

# Serum zinc levels in hospitalized children with pneumonia: a hospital-based case–control study

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**Background** Zinc is an important micronutrient in humans. Globally, pneumonia represents 18% of mortality in children under 5 years of age and the main infectious purpose of early life mortality. There is a higher pneumonia risk in a population with zinc deficiency. The aim of our study is to compare the level of serum zinc in children with pneumonia with age, sex, and nutritional matched healthy controls.

**Patients and methods** Serum zinc level in 90 children admitted with pneumonia was compared with the matched controls.

**Results** The mean level of serum zinc in children with pneumonia ( $67.5 \pm 21.8$ ) is significantly lower than that of controls ( $91.8 \pm 19.94$ ) with ( $P < 0.001$ ).

**Conclusion** Children with pneumonia has a significantly lower serum zinc levels than matched healthy controls.

## Introduction

Acute respiratory tract infection is the leading cause of below-five mortality in kids [1]. Pneumonia is an acute form of respiratory infection that impacts the lungs. It is defined as an inflammation of the lung tissue due to an infectious agent. The commonly used clinical WHO operational definition is based only on clinical symptoms (cough or difficulties in breathing and tachypnea). In the developing world, the term lower respiratory tract infection is widely used instead of pneumonia, because of poor access to radiography and difficulties in radiological confirmation of diagnosis [2].

Pneumonia is the only major infectious cause of pediatric mortality internationally. Pneumonia death is about 920 000 children under the age of 5 years in 2015, representing 16% of all pediatric mortality below 5 years old. Pneumonia influences children and families everywhere, however, is most usual in South Asia and Sub-Saharan Africa. Children can be avoided with easy interventions and treated with low-cost, low technical medication, and care [3]. In Egypt, it was estimated that 10% of deaths in children under the age of 5 years is probably caused by pneumonia and other acute respiratory infections [4].

Zinc affects many elements of the immune device, from the skin barrier to gene regulation inside lymphocytes. The function of macrophage is adversely affected by zinc deficiency. Zinc plays a crucial role in the development of acquired immunity, immunoglobulin

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G production, intracellular killing, cytokine production, and phagocytosis, thus regulating the defense mechanism in children with acute infection [5]. Prophylactic zinc therapy decreases the rate of infection in children with pneumonia [6].

Deficiency of zinc reduces the body's ability to reply to infection and additionally adversely influences both cell-mediated and humoral immune responses. The impaired immunocompetence due to low zinc states enhances the establishment of a particular infection due to a reduction in the clearance of infectious agents [7].

The purpose of our study was to compare the serum zinc level in children admitted with pneumonia to the matched controls and assess its relationship to the grade of respiratory distress.

## Patients and methods

A comparative, cross-sectional hospital-based study was carried out from November 2016 to October 2018. The total of 180 children included in the study was classified into two groups as follows: group I, the cases group: included 90 children with clinical and laboratory evidence of pneumonia

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attending the pediatric department and group II, the control group: included 90 children who are seemingly healthy controls who attended for nonchest problem or dangerous medical condition. Parents of all patients and controls gave their informed consents and written approval for their children's participation before their enrollment in the study. The study was approved by the local moral committee of our university, to assess and submit facts. Written or verbal consent was taken from parents or from close guardian.

#### Inclusion criteria

Children aged between 2 months and as much as 5 years on admission identified as pneumonia were recruited as patients.

#### Exclusion criteria

(a) Children of age less than 2 months; (b) children over 5 years of age; (c) children who had upper respiratory tract infection or viral infection such as bronchiolitis; (d) children with diarrhea in the previous 1 month; (e) excessive form of malnutrition such as marasmus; (f) history and manifestation of liver, heart illness, or history of intake of zinc supplements within the preceding 1 month.

All children were clinically examined by the treating physician and treatment ordered by way of them was abstracted. These children were confirmed radiologically with a chest radiograph. All cases were subjected to a complete clinical study (through history and physical examination) upon study inclusion, with emphasis on symptoms and signs of pneumonia.

