

## Serum zinc levels in children hospitalized with pneumonia – A cross-sectional study

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### ABSTRACT

**Background:** Zinc deficiency is associated with high rates of infections such as diarrhea, skin, and respiratory infections. **Objective:** The objective of the study was to determine serum zinc levels in children hospitalized with pneumonia and to study the correlation between serum zinc levels and severity and complications of pneumonia. **Materials and Methods:** A cross-sectional study was conducted in a hospital of South India, which included 120 subjects aged between 6 months and 5 years. A detailed history, clinical examination, severity of pneumonia according to the WHO criteria, chest X-ray findings, arterial oxygen saturation, hemoglobin, and total white blood cell count were noted. **Results:** Mean serum zinc levels in pneumonia cases were significantly lower compared to healthy age- and sex-matched controls ( $p=0.001$ ). Low serum zinc was associated with increasing severity of pneumonia. Serum zinc levels in pneumonia, severe pneumonia, and very severe pneumonia were 118.4, 67.7, and 45.7  $\mu\text{g/dl}$ , respectively. Out of 60, 3 were complicated with empyema and 3 cases expired. The mean serum zinc levels in cases complicated with empyema and in expired cases were very low compared to those with no complications. **Conclusions:** Serum zinc level is low in children with pneumonia and lower serum zinc is associated with increased severity of pneumonia.

**Key words:** Mortality, Pneumonia, Serum zinc

Acute respiratory infections may cause inflammation of the respiratory tract anywhere from nose to alveoli [1]. Pneumonia is a severe form of lower respiratory tract infections (LRTIs) that specifically affect lungs [2]. Pneumonia is an important cause of mortality and morbidity in children throughout the world. The annual estimated global incidence of pneumonia is 158 million new cases per year, of which 154 million are occurring in developing countries. It is estimated to cause 3 million deaths or an estimated 29% of all deaths among children younger than 5 years of age, worldwide [3]. Pneumonia was responsible for about 18% of all under 5-year deaths in India [1].

Zinc is a trace element and an essential mineral which is present in all tissues, fluids, and secretions in the body. It is crucial for cellular metabolism, physical growth, immunocompetence, reproductive functions, integrity of intestinal mucosa, and neurobehavioral development [4]. Zinc deficiency is associated with decreased immunocompetence, and high rates of infections such as diarrhea, skin, and respiratory infections [5,6]. Zinc is routinely supplemented in children with diarrhea for 14 days [7].

Zinc is known to protect children from RTI by its role in immunomodulation, protection of epithelium of respiratory tract from infections, and improvement of T-lymphocytes function [8]. It also acts as an antioxidant and a cytoprotective agent against the toxins and inflammatory mediators which damage the

respiratory epithelium [9]. Even a mild-to-moderate zinc deficiency impairs the function of immune system, thus resistance against infection is reduced and T-lymphocytes cannot exhibit sufficient effectiveness [10].

Recent studies have shown conflicting evidence on the role of zinc against pneumonia. While few studies reported no significant difference in serum zinc levels in pediatric pneumonia [11], some have shown significantly lower serum zinc levels in children with pneumonia in comparison to controls [12]. Some Indian studies are also revealing conflicting results [13]. In view of conflicting reports about the role of zinc in pneumonia and paucity of data from Southern India, the present study was undertaken to determine serum zinc levels in children hospitalized with pneumonia and to study the correlation between zinc levels and severity and complications of pneumonia.

### MATERIALS AND METHODS

This cross-sectional study was conducted in a hospital of South India from June 2016 to May 2017. The sample size was 60, each for case and control groups. All children between 2 months and 5 years of age admitted to pediatric wards with a diagnosis of pneumonia (of any severity according to the WHO criteria [1]) were taken as cases and those admitted for other infections were considered as controls. The children diagnosed with

protein–energy malnutrition according to the Indian Academy of Pediatrics classification or as severe acute malnutrition according to the WHO criteria were excluded from the study. The children with associated diarrhea or on zinc supplements presently or who had received zinc supplements in the past 6 months were also excluded from the study.

