



SERUM ZINC LEVELS IN CHILDREN WITH ACUTE LOWER RESPIRATORY INFECTIONS

Paediatrics

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ABSTRACT

Introduction Acute Lower Respiratory Tract Infection (ALRTI) is an important cause of morbidity and mortality in the developing world. Deficiency of micronutrients such as zinc may increase the risk of ALRTI. The aim of this study was to estimate serum zinc levels in children of under-5 year's of age admitted with acute lower respiratory tract infection and to compare with healthy controls. **Methods** A case control Study was carried out in the Department of Pediatrics of National Institute of Medical Sciences & Research, Jaipur. 70 children with Acute Lower Respiratory Tract Infections, and another 70 served as controls. Blood samples were collected for zinc estimation in both case and control groups. **Results** Of the 70 cases, Demographic data was comparable amongst gender groups. Baseline clinical characteristics of cases and control group were comparable. Amongst the cases, 54 were diagnosed as bronchiolitis and 16 as bronchopneumonia. The mean ($\pm$ SD) zinc levels among the cases was $90.8 \pm 59 \mu\text{g/dl}$ and in the control group, it was $98.78 \pm 66.26 \mu\text{g/dl}$ which was statistically non-significant ($p = 0.4526$). Zinc deficiency was observed to be significantly associated with the severity of bronchiolitis ($p=0.00001$) and bronchopneumonia ($p=0.011$) and prolonged hospital stay ($p=0.017$) as a consequence. **Conclusion** The results of our study revealed that there was no significant difference in the zinc level between children having Acute Lower Respiratory Tract Infection and controls. Zinc deficiency was significantly associated with severity of pneumonia (bronchiolitis and bronchopneumonia). However to further validate we need to have good quality studies with larger sample size and proper follow-up.

KEYWORDS

Zinc, Children, Pneumonia

INTRODUCTION

Pneumonia, acute bronchitis, and bronchiolitis are typically included in the definition of Acute Lower Respiratory Illnesses. In underdeveloped nations, Acute Lower Respiratory Infections are frequent cause of morbidity and mortality in children under the age of five¹.

Febrile children can be diagnosed with Acute Lower Respiratory Tract Infection (ALRTI) based on their respiratory rate and respiratory distress. Lower chest wall indrawing indicates severe illness. Bronchiolitis and Pneumonia are the most frequent causes of ALRTI in young children². Viral or bacterial infection are the most frequent cause of the ALRTI in children³. RSV and Parainfluenza viruses are frequent sources of viral bronchiolitis⁴. Common causes of bacterial pneumonia are Streptococcus pneumonia (pneumococcus), haemophilus influenzae (mostly type b, hib), Staphylococcus Aureus, and Group A Streptococci. Atypical pneumonias are caused by Chlamydia pneumonia and Mycoplasma pneumonia⁵.

Lower respiratory tract infections occur 0.25–0.5 episodes per child per year⁶. Pneumonia killed 7,40,180 children worldwide in 2019—14% of all pediatric deaths as per WHO.

Malnutrition is important risk factors for contracting illnesses like ALRTI. A shortage of zinc has been linked in certain studies to Acute Lower Respiratory Tract Infections, and zinc supplementation was found to reduce the frequency of Acute Lower Respiratory Tract Infections⁷.

Important micronutrients like zinc are needed for healthy skeletal development, intestinal mucosal integrity, and immune system performance, especially cellular immunity and antioxidant activity.

Research from all around the world has unequivocally demonstrated the role of zinc in treating childhood diarrhea and reducing its severity and susceptibility; however, studies on the relationship between zinc and reducing risk of Acute Lower Respiratory Tract Infections (ALRTI) have produced mixed findings. Furthermore, there is a lack of research on the relationship between zinc and the clinical course of ALRTI⁸. In view of the above facts, this study was planned to estimate

the zinc levels in children suffering from Acute Lower Respiratory Tract Infections and to compare them with normal healthy children.

MATERIALS AND METHOD

A case control study was carried out among children < 5 years of age admitted with a diagnosis of ALRTI in Department of Paediatrics, NIMS Hospital, Jaipur after obtaining clearance from the Institutional Ethics Committee. We included 70 cases of acute lower respiratory tract infections and 70 children who were matched for age, sex, and nutritional status served as controls.

The inclusion criteria were Children less than 5 years of age admitted in the Department of Paediatrics, Nims Hospital, Jaipur with a diagnosis of Acute Lower Respiratory Tract Infection. Children with a clinical diagnosis of chronic lung diseases, cardiac diseases, acute and chronic diarrhoea, malabsorption syndromes, history of zinc intake in the previous one month, and children of parents who did not consent for participation were excluded.

Methodology

70 children with diagnosis of ALRTI were enrolled in the study. The details of study procedure were explained and an informed consent of all screened cases was obtained from the parents/ guardian. 2 ml of venous blood was taken by the standard venipuncture technique from the all patients and controls and under aseptic conditions. Samples were analyzed for serum zinc level estimation.