Complete diagnostic workup including complete blood count, C-reactive protein (CRP), renal function test, and blood culture was done. In all children, serum zinc level was measured in 2 ml of a venous blood sample taken at the time of admission or within 24 h of admission after obtaining consent from parents. Serum zinc level was measured by spectrophotometry using the calorimetric method (Quanticore™ Zinc Assay Kit; Bioassay Systems, Hayward, USA).

## Results

The study population consists of 180 children with 90 cases with pneumonia (48 men and 42 women) and 90 healthy controls of matched age and sex (48 men and 42 women). The mean age of the patient group was  $20.6 \pm 15.7$  and  $22.3 \pm 19.9$  months for the control group and there was no statistically significant difference between groups ( $P > 0.05$ ). There is no significant difference between patients and control group as

regards sex, residence, history of exposure to smoking, weight, and height ( $P > 0.05$ ) while there was significant difference between patients and controls as regards the type of supplementation ( $P < 0.05$ , Table 1), where supplementation is significantly lower in children with pneumonia than their matched controls ( $P < 0.05$ , Table 2).

There was a statistically significant decrease in mean corpuscle volume, mean corpuscle hemoglobin, and lymphocyte percentage in patients when compared with controls ( $P < 0.05$ ), while there was a statistically significant increase in white blood cell and its differential (neutrophil, staff) count and CRP level in patients when compared with controls ( $P < 0.05$ ).

Mean serum zinc level in children with pneumonia was  $67.5 \pm 21.8 \mu\text{g/dl}$ , while that of matched controls was  $91.8 \pm 19.94 \mu\text{g/dl}$ . Mean serum zinc level is significantly lower in children with pneumonia than

**Table 1 Demographic data and anthropometric measurements among patients and control**

| Parameters                             | Patients (N=90) | Controls (N=90) | P value |
|--|-----------------|-----------------|---------|
| Age of the child (months) (mean±SD)    | 20.6±15.7       | 22.3±19.9       | 0.16    |
| Range (minimum–maximum)                | 58 (2–60)       | 57 (3–60)       |         |
| Sex [n (%)]                            |                 |                 |         |
| Male                                   | 48 (53.3)       | 39 (43.3)       | 0.44    |
| Female                                 | 42 (46.7)       | 51 (56.7)       |         |
| Residence [n (%)]                      |                 |                 |         |
| Urban                                  | 30 (33.3)       | 27 (30.0)       | 0.78    |
| Rural                                  | 60 (66.7)       | 63 (70.0)       |         |
| History of exposure to smoking [n (%)] |                 |                 |         |
| No                                     | 72 (80.0)       | 75 (83.3)       | 0.5     |
| Yes                                    | 18 (20.0)       | 15 (16.7)       |         |
| Place of admission [n (%)]             |                 |                 |         |
| Ward                                   | 54 (60)         | –               |         |
| PICU                                   | 36 (40)         | –               |         |
| Weight-for-age [n (%)]                 |                 |                 |         |
| <5th                                   | 18 (20.0)       | 9 (10.0)        | 0.74    |
| ≥5th                                   | 72 (80.0)       | 81 (90.0)       |         |
| Height-for-age [n (%)]                 |                 |                 |         |
| <5th                                   | 9 (10.0)        | 6 (6.7)         | 0.8     |
| ≥5th                                   | 81 (90.0)       | 84 (93.3)       |         |

PICU, pediatric intensive care unit.

**Table 2 Comparison between patients and controls regarding the type of supplementation (total N=180)**

| Supplementation      | Patients [n (%)] | Controls [n (%)] |        |
|----------------------|------------------|------------------|--------|
| No (N=48)            | 33 (36.7)        | 15 (16.7)        | 0.041* |
| Iron (N=12)          | 3 (3.3)          | 9 (10)           |        |
| Iron+vitamins (N=69) | 21 (23.3)        | 48 (53.3)        |        |
| Vitamins (N=51)      | 33 (36.7)        | 18 (20)          |        |

\*P value is statistically significant.

