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**Original Research Article**

# A Case Control Study on Estimation of Zinc Levels in Children with Acute Lower Respiratory Tract Infection

**Sunil Kumar Agrawal**

**Associate Professor, Department of Paediatrics, Varun Arjun Medical College and Rohilkhand Hospital, Shahjahanpur, U.P.**

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**Corresponding author: Dr. Sunil Kumar Agrawal**
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**Abstract:**

**Background:** With regard to conditions like acute lower respiratory tract infection (ALRTI), the significance of zinc in treating illnesses in children has been established, which has sparked a larger interest among researchers. Therefore, the purpose of this study was to assess serum zinc levels in ALRTI cases and to connect those levels with the clinical course of the disease.

**Methods:** ALRTI was present in 61 patients, aged 2 months to 5 years, who participated in the hospital-based case-control study, along with 61 nutritionally and age-matched control subjects. At admission, the serum zinc level was estimated. Along with details of the clinical course such length of stay, oxygen needs, severity of disease, and outcome, a thorough history, sociodemographic information, and examination were recorded.

**Results:** The difference between the mean serum zinc levels of patients and controls (patients 58.88±12.40 μg/dl, Controls 85.36±16.27 μg/dl) was determined to be statistically significant (p value = 0.0001). Zinc levels and length of stay had a negative connection (r = -0.052, p value = 0.691). When compared to cases of pneumonia (WHO IMNCI grading), cases of severe pneumonia had considerably lower mean serum zinc levels (p value = 0.0001). As compared to the patients who were released, those who required higher $O_2$ concentrations and those who died had considerably lower mean serum zinc levels (p value = 0.0001) and respectively.

**Conclusion:** Lower serum zinc levels are significantly associated with ALRTI and the lower the serum zinc levels; the more is the severity of disease and duration of stay in hospital for the patient, along with increased oxygen requirement and also increased incidence of mortality.

**Keywords:** Serum zinc estimation, acute lower respiratory tract infection, Children, Pneumonia.



## Introduction

Acute lower respiratory tract infections, or ALRTIs, are still a major global public health issue, particularly when they manifest as paediatric pneumonia. Although its impact on wealthy nations has considerably lessened, developing nations like India are still subject to its wrath. In 2016, it was responsible for around 125,333 fatalities in the postnatal age range of children under the age of five. This represented 28% of all deaths among people in this age range [1].Malnutrition is frequently regarded as one of the major risk factors for contracting illnesses like ALRTI [2]. The issue of macronutrient insufficiency has greatly decreased, and new research has focused on the micronutrient deficiency with trace elements like zinc in particular as a cause of children's higher susceptibility to ALRTI. More than 300 different enzymes involved in a variety of processes, including the creation of nucleic acids, proteins, hormones, their receptors, and some immunoregulatory molecules, as well as pathways, have been related to zinc's activity[3]. Due to its function in the creation of Interferon, zinc has also been shown to have intrinsic antiviral action [4]. Zinc has a well-established role in treating children's diarrhoea and reducing its severity and susceptibility, according to research conducted around the world, but studies on how it treats Acute Lower Respiratory Tract Infections (ALRTI) have produced mixed results.

There are also few investigations on the relationship between zinc and the ALRTI clinical course. Therefore, this study was conducted with the intention of quantifying the Zinc levels in the population not suffering from ALRTI and comparing it to the population suffering from ALRTI as a Case-Control Study, along with further evaluation of the association of Zinc levels with the clinical course of ALRTI, in order to better assess the role of Zinc in ALRTI.

## Material and Methods

It was a Hospital based Case-Control Study that was conducted in Department of Paediatrics, Varun Arjun Medical College and Rohilkhand Hospital, Shahjahanpur, U.P. from November 2022 to May 2023. After receiving informed consent, participants in the study were enrolled. Cases were determined to be children between the ages of 2 months to 5 years who were admitted from the OPD or a casualty for an acute lower respiratory tract infection during the study period. Children who had acute gastroenteritis or diarrhea prior to or during study enrollment, or who had a clinical diagnosis of reactive airway disease or asthma, or who had underlying chronic illnesses or congenital heart disease, or who had started taking zinc supplements within one month of enrolling in the study, were excluded. As Controls, age-, sex-, and nutritionally matched OPD or casualty patients admitted for reasons other than the inclusion and exclusion criteria were included. Within six months, the controls' ages matched the samples'. In this two-sided investigation, the sample size was statistically calculated to be 61, with an alpha error of 0.5% and an 80% power. So, 61 cases and 61 controls in all were included in the study.

