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Dr. Uma Maheswar Rao
Assistant Professor, Department of Paediatrics, Bharat Medical College, Chennai, Tamil Nadu, India

Dr. S Sailaja Suresh Kumar
Assistant Professor, Department of Community Medicine, Sambhram Institute of Medical Sciences and Research, Bangalore, Karnataka, India

Corresponding Author:
Dr. S Sailaja Suresh Kumar
Assistant Professor, Department of Community Medicine, Sambhram Institute of Medical Sciences and Research, Bangalore, Karnataka, India

Investigation of zinc levels in the blood of children between the ages of six months to five years old with acute respiratory tract infections

Dr. Uma Maheswar Rao and Dr. S Sailaja Suresh Kumar

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Abstract
Background and Objectives: One of the leading causes of death and illness among children in underdeveloped nations is acute respiratory tract infections. Zinc serum levels in patients with acute lower respiratory tract infections are the focus of this investigation. This is associated with acute lower respiratory tract infection severity, the requirement for intravenous antibiotics, and the pattern of recovery.
Materials and Methods: This study is a case-control investigation that was carried out in the Department of Community Medicine, Sambhram Institute of Medical Sciences and Research, Bangalore, Karnataka, India. The study was done from February 2019 to January 2020. The study's sample consisted of 50 instances of acute lower respiratory tract infection, along with 50 children who were matched in terms of sex, age, and nutritional condition, serving as controls.
Results: Prolonged hospital stay was associated with a reduction in mean serum zinc levels. The average zinc concentration decreased within the range of normal zinc levels in children who were hospitalized for a duration of less than 7 days. In addition, a higher prevalence of zinc insufficiency was observed when comparing patients and controls. A greater proportion of children with bronchiolitis exhibited a normal zinc level. A higher proportion of children with pneumonia and lobar pneumonia exhibited a zinc deficiency. In addition, a greater proportion of children with severe acute lower respiratory tract infections exhibited zinc deficiency compared to those with mild and moderate acute lower respiratory tract infections.
Conclusion: In severe acute lower respiratory tract infections, there was a notable decrease in serum zinc levels in comparison to mild and moderate acute lower respiratory tract infections. Additionally, it was observed that children requiring an extended hospital stay exhibited a deficiency in serum zinc levels.

Keywords: Zinc level, children, acute respiratory tract infections

Introduction
One of the leading causes of death and illness among children in underdeveloped nations is acute respiratory tract infections. The most prevalent causes of acute infections of the lower respiratory tract in children under the age of five are bronchiolitis and pneumonia. Infections with bacteria or viruses can cause children to suffer from acute lower respiratory tract infections. Parainfluenza and RSV viruses are leading causes of viral LRIs. Bronchiolitis is the most common symptom. Bacteria and viruses are both capable of causing pneumonia. Pneumococcus pneumoniae, Staphylococcus aureus, group A streptococci, and *Haemophilus influenzae*, particularly type b, are among the bacteria that can cause bacterial pneumonia. Atypical pneumonias can be caused by Mycoplasma pneumonia and Chlamydia pneumonia. Acute respiratory tract infections have an incidence of 21.7% to 40% in underdeveloped nations [1-3].
Between 30 and 60 million cases of moderate to severe ARI occur annually in India, out of an estimated 300 million cases. Although Indian children make up one in six worldwide, they also account for one in four infant fatalities. In India, children under the age of five account for a quarter of the population and a quarter of the deaths. Twenty percent to thirty-five percent of the deaths in children less than five in India are attributable to ARIs. Between 0.25 and 0.5 episodes per child each year occur due to lower respiratory tract infections. Acute lower respiratory tract infections account for 10%-13% of ARI episodes in children, while upper respiratory tract infections account for 87% to 90%. Additionally, 96.5% of respiratory-related deaths are attributable to infections in the lower respiratory tract.

Acute respiratory events account for 33% of paediatric outpatient visits and admissions, with lower respiratory tract infections accounting for almost 90% of those admissions, according to studies [4-6].