CT-180 fully automated hematology analyzer was used to estimate serum zinc levels by using colorimetric, endpoint, increasing reaction. Zinc forms a red chelate complex with 2-(5-bromo-2- pyridylazo)-5- (n-propyl-n-sulfopropylamino)-phenol. The increase in absorbance of this complex is proportional to the concentration of total zinc in the sample. The results of the serum zinc levels were then entered in the master chart and was subjected for statistical analysis.

Statistical Analysis

The data was collected and entered in MS excel. Different statistical analysis were performed using SPSS software version 22. The one sample Kolmogorov Smirnov test was employed to determine whether the data sets differed from a normal distribution or not. Normally

distributed data was analyzed using parametric tests and non-normally distributed data was analysed using non parametric tests.

RESULTS

The majority of children were in the age group of ≤ 1 year in both cases and controls. (Table 1)

Table 1: Frequency distribution of age in both groups

Age interval	Control group		Case group	
	N = 70	In %	N = 70	In %
≤ 1 yr.	37	52.86%	51	72.86%
1 - 3 yr.	15	21.43%	12	17.14%
3 - 5 yr.	18	25.71%	7	10.00%

In our study, out of 70 cases there were 51 (72.86%) males and 19 (27.14%) females out of 70 controls there were 51 (72.86%) males and 19 (27.14%) females. (Table 2)

Table 2: Frequency distribution of gender in both groups

Gender	Control group		Case group	
	N = 70	In %	N = 70	In %
Male	51	72.86%	51	72.86%
Female	19	27.14%	19	27.14%

On the basis of diagnosis, the cases were categorized in the following two categories i.e. Children with bronchiolitis and Children with bronchopneumonia. 54 (77.14%) patients were diagnosed with bronchiolitis and 16 (22.86%) patients with bronchopneumonia. The mean serum zinc in bronchiolitis was 93.45 ± 56.41 $\mu\text{g/dl}$ and the mean serum zinc in bronchopneumonia was 81.81 ± 68.3 $\mu\text{g/dl}$. The difference in the zinc levels between the two groups was found to be statistically non significant with p value of 0.5362. (Table 3)

Table 3: Frequency distribution of diagnosis and serum zinc level in the case group

Diagnosis	N = 70	In %	Serum zinc level	P - value	Significance
Bronchiolitis	54	77.14%	93.45 ± 56.41	0.5362	Non significant
Bronchopneumonia	16	22.86%	81.81 ± 68.3		

On comparing the mean value of serum zinc between the case and control groups by using t-test the difference in the zinc levels between cases and controls was found to be non significant with p value of 0.4526. (Table 4)

Table 4: Comparing the mean of serum zinc level between the control & case groups by using a t-test

Variable	Control group	Case group	T-test	P - value	Significance
Serum zinc level ($\mu\text{g/dl}$)	98.78 ± 66.26	90.8 ± 59	0.753	0.4526	Non significant

We compared the association of the severity of disease according to diagnosis and serum zinc level by using the chi-square test which was found to be statistically significant with a p value of 0.00001 in bronchiolitis patients and p value of 0.01174 in bronchopneumonia patients. (Table 5)

Table 5: Association of severity of disease according to diagnosis and serum zinc level by using chi-square test

Category		≤ 65 ($\mu\text{g/dl}$)	>65 ($\mu\text{g/dl}$)	Chi-square test	P - value	Significance
Bronchiolitis	Mild	1	27	28.96	0.00001	Significant
	Moderate	12	6			
	Severe	7	1			
Bronchopneumonia	No pneumonia	0	6	6.349	0.01174	Significant
	Severe pneumonia	1	0			
	Very severe pneumonia	7	2			

The association of hospital stay with zinc deficiency was found to be statistically significant with p value of 0.01712. (Table 6)

Table 6: Association of hospital stay and serum zinc level by using chi-square test

Category	≤ 65 ($\mu\text{g/dl}$)	>65 ($\mu\text{g/dl}$)	Chi-square test	P - value	Significance
< 7 days	9	4	5.684	0.01712	Significant
> 7 days	19	38			

DISCUSSION

It is well established in literature that zinc modulates the host's immune response to infection by improving the function of leukocytes, cytokines, and mucous membrane barriers. There is a dearth of research on the relationship between zinc and the clinical course of ALRTI. We enrolled 70 cases of Acute Lower Respiratory Tract Infection in children < 1 yr. Out of the 70 children in the control group there were 37 children (52.86%) of age ≤ 1 year; 15 children (21.43%) of age 1 to 3 years; and 18 children (25.71%) of age 3 to 5 years. So the majority of children were in the age group of < 1 yr.

On the basis of diagnosis, the cases were categorized in the following two categories i.e. Children with bronchiolitis and bronchopneumonia. 54 (77.14%) patients were diagnosed with bronchiolitis and 16 (22.86%) patients with bronchopneumonia. The mean serum zinc in bronchiolitis was 93.45 ± 56.41 $\mu\text{g/dl}$ and the mean serum zinc in bronchopneumonia was 81.81 ± 68.3 $\mu\text{g/dl}$ and the results were found to be statistically non significant with p value of 0.5362.

