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Original Research Article

Zinc Level Estimation in Children with Acute Lower Respiratory Tract Infection: A Case Control Study

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Conflict of interest: Nil

Abstract:

Background: Because of the recognized importance of zinc in treating pediatric disorders, such as acute lower respiratory tract infections (ALRTI), researchers are becoming more interested in this area. So, the aim of this study was to determine the serum zinc levels in instances of ALRTI and to establish a relationship between those levels and the disease's clinical progression.

Methods: In the hospital-based case-control trial, 61 patients between the ages of 2 months and 5 years had ALRTI in addition to 61 age- and nutritionally-matched control subjects. The serum zinc level was assessed at admission. A comprehensive history, sociodemographic data, and examination were documented in addition to specifics of the clinical course, such as duration of stay, oxygen requirements, degree of disease, and result.

Results: It was found that there was a statistically significant difference (p value = 0.0001) in the mean blood zinc levels of the patients and controls (patients 58.88±12.40 µg/dl, Controls 85.36±16.27 µg/dl). There was a negative correlation between zinc levels and length of stay (r = -0.052, p value = 0.691). Severe pneumonia cases had far lower mean serum zinc levels (p value = 0.0001) compared to pneumonia cases (WHO IMNCI grade).The patients who required greater amounts of oxygen and those who passed away had significantly lower mean serum zinc levels (p value = 0.0001) and correspondingly, in comparison to the patients who were released.

Conclusion: Reduced serum zinc levels are strongly linked to ALRTI; the lower the serum zinc levels, the more severe the illness, the longer the patient stays in the hospital, the higher the oxygen requirement, and the higher the fatality rate.

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

Introduction

Acute lower respiratory tract infections, or ALRTIs, continue to pose a serious threat to international public health, especially when they cause pneumonia in children. Its effect on affluent countries has significantly diminished, but emerging countries like India continue to feel its wrath. About 125,333 deaths in the postnatal age range of children under five were caused by it in 2016.

This accounted for 28% of all deaths in this age group [1].One common belief is that malnutrition poses a significant risk of acquiring infections such as ALRTI [2]. The problem of inadequate intake of macronutrients has significantly diminished, and recent studies have concentrated on the shortage of some micronutrients, including trace elements like zinc, as a reason for children's increased vulnerability to ALRTI. Zinc activity has been linked to more than 300 distinct enzymes that are involved in a range of processes, such as the synthesis of proteins, nucleic acids, hormones, their receptors, and some immunoregulatory molecules, as well as pathways[3].Zinc has demonstrated inherent antiviral activity as well as its role in the synthesis of Interferon [4].

Studies conducted globally have demonstrated the effectiveness of zinc in treating diarrhea in children and lowering their susceptibility to illness. However, studies investigating zinc's effect on Acute Lower Respiratory Tract Infections (ALRTI) have yielded inconsistent findings. On the connection between zinc and the clinical course of

ALRTI, there are also not many studies. In order to better understand the role of zinc in ALRTI, this study was carried out with the goal of measuring the levels of zinc in the population not suffering from ALRTI and comparing them to the population suffering from ALRTI as a Case-Control Study. It also included additional analysis of the relationship between zinc levels and the clinical course of ALRTI.

Material And Methods

From January 2023 to December 2023, a hospital-based case-control study was carried out in the pediatric department of the Netaji Subhas Medical College and Hospital in Bihta, Patna, Bihar.

The study enrolled participants after obtaining informed permission. Children between the ages of two months and five years who were hospitalized for an acute lower respiratory tract infection in the OPD or who were casualties throughout the study period were identified as cases. Acute gastroenteritis or diarrhea, a clinical diagnosis of asthma or reactive airway disease, underlying chronic illnesses, congenital heart disease, or beginning zinc supplementation within one month of study enrollment were all grounds for exclusion from the study for children. OPD or casualty patients admitted for reasons other than the inclusion and exclusion criteria were included as controls, along with age, sex, and nutritional matching.

The ages of the samples and the controls coincided within six months. The statistical calculation for this two-sided study yielded a sample size of 61 with an 80% power and an alpha error of 0.5%. There were 61 cases and 61 controls total in the research. The complete demographic information, history, clinical findings, laboratory results, and details about the clinical progression of the study's cases and controls were entered into a predesigned and validated proforma. The socioeconomic status (SES) was ascertained using the 2017[5] Modified Kuppuswamy scale.

Specific a clinical diagnosis was made and entered into the proforma after the patients underwent general examination, systemic, respiratory, and other exams. The specifics of the imaging and blood tests performed for clinical diagnostic confirmation were also documented during the patient's hospital stay. The serum zinc estimation was done by using colorimetric test to used kit. Serum was the sample that was used, and it was created by centrifuging two milliliters of blood samples at 3000 rpm for three to five minutes. On the first day of the patients' and controls' admission, a blood sample was obtained. Two ependoff tubes were filled with 1000 µl of reagent each, 50 µl of serum in one tube, and standard solution in the other. The tubes were then incubated at 370C for five minutes. The concentration of total zinc in the sample was calculated using a spectrophotometer by comparing the absorbance of the standard A (Standard) and sample A (Sample) against the reagent blank A (Blank) [6].

The clinical information of the cases, such as the duration of stay, oxygen requirements, severity of disease as assessed by the WHO IMNCI grading system for 2014, and case outcomes, were documented in addition to the serum zinc levels.