**Table 3 Comparison between patients and controls regarding complete blood count, serum zinc level, and C-reactive protein (N=180)**

| Parameters                                   | Patients (N=90)   | Controls (N=90)  | P value |
|--|-------------------|------------------|---------|
| RBCs $\times 10^6$ (cm) (mean $\pm$ SD)      | 4.46 $\pm$ 0.9    | 4.18 $\pm$ 0.49  | 0.13    |
| HB (g/dl) (mean $\pm$ SD)                    | 10.12 $\pm$ 2.06  | 10.53 $\pm$ 1.23 | 0.36    |
| HCT (mean $\pm$ SD)                          | 29.7 $\pm$ 6.04   | 31.8 $\pm$ 4.56  | 0.13    |
| MCV (fl) (mean $\pm$ SD)                     | 67.3 $\pm$ 10.8   | 75.74 $\pm$ 7.25 | 0.001** |
| MCH (pg) (mean $\pm$ SD)                     | 23.09 $\pm$ 3.56  | 24.88 $\pm$ 2.44 | 0.028*  |
| MCHC (pg) (mean $\pm$ SD)                    | 34.14 $\pm$ 3.11  | 33 $\pm$ 1.57    | 0.75    |
| Platelet count $\times 10^3$ (mean $\pm$ SD) | 373.4 $\pm$ 139.5 | 321.8 $\pm$ 89.2 | 0.094   |
| Lymphocyte (mean $\pm$ SD)                   | 29.06 $\pm$ 14.6  | 37.42 $\pm$ 11.5 | 0.016*  |
| WBCs $\times 10^3$ (cm) (mean $\pm$ SD)      | 18.53 $\pm$ 9.66  | 9.81 $\pm$ 4.9   | 0.001** |
| Eosinophil (mean $\pm$ SD)                   | 2.13 $\pm$ 0.83   | 3.12 $\pm$ 1.75  | 0.14    |
| Neutrophil (mean $\pm$ SD)                   | 63 $\pm$ 15.3     | 54.1 $\pm$ 11.9  | 0.013*  |
| Monocyte (mean $\pm$ SD)                     | 6.15 $\pm$ 4.9    | 3.8 $\pm$ 1.92   | 0.32    |
| Staph (mean $\pm$ SD)                        | 2.43 $\pm$ 1.61   | 0.67 $\pm$ 0.13  | 0.011*  |
| Segmented (mean $\pm$ SD)                    | 55.6 $\pm$ 17.5   | 52.7 $\pm$ 19.7  | 0.073   |
| Serum zinc ( $\mu$ g/dl) (mean $\pm$ SD)     | 67.5 $\pm$ 21.8   | 91.8 $\pm$ 19.94 | 0.001** |
| CRP [n (%)]                                  |                   |                  | 0.001** |
| -ve  | 24 (26.7)         | 72 (80)          |         |
| +ve  | 66 (73.3)         | 18 (20)          |         |

CRP, C-reactive protein; HB, hemoglobin; HCT, hematocrit; MCH, mean corpuscle hemoglobin; MCHC, mean corpuscle hemoglobin concentration; MCV, mean corpuscle volume; RBCs, red blood cells; WBCs, white blood cells. \*P value is statistically significant. \*\*P value is statistically highly significant.

their matched controls ( $P < 0.001$ ) (Table 3). There was no significant correlation between CRP results and serum zinc level in patients ( $r = -0.1$ ,  $P = 0.49$ ) and controls ( $r = -0.28$ ,  $P = 0.29$ ) (Figs 1, 2).

Mean serum zinc level in the patient group is compared with the degree of respiratory distress. There was a significant difference in mean serum zinc level between patients when compared with the degree of respiratory distress ( $P < 0.05$ ), where higher values of zinc were reported with lower grades of respiratory distress (Table 4).

There was no significant difference in serum zinc level between patients as regards the type of feeding ( $P > 0.05$ ), while there was a significant difference in serum zinc level between controls as regards the type of feeding ( $P < 0.05$ ) (Table 5).

There was a highly significant decrease in serum zinc level of patients with complications such as pleural effusion or empyema (43.8 $\pm$ 15.4) than that without complications (72.25 $\pm$ 19.8) ( $P < 0.001$ ) (Fig. 3).

There was a significant difference in mean serum zinc level of patients as regards the place of admission in a ward (66.7 $\pm$ 16.6) or PICU (60.3 $\pm$ 11.6) ( $P < 0.05$ ).

