

Original Research Article

Serum zinc level: a prognostic marker for severe pneumonia in children

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ABSTRACT

Background: Pneumonia is one of the leading causes of under 5 mortality among children in developing countries. Zinc deficiency is postulated as cause of severe pneumonia, but evidences shows conflicting results on whether serum zinc levels predicts the severity of pneumonia. So prospective study was undertaken to study the relationship between serum zinc levels and severity of pneumonia in children with community acquired pneumonia.

Methods: Fifty cases of pneumonia (group 1) and 50 cases of severe pneumonia (group 2) according to WHO classification were enrolled into the study. Demography, anthropometry and immunization status were recorded. A single zinc measurement was performed for all the patients within 24 hours of admission. The severity, clinical course including recovery to discharge was compared between two groups with respect to their serum zinc levels.

Results: Mean ($\pm$ SD) age group of the study population was 22 months $\pm$ 16.05 and 21.88 months $\pm$ 15.97 months in boys and girls respectively. Pneumonia was high in girls (59%) and children between 2 to <12 months had higher (36%) infection rate. Mean zinc level in pneumonia and severe pneumonia group were 68.69 μ g/dl $\pm$ 28.77 and 68.08 μ g/dl $\pm$ 27.55 respectively. There was no difference in the nutritional status (weight for height and height for age) of the study group. Serum Zn level was low in 56 % and 52% of pneumonia and severe pneumonia group respectively. Comparison of serum zinc levels between the ARTI groups did not achieve statistical significance ($p=0.430$). However, the duration of recovery is earlier than 1 week in pneumonia cases when compared to severe pneumonia patients ($p<0.001$, OR 1.375).

Conclusions: Normal zinc levels was associated with early recovery in simple pneumonia patient, so study of serum zinc levels in severe pneumonia patients has prognostic value.

Keywords: Children, Pneumonia, Zinc

INTRODUCTION

Acute respiratory tract infection (ARTI) is the leading cause of under-five mortality in children.¹ Zinc affects multiple aspects of the immune system, from the barrier of the skin to gene regulation within lymphocytes. Macrophage function is adversely affected by zinc deficiency. Zinc plays an important role in development of acquired immunity, production of immunoglobulin G, intracellular killing, cytokine production and

phagocytosis, thereby regulating defense mechanism in children with acute infection.² Role of zinc in diarrhea and pneumonia are well documented by studies. Prophylactic zinc therapy reduces the infection rate in children with pneumonia.³ Studies show that zinc supplementation reduces the incidence of acute lower respiratory tract infection by 45%.⁴⁻⁶ Prevalence of zinc deficiency is high in developing countries and in India ranges from 44% to 72%.⁷ Since regular supplementation and fortification of foods with zinc is not practiced in

developing countries, placing our children at risk of infection with pneumonia.

Still there is an existing debate and lack of data regarding effect of low zinc levels in pneumonia, so this study was undertaken to find association between zinc level and severity of pneumonia in children.

METHODS

The study was conducted in a tertiary care hospital from October 2016 to December 2017 after approval from the institute ethics committee.

Inclusion criteria

- After obtaining parental consent, children of age >2 months to 59 months clinically diagnosed as pneumonia according to WHO revised guidelines were included in the study.⁸

Exclusion criteria

- Children with acute diarrhoea, chronic medication, severe acute malnutrition, on zinc supplementation were excluded from the study.
- Severe pneumonia children requiring invasive ventilation were excluded from the study so as to remove the confounding factor affecting the time to discharge.

They were divided into two groups namely pneumonia (50 cases) and severe pneumonia (50 cases). Data regarding age, sex, anthropometry (height, weight, weight for age, height for age, and weight for height) and immunization status was recorded. All children were clinically examined by the treating physician and treatment ordered by them was abstracted. These children were confirmed radiologically with chest radiograph, the gold standard test for diagnosis of pneumonia. Complete diagnostic work up such as complete blood count, C-reactive protein, renal function test and blood culture was done. Other investigations were performed on individualized case basis. Severe pneumonia cases with respiratory insufficiency were admitted to PICU. In all children serum zinc level was measured in 2ml of venous blood sample taken at the time of admission or within 24 hours of admission after obtaining consent from parents. Serum zinc level was measured by spectrophotometry using calorimetric method (Quanticore™ Zinc assay kit- Bioassay systems, USA). Serum zinc level <65µg/dl was considered low in children.⁹ All children were treated according to existing institute protocol. In all cases record of the treatment given and outcome of the disease was also maintained.

Statistical analysis

Data were analysed using SPSS Version 21 (IBM Corp). Descriptive data were presented using Percentages or by

using mean and standard deviation as the case may be. Chi square test was used to test the association of severity of pneumonia with factors like zinc level, anthropometric indicators, etc. Binary logistic regression was used to calculate the causal association (Odds ratio) of various factors with severity of pneumonia. P value of <0.05 was considered as significant association.

RESULTS

Mean (±SD) age group of the study population was 22 months±16.05 and 21.88 months±15.97 months in boys and girls respectively (Table 1).

Table 1: Mean distribution of age group (in months) according to gender.

Gender	Age group	
	Mean	SD
Boys	22	16.05
Girls	21.88	15.97

Mean zinc level in pneumonia and severe pneumonia group were 68.69µg/dl±28.77 and 68.08µg/dl±27.55 respectively (Table 2).

Table 2: Gender and severity of pneumonia wise distribution of mean serum zinc levels.

Category	Serum zinc level	
	Mean	SD
Gender		
Boys	67.77	27.51
Girls	68.69	28.77
Severity of pneumonia		
Pneumonia	68.69	28.77
Severe pneumonia	68.08	27.55

A total of 100 cases (50 cases of pneumonia and 50 cases of severe pneumonia) were taken into study, among them 41 male and 59 female children had acute respiratory tract infection. Children between ages 2 months to <12 months had higher percentage (36%) of infection as shown in Table 3.

