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Original Research Article

Zinc deficiency as a key risk factor for pneumonia in early childhood: a hospital-based case-control study

Linda Jacob*, Carol Sara Cherian

Department of Pediatrics, Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India

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***Correspondence:**
Dr. Linda Jacob,
E-mail: lindajacob123@gmail.com

ABSTRACT

Background: Pneumonia remains the leading infectious cause of under-five mortality globally. Zinc deficiency impairs immune function and is prevalent among children in low- and middle-income countries. This study examined the association between serum zinc status and pneumonia in hospitalised children aged 6-59 months at a tertiary care centre in Kerala, India.

Methods: A prospective hospital-based case-control study was conducted from May 2023 to November 2024. Thirty children with WHO-defined pneumonia (cases) were compared with 30 age- and sex-matched healthy controls. Serum zinc was measured by atomic absorption spectrometry. Zinc deficiency was defined per IZiNCG criteria as <65 µg/dl. Logistic regression estimated the odds of pneumonia per 1 µg/dl decrease in serum zinc.

Results: Mean serum zinc was significantly lower in cases than controls (54.0±11.6 µg/dl versus 76.8±13.6 µg/dl; mean difference 22.8 µg/dl, 95% CI 16.2-29.3; p<0.001). Zinc deficiency was present in 86.7% of cases (33.3% severe, 53.3% mild) versus 26.7% of controls (p<0.001). Each 1 µg/dl decrease in serum zinc was associated with 1.15-fold greater odds of pneumonia (OR 1.15, 95% CI 1.07-1.24; p<0.001). No significant associations were found with anthropometric indices, disease severity, or length of hospital stay.

Conclusions: Low serum zinc was strongly associated with childhood pneumonia, even among children with normal growth parameters, consistent with the 'hidden hunger' phenomenon. Prospective multi-centre studies are needed to confirm these findings.

Keywords: Case-control study, Childhood pneumonia, Micronutrient deficiency, Pediatric nutrition, Serum zinc

INTRODUCTION

Pneumonia is the leading infectious cause of death in children under five worldwide, accounting for approximately 740,000 deaths and 14% of child mortality in 2019, with the highest burden in South Asia and sub-Saharan Africa.[1] In India, the disease contributes to nearly one-quarter of under-five mortality, with close to 30 million episodes reported annually.[2] Malnutrition, poor living conditions, and low vaccination coverage amplify pneumonia risk.[1,3]

Zinc is an essential trace element required for epithelial barrier integrity, macrophage and T-lymphocyte function, antimicrobial peptide production, and cytokine regulation.[4] Globally, approximately 17% of the population is at risk of zinc deficiency, with the highest proportions in South Asia.[5] In India, the Comprehensive National Nutrition Survey 2016-18 reported zinc deficiency in approximately 17% of preschool-aged children, with higher rates in rural and low-income populations.[6] Pooled evidence from randomised controlled trials indicates zinc supplementation can reduce childhood pneumonia incidence by approximately 20%.[4,7]

Despite this background, few Indian studies have biochemically characterised serum zinc in children with pneumonia. This study tested the hypothesis that

hospitalised children with pneumonia would have significantly lower serum zinc levels than age- and sex-matched controls. The primary aim was to quantify the association between zinc status and pneumonia; the secondary aim was to examine whether zinc deficiency correlated with anthropometric measures.

METHODS

Study design and setting

This was a prospective hospital-based case-control study conducted at Pushpagiri Institute of Medical Sciences and Research Centre, Thiruvalla, Kerala, India, from May 2023 to November 2024. Institutional Ethics Committee approval was obtained prior to enrolment (No. PIMSRC/E1/388A/14/2023). Written informed parental consent was obtained for every participant.

Participants

Cases were children aged 6-59 months admitted with WHO-defined pneumonia: cough or difficulty breathing with age-specific tachypnoea and/or chest indrawing.[3] Severity was classified per revised WHO 2014 criteria.[3] Controls were age- and sex-matched healthy children with no pneumonia in the preceding four weeks. One control was selected consecutively for each enrolled case.

Exclusion criteria for both groups included

Chronic cardiac or pulmonary disease; primary immunodeficiency; severe acute malnutrition (weight-for-age or height-for-age Z-score <−3 SD); current zinc supplementation; chronic diarrhoea; aspiration or hospital-acquired pneumonia; chronic medication use; and refusal of consent.

