

## Serum zinc level in patients with pneumonia: a six-month long cross-sectional descriptive study at Liaquat University Hospital Hyderabad, Sindh, Pakistan

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### Abstract

**Objective:** To determine the serum zinc level in patients with pneumonia.

**Methods:** The descriptive cross-sectional study was conducted at the Liaquat University Hospital, Hyderabad, Pakistan, from September 2008 to February 2009. All patients above 12 years of age and of either gender who had been diagnosed with pneumonia were further evaluated for their serum zinc status. The data was analysed through SPSS 10.00, and  $p < 0.05$  was considered statistically significant.

**Result:** The mean age of the 118 patients in the study was  $25.64 \pm 6.53$  years. The mean serum zinc level was  $8.279 \pm 2.77$  mmol/L, while the mean serum zinc levels in patients having low and normal levels was  $6.740 \pm 1.47$  mmol/L and  $13.243 \pm 1.52$  mmol/L respectively ( $p < 0.001$ ). The serum zinc was low in 42 of the 72 (58%) males, and 35 of the 46 (76%) females ( $p < 0.04$ ). There was also significant difference between mean serum zinc level in male and female patients ( $p < 0.03$ ). Out of 77 (65%) hypozincaemic patients, 69 (90%) recovered, while 08 (10%) failed to recover) during their hospital stay ( $p < 0.33$ ). Of the 69 who recovered, 29 (42%) patients did so in less than 2 weeks, while 40 (58%) patients recovered in more than 02 weeks.

**Conclusion:** Serum zinc level was found to be low in patients with pneumonia.

**Keywords:** Pneumonia, Zinc, Trace elements. (JPMA 63: 369; 2013)

### Introduction

Zinc is a trace mineral and has fundamental role in gene expression, cell development and replication. Severe or clinical zinc deficiency is associated with various health consequences.

The need to assess the prevalence of zinc deficiency in representative samples of populations have been acknowledged, and currently, serum or plasma zinc concentration is the most widely used biochemical indicator of zinc status. Since the second National Health and Nutrition Examination Survey (NHANES II) of the United States (1976-1980) included serum zinc concentration in its biochemical assessments.<sup>1</sup>

Pneumonia has been recognised as a common and potentially lethal condition for nearly two centuries and over 80 per cent of the cases have been found to be due to streptococcus pneumoniae. Physical findings include fever in 80 per cent of patients; most have a respiratory rate exceeding 20 breaths per minute; crackles are heard on auscultation in 80 per cent; and up to 30 percent have signs of

consolidation.<sup>2</sup> Mortality varies depending on the etiologic organism and host defense status; for outpatients, the mortality is low at about 5% with even higher rates for patients requiring intensive care unit (ICU) stay.<sup>3</sup> Radiographic changes usually cannot be used to distinguish between bacterial and non-bacterial pneumonia, but they are often important for evaluating the severity of the illness and in determining the need for diagnostic studies.

Evidence from low-income countries indicate that detrimental effects on host immunity can occur rapidly in people with mild zinc deficiency and there is an increased risk of microbial infections in such individuals. Results from preventive trials have shown that zinc supplementation significantly reduces the duration and recovery time of pneumonia in people living in areas of endemic zinc deficiency.<sup>4</sup> The prevalence of serum zinc disturbance pneumonia is 26.2%.<sup>5</sup>

The current study was conducted to assess the disturbance in serum zinc level in patients with pneumonia.

### Patients and methods

The descriptive cross-sectional study was conducted at Liaquat University Hospital — a tertiary care teaching 1500-bed hospital — Hyderabad from September 2008 to February 2009. All patients between 12-35 years of

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age, of either gender, who had come through outdoor patient department (OPD), or were indoor patients, or had been referred by the casualty outdoor department (COD) with history of fever  $\geq 37.8^{\circ}\text{C}$  plus respiratory symptoms (cough, dyspnoea, sputum), shaking chills or chest pain were admitted, evaluated and enrolled in the study.