#### Statistical analysis

The collected data were collected, prepared, tabulated, and statistically analyzed using the Statistical Package

for the Social Sciences (SPSS), version 23.0 for Windows. Enumeration data were presented as mean $\pm$ SD and were analyzed with an unpaired  $t$  test. Categorical variables were analyzed with Pearson  $\chi^2$  and Fisher's exact tests. The statistical methods were verified, assuming a significance level of  $P$  value less than 0.05 and a highly significant level of  $P$  value less than 0.001.

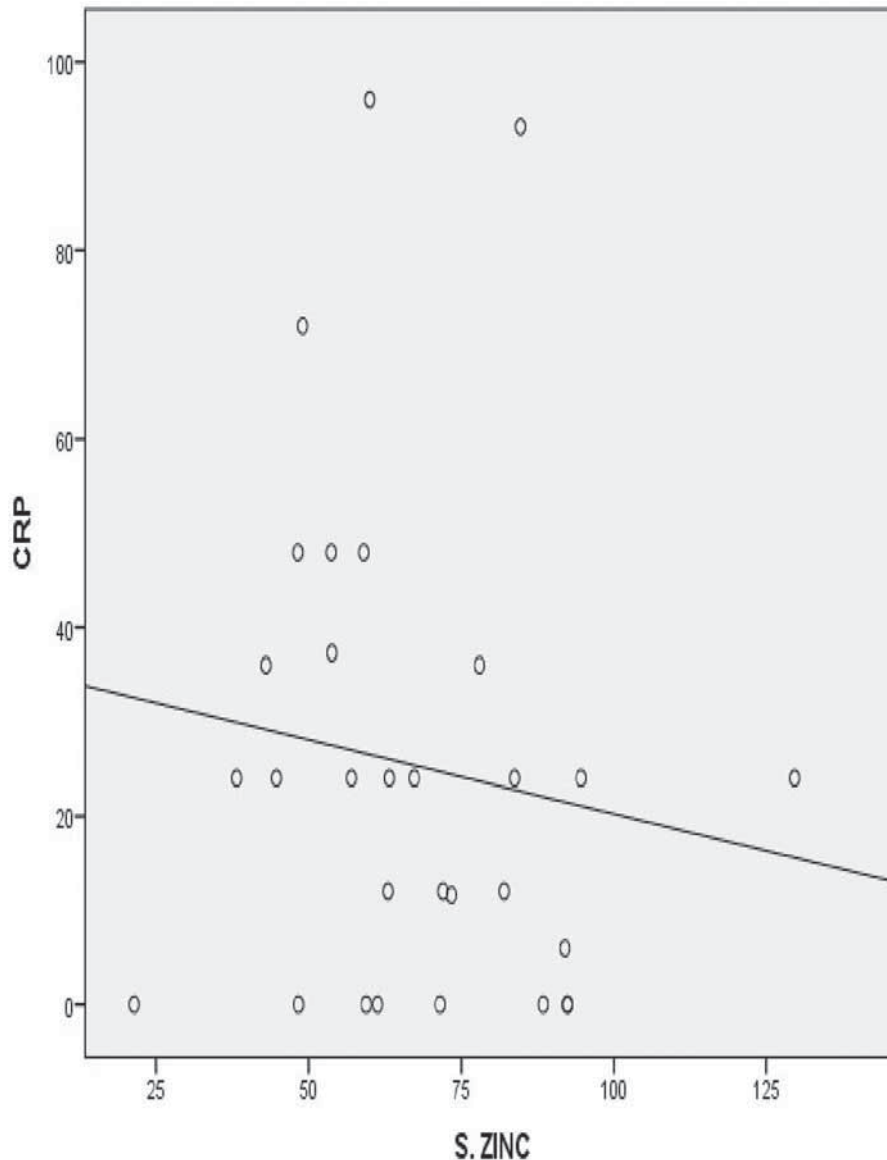
#### Discussion

Pneumonia is one of acute lower respiratory infections that involve the airways and parenchyma with a consolidation of alveolar spaces (infection of the lung alveoli) [8]. In Egypt, it was estimated that 10% of death in children under the age of 5 years is usually caused by pneumonia and other acute respiratory infections [3]. The occurrence and mortality of pneumonia is adversely affected by malnutrition. Malnutrition has been identified as an important determinant of pneumonia-related mortality [7].

