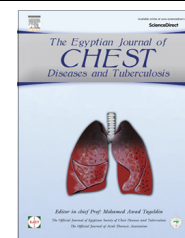




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## ORIGINAL ARTICLE

# Zinc Levels in community acquired pneumonia in hospitalized patients; a case control study



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### KEYWORDS

Pneumonia;  
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**Abstract** *Introduction:* Pneumonia usually connotes the infection of pulmonary parenchyma. Pneumonia is best classified according to the setting in which it occurs i.e community acquired pneumonia (CAP) hospital acquired or immunodeficiency associated. Dietary zinc deficiency is widespread in developing countries. Zinc deficiency is related to the morbidity and mortality in CAP.

*Aims and objectives:* To compare serum zinc values of community acquired pneumonia patients with healthy controls and to see the effect of zinc levels with severity of pneumonia.

*Methods and materials:* A case control study involved 100 patients of community acquired pneumonia with age and sex matched healthy controls, after getting informed consent from all subjects. The serum zinc level was measured, analyzed and interpreted with regard to age, CURB-65, comorbidity and hospital stay.

*Results and observation:* The mean age of patients was 59.74 years. 53 patients were males and 47 were females. Smoking history was present in 55 patients. The mean serum zinc level in patients was 89.9 µg/dl whereas in controls it was 105.65 µg/dl, which was statistically significant. The zinc levels were low in elderly patients and controls as compared to young ones. Mean zinc level was lower in patients of high CURB-65 score and vice versa.

*Summary:* Our study revealed a definite relation of low serum levels of zinc with community acquired pneumonia and there is definite decrease in serum zinc levels as the age increases. Considering the morbidity, mortality, hospital stay and financial burden and to reduce the use of antibiotics for pneumonia, especially in developing countries like ours, serum zinc levels should be routinely measured and thereby supplemented.

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### Introduction

Pneumonia is an inflammation of pulmonary parenchyma resulting in exudative solidification (consolidation) of

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pulmonary tissue that may be infectious or non infectious in nature; however in medical parlance, pneumonia usually connotes the infection of pulmonary parenchyma [1]. From the patient management point of view pneumonia is best classified according to the setting in which it occurred i.e community acquired pneumonia (CAP), hospital acquired or immunodeficiency associated infection.

Community acquired pneumonia is a common and major cause of mortality and morbidity especially in developing world. Its incidence is 20–30% in developing world compared to 3–4% in developed world [2]. Risk factors for community acquired pneumonia include increasing age and comorbid illnesses like cardiac failure, diabetes, neoplasia and COPD.

Five decades back it was considered improbable that zinc deficiency could occur and lead to any significant clinical problems. Zinc has been shown to play an important role in the regulation of the T cell-mediated function [3–5]. Dietary zinc deficiency is widespread in developing countries [6] and is often aggravated by intercurrent acute and chronic infections [7]. Zinc is involved in numerous aspects of cellular metabolism. It is required for the catalytic activity of approximately 100 enzymes [8–10] and it plays a role in immune function [10,11], protein synthesis, wound healing, DNA synthesis, and cell division [10]. Zinc also supports normal growth and development during pregnancy, childhood, and adolescence [12,13] and is required for proper sense of taste and smell [14]. A daily intake of zinc is required to maintain a steady state because the body has no specialized zinc storage system [15].

Recently some investigators have found that zinc deficiency is related to the morbidity and mortality in community acquired pneumonia. These studies have been done in children [16,17].

Until recently very few studies have been done to elucidate the role and relationship of zinc with the morbidity and mortality in community acquired pneumonia. Some investigators have found that patients with normal serum zinc levels are less likely to have infections like community acquired pneumonia and less frequent antibiotic use [18].

### Aims and objectives

1. To compare the serum zinc values of community acquired pneumonia patients with healthy controls.
2. To see the effect of serum zinc levels with severity of pneumonia.