Detailed history of all patients was taken and complete physical and relevant clinical examination to detect signs of consolidation were performed. The diagnosis of pneumonia was made on the basis of (1) acutely presenting clinical findings of either one major criterion (axillary temperature  $>37.8^{\circ}\text{C}$ , cough, or expectoration) or at least two minor criteria (pleuritic chest pain, dyspnoea, leukocytosis [white blood cell count  $>12,000/\text{mL}$ ], altered mental status or sign of lung consolidation by clinical examination). All such patients were advised for chest radiograph to detect any pneumonic patch, and pleural fluid examination was also done. The sputum gram stain and culture was also advised and considered to be positive for pneumonia when the white blood cell (WBC) count was more than 25 and  $<10$  squamous epithelial cells per low-power field. Thoracocentesis was performed and obtaining fluid (pleural effusions and frank empyema fluid identified by obliteration of costophrenic angles on chest x-ray) from the pleural space was tested for gram stain and culture to isolate pneumonic infection by biochemical analysis.

The referred suspicious patients with different respiratory symptoms from various departments were also included in the study and were then evaluated according to the above mentioned criteria for inclusion in the study.

The presenting chest X-ray pattern (airspace pneumonia, interstitial infiltrate and bronchopneumonia), extension (number of lobes involved, unilateral or bilaterality patches) and physical examination (respiratory rate, heart rate, blood pressure and respiratory signs such as consolidation, rales, reduced breath sounds, rhonchi, or evidence of pleuritis or effusion) were also recorded. The severity of pneumonia was assessed according to the CURB-65 score,<sup>6</sup> which is an acronym for each of the risk factors measured. Each risk factor scores one point, for a maximum score of 5: Confusion, of new onset (defined as an abbreviated mental test score of 8 or less); Urea greater than  $19\text{mg/dL}$ ; Respiratory rate of 30 breaths per minute or greater; Blood pressure less than  $90\text{mmHg}$  systolic or diastolic blood pressure  $60\text{mmHg}$

or less; and age 65 or older.

The risk of complications and mortality increases as the score goes higher. After the confirmatory diagnosis of pneumonia, all patients were then evaluated for serum zinc level by taking 2cc fasting venous blood sample and sending it to laboratory for analysis. The normal range of serum zinc level is  $11\text{-}19\text{mmol/L}$  and the value  $< 11\text{mmol/L}$  was considered low.<sup>7</sup> As far as severity of hypozinaemia is concerned, it was categorised into mild, moderate and severe. Informed consent was taken from every patient or from attendants of patients after explaining the procedure regarding the study. Patients who were diagnosed with pneumonia but refused hospitalisation were advised fasting serum zinc level on follow-up visit to assess their serum zinc status.

Those excluded were patients already on zinc therapy; non-cooperative patients or those who refused to give consent; patients who were known cases of any autoimmune disease, immunodeficiency disorder ( $\text{CD4}+$  count  $< 200$ , granulocytopenia  $< 500/\text{mm}^3$ ) or already on chemotherapy; patients with pulmonary oedema, tuberculosis and lung cancer; patients already on hormonal therapy; patients with acute or chronic diarrhoea; and patients who were pregnant.

All blood investigations and chest radiographs were reviewed by a panel of expert consultant physicians of the ward and labelled "no pneumonia" if review of chest X-ray did not reveal infiltrate, or if the infiltrates were non-infectious (malignancy, pulmonary oedema, atelectasis etc).

The data was then analysed through SPSS version 10.00. Frequency and percentage of gender and serum zinc disturbance in the patients was calculated. The mean and standard deviation (SD) was calculated for age. Independent samples t-test was applied on categorical variables, while chi-square was applied to determine the statistical difference in gender. P-value  $<0.005$  was considered statistically significant. The tests were applied at 95% confidence interval.

## Results

During the study period 118 patients were diagnosed with pneumonia. The mean age was  $25.64 \pm 6.53$  years. Of the total, 104 (88%) patients had come directly to the Medical Ward, while 14 (12%) were referred by different units for expert opinion; 23 (19%) patients refused hospitalisation and were advised for follow-up visits. Fever was detected in all 118 patients, while productive cough was observed in 98 (83%); dyspnoea in 92 (78%), chest pain in 94 (80%); and shaking chills in 48 (41%);

Table-1: Gender distribution of pneumonia patients in relation to serum zinc status.