Bronchiolitis was further categorized into the following three categories i.e. mild, moderate, and severe. Out of 54 (77.14%) patients, 28 (40.0%) children suffered from mild disease, 6 (8.57%) children suffered from moderate disease and the remaining 8 (11.43%) children suffered from severe disease and the results were found to be statistically significant with p value of 0.00001. Similarly, bronchopneumonia was further categorized into the following three categories i.e. No pneumonia, severe pneumonia, and very severe pneumonia, and it was found that 6 (8.57%) children suffered from no pneumonia, 1 child suffered from severe pneumonia (1.42) and 9 (12.86%) children suffered from very severe pneumonia with and the results were found to be statistically significant with a p value of 0.01174.

Zinc deficiency status was seen more in children with Acute Lower Respiratory Tract Infections who needed a prolonged hospital stay. 9 cases (12.86%) whose hospital stay was < 7 days had zinc deficiency. In cases whose hospital stay was > 7 days, 19 (27.14%) had zinc deficiency. The association of hospital stay with zinc deficiency is found statistically significant with p value of 0.01712.

The above mentioned findings showed that children with zinc deficiency were not predisposed to an increased incidence of ALRTI. However, we also discovered that children with higher serum zinc levels had shorter hospital stays, and less severe illness.

Our study results show that the difference observed between the zinc levels of cases and controls was not statistically significant which was similar to the findings from a study done by Zainab Ismaeel El-Drwany et al⁹ in the year 2022 as their study showed that the average serum zinc level in the individuals under investigation was 200.75 ± 37.44 $\mu\text{g/dl}$, which is regarded as normal or marginally above normal. They found that there was no statistically significant difference (p value 0.551) in serum zinc levels between various lower respiratory illnesses, nor between serum zinc levels and other disease risk factors, in participants ranging in age from two months to five years.

In the literature, we found a number of studies which showed that zinc deficiency was associated with an increased risk of Acute Lower Respiratory Tract Infections. Puneet Kumar Gupta¹⁰ conducted a study in the year 2021 in which he formed two distinct groups. Group I consisted of 68 children who had acute lower respiratory infections, while group II had an equal number of controls. Children with LRTI had a mean zinc level of 56.8 $\mu\text{g/dl}$, while controls had a mean zinc level of 84.2 $\mu\text{g/dl}$ (the difference observed was statistically significant p value < 0.05). The difference observed from our study in findings is probably because of the inclusion of only pneumonia and severe pneumonia patients in their case group whereas we included all cases of ALRTI of varied etiology.

A study Anil Sharma et al¹¹ in the year 2020 in which they involved 51

cases and 31 controls. On comparing cases of ALRI to controls, blood levels of zinc, vitamin D, and A were significantly low ($p < 0.001$). The difference observed in the results from our study was probably because they used the atomic absorption spectroscopy method in their study whereas in our study we used the colorimetric method.

Our study results also revealed that the difference observed in serum zinc levels between children who had hospital stay of less than 7 days and more than 7 days was statistically significant. Children who had prolonged hospital stay had significantly lower zinc levels.

Shreyas Rajendra Borkar et al⁸ in the year 2019 carried out a case control study in which they compared zinc levels and length of stay and their results were suggestive of a negative correlation ($r = -0.052$) ($p = 0.691$) between zinc levels and the length of stay. They found that reduced serum zinc levels resulted in longer stay of patient in the hospital which were similar to the findings seen in our study wherein children with prolonged hospital stay had significantly lower zinc levels.

In our study, we observed statistically significant difference amongst the groups of bronchiolitis based on severity and amongst those of bronchopneumonia based on the severity of the disease. Shisira Philip et al¹² in the year 2020 found that while comparing children with varying stages of pneumonia to those with wheeze associated LRTI/bronchiolitis and between children with severe pneumonia and those with pneumonia, significantly lower mean serum zinc levels were seen and on comparing bronchiolitis according to severity the results were found to be statistically significant with p value of 0.000. The findings of their study were similar to our findings with respect to severity of bronchiolitis.

Shreyas Rajendra Borkar et al⁸ in the year 2019 carried out a case control study that compared cases of severe pneumonia to cases of pneumonia (WHO IMNCI grade), the mean serum zinc levels were considerably lower (p value = 0.0001). They found that reduced serum zinc levels are strongly linked to ALRTI; the lower the serum zinc levels, the more severe the illness. Similar to our study their study too showed statistically significant results with respect to the severity of bronchiolitis and severity of bronchopneumonia between both groups.

CONCLUSION

This case control study was conducted on the estimation of serum zinc levels in 70 children of less than 5 years of age with Acute Lower Respiratory Tract Infection and 70 healthy controls.

The results of the study revealed that there was no significant difference in the zinc level between children having Acute Lower Respiratory Tract Infection and controls.

The hypothesis of zinc deficiency predisposing to increased incidence of ALRTI is being supported by many studies in literature but has not been proved in our study. The difference in observation may be attributed to different variables in different studies.

However to further validate this hypothesis we need to have studies with larger sample size and proper follow-up

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