After obtaining the institutional ethical committee clearance and written informed consent from the parents/guardian of subjects, a detailed history, demographic data, clinical examination, severity of pneumonia, chest X-ray findings consistent with pneumonia, arterial oxygen saturation measured by pulse oximetry (SpO<sub>2</sub>), hemoglobin (g/dl), and total white blood cell count were noted down. Within 24 h of hospitalization, 3 ml of venous blood was collected under strict aseptic conditions in a tube with clot activator. The sample was centrifuged for 10 min at 3000 rpm and serum was separated. All serum samples were stored at 2–8°C until estimation. Determination of zinc levels in serum was done by colorimetric method [14].

All the statistical methods (descriptive statistics, contingency table analysis, paired sample t-test, and repeated measure ANOVA) were carried out through SPSS for Windows (version 17). Serum zinc level was expressed as mean and standard deviation.  $p < 0.05$  was considered as statistically significant.

## RESULTS

Out of 60 cases of pneumonia, 38 (63.3%) were male and 22 (36.7%) were female and 42 (70%) cases were in the age group of 7–18 months. A total of 56 (93.3%) cases were exclusively breastfed till 6 months of age and 4 (6.7%) were started on complementary feeds before completion of 6 months. Demographic details are given in Table 1. There was no statistically significant difference between cases and controls in terms of overcrowding, usage of fuel, and ventilation. Out of 60 cases, 15 (25%) were exposed to indoor smoking compared to only 6 (10%) among controls ( $p = 0.031$ ) (Table 1).

Mean serum zinc level in pneumonia cases was 100.6 µg/dl, and in controls, it was 165.82 µg/dl ( $p = 0.001$ ). Mean serum zinc values among cases with pneumonia, severe pneumonia, and very severe pneumonia were 118.4, 67.7, and 45.7 µg/dl, respectively. Inverse relationship between serum zinc levels and severity of pneumonia was observed. Although mean serum zinc was decreasing with the severity of pneumonia, it was not statistically significant ( $p = 0.05$ ).

Comparison of mean serum zinc levels and other parameters among cases is presented in Table 2. Out of 60 cases, 13 were hypoxic at the time of admission and serum zinc level among them was found to be very low (53.27 µg/dl). There was a significant relation difference between lower zinc levels and SpO<sub>2</sub> at the time of admission ( $p = 0.033$ ). Out of 60 cases, 3 children died and 3 were complicated with empyema. The mean serum zinc among expired and empyema cases was 33.6 µg/dl and 70 µg/dl, respectively. Inverse relation was seen between the duration of hospital stay and mean serum zinc levels. Those with prolonged duration of stay in hospital had very low zinc values.

## DISCUSSION

Recent studies have shown conflicting evidence on the role of zinc against pneumonia. In our study, the mean serum zinc levels in pneumonia cases were significantly lower compared to healthy age- and sex-matched controls ( $p = 0.001$ ), and lower serum zinc was associated with increasing severity of pneumonia. This is consistent with earlier studies by Kumar *et al.*, Pushpa *et al.*, Devrajani *et al.*, and Kumar *et al.* [12,15–17]. Most of the cases in the present study were in the age group of 7–18 months (74%) which is in accordance with other studies [12,15]. Increased susceptibility of this group may be due to decreased immunity making them more prone to infections.

In this study, the environmental risk factors for pneumonia analyzed were overcrowding, poor ventilation, indoor smoking, and biomass fuel usage. Significant association was seen between indoor smoking and increased incidence of pneumonia. As studied by Gupta *et al.*, passive smoking and parental smoking increase the risk of LRTIs [18]. Kumar *et al.* found that the use of biomass fuels was significantly associated with severe pneumonia [12]. Biomass fuel when burnt with incomplete combustion generates a lot of toxic products that adversely affect specific and non-specific local defense mechanisms of respiratory tract [19]. However, in this study, the use of biomass fuel was not found to be a significant risk factor for pneumonia.