Zinc is an essential element required for cell metabolism and immunity. Therefore, zinc deficiency leads to susceptibility to infections and may affect pulmonary epithelial cell integrity. Several investigators have used zinc supplementation to see its effect on many diseases mainly diarrheal diseases and severe pneumonia [9].

The incidence of pneumonia is high in the young age that may be due to a defect in the complex system of

Figure 1



Scatter diagram showing the correlation between CRP results and serum zinc among patients. CRP, C-reactive protein.

defense mechanisms which normally protect the lungs from a hostile microbiological environment. These include physical defenses such as cough and mucociliary clearance, circulating and resident cellular defenses, and a range of humeral or secretory mechanisms and may be due to restricted access to zinc-rich ingredients (animal products, oysters, and shellfish) and the abundance of zinc inhibitors which include phytate [10].

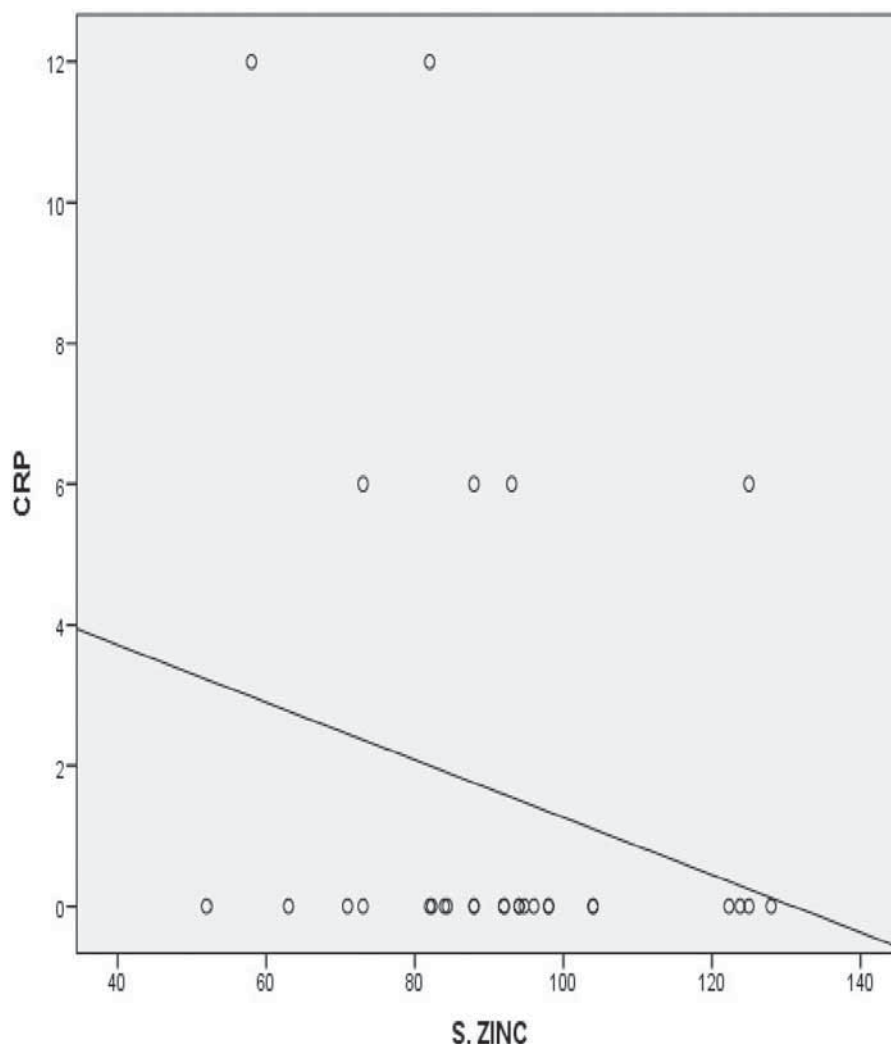
Our study reported that the mean age for children with pneumonia was 20.6 months. This result was higher than the results found in studies undertaken in Uganda and Nepal by Srinivasan *et al.* [11] and Basnet *et al.* [12], respectively, who reported that the mean age of their children was  $17.9 \pm 12.2$  and  $7.8 \pm 6.0$  months, respectively. The mean age of our patients was lower

than that reported by Shah *et al.* [13] in their cases ( $108 \pm 60$  months). This difference found in the studied patients may be due to a wide variation in the causative organisms.