### Methods and materials

The study was a hospital based prospective study comprising 100 patients attending inpatient department of Sher-I-Kashmir Institute of Medical Sciences (SKIMS), a tertiary care institute in an urban area of Kashmir, India. For the purpose of the present study, serum zinc levels were taken at the time of admission and the CURB 65 score was evaluated at that time. In addition demographic characteristics, comorbidities, clinical features, vaccination status, causative agents, therapy, and outcomes were noted. An informed consent was taken from patients as well as controls.

### Inclusion criteria

Community acquired pneumonia was defined as an acute illness (fewer than 14 days of symptoms), the presence of new chest infiltrates, and clinical features suggestive of acute pneumonia. The clinical features required will be one of group A (fever > 37.8 C, hypothermia < 36 C, cough and sputum production) or two of B (dyspnea, pleuritic pain, physical findings suggestive of lung consolidation and leukocyte count greater than 12,000 or less than 4000). These criteria are consistent with the published guidelines of community acquired pneumonia.

### Exclusion criteria

These include:

- (1) Patients with severe immunodeficiency as defined by the Centres for Disease Control Criteria for patients with acquired immune deficiency syndrome.
- (2) Patients receiving chemotherapy in the past 60 days.
- (3) Patients receiving treatment with corticosteroids equivalent to prednisolone at more than 20 mg/day for more than 14 days.
- (4) Patients receiving immunosuppressive drugs.
- (5) Active neoplastic disease.

### Other investigations

- Basic chemistry and hematology tests.
- Arterial blood gas.
- Chest radiography.
- Sputum for Gram staining and culture.

Serum zinc levels were taken from the patients of CAP. Also samples were taken from the age and sex matched control, which were taken from the general population.

While taking blood samples for serum zinc levels in CAP patients strict septic precautions were taken and it was made compulsory to avoid contamination of sample. Later zinc levels were measured by Colorimetric method with 5-Bromo-PAPS.

### Results and observation

Our study comprised 100 patients of community acquired pneumonia. The mean age of patients was 59.74 years. From the total number of patients 53 were males and 47 patients were females. Smoking history was present in 55% of patients of community acquired pneumonia. Cough was the commonest symptom present in 89% of patients followed by breathlessness in 76% of patients, altered sensorium in 21% of patients, with the least common symptom being hemoptysis present in only 7% of CAP patients. 65% our patients had a curb-65 score of 2–3 (Table 1). More than half of our patients were hypertensive (55%), with COPD being present in 42% of patients, 17% were diabetic, 6 patients were labeled as having coronary artery disease. 7 patients were suffering from chronic kidney disease, 2 patients were having chronic liver disease. 71% of our patients had consolidation on chest X-ray, infiltrates in 21 patients with 4 patients had both. Pleural effusion was seen in 4 patients (Table 3). The mean PH value

**Table 1** Basic characteristics, Clinical feature, and CURB 65 score.

	< 40	40–60	> 60
Age (yrs)			
No.	06	58	36
Sex	Male	Female	
No.	53	47	
Smoking	Present	Absent	
No	55	45	
Symptom	Present	Absent	
Cough	89	11	
Breathlessness	76	24	
Fever	63	37	
Altered sensorium	21	79	
Chest pain	13	87	
Hemoptysis	7	93	
CURB-65	No.		
0–1	24		
2–3	65		
4–5	11		

**Table 2** CBC, biochemistry and arterial blood gases.

Variable	No.	Min	Max	Mean	SD
Hemoglobin (g/dl)	100	6.2	18.6	11.9	2.36
TLC ( $\mu$ l)	100	1.5	24.6	11.6	4.77
Platelets	100	26.0	426.0	151.0	70.48
Urea (mg/dl)	100	16.0	272.0	79.0	47.68
Creatinine (mg/dl)	100	0.8	11.3	1.8	1.48
Bilirubin (mg/dl)	100	0.3	13.5	1.3	1.47
ALT (mg/dl)	100	7.0	714.0	89.3	131.54
Total protein (g/dl)	100	3.8	9.8	6.1	0.73
Albumin (g/dl)	100	1.9	4.3	3.1	0.50
Calcium (mg/dl)	100	6.8	10.2	8.8	0.65
LDH	100	108	2359	597.5	385.80
PH	100	7.13	7.52	7.4	0.09
PAO <sub>2</sub> mm hg	100	26	77	56.3	9.55
PCO <sub>2</sub> mm hg	100	19	90	42.4	14.43
SAO <sub>2</sub> %	100	46	98	84.0	11.00
Sodium (meq/l)	100	117	155	139.0	7.04
Potassium (meq/l)	100	1.7	5.4	3.5	0.73
HCO <sub>3</sub>	100	9.3	52.6	23.9	7.00