Sample size

Sample size was calculated using data from Rajasekaran et al. 8 (mean zinc: cases 60.36 µg/dl, SD 29.23; controls 80.54 µg/dl, SD 25.70; pooled SD 27.52). With α=0.05 (two-tailed) and 80% power, the minimum required was 29 subjects per group; 30 per group were enrolled.

Data collection and laboratory methods

A standardised proforma recorded age, sex, clinical parameters, and anthropometry. Nutritional status was assessed using WHO 2006 Z-scores for weight-for-age (WAZ) and height-for-age (HAZ). Blood samples (2 ml) were collected at admission alongside routine investigations, avoiding additional venepuncture. Serum was separated within 30 minutes by centrifugation and stored at −20°C until analysis. Serum zinc was measured by atomic absorption spectrometry under standardised, quality-controlled laboratory conditions. Zinc deficiency was defined using IZiNCG thresholds for non-fasting samples in children under five: <65 µg/Dl.[9] Hemoglobin was classified per WHO criteria for children aged 6-59 months (normal ≥11 gm/dl; mild anemia 10-10.9 gm/dl; moderate anemia 7-9.9 gm/dl).

Statistical analysis

Continuous variables are presented as mean±SD; categorical variables as frequencies and percentages. Normality was assessed using the Shapiro-Wilk test. Normally distributed variables were compared using independent samples Student's t-test; non-normal variables using the Mann-Whitney U test. Categorical variables were compared using Fisher's exact test. Logistic regression was performed with pneumonia status as the binary outcome and serum zinc (continuous, per 1 µg/dl decrease) as the primary predictor, adjusted for age and sex. Statistical significance was set at $p<0.05$ (two-tailed). Analyses were performed using SPSS version 26 (IBM Corp.).

RESULTS

Participant characteristics

Sixty children were enrolled (30 cases, 30 controls). Mean age was 3.01±1.44 years (range 8 months-5 years). Groups were well matched for age, sex, weight-for-age, height-for-age, and haemoglobin. Among cases, 20 (66.7%) had pneumonia with chest indrawing and 10 (33.3%) had severe pneumonia; none required intensive care beyond supplemental oxygen.

Serum zinc levels

The Shapiro-Wilk test confirmed approximate normality in both groups ($p>0.05$). Mean serum zinc was significantly lower in cases than controls (54.00±11.57 µg/dl versus 76.76±13.61 µg/dl; mean difference 22.76 µg/dl, 95% CI 16.23-29.29; $t=6.97$; $p<0.001$) (Table 1).

Table 1: Comparison of mean serum zinc levels between cases and controls.

Group	N	Mean zinc (µg/dl)	SD (µg/dl)	Mean difference (95% CI)	t	P value
Cases	30	54.00	11.57	22.76 (16.23-29.29)	6.97	<0.001
Controls	30	76.76	13.61			

CI confidence interval; SD standard deviation.

Table 2: Distribution of serum zinc categories among cases and controls.

Zinc category	Cases (%)	Controls (%)	Fisher's exact value	P value
Severe deficiency (<50 µg/dl)	10 (33.3)	0 (0)	25.12	<0.001
Mild deficiency (50-64.9 µg/dl)	16 (53.3)	8 (26.7)		
Normal (≥65 µg/dl)	4 (13.3)	22 (73.3)		
Total	30 (100)	30 (100)		

Normal serum zinc ≥65 µg/dl; mild zinc deficiency 50-64.9 µg/dl; severe zinc deficiency <50 µg/dl.

Table 3: Logistic regression analysis: serum zinc and odds of pneumonia.

Variables	Crude OR	95% CI	Wald χ^2	P value
Serum zinc (per 1 µg/dl decrease)	1.15	1.07-1.24	15.2	<0.001

OR odds ratio; CI confidence interval. Model adjusted for age and sex.

Table 4: Comparison of serum zinc by pneumonia severity.

Severity	N	Mean zinc (µg/dl)	SD (µg/dl)	t	P value
Pneumonia (chest indrawing)	20	55.24	10.39	0.76	0.45
Severe pneumonia	10	49.25	10.32		

NS not statistically significant (p>0.05).