Gender	Pneumonia (n = 118) Serum zinc		P-value
	Normal	Low	
Male	30 (41.7%)	42 (58.3%)	0.04*
Female	11 (23.9%)	35 (76.1%)	

Chi-square with one degree of freedom = 3.90.

\*P-value is statistically significant.

Table-2: Severity of hypoziacaemia in relation to severity of pneumonia.

Hypoziacaemia	CURB-65 score			Total	P-value
	0 - 1	02	03 - 05		
Mild	07(33.3%)	08(26.7%)	09(34.6%)	24(31.2%)	<0.01*
Moderate	12(57.1%)	15(50.0%)	03(11.5%)	30(39.0%)	
Severe	02(9.5%)	07 (23.3%)	14(53.8%)	23(29.9%)	
Total	21(100%)	30(100%)	26(100%)	77(100%)	

\*P-value is statistically significant.

 $\chi^2$  value = 16.40; df = 4.

Table-3: Severity of hypoziacaemia in relation to recovery.

Hypoziacaemia	Recovery		Total	P-value
	≤02 weeks	>02weeks		
Mild	14(48.3%)	09(22.5%)	23(33.3%)	0.03*
Moderate	11(37.9%)	16(40.0%)	27(39.1%)	
Severe	04(13.8%)	15(37.5%)	19(27.5%)	
Total	29(100%)	40(100%)	69(100%)	

\*P-value is statistically significant.

 $\chi^2$  value = 6.80; df = 2.

108 (92%) presented with multiple symptoms i.e. the combination of two or more symptoms; while 10 (8%) patients had single symptom. Signs of consolidation and lung crackles were detected in all patients.

Chest radiograph showed air space pneumonia in 86 (73%) patients; interstitial infiltrate in 22 (19%); and bronchopneumonia in 10 (8%). Bilateral pulmonary involvement was observed in 98 (83%) patients, while 20 (17%) had unilateral pulmonary involvement. Pleural effusion was seen in 21 (18%) patients. The flow of pneumonic patients was seen more in the month of November and December 2008, and the majority of the subjects (n=92; 78%) belonged to rural population. The mean serum zinc level of the overall study population was  $8.27 \pm 2.77$  mmol/L; 77 (65%) patients were found to have serum zinc level below the cut-off value, while 41 (35%) had normal serum zinc levels. Of the 118 patients, 72 (61%) were males and 46(39%) were females (Table-

1). The overall mean of serum zinc in male and female population was  $9.472 \pm 3.63$  and  $8.130 \pm 2.94$  respectively ( $p < 0.03$ ), while the mean of serum zinc levels in patients having low and normal levels were  $6.740 \pm 1.47$  mmol/L and  $13.243 \pm 1.52$  mmol/L respectively ( $p < 0.001$ ). Out of 77 hypoziacaemic patients, 69(90%) patients recovered, while 08(10%) expired during their hospital stay ( $p < 0.33$ ). The severity of hypoziacaemia in relation to severity of pneumonia (Table-2), and the severity of hypoziacaemia in relation to recovery from pneumonia (Table-3) were also worked out.

## Discussion

The low concentrations of circulating zinc is associated with an increased risk of respiratory morbidity, and zinc supplementation has been shown to reduce the duration of pneumonia and deaths due to pneumonia.<sup>8</sup>

Our study identified 118 patients with a mean age of  $25.64 \pm 6.53$  years. This was similar to earlier studies.<sup>9,10</sup> In the present study, the frequency of pneumonia was more marked in November and December, and the observation was consistent with literature.<sup>11</sup>

Chest pain was observed in 80% patients, sign of consolidation in all patients, air space pneumonia in 86% patients, interstitial infiltrate in 22% subjects and bilateral opacities in 83% patients. All such findings and features correlate to an earlier study.<sup>12</sup> Clinical features cited by an earlier study<sup>13</sup> — fever, cough, chest pain, leucocytosis etc — were also identified by our study. Radiographic studies are the best tool to diagnose pneumonia. As such, the present study also followed the protocol to identify pneumonia in patients presenting with fever and respiratory symptoms. This was in contrast with an earlier study.<sup>14</sup>