**Table 1: Comparison of demographic details among cases and controls**

Parameter (number/%)	Cases (n=60)		Controls (n=60)		p-value
Gender					
Male	38	63.3	37	61.7	0.85
Female	22	36.7	23	38.3	
Age: 7–18 months	37	61.7	22	36.7	0.05
Exclusive breastfeeding	56	93.3	58	96.7	0.402
Overcrowding	11	18.3	6	10	0.191
Biomass fuel	10	16.7	6	10	0.484
Ventilation	14	23.3	9	15	0.246
Indoor smoking	15	25	6	10	0.031

**Table 2: Correlation of mean serum zinc levels and other parameters among cases**

Parameter	n	Mean serum zinc (µg/dl)
Severity of pneumonia		
Pneumonia	42	118.4
Severe pneumonia	11	67.7
Very severe pneumonia	7	45.7
SpO <sub>2</sub> < 94%	13	53.27 ( $p = 0.033$ )
Shock	6	46.17
Anemia < 11 g/dl	42	87.01
Chest X-ray (bilateral interstitial infiltrates)	39	78.5 ( $p = 0.001$ )
Death	3	33.6
Empyema	3	70

The overall high prevalence of low serum zinc levels in the current study may be due to local food habits rich in phytates and fiber contents which potentially inhibit the absorption and utilization of zinc. It may also be due to pre-existing zinc deficiency due to inadequate intake of food-containing zinc or decreased absorption which is commonly seen in developing countries. The benefit of zinc supplementation to prevent and decrease the severity of pneumonia is mainly due to the correction of zinc deficiency. We observed that lower serum zinc was associated with increasing severity of pneumonia (118.4 µg/dl in pneumonia vs. 67.7 µg/dl in severe pneumonia vs. 47.7 µg/dl in very severe pneumonia). This is in accordance with earlier studies done by Pushpa *et al.* and Hussain *et al.* [15,20].

Zinc deficiency leads to increased apoptosis of pre-B and pre-T cells resulting in lymphopenia and decreased B-cell production. In zinc-deficient individuals, there is a decrease in T helper type 1 function, leading to decreased interleukin (IL)-2 and interferon-gamma. This results in impairment in the function of natural killer (NK) cells and cytolytic activity of T cells. IL-10 is increased in zinc deficiency which results in increased production of IL-1B, IL-8, and tumor necrosis factor-alpha. Therefore, overall, the programming of the immune system is impaired, decreasing the NK cell activity in zinc deficiency [21].

Hussain *et al.* have studied the association between severity of pneumonia, X-ray finding, and anemia and reported that there is no significant difference between anemia and severity of pneumonia, and pulmonary infiltrate on X-ray was the common finding with pneumonia cases [20]. Similar observation was seen in this study. Kumar *et al.* reported no significant difference between the duration of hospital stay and mean serum zinc levels [17]. Inverse relationship was seen between the duration of hospital stay and mean serum zinc levels in the present study; although, it was statistically insignificant.

Zinc has antioxidant and anti-inflammatory properties. Zinc also acts as growth factor for regeneration of damaged epithelial cells, a process needed for restoration of damaged lungs following severe pneumonia [22]. Thus, zinc deficiency impairs faster restoration of damaged lung tissue to normal and thereby causing prolonged hospital stay. In our study, out of 60 cases, 3 were complicated with empyema and 3 cases expired. The mean serum zinc levels in both the groups were very low compared to those with no complications. The study was limited by the small sample size with complicated pneumonia; hence, the significance of low serum zinc in these groups could not be assessed.

## CONCLUSIONS

Serum zinc levels are significantly low in children with pneumonia compared to age- and sex-matched controls. Low serum zinc is associated with increased severity of pneumonia.

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