Zinc deficiency distribution

Zinc deficiency was present in 86.7% of cases (severe in 33.3%, mild in 53.3%) versus 26.7% of controls (all mild; no severe deficiency). This difference was highly significant (Fisher's exact value 25.12; p<0.001) (Table 2).

Association between serum zinc and pneumonia risk

Logistic regression demonstrated a significant inverse association between serum zinc and pneumonia. Each 1 µg/dl decrease in serum zinc was associated with 1.15-fold greater odds of pneumonia (OR 1.15, 95% CI 1.07-1.24; p<0.001), adjusted for age and sex (Table 3).

Zinc status and pneumonia severity

Mean serum zinc was lower in severe pneumonia cases (49.25±10.32 µg/dl, n=10) than in non-severe cases (55.24±10.39 µg/dl, n=20), but the difference did not reach statistical significance (t=0.76; p=0.45) (Table 4).

Zinc status and other clinical variables

No significant association was found between zinc status and WAZ category (Fisher's exact p=0.264), HAZ category (p=0.680), anaemia within cases (p=0.78), or length of hospital stay (p=0.15). Zinc deficiency occurred largely independently of anthropometric malnutrition in this cohort.

DISCUSSION

Children hospitalised with pneumonia had substantially lower serum zinc than age- and sex-matched controls (mean difference ~23 µg/dl; 86.7% deficiency in cases versus 26.7% in controls). This magnitude and direction are consistent with findings from comparable studies in India, Egypt, and Vietnam, suggesting a biologically plausible immunological relationship rather than a population-specific finding.[8,10,11]

The logistic regression finding- a 1.15-fold increase in pneumonia odds per 1 µg/dl decrease in serum zinc- indicates a dose-response relationship, consistent with zinc's established roles in maintaining airway epithelial integrity, supporting macrophage and T-lymphocyte function, modulating NF-κB-mediated inflammation, and providing antioxidant protection to lung tissue.[4,7]

A noteworthy finding was the dissociation between serum zinc and anthropometric indices. Neither WAZ nor HAZ was significantly associated with zinc status, reinforcing the concept of 'hidden hunger': micronutrient deficiency occurring in children who appear nutritionally adequate on standard growth monitoring. This has direct clinical implications- routine anthropometry alone may not identify children at elevated pneumonia risk due to zinc insufficiency.

The study found no statistically significant association between zinc levels and pneumonia severity. This may reflect limited statistical power with n=30 cases, the narrow severity range (no cases required ICU admission), or the possibility that zinc deficiency primarily increases susceptibility to infection rather than determining downstream severity once infection is established- an interpretation supported by some earlier reports. [11]

The demographic characteristics of our cohort align with those reported in similar studies. La et al reported that 72% of their Vietnamese cohort was aged 12-59 months, and

Hamed et al documented similar age distribution in Egyptian children.[10,11] The male predominance noted in our cohort (63.3% in cases) corresponds closely to the 63.5% male proportion reported by La et al, suggesting our sample is representative of the broader paediatric population at greatest risk for pneumonia.[11]

The high prevalence of zinc deficiency (86.6% of cases) aligns with reports from Nigeria and other Indian studies, indicating that zinc deficiency constitutes a widespread and significant risk factor for childhood pneumonia in developing regions.[12,13]

This study has several limitations that should be considered. As a case-control study, it cannot establish cause-and-effect relationships or confirm the sequence of events. Serum zinc levels were measured during acute illness, and these values may be influenced by the acute-phase response rather than reflecting true baseline levels. The sample size was relatively small (30 participants in each group), and the study was conducted at a single centre, which may limit the generalisability of the findings, particularly for subgroup analyses.

CONCLUSION

This case-control study found a strong and statistically significant association between low serum zinc and pneumonia in hospitalised children aged 6-59 months in Kerala, India. Zinc deficiency was observed in 86.7% of pneumonia cases versus 26.7% of controls, and each 1 µg/dl decrease in serum zinc was associated with 1.15-fold greater odds of pneumonia. Zinc deficiency occurred independently of anthropometric malnutrition, highlighting an important gap in conventional nutritional assessment. These findings support existing evidence for zinc's relevance to paediatric pneumonia prevention and should be considered in integrated child health strategies. Confirmation requires larger multi-centre prospective studies with comprehensive confounder assessment and longitudinal zinc measurement.

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