusted odds ratio; CI indicates confidence interval

^aThe model included all variables (age, sex, anthropometric indices, family members, passive smoking, immunisation, exclusive breastfeeding, maternal education, serum zinc)

^bP≤0.01

Discussion

In this hospital-based case-control study, children with ALRTI had significantly lower serum zinc levels than controls without respiratory disease. Severe zinc deficiency was strongly associated with ALRTI, highlighting a possible role of zinc deficiency in susceptibility to lower respiratory tract infections among Bangladeshi children aged 2–60 months.

Nearly one-third of the ALRTI cases in the current study were infants aged around 1 year. This finding is consistent with recent global evidence showing that infants and young children bear the highest burden of acute lower respiratory tract infections [13]. Infants are more vulnerable to ALRTI probably due to several anatomical and physiological factors, including narrow airways, short bronchial tree, immature lung development, and poor immune responses. In addition, nutritional vulnerabilities during early childhood may further contribute to the risk of respiratory infections [14].

A male predominance was observed among ALRTI cases in this study. This trend suggests that male children may have a slightly higher biological susceptibility to respiratory infections. However, socio-cultural biases favouring earlier medical attention and hospital admission for boys may also play a role in countries like Bangladesh.

One of the major findings of this study was significantly lower serum zinc levels among ALRTI cases compared with controls. This finding is supported by earlier studies suggesting that zinc deficiency is associated with increased susceptibility to respiratory infections in children [10, 15]. Zinc is an essential micronutrient that plays a vital role in maintaining immune function. Its deficiency may weaken host defences and increase vulnerability to respiratory pathogens. The markedly higher risk of pneumonia among children with severe zinc deficiency further strengthens the potential role of zinc in respiratory health. Previous clinical trials have shown that zinc supplementation as adjunct therapy in children with pneumonia has yielded inconsistent results regarding the duration of hospital stay and clinical recovery [16, 17]. This may be due to differences in baseline zinc status, participants' nutritional status, severity of pneumonia, and variations in zinc dosage and treatment protocols across studies.

Although zinc deficiency was associated with ALRTI, anthropometric indices were not significantly associated with disease occurrence in either univariable or multivariable analysis. This finding should be interpreted cautiously and should not be considered inconsistent with the established evidence linking undernutrition and childhood pneumonia [3–5]. A likely explanation is that children with overt malnutrition were excluded from both case and control groups, resulting in a relatively homogeneous nutritional profile among participants. Furthermore, anthropometric indicators such as weight-for-age and height-for-age reflect overall growth status but may not adequately capture micronutrient deficiencies or functional immune impairment. Therefore, children with apparently normal anthropometric measurements may still have clinically important zinc deficiency, particularly in low- and middle-income settings where dietary quality may be inadequate despite sufficient caloric intake [18]. The absence of a significant association in the present study may thus reflect the study population and sample size rather than the absence of a true relationship between nutritional status and ALRTI.

Age, sex, maternal education or family size were not significantly associated with disease occurrence in this study. Another important finding was the independent association between passive smoking exposure and ALRTI. Children exposed to environmental tobacco smoke had more than five-fold higher odds of ALRTI after adjustment for other risk factors. Exposure to tobacco smoke is known to impair

mucociliary clearance, increase oxidative stress, promote airway inflammation, and alter both innate and adaptive immune responses [19]. Several studies have demonstrated an increased risk of pneumonia and other lower respiratory tract infections among children exposed to household smoking [20, 5]. The persistence of the association after multivariable adjustment in the current study suggests that passive smoking represents an important and potentially preventable risk factor for childhood ALRTI.

The wide confidence interval observed in the logistic regression analysis may reflect the relatively small sample size and potential instability of the model. Therefore, the magnitude of the observed associations should be interpreted with caution. Nevertheless, the direction of these associations was consistent with biological plausibility and findings from previous studies. Despite its limitations, this study contributes valuable local data on the relationship between serum zinc status and ALRTI among Bangladeshi children.

Conclusion

Children with ALRTI had significantly lower serum zinc levels than controls and were more likely to have zinc deficiency. Low serum zinc levels were independently associated with ALRTI after adjustment for potential confounding factors. These findings highlight the importance of assessing zinc status in children and support strategies to improve zinc nutrition as a potentially beneficial approach to reducing the burden of ALRTI.

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Author contributions

Concept or design of the work; or the acquisition, analysis, or interpretation of data for the work: TM, ND, NG. *Drafting the work or reviewing it critically for important intellectual content:* TM, ND. *Final approval of the version to be published:* TM, ND. *Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved:* TM, ND, NG.

Conflict of interest

We do not have any conflict of interest.

Data availability statement

We confirm that the data supporting the findings of the study will be shared upon reasonable request.

AI disclosure

The authors take full responsibility for the content of this manuscript. ChatGPT (OpenAI) was used solely to assist with English-language editing and improve clarity, grammar, and overall structure. All AI-generated suggestions were carefully reviewed, revised, and approved by the authors. The authors confirm that all scientific content, data analysis, interpretations, and conclusions are their own, and the integrity and originality of the work were maintained.

Supplementary file

None

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