In our study, we reported that male patients were affected by pneumonia more than females. This male predominance was also recorded by Valentinier-Branth *et al.* [14] (58%), Basnet *et al.* [12] (59.2%), and Jagnoor *et al.* [15] (52.8%).

Anatomic, way of life, behavioral, and socioeconomic differences between men and women may explain the located findings. The role of sex hormones in the regulation of the immune system can be additionally contributing to the reported sex differences in the occurrence and

Figure 2



Scatter diagram showing the correlation between CRP results and serum zinc among controls. CRP, C-reactive protein.

severity of the several types of respiratory tract infections [16].

The current study observed that there was a significant increase in CRP level in patients when compared with controls (Table 3). This may be due to the manufacturing of plasma CRP from the liver in response to an infection or harm to the tissue and inflammatory processes, so the anti-inflammatory effect of zinc may increase the CRP level [17].

Our study was consistent with the results observed by Cvijanovich *et al.* [18] who observed low plasma zinc levels in 20 critically ill children and its levels correlated inversely with markers of inflammation such as CRP and grade of organ failure.

There was a significant difference in serum zinc level between patients and controls as regards the type of

**Table 4 Comparison of serum zinc level according to the degree of respiratory distress among patients (N=90)**

|                              | Mild (N=27) | Moderate (N=39) | Severe (N=24) | P value |
|------------------------------|-------------|-----------------|---------------|---------|
| Serum zinc (µg/dl) (mean±SD) | 72.5 ±24.7  | 61.4±21.5       | 55.2±17.2     | 0.002*  |

\*P value is statistically significant.

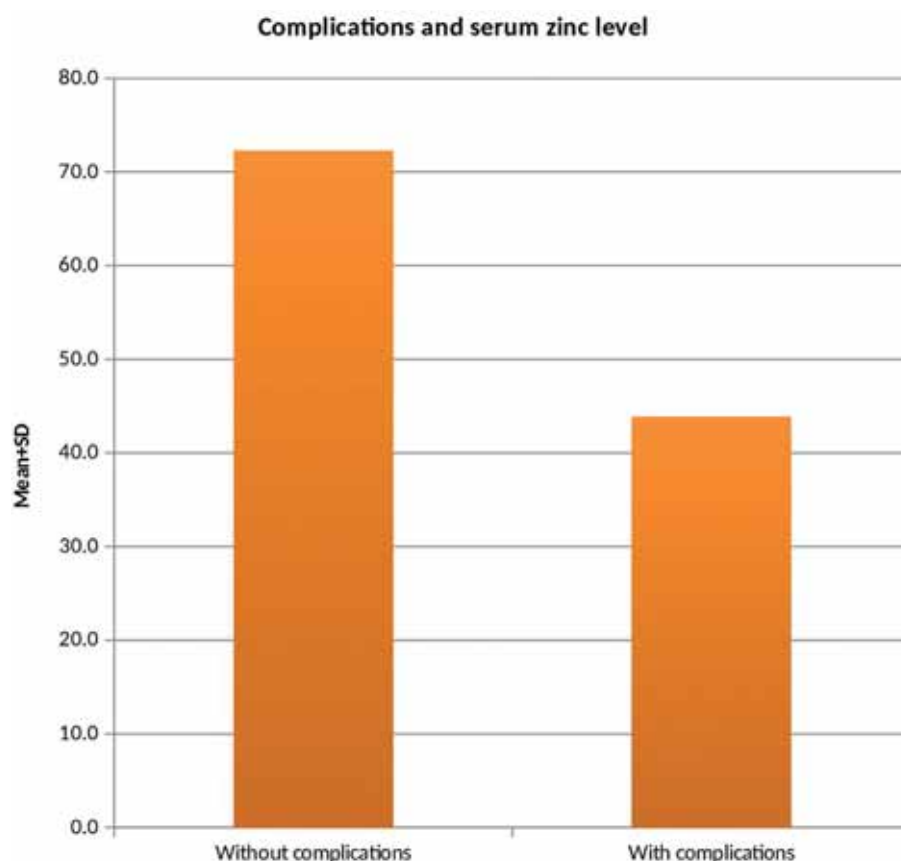
feeding and supplementation (Table 4). There was a significant difference in serum zinc level between controls as regards the type of feeding (Table 4). This may be due to that breastfeeding protects the infants from getting pneumonia by way of boosting their infection-fighting (immune) system. Breastfeeding beyond 4 months of age offers satisfactory protection [19].