was 7.4 with mean PaO<sub>2</sub> of 56.3 mm hg. The mean PCO<sub>2</sub> was 42.4 mm hg with highest value being 90 mm hg (Table 2). In all age groups the serum zinc levels in patients were lower than those of controls. The mean serum zinc level in patients of community acquired pneumonia was 89.9  $\mu$ g/dl whereas that of age and sex matched healthy controls was 105.65  $\mu$ g/dl which was statistically significant. The mean serum zinc level in patients below age of 40 years was 96.38  $\mu$ g/dl and above 65 years of age was 87.04  $\mu$ g/dl. There was a decreasing trend of serum zinc levels as the age group increased. The mean serum zinc value in healthy controls less than 40 years of age was 118.96  $\mu$ g/dl whereas those above 40 years of age had 105.05  $\mu$ g/dl (Tables 4–6). The mean serum zinc level in patients with CURB-65 score of 1 was 98.3  $\mu$ g/dl whereas that with CURB-65 score of 4 had 81.0 98.3  $\mu$ g/dl. The serum zinc level in patients having hospital stay of less than 1 week was

**Table 3** Various comorbidities present in our patients.

		Frequency	Percent
Sex	Male	53	53
	Female	47	47
COPD	Present	42	42
	Absent	58	58
Diabetes	Present	17	17
	Absent	83	83
Hypertension	Present	55	55
	Absent	45	45
Coronary artery disease	Present	6	6
	Absent	94	94
Congestive heart failure	Present	17	17
	Absent	83	83
Chronic kidney disease	Present	7	7
	Absent	93	93
Chronic liver diseases	Present	2	2
	Absent	98	98
Chest X-ray	Consolidation	71	71
	Consolidation & infiltrates	4	4
	Consolidation & pleural effusion	1	1
	Infiltrates	21	21
	Infiltrates & pleural effusion	1	1
	Pleural effusion	2	2

91.0  $\mu$ g/dl whereas that having more than 1 week was 89.1  $\mu$ g/dl (Tables 7 and 8). There was no significant association between the serum zinc levels and underlying comorbidities in patients of community acquired pneumonias, although they are independent risk factors for the CAP.

## Discussion

The present study was conducted to assess the possible application of serum zinc levels as an ancillary tool in the diagnosis and assessment of severity of community acquired pneumonia. The serum zinc levels were measured from community acquired pneumonia patients. The sample was drawn as soon as the diagnosis was suspected and only those cases were included in whom diagnosis was confirmed by radiology or cultures.

The measured mean serum zinc level in patients of community acquired pneumonia was 73.3  $\pm$  10.83  $\mu$ g/dl, whereas that of controls was 98.4  $\pm$  12.89  $\mu$ g/dl. This variation is statistically highly significant.

Only one study has been done in adults who compared serum zinc levels in pneumonia patients. Devrajani [19] found that mean serum zinc level was 8.279  $\pm$  2.77 mmol/L (54.11  $\pm$  18.1  $\mu$ g/dl), while it was higher in our patients. Hypozincemia was defined as serum zinc levels of less than 11  $\mu$ mol/L (72  $\mu$ g/dl). They however interpreted the measured serum zinc levels without showing any correction with serum protein levels. 39% of our patients also had measured serum zinc levels  $\leq$  70  $\mu$ g/dl and 78% of our patients has measured serum zinc levels < 80  $\mu$ g/dl. However the corrected serum zinc levels were greater as most of our patients had hypoproteinemia. Meydani [18] also found that individuals with low serum zinc levels also had low serum albumin concentration.