Table 3: Age and sex wise distribution of children with pneumonia.

Age group	Male n (%)	Female n (%)	Total
2 months to <12 months	16 (44.4)	20 (55.6)	36
12 months to <24 months	8 (33.3)	16 (66.7)	24
24 months to <36 months	5 (27.7)	13 (72.3)	18
36 months to <48 months	5 (55.5)	4 (44.5)	9
48 months to <60 months	7 (53.8)	6 (46.2)	13
Total n (%)	41	59	100

Moderate acute malnutrition (weight for height between $<-2SD$ to $>-3SD$) was seen in 44% of pneumonia and 40% of severe pneumonia group respectively. Moderate stunting was seen in 6% and 28% of pneumonia and severe pneumonia group respectively. Stunting ($P=0.965$) and wasting ($P=0.064$) was not statistically significant between the 2 groups as shown in Table 4.

Table 4: Nutritional status of pneumonia cases.

Nutritional status	Pneumonia severity		p value
	Pneumonia n (%)	Severe pneumonia n (%)	
Weight for height			
Normal	28 (56)	30 (60)	0.064
<-2SD to >-3SD	22 (44)	20 (40)	
Height for age			
Normal	47 (94)	36 (72)	0.965
<-2SD to >-3SD	3 (6)	14 (28)	

Children with $<-3SD$ are not taken into study in view of severe acute malnutrition/severe stunting.

Serum zinc levels were low in 52% of pneumonia cases which is equally comparable to the severe pneumonia group, where 56% had low Zn levels. Comparison of serum zinc level between the groups was not significant ($p=0.430$) as shown in Table 5.

Table 5: Comparison of serum zinc levels in children with pneumonia vs severe pneumonia.

Zinc level	Pneumonia severity		p value
	Pneumonia n (%)	Severe pneumonia n (%)	
Low	26 (52)	28(56)	0.430
Normal	24 (48)	22(44)	

Nearly majority (96%) pneumonia group recovered within 1 week and recovery was prolonged >1 week in 60% of severe pneumonia group. Comparison of zinc levels with recovery/ discharge showed that severe pneumonia group had prolonged stay (>1 week) in hospital and it was statistically significant ($p<0.001$, OR 1.375).

Table 6: Comparison of zinc level vs recovery in children with pneumonia severity.

Pneumonia severity	Zinc level		Recovery		OR	p value
	Normal n (%)	Low n (%)	<1 -week n (%)	>1 -week n (%)		
Pneumonia	24 (48)	26 (52)	48 (96)	2 (4)	0.090	0.410
Severe pneumonia	22 (44)	28(56)	20 (40)	30(60)	1.375	<0.001

However, serum zinc levels did not affect the recovery or time to discharge in pneumonia group as shown Table 6.

DISCUSSION

Zinc is an important trace element necessary for growth, wound healing, oxidative stress response and immunological function. Zinc deficiency results in altered cytokine secretions due to loss of T and B cell maturation.² Present study was conducted to find the correlation between severity of pneumonia and zinc levels. At baseline serum Zn levels were low in 56% of the ARTI cases which shows declining trend in the prevalence of deficiency as compared to study done by Dhingra et al in preschool children where zinc deficiency was high as 73.3%.¹⁰

Majority of the ARTI cases (36%) were less than 12 months of age which is similar to study by kumar et al.¹¹ However pneumonia was high (59%) in girls in present study in contrast to finding recorded by other studies.¹²⁻¹⁴ Difference in the serum zinc levels was not statistically significant in both pneumonia and severe pneumonia group in present study because of the relatively well nourished children were taken into study, which is similar

to study done by Pedraza et al found no significant association between zinc deficiency and anthropometric indices.¹⁵

In present study there is no substantial association between gender, anthropometry, and severity of pneumonia with regards to low zinc levels. A cross sectional study done by Arica et al showed children between age group 0- 24 months were susceptible to pneumonia when serum zinc level was low, which is contrast to present study where both groups zinc deficiency was equally distributed, and they were not significant statistically between the groups.¹⁶ This shows nutritional status was relatively well between both the groups in present study.

Although in developing countries there will be substantial prevalence of zinc deficiency, present study children were not preselected on the basis of nutrition status. Recovery rate was prolonged in severe pneumonia cases for >1 week, this could be due to reduction in pre-B and pre-T cells leading to reduced lymphocytes due to zinc deficiency and also due to critically ill nature of disease which could have resulted in prolonged ventilation,

oxygen requirement and time taken to recover from inflammatory cascade.

There was no positive co-relation between low zinc levels and recovery/discharge rate in pneumonia group which is similar to study done by Shakur et al showed negative correlation between severity of pneumonia and low zinc levels.¹⁷

Study done by Mahanlabis et al showed that recovery rates from very ill status and from fever in zinc-treated boys were 2.6 times ($P=0.004$) and 3 times ($P=0.003$) than those in non-zinc-treated children with pneumonia.¹⁸ Zinc supplementation resulted in a lower incidence of pneumonia than placebo (absolute risk reduction 2.5%, 95% confidence interval 0.4% to 4.6%) in a study done by Bhandari et al.¹⁹

Small sample size, clinical improvement before and after zinc supplement during acute phase, exclusion of severe pneumonia cases in ventilators are the limitations of present study.

CONCLUSION

Mean duration of hospital stay was prolonged in severe pneumonia cases with low zinc levels, thus serum low zinc levels prolong recovery rate which can be used as a prognostic marker in children with pneumonia.

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