In agreement with our results, Arica *et al.* [20] reported that there is a high concentration of zinc in breast-fed infants especially colostrum.

**Table 5 Comparison of serum zinc level according to feeding type among patients and controls (N=60)**

| Serum zinc ( $\mu\text{g/dl}$ ) (mean $\pm$ SD) | Breastfeeding    | Breast and artificial feeding | Artificial feeding | P value |
|---|------------------|-------------------------------|--------------------|---------|
| Total number of patients                        | N=111            | N=39                          | N=30               |         |
|   | 85.07 $\pm$ 23.9 | 75.7 $\pm$ 22.5               | 64.6 $\pm$ 19.2    | 0.041*  |
| Patient group                                   | N=45             | N=30                          | N=15               |         |
|   | 67.1 $\pm$ 19.2  | 75 $\pm$ 24.4                 | 53.8 $\pm$ 21.03   | 0.21    |
| Control group                                   | N=66             | N=9                           | N=15               |         |
|   | 97.33 $\pm$ 18.8 | 78.1 $\pm$ 13.36              | 75.4 $\pm$ 9.76    | 0.027*  |

\*P value is statistically significant.

**Figure 3**

Comparison of serum zinc level according to complications among patients (N=90).

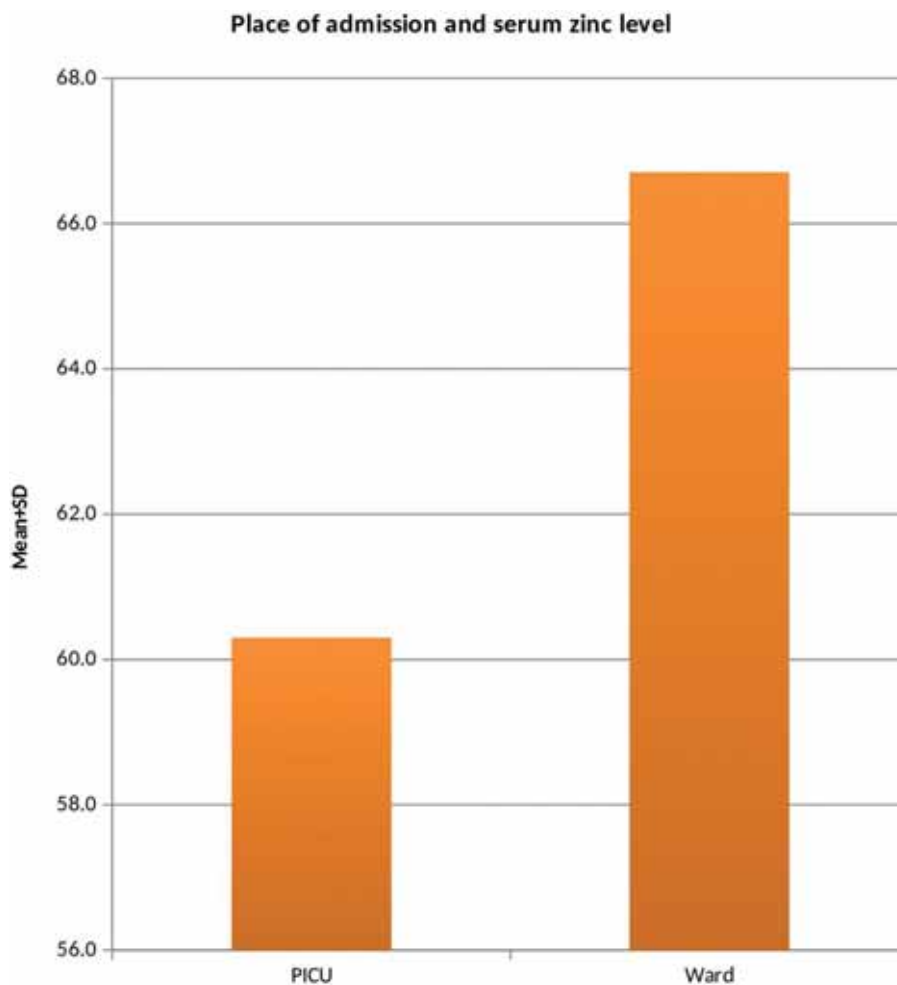
The current study found that there was a significant difference in serum zinc level between patients as regards the grading of respiratory distress. Our results agreed with Bhandari *et al.* [21] who found that there was a wide decrease in the duration of hospitalization and recovery from pneumonia in zinc receiving children. This suggests the effect of zinc therapy and a change in the clinical course of pneumonia among the children.

