



Original Research Article

Correlation between serum Zinc and C-reactive protein (CRP) levels severity of clinical presentation in children with Acute Lower Respiratory Tract Infections (ALRI)

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ABSTRACT

Introduction: Acute lower respiratory infections (ALRI) is a substantial cause of mortality and morbidity in children less than 5 years of age. ALRI is one of the major reasons for which children are brought to the hospitals and seek health facilities. Pneumonia was responsible for about 18% of all under 5 year death in India. Zinc (Zn) is a trace element with demonstrable effect on immune mediated production of interferon. Low zinc levels not only impairs the immunity but it also enhances the infection along with a reduction in the clearance of infectious agents. Hence present study was undertaken with intention to assess the serum zinc levels in children suffering from pneumonia.

Material and Methods: Study protocol was approved by the Institutional Ethics Committee (IEC) of the college and written informed consent was taken from all children parents/guardians before conducting the study. Study comprises sixty children with clinically diagnosed pneumonia (according to WHO criteria) and sixty were healthy controls of the age group between six months to five years. Under aseptic precaution 2mL of venous blood was drawn and used for estimation of zinc by NITRO-PAPS method and CRP by immunoturbidimetric method.

Results: There was significant decrease ($p < 0.05$) in serum zinc levels and significant increase in CRP levels in pneumonia children compared to healthy children. Serum zinc levels goes on decreases with severity of the disease hence it was negative correlation.

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1. Introduction

Acute lower respiratory infections (ALRI) predominantly pneumonia is a substantial cause of mortality and morbidity in children less than 5 years of age.¹ ALRI is one of the major reasons for which children are brought to the hospitals and seek health facilities. According to the statistics 26.3 million cases of ALRI were reported which gives an incidence rate of about 2,179 cases per lakh population in India. Pneumonia cases were about 59 cases per lakh population. Pneumonia was responsible for about 18% of

all under 5 year death in India.² Well designed randomized controlled trials experience lower mortality and morbidity due to infectious diseases among zinc supplements in young children has highlighted zinc deficiency as public health problem.

Zinc is a micronutrient with direct anti-viral activity and demonstrable effect on immune mediated production of interferon. It also prevents pathogens from gaining entry into cells and hinders their intra cellular multiplication.³ There are more than three hundred zinc dependent enzymes. It has an antioxidant property. Trace mineral deficiencies have long been implicated in causation of many diseases.

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Zinc deficiency is common in children from developing countries due to high incidence of malnutrition, lack of intake of animal food, high dietary phytate contents and in adequate food intake with increased fecal loss during diarrhea. About 30% of the world's population is zinc deficient, most prevalent in children.⁴ Zinc deficiency is associated with impaired immune function which results in an increase in morbidity due to infections, growth retardation, hypogonadism and cognitive dysfunction.⁵ Zinc deficiency decreases the ability of the body to respond to infection and also adversely affects both cell mediated and humoral immune responses. Low zinc levels not only impairs the immunity but it also enhances the infection along with reduction in the clearance of infectious agents. Various studies reveal that zinc deficient population are at increased risk of developing diarrheal diseases, respiratory infections and growth retardation. Among the individual interventions zinc supplementation with universal coverage ranks fifth in preventing under five mortality in India.

Role of zinc supplementation in diarrhea is now well established and there are specific guidelines and recommendations whereas role of zinc in acute respiratory infections is controversial.

C-reactive protein (CRP) is gold standard marker of inflammation. It is a member of the pentraxin family of proteins. It is an acute phase reactant protein synthesized by the liver. These levels are elevated in response to acute infections and inflammatory conditions. Serum CRP levels raise rapidly with a concomitant elevation of erythrocyte sedimentation rates (ESR).⁶ CRP levels are stable as these do not exhibit diurnal variations or the food intake.

Hence present study was undertaken with intention to assess the serum zinc and CRP levels in children suffering from ALRI and to evaluate the association between serum zinc and CRP levels to its severity of clinical presentation.

2. Materials and Methods

Study protocol was approved by the Institutional Ethics Committee (IEC) of the college. Written Informed consent was taken from all children parents/guardians before conducting the study.

2.1. Study design

This is an observational case control study, which was conducted in the department of Biochemistry along with pediatric department at S.Nijalingappa Medical College and Hanagal Sri Kumareshwara Hospital and Research centre, Bagalkot, Karnataka, a tertiary care teaching hospital. Study was conducted from January to August 2016. Sample size was calculated using open Epi software version 2.3.1 taking 95% confidence level and absolute precision 10%.

2.2. Inclusion criteria

Sixty children newly diagnosed and admitted in the pediatric ward/ PICU with acute lower respiratory tract infection of the age group between 6 months to 5 years were included in the study. Cases were further grouped into four categories depending on the severity of the clinical presentation as per WHO criteria of severe pneumonia.⁷ Grade-I presents with only tachypnea, grade-II with tachypnea and chest retraction, grade-III with tachypnea, chest retraction and grunting and the grade-IV presented with tachypnea, chest retraction, grunting and cyanosis. A detailed history was taken, anthropometric and physical examination was done according to the predesigned proforma. Sixty healthy children between the age group of 6 months to 5 years who are normal siblings admitted children and children admitted for nonrespiratory complaints were selected as controls.