**Table 4** Comparison of uncorrected zinc levels ( $\mu\text{d}/\text{dl}$ ) in cases and controls.

Age group (years)	Cases			Controls			<i>p</i> -Value	Remarks
	No.	Mean	SD	No.	Mean	SD		
< 40	6	80	7.38	6	107.2	13.51	0.002	Sig.
40–65	58	74.7	11.60	67	98.9	12.62	< 0.001	Highly Sig.
> 65	36	70.3	9.21	27	95.2	12.83	< 0.001	Highly Sig.

**Table 5** Corrected serum zinc levels ( $\mu\text{g}/\text{dl}$ ).

Group	No.	Mean	SD	<i>p</i> -Value	Remarks
Case	100	89.90	13.64	< 0.001	Highly Sig.
Control	100	105.65	13.89		

So all our results were interpreted after correcting the zinc values with their respective protein levels.

The calculated mean serum zinc level in patients of community acquired pneumonia was  $89.90 \pm 13.64$  mcg/dl, whereas that of controls was  $105.65 \pm 13.89$  mcg/dl. This variation is statistically highly significant. It established that serum zinc levels show a definite fall in pneumonia.

The patients belonged to all the age groups ranging from 15 to 95 years. Majority of the patients were in the age group of 40–65 years (58%). 36% of patients were above 65 years of age. Only 6% of patients were below 40 years of age.

On the other hand the control group cases were in the range of 15–83 years with 67% in the age group of 40–65 years, 6% below 40 years and rest above 65 years.

The age variation between cases and controls is statistically insignificant. The calculated or corrected mean serum zinc level in patients of community acquired pneumonia aged less than 40 years is  $96.38 \pm 15.75$   $\mu\text{g}/\text{dl}$  and that of 40–65 years is  $90.98 \pm 14.35$   $\mu\text{g}/\text{dl}$ . As the age group increased the mean serum zinc levels decreased. The mean serum zinc level of patients aged more than 65 years is  $87.04 \pm 11.74$   $\mu\text{g}/\text{dl}$ , although it was not statistically significant. Similarly the corrected zinc level in controls of age group less than 40 years is  $118.96 \pm 6.63$   $\mu\text{g}/\text{dl}$  while that of 40–65 years of age is  $105.05 \pm 13.91$   $\mu\text{g}/\text{dl}$ . Controls again showed the same trend of decreasing serum zinc levels with increasing age. The zinc level in the age group of more than 65 years is  $104 \pm 13.82$   $\mu\text{g}/\text{dl}$ . This comparison showed that values of serum zinc level in controls in the age group of less than 40 years in relation to the rest of the 2 groups is statistically significant. But comparison between 40 and 65 years age group versus more than 65 years was not statistically significant. While com-

**Table 7** Corrected zinc levels ( $\mu\text{g}/\text{dl}$ ) on the basis of CURB-65 score.

CURB-65 score	No.	Mean	SD	Min	Max	<i>p</i> -Value	Remarks
1	24	98.3	13.74	66.2	127.1	0.001	Sig.
2	42	90.0	13.29	54.1	120.7		
3	23	85.2	10.47	72.8	112.8		
4	11	81.0	11.59	62.0	106.7		

**Table 8** Comparing corrected zinc levels ( $\mu\text{g}/\text{dl}$ ) depending on hospital stay (in days).

Hospital stay	No.	Mean	SD	<i>p</i> -Value	Remarks
< 8	44	91.0	13.15	0.491	Not Sig.
$\geq 8$	56	89.1	14.07		

paring the serum zinc levels in patients (mean  $96.38 \pm 15.75$   $\mu\text{g}/\text{dl}$ ) in the age group of less than 40 years with corresponding controls ( $118.96 \pm 6.63$   $\mu\text{g}/\text{dl}$ ) the results were statistically significant ( $p = 0.009$ ). Similarly comparing the mean zinc values in the age group of 40–65 years, between cases ( $90.98 \pm 14.35$   $\mu\text{g}/\text{dl}$ ) and control ( $105.05 \pm 13.91$   $\mu\text{g}/\text{dl}$ ), the variation is statistically highly significant ( $p < 0.001$ ).