This agreed with the study by Rahim *et al.* [22] who suggested that zinc through its antioxidant effect may improve symptoms of respiratory tract infection.

There was a significant decrease in serum zinc level of patients with complications (pleural effusion or empyema) than that without complications of pneumonia (Figs 3 and 4). This may be due to that zinc reduces susceptibility to pneumonia by regulating several immune functions, including protecting the health and integrity of the respiratory cells during lung inflammation or injury resulting in improvement of respiration [23].

Our study has shown that there was a significant difference in serum zinc level between patients as regards the site of admission which is either in a ward or PICU. This can be explained by the role of

Figure 4



Comparison of serum zinc level according to the place of admission, among patients ( $N=90$ ).

zinc in decreasing inflammation resulting in an improvement of respiratory distress. Zinc deficiency may harm mucosal integrity. Zinc helps revitalize mucus membranes. It is suggested that the antioxidant effect of zinc may improve symptoms of respiratory tract infection [23].

The mean serum zinc levels in patients were significantly lower than the corresponding level for controls. This may be due to that a defensive reaction to infection as zinc has a direct antiviral effect and an observable impact on immune-mediated production of interferon. Additionally, zinc prevents pathogens from gaining entry into cells and hinders their intracellular multiplication [7]. Also, perhaps because zinc deficiency impairs standard immune feature and resistance to infection [24]. In agreement with our study, Panneerselam and Marimuthu [25] mentioned that their mean serum zinc level in the patient group (60.98) is significantly lower than that of controls (73.124) with ( $P=0.001$ ).

Our result was in agreement with the results reported by Brooks *et al.* [26], Mahalanabis *et al.* [27], and Srinivasan *et al.* [14] studies. They reported that their mean serum zinc levels were 52.7, 66.01, and 62.75  $\mu\text{g}/\text{dl}$ , respectively.

Our study was consistent with the results documented by the Shakur *et al.* [28] and Shakur *et al.* [9] studies. They reported that their mean serum zinc levels were 63.7 and 57.9  $\mu\text{g}/\text{dl}$ ; respectively. In India, Kumar *et al.* [29] reported that serum zinc level was significantly lower in patients with pneumonia compared with the control cases.

Our results disagreed with the results observed by Anuradha *et al.* [30] (71.9  $\mu\text{g}/\text{dl}$ ) and Rady *et al.* [31] (80.77  $\mu\text{g}/\text{dl}$ ). This may be explained by a longer period of breastfeeding in her study group and the known fact that high concentration of zinc is included in colostrum.

Further studies are required to recommend routine intake of zinc in children to prevent pneumonia and the therapeutic use of zinc in pneumonia. The chief limitation of our study is follow-up with zinc intake and its impact is not recorded.

## Conclusion

Serum zinc levels are significantly low in children with pneumonia when compared with healthy controls. There is a negative correlation between serum zinc level and the grade of respiratory distress among children with pneumonia. The low serum zinc level determined in children with pneumonia usually due to zinc deficiency highlights the significance of the inclusion of food items containing good amounts of zinc in children's diet.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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