2.3. Exclusion criteria

Children with chronic diarrhea, bronchial asthma, congenital heart disease, anomalies which cause recurrent chest infections, malnourished children and patients on zinc supplementation were excluded from the present study.

2.4. Sample collection

Under aseptic precaution 2 mL of venous blood was drawn from prominent visible veins and collected in a vacutainer. Blood was allowed to clot and serum was separated after centrifugation and used for analysis of biochemical parameters like zinc and CRP. Zinc was estimated by NITRO-PAPS method⁸ using commercially available kit by end point method and CRP by immunoturbidimetric method⁹ using Biosystem kit in semi autoanalyser Erba Chem-5 plus.

2.5. Statistical analysis

Statistical analysis was done using statistical package social system (SPSS) version 13. Results are expressed in terms of mean \pm SD, proportions and percentages. Student 't' test and to see the association person correlation test was applied. $p < 0.05$ was considered as statistical significance.

3. Results

The present study comprises of 120 children in the age group of 6 to 60 months with 60 cases and 60 healthy controls. There were 37 male children and 23 female children with acute respiratory tract disease were recruited in the study. In controls there were 35 male and 25 female participants.

1 depicts the age distribution of cases and controls. Fifty percent of the children are in the age group of 12 to 24 months.

Table 1: Age distribution of cases and controls

Age in months	Case	Control
6 - 12	18(30%)	20(33.33%)
13 – 24	32(53.33%)	30(50%)
25 – 60	10(16.66%)	10(16.66%)
Total	60(100%)	60(100%)

Table 2: Mean values of serum zinc and CRP levels in cases and controls

Parameters	Cases	Controls	p - value
Male: Female	37:23	35:25	-
Serum Zinc ($\mu\text{g/dL}$)	57.09 ± 19.36	83.65 ± 21.6	0.001
Serum CRP (mg/L)	11.62 ± 3.47	2.35 ± 1.44	0.001

Table 3: Serum zinc and CRP levels among children with different grades of respiratory distress

Parameters	Grade-I	Grade-II	Grade-III	Grade-IV	p-value
Male: Female	16:10	14:9	4:3	3:1	-
Serum Zinc ($\mu\text{g/dL}$)	59.97 ± 18.61	62.08 ± 23.43	48.3 ± 12.54	42.05 ± 15.63	-0.001
CRP (mg/L)	6.8 ± 2.75	7.92 ± 3.63	10.65 ± 4.58	12.8 ± 4.07	0.001

Mean levels of serum zinc and CRP are shown in the Table 2. In our study male children were affected more compared to female children. There was significant decrease ($p < 0.01$) in the serum zinc levels and significant increase ($p < 0.01$) in the serum CRP levels in cases compared to controls.

3 shows the mean serum zinc and CRP levels in children with different grades of respiratory distress. Zinc levels goes on decreases as the severity of the respiratory distress increases. Hence there was negative correlation between serum zinc levels and grades of respiratory distress. At the same time CRP levels increased proportionately with the severity of the disease hence there was positive correlation.

4. Discussion

In India nutritional disorders are more common, among them vitamin-A, iron, iodine, vitamin-D and zinc deficiency.

In our study more than 80% of the pneumonia affected children are infants and toddlers of less than two years. It indicates that infants and toddlers are vulnerable age group for childhood pneumonia and susceptible for frequent multiple viral infections.¹⁰ In present study there was male predominance which is in consistent with other studies.^{11,12} It reflects the societal importance to male child and parents give more prompt attention and hence higher hospital admission.¹³

In our study there was significant decrease in the serum zinc levels in cases compared to controls. This was similar to results found by many other authors.^{11,14–16} Zinc deficiency is more common in children in developing countries because of decreased food intake, limited bioavailability from regional i.e local diet, decreased absorption because of increased phytates has many are

vegetarians and loss of zinc during recurrent diarrheal diseases.¹⁷ To some extent these could be the reasons for low serum zinc levels in our study too. Existing low zinc levels increases the susceptibility of the child to get pneumonia by impairing the children immunity.¹⁸

According to Rady HI¹⁴ lower zinc levels were associated with more advanced respiratory support. Death was more prevalent among patients with low serum zinc level. According to Reddy LN,¹⁹ malnutrition was significantly associated with ALRI. A western study reveals that highest risk of death from ALRI due to malnutrition among those aged between 12 to 22 months.

In the present study we classified the pneumonia children into four groups depending on their symptoms according to WHO classification. It shows that serum zeinc levels goes on decreases with severity of the disease hence it was negative correlation. Our results are in accordance with few other studies.^{14,20}

Many trials have been conducted and that interpreted adjuvant treatment with 20 mg zinc per day accelerates recovery from severe pneumonia in children and could reduce antimicrobial resistance by decreasing multiple antibiotic exposure thus intern lessen complications and death.²¹

5. Conclusion

Pneumonia is more prevalent in developing countries like India among the preschool children. Zinc plays important role in immunity development and inturn helps in reduction of infections. Since the serum zinc levels are direct correlation with severity of pneumonia. There is an opportunity to supplement the zinc as a part of their routine treatment which inturn can improve the immunity thus

expected to reduce the morbidity and mortality.

5.1. Limitation of the study

Small sample size, socio-economic status of the family and dietary intake of the child was not taken into consideration.

6. Source of funding

None.

7. Conflict of interest

None.

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