In every cell in your body, you'll find the catalytic metal ion zinc in the cytoplasm. Although all cells contain zinc, the concentration in bones and muscles is around 80%. The blood's plasma and red cells both contain it. Macroglobulin and albumin bind one third of the zinc in the blood plasma. Zinc is an essential mineral for healthy gut lining, strong bones, and a strong immune system, especially for cellular immunity and antioxidant defenses. It permeates every part of the body, from organs to tissues to fluids [7-9].

There is a larger concentration of zinc in seminal fluid. Iron is an essential component of many enzymes, including superoxide dismutase, carbonic anhydrase, alkaline phosphatase, DNA and RNA polymerase, and reverse transcriptase. It serves several physiological purposes. Cell division and DNA replication both rely on it. In cells with a high rate of turnover, it is essential for preserving cell integrity and immunity. So, it's really important for keeping infections under control and preventing them [8-10].

Zinc is not stored by the body despite its many uses. Zinc is essential but cannot be stored in the body like iron and must be consumed continuously. Zinc can be found in foods such as nuts, grains, shellfish, dairy, red meat, and other animal proteins. Because of the presence of phytate, which chelates zinc and hinders its absorption, most vegetables are not good sources of zinc. While the significance of zinc in diarrhoea is well-established, multiple investigations have shown that zinc can reduce the intensity, length, and frequency of diarrhoea, thus it is recommended to take zinc supplements while you're sick [9-11].

A few studies have linked zinc shortage to an increased likelihood of acute lower respiratory tract infections, and taking zinc supplements has been shown to lessen the frequency of these illnesses. Fewer cases of acute lower respiratory tract infections were observed in trials when zinc supplementation was administered to patients with pneumonia. Additionally, adding zinc to antibiotic treatment has not been found to have any therapeutic advantage in trials.

Zinc serum levels in patients with acute lower respiratory tract infections are the focus of this investigation. This is associated with acute lower respiratory tract infection severity, the requirement for intravenous antibiotics, and the pattern of recovery [10-12].

Materials and Methods

The present investigation is a case-control study conducted at the Department of Community Medicine, Sambhram Institute of Medical Sciences and Research, Bangalore, Karnataka, India. The research was conducted between the months of February 2019 to January 2020. The sample for this study comprised 50 cases of acute lower respiratory tract infection, together with a control group of 50 children who were matched in terms of sex, age, and nutritional condition.

Inclusion Criteria

Tachypnea, chest retractions, and other symptoms of severe illness such high fever, convulsions, excessive lethargy, or incapacity to suck or drink were used to diagnose a severe acute lower respiratory tract infection.

Exclusion Criteria

- Kids who had diarrheal episodes in the previous three months were not allowed to participate in the trial;
- Kids who were already taking zinc supplements were not allowed to participate either.

Results

A total of 50 cases of acute lower respiratory tract infections were examined and categorized based on age, sex, and nutritional status. Age and nutritional status were matched within a 3-month timeframe, and weight for age was measured to ensure compatibility. Given that the children in both the cases and controls were matched in terms of age and sex, the counts of children in each age group and the counts of males and females in both cases and controls were identical.

Table 1: Sex wise patient distribution

Sr. No.	Gender	Number	%
1.	Male	33	66
2.	Female	17	34
	Total	50	100

Each group consisted of 33 males (66%) and 17 females (34%). Both males and females had an average age of 2 years.

Age-based distribution

The age group consisted of 26 children under the age of 1, 10 children aged 1 to 3, and 14 children aged 3 to 5. In the cases, the average age group for those under 1 year, 1 to 3 years, and 3 to 5 years was 9 months, 2 years, and 3.75 years, respectively. In the control group, the average age for individuals under 1 year, 1 to 3 years, and 3 to 5 years was 9.5, 2.25 years, and 3.75 years, respectively.