The patients aged more than 65 years also showed a variation, when compared to age matched controls, that was highly significant. Their mean serum zinc levels were  $98.3 \pm 13.74$   $\mu\text{g}/\text{dl}$  (range 66.2–127.1). 42% patients had CURB-65 score of 2 with serum zinc levels of  $90.0 \pm 13.29$   $\mu\text{g}/\text{dl}$  (range 54.1–120.7). Patients with CURB score-65 of 3 (23%) had a mean serum zinc level of  $85.2 \pm 10.47$   $\mu\text{g}/\text{dl}$  (range 72.8–112.8) while those with score of 4 had zinc concentration of  $81 \pm 11.59$   $\mu\text{g}/\text{dl}$  (62–106.7). The results were statistically significant ( $p$  value = 0.001). Devrajani also found that the severity of hypozincemia was correlated with CURB-65 score.

**Table 6** Comparison of corrected zinc levels ( $\mu\text{d}/\text{dl}$ ) in cases and controls on the basis of age (years).

Age group	Cases			Controls			<i>p</i> -Value	Remarks
	No.	Mean	SD	No.	Mean	SD		
< 40	6	96.38	15.75	6	118.96	6.63	0.009	Sig.
40–65	58	90.98	14.35	67	105.05	13.91	< 0.001	Highly Sig.
> 65	36	87.04	11.74	27	104.18	13.82	< 0.001	Highly Sig.

The higher the CURB-65 score, the lower the serum zinc levels. Our study also showed that the serum zinc levels decreased as the CURB-65 score of patients increased, although our corrected zinc values were higher as most of our patients had low serum proteins due to the presence of multiple comorbidities.

In the patient group, males had slightly higher zinc values as compared to females ( $90.0 \pm 16.41 \mu\text{g/dl}$  versus  $89.7 \pm 9.79 \mu\text{g/dl}$ ) which was not statistically significant. In the control group males had a mean serum zinc level of  $108.4 \pm 14.22 \mu\text{g/dl}$  while females had  $102.5 \pm 12.96 \mu\text{g/dl}$  which was statistically significant. Devrajani also found that males had higher serum zinc levels as compared to females although that was statistically insignificant. The overall mean of serum zinc in male and female population was  $9.472 \pm 3.63 \text{ mmol/l}$  ( $61.89 \mu\text{g/dl}$ ) and  $8.130 \pm 2.94 \text{ mmol/l}$  ( $53.1 \mu\text{g/dl}$ ) respectively ( $p < 0.03$ ). Although, multiple studies have been done in children showing decreased serum zinc levels in pneumonia patients as compared to age matched controls. Also various studies have shown that the introduction of zinc in the management of pneumonia patients in children decreased duration of severe pneumonia and hospital stay as well as mortality. But further studies are needed to be done whether true hypozincemia also occurs in adult pneumonia patients and whether the introduction of zinc in pneumonia patients will also reduce the hospital stay, duration of severe illness as well as mortality. There was no significant relation between zinc levels and associated co-morbidities.

### Summary

Our study revealed a definite relation of low serum levels of zinc with community acquired pneumonia and there is a definite decrease in serum zinc levels as the age increases. There was no definite relation between the zinc levels, smoking and other comorbidities, although they are independent risk factors for developing pneumonia. The level of low serum levels is associated with severity of pneumonia and associated morbidity and mortality.

Considering the morbidity, mortality, hospital stay and financial burden thereof in pneumonia patients especially in developing countries like ours, serum zinc levels should be routinely measured and thereby supplemented. Although till now studies have been predominantly performed in children which recommended prophylactic and therapeutic administration of zinc in children to reduce morbidity, mortality and to lessen antibiotic use, same needs to be studied in adults also in large studies.

### Conflict of interest

None.

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