In our series the bilateral patchy air space consolidation in both mid and lower zones of lungs was observed in 26% subjects. Similar finding was also detected in a previous study.<sup>15</sup> Bronchopneumonia was assessed in 8% subjects, which was also in line with literature.<sup>16</sup> The age limit criteria of pneumonic patients in our study was 12-35 years, and respiratory features were more prominent in the age group. Earlier studies also identified that respiratory and non-respiratory symptoms were less commonly reported in older patients with pneumonia, even after controlling for the increased co-morbidity and illness severity in these older patients. Therefore, recognition of this phenomenon by clinicians and patients is essential given the increased mortality in elderly patients with pneumonia.<sup>17</sup> In our study the majority of pneumonic patients belonged to rural areas and it correlated to

earlier findings.<sup>18</sup>

The present study also identified that the serum zinc level of patients with pneumonia was disturbed (low/deficient). Similar observations have been made previously as well.<sup>19</sup> Severe zinc deficiency can impair immunity and increase susceptibility to infectious diseases. The risk of mortality was reduced by 27% in participants of eye diseases who received supplementation with 80mg Zn/d.<sup>20</sup> A recent zinc mortality trial in Zanzibar found a 7% reduction in the relative risk of all cause mortality in patients supplemented with zinc.<sup>21</sup> The gender distribution of our study was statistically significant ( $p < 0.04$ ), which was also the case in another study.<sup>22</sup>

In our study we evaluated fasting serum zinc in pneumonic subjects because meal consumption results in a decrease in serum zinc concentrations which is cumulative with repeated meals. Oestrogen and progesterone are associated with lower serum zinc concentrations in women when these hormones are at their highest concentrations during the ovulatory and luteal phases of the menstrual cycle, and use of oral contraceptive agents has been documented to affect serum zinc concentration. We excluded subjects who were using steroids or other hormones because of the observed effects of physiologic or pharmacologically-induced changes in hormones or steroid concentrations on serum zinc concentration. Acute diarrhoea may result in large losses of endogenous zinc through the intestine. Therefore, serum zinc concentrations during diarrhoea may reflect acute changes in zinc metabolism and not necessarily the true zinc status. All these conditions were considered to be possible confounding factors in the analysis of serum zinc status in the study population. Serum zinc concentrations decrease during pregnancy as a consequence of blood volume expansion and possibly because of hormonal changes and, therefore, this was another confounding factor which was excluded.

A study detected that pneumonic patient with zinc deficiency showed delayed or prolonged recovery from illness.<sup>22</sup> At the onset of infection, plasma zinc concentrations decline rapidly by 10-69% and zinc supplementation in zinc deficient subjects may improve host responses in acute infection.<sup>23</sup> Thus, zinc status and the timing of supplementation are important factors in the recovery phase. Results from several trials conducted in populations that have endemic zinc deficiency indicate that zinc prophylaxis will also reduce the incidence of severe pneumonia,<sup>24</sup> which may

suggest that the up-regulation of pro-inflammatory cytokines may serve to potentiate the immune system against future severe infection in zinc-deficient individuals.

The present study did not assess the cause of disturbance in serum zinc levels in the study population. However, dietary insufficiency and the high incidence of infection in our population were findings that were consistent and correlated with a pattern of zinc deficiency. A study on zinc-deficient pneumonic patients has shown cessation of pneumonia, reduction of duration of pneumonia, fever and tachypnoea after zinc supplementation.<sup>25</sup> Serum zinc is fairly well maintained within a normal range during short-term zinc depletion because of efficient homeostatic mechanisms and, therefore, may show measurable changes only when zinc depletion is prolonged or severe. Therefore, zinc supplementation reduces the inflammation and contributes to faster inflammation resolution time in pneumonic patients with serum zinc disturbance. As such, further studies are needed to update the data, knowledge and information regarding medical workup of pneumonia patients.

## Conclusion

Disturbance in serum zinc level (low/deficient) was detected in patients with pneumonia. The disturbance was more marked in rural population. Hospital-based nutrition surveys should include biochemical assessments of zinc status in patients with pneumonia.

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