Using the data acquired from the cases and controls, a Microsoft Excel case sheet was made and completed. The statistical analysis used both descriptive and inferential statistics, such as Pearson's correlation coefficient and chi ANOVA. The analysis software used was GraphPad Prism 6.0 and SPSS 22.0, with a significance threshold set at $p < 0.05$.

Results

The mean age of the cases was 1.55±1.29 years, whereas the mean age of the controls was 1.95±1.63 years. Gender-wise, there were 36 (59.02%) male cases and 25 (40.98%) female controls among the cases and controls, compared to 35 (57.38%) male controls and 26 (42.62%) female cases. When compared, the distribution of cases and controls in this study by age, sex, socioeconomic status, and nutritional status was statistically insignificant.

After comparison, the mean serum zinc levels in the patients and controls were found to be substantially different [p=0.0001], with the mean value for the cases being 58.88 ± 12.40 µg/dl and the control group's mean value being 85.36 ± 16.27 µg/dl (Table 1). Zinc deficiency was discovered in 33 cases and controls (27.05%), the majority of which (93.93%) were cases (normal range of 60 to 150 µg/dl). [7]

Table1: Comparison of Zinc level in cases and controls

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

Serum zinc levels are compared in Table 2 based on the clinical features of the cases. The WHO IMNCI grading of the cases showed a statistically significant difference in mean serum zinc levels (p value = 0.0001), with cases in the Severe Pneumonia group (Mean = 42.88 ± 5.93 µg/dl) having a significantly lower value than those in the 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).Zinc concentrations were significantly lower (p value = 0.0001) in cases where the ALRTI and related repercussions finally led to death (n = 9), compared to cases where the patient was released from therapy (n = 52) (Table 2).

Table 2: Zinc level according to clinical characteristics incases

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	
O2 Requirement				
Room Air	27(44.26%)	66.03	7.69	35.14 p=0.0001, S
Supplemental Oxygen	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	

It was shown that there was a negative correlation (r = -0.052) between the average serum zinc level and the average duration of stay for cases; however, this correlation was statistically insignificant (p value = 0.691).

Discussion

The average serum zinc levels matched those found in the study by Hussain et al. [8].Studies by Shakur et al. in Bangladesh and Rady et al. in Egypt revealed that patients' mean serum zinc levels were higher[9][10]. However, the mean serum zinc levels of the patients were lower, according to a study done in Nigeria by Ibraheem et al.[4]. This variation in mean zinc values can be attributed to national dietary patterns and the overall nutritional condition of study participants [4], [9] [10].

The differences in serum zinc levels between the patients and controls in this study and the ones mentioned above are statistically significant (p value = 0.0001).Studies by Arica et al. in Greece and Kumar et al. in India also produced results that were similar [11][12]. These findings could be explained by the fact that interleukins and the tumor cute phase reaction reduce serum zinc levels in response to inflammatory stimuli [11].

Severe pneumonia cases had a substantially lower value in terms of illness severity than pneumonia patients, according to WHO IMNCI grading 2014; similar results were reported in research by Rady et al., Hussain et al., and Brooks et al.[8][10][13]. This could be as a result of zinc's immunomodulatory role being lacking, which raises the risk of airway damage and causes an uncontrollable immune response in the respiratory tract [13].On the other hand, research by Valentiner-Branth et al. and Bose et al. showed the opposite [14] [15]. According to the aforementioned research, increased damage to the respiratory epithelium due to the heightened immune response caused by zinc deficiency will exacerbate symptoms by causing the host to mount a stronger defense against infection [15].When it came to the duration of stay for patients, Basnet et al. found that those who took zinc supplements had shorter stays than those who took a placebo [19], but the difference was not statistically significant. However, Brooks et al., Singh et al., and Malik et al. found that patients with ALRTI had a considerably reduced length of stay after taking a zinc supplement [13][16][17].During this time, Bose et al., Valentiner - Branth et al., and Yuan et al. found that increasing a patient's zinc intake either had no effect or caused the patient to stay in the hospital longer [14][15][18].

A comparable pattern is also seen when determining the patients' oxygen requirements during therapy. The results of our investigation are corroborated by studies conducted by Rady et al., Brooks et al., and Valentiner-Branth et al., while Bose et al. and Valentiner-Branth et al. have not observed a discernible drop in oxygen consumption [10][13][14][15].

Comparing the case outcomes based on serum zinc levels, our findings concurred with those of Rady et al., Brooks et al., and Basnet et al.[10][13][19]. Furthermore, Mayo-Wilson et al.'s comprehensive systematic research of zinc supplementation demonstrated that giving zinc to kids may reduce their chance of dying from lower respiratory tract infections as well as their overall risk of death[20].

Conclusion

When compared to age-, sex-, and nutritionally matched controls, ALRTI patients had significantly lower zinc levels. This suggests that zinc is important for the onset and progression of ALRTI in children between the ages of two months and five years. A zinc deficiency also causes a more severe type of the illness, which means the patient needs to be in the hospital longer, requires more oxygen, and has a higher chance of dying. Randomized trials on zinc supplementation have produced inconsistent results regarding the therapeutic and prognostic utility of zinc, highlighting the ongoing need for large-scale, community-based longitudinal studies. A small sample size and hospital setting limited the study's ability to provide an accurate picture of the prevalence of zinc deficiency in the general population.

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