In a predesigned and validated proforma, the full demographic data, history, clinical findings, laboratory findings, and information regarding the clinical course of the study's cases and controls were input. The Modified Kuppuswamy scale, which was modified in 2017[5], was used to determine socioeconomic status (SES).

Detailed the patients underwent a general examination, as well as systemic, respiratory, and other examinations, and a clinical diagnosis was determined and put into the proforma. During the patient's hospital stay, the specifics of blood tests and imaging for clinical diagnostic confirmation were also recorded.

The serum zinc estimation was done by using colorimetric test to used kit.

The sample that was used was serum, which was produced by centrifuging 2 ml of blood samples for 3 to 5 minutes at 3000 rpm. The blood sample was taken on the first day when patients and controls were admitted. 1000 µl of reagent in each of two ependoff tubes, along with 50 µl of serum in one tube and standard solution in the other, were combined and incubated at 370C for five minutes. By using a spectrophotometer and measuring the absorption of the standard A (Standard) and sample A (Sample) against the reagent blank A (Blank), the concentration of total zinc in the sample was determined [6].

In addition to determining the serum zinc levels, the clinical data of the cases were recorded, including the length of stay, oxygen needs, severity of disease as determined by the WHO IMNCI grading system for 2014, and case outcomes.

A Microsoft Excel case sheet was created and filled out using the information gathered from the cases and controls. Descriptive and inferential statistics, including chi ANOVA and Pearson's correlation coefficient, were employed in the statistical analysis. SPSS 22.0 and GraphPad Prism 6.0 versions of the analysis software were utilized, and a significance level of p <0.05 was used.

**Results**

Cases had a mean age of 1.55±1.29 years, while controls had a mean age of 1.95±1.63 years. In terms of gender, the cases and controls were split into 36 (59.02%) male cases and 25 (40.98%) female controls, as opposed to 35 (57.38%) male controls and 26 (42.62%) female cases. The distribution of cases and controls in this study by age, sex, nutritional status, and socioeconomic position was statistically insignificant when compared.

The Mean serum zinc levels in the cases and controls, after comparison, were found to be significantly different [p=0.0001], with mean value for the cases being 58.88 ± 12.40 µg/dl as compared to 85.36 ± 16.27 µg/dl for the controls (Table 1). A total of 33 cases and controls (27.05%) were found to have deficiency of zinc, of which majority (93.93%) were cases (normal range of 60 to 150 µg/dl) [7].

**Table 1: Comparison of Zinc level in cases and controls**

| Group | No. | Mean(µg/dl) | Std. Deviation(µg/dl) | Std. ErrorMean | t-value |
|---|---|---|---|---|---|
| Cases | 61 | 58.88 | 12.40 | 1.54 | 10.10<br>p=0.0001, S |
| Controls | 61 | 85.36 | 16.27 | 2.08 | |

Table 2 shows comparison of serum zinc levels according to the clinical characteristics of cases. Here, the difference in mean serum zinc levels of cases according to WHO IMNCI grading was statistically significant (p value = 0.0001) with cases belonging to Severe Pneumonia group (Mean = 42.88 ± 5.93 µg/dl) having significantly lower value than that of Pneumonia group (Mean = 65.06 ± 7.81 µg/dl).This is also reflected when we see serum zinc levels according to oxygen requirements, with cases managed on room air having mean of 66.03 ± 7.69 µg/dl, cases requiring supplemental oxygen by nasal prongs having mean of 59.63 ± 10.00 µg/dl and cases requiring mechanical ventilation having mean of 41.41 ± 6.93 µg/dl(Table 2).

In situations where the ALRTI and associated consequences ultimately resulted in death (n = 9), there were considerably lower zinc concentrations (p value = 0.0001) than in cases where the patient was discharged following treatment (n = 52) (Table 2).

**Table 2: Zinc level according to clinical characteristics in cases**

| IMNCI Grading | No. of cases | Mean (μg/dl) | SD | t-value |
|---|---|---|---|---|
| Pneumonia | 44(72.13%) | 65.06 | 7.81 | 10.56 p=0.0001,S |
| Severe Pneumonia | 17(27.86%) | 42.88 | 5.93 | |
| Total | 61(100%) | 58.88 | 12.40 | |
| **$O_2$ Requirement** | | | | |
| Room Air | 27(44.26%) | 66.03 | 7.69 | 35.14 p=0.0001,S |
| SupplementalOxygen | 22(36.07%) | 59.63 | 10.00 | |
| Mechanical Ventilation | 12(19.67%) | 41.41 | 6.93 | |
| **Outcome** | | | | |
| Discharge | 52(85.25%) | 62.13 | 10.15 | 39.88 p=0.0001,S |
| Death | 9(14.75%) | 40.11 | 6.09 | |

The relationship between zinc levels and duration of stay, it was discovered that the average serum zinc level correlated negatively (r = -0.052) with the average duration of stay for cases, however this link was statistically insignificant (p value = 0.691).

## Discussion

The mean serum zinc levels were similar to those discovered in Hussain et al. study[8].The mean serum zinc levels in patients were found to be higher in studies conducted in Bangladesh by Shakur et al. and Egypt by Rady et al. [9][10]. On the other hand, a study conducted in Nigeria by Ibraheem et al. revealed that the cases' mean serum zinc levels were lower [4]. The dietary practices of the nation and nutritional status of the study's participants as a whole can be blamed for this difference in mean zinc values [4] [9] [10].

It is statistically significant (p value = 0.0001) that the patients and controls in this study and the studies listed above have different serum zinc levels.

Similar findings were also found in studies conducted by Kumar et al. in India and Arica et al. in Greece [11][12]. These results may be explained by the fact that, in response to an inflammatory stimulus, interleukins and the tumor cute phase reaction lower serum zinc levels [11].

According to WHO IMNCI grading 2014, severe pneumonia cases had a much lower value than pneumonia cases in terms of illness severity, and comparable findings were found in studies by Rady et al., Hussain et al., and Brooks et al.[8][10][13]. This may be because to the lack of zinc's immunomodulatory function, which leads to an uncontrolled immunological response in the respiratory tract and increases airway injury [13].Studies by Valentiner - Branth et al. and Bose et al., however, provided evidence to the contrary [14] [15]. The aforementioned studies have made the case that because zinc is needed for the host to generate a greater immune response against infection, there would be increased damage to the respiratory epithelium as a result of the heightened immunological response, which will worsen the symptoms [15].

In terms of the length of stay for cases, Basnet et al. discovered a shorter length of stay in the zinc supplemented group as compared to the placebo group [19], but the difference was statistically not significant. However, after taking a zinc supplement, patients with ALRTI had a significantly shorter length of stay, according to Brooks et al., Singh et al., and Malik et al. [13][16][17]. While this was going on, Bose et al., Valentiner-Branth et al., and Yuan et al. discovered that adding zinc to a patient's diet either had no benefit or lengthened their hospital stay [14][15][18].

When assessing the patients' oxygen needs during treatment, a similar pattern is also visible. Although research by Rady et al., Brooks et al., and Valentiner-Branth et al. support our study's findings, Bose et al. and Valentiner-Branth et al. have reported no appreciable decrease in oxygen consumption [10][13][14][15].

The results of our investigation agreed with those of Rady et al., Brooks et al., and Basnet et al. when comparing the outcomes of cases according to serum zinc levels[10][13][19]. Additionally, Mayo-Wilson et al. showed in their extensive systematic analysis of zinc supplementation that administering zinc to children may lessen both their risk of death overall and their risk of death from lower respiratory tract infection[20].

## Conclusion

ALRTI patients have considerably lower zinc levels than age-, sex-, and nutritionally matched controls, suggesting that zinc plays a significant role in the development and progression of ALRTI in children between the ages of 2 months and 5 years. Additionally, a zinc shortage results in a more severe form of the disease in the patient, necessitating a longer stay in the hospital as well as higher oxygen demands and a higher risk of fatality. There is still a need for sizable, community-based longitudinal research because the outcomes of randomized trials on zinc supplementation have yielded conflicting results for the therapeutic and prognostic usefulness of zinc. The study's weaknesses included its small sample size and hospital setting, which prevented it from accurately portraying the extent of zinc insufficiency in the general population.

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