Table 2: Age wise patient distribution

Sr. No.	Age	Number	%
1.	<1 year	26	52
2.	1-3 years	10	28
3.	3 -5 years	14	20
	Total	50	100

Morbidity Pattern

Out of the 50 instances of acute lower respiratory tract infections, there were 16 cases of bronchiolitis, 21 cases of pneumonia, 12 cases of lobar pneumonia, and 21 cases with a clinical diagnosis of acute lower respiratory tract infections but no radiological abnormalities. In the present investigation, pneumonia accounted for the majority of the cases. The average age of bronchiolitis, pneumonia, and lobar pneumonia were 1 year, 2 º years, and 1 º years, respectively. Bronchiolitis was observed in a cohort consisting of 11 males and 5 females. The pneumonia study included a total of 22 males and 29 females. The lobar pneumonia case consisted of six males and six females. The average age for individuals with bronchiolitis, pneumonia, lobar pneumonia, and cases diagnosed with acute lower respiratory tract infections without any radiological abnormalities was 1 year, 2 º years, 1 º years, and 2 º years, respectively. Bronchiolitis was more prevalent among individuals under the age of 1 year. The incidence of lobar pneumonia was found to be higher among individuals aged 1 to 3 years, whereas pneumonia was seen to be more

prevalent among those aged 3 to 5 years.

IAP classification

The graphic below displays the distribution of cases based on nutritional status across different disease patterns. Malnutrition was assessed using the IAP classification to determine the nutritional status. A normal nutritional status was seen in individuals with bronchiolitis, as indicated by the study. Localized pneumonia was seen to be more prevalent in cases of grade II and grade III malnutrition. The study observed that the nutritional condition of the children with pneumonia was predominantly within the normal range or grade I PEM.

Table 3: IAP classification

1.	Normal	> 81%
2.	Grade I PEM	70 to 81%
3.	Grade II PEM	60 to 70%
4.	Grade III PEM	51 to 60%
5.	Grade IV PEM	< 50%

The table presented above illustrates the distribution of patients across different illness patterns in acute lower respiratory tract infections, categorized by severity. This study observed that the majority of cases of bronchiolitis and pneumonia had intermediate acute lower respiratory tract infections, whereas lobar pneumonia predominantly manifested as severe instances.

Distribution of Cases According to the Severity

Acute lower respiratory tract infections, both serious and mild, were the majority of patients seen in our hospital. There was no statistically significant variation in the presentation between mild and moderate. The above bar chart shows the breakdown of cases by age and severity. Children between the ages of one and three, or toddlers, accounted for a disproportionate share of the serious cases in our research. The severity of acute lower respiratory tract infections was usually moderate to mild in children aged 3 to 5, who were in the preschool age group, and there was little to no difference in this group compared to babies. The following bar chart shows the gender breakdown of instances of acute lower respiratory tract infections, broken down into mild, moderate, and severe. When looking at the severity of acute lower respiratory tract infections, there was no statistically significant difference between males and females.

Zinc Deficiency Status

Zinc levels in children's serum should typically range from 60 to 120 µg/dl. Zinc deficiency status was determined when the serum zinc level was less than 60 µg/dl. Of the fifty instances of acute lower respiratory tract infections included in this investigation, fifty-two percent were found to have zinc deficiency, whereas forty-eight percent had normal serum zinc status.

Table 4: Zinc Deficiency

Sr. No.	Serum Zinc average	Case	%
1.	< 60	26	52%
2.	> 60	14	48%
	Total	50	100

Status of Zinc Deficiency and Distribution by Sex

Zinc deficiency was found in 21 out of 33 male children with acute lower respiratory tract infections, while 12 children had normal zinc levels. Also, 13 out of 33 children who were considered controls had zinc deficiencies. Ten of the seventeen female children sick with acute lower respiratory tract infections were zinc deficient, whereas seven others tested normal.

Deficiency of zinc intake across various age groups

Of the 25 children who were diagnosed with an acute lower respiratory tract infection, 9 had normal zinc levels and 16 had zinc deficiency. Six babies used as controls had low levels and nineteen babies had normal levels. There were 39 instances of zinc deficiency and 10 cases of normal zinc levels among toddlers. Eight toddlers tested negative for zinc deficiency and forty-two tested normal for zinc levels within the control group. Out of 26 cases in the preschool age range, 5 had normal zinc level and 21 had zinc deficiency. Twenty people in the control group had normal zinc levels, while five people were zinc deficient.

Antibiotics and the state of serum zinc

For children requiring oral antibiotics, the average zinc level was 60.78 µg/dL, while for those requiring intravenous antibiotics, it was 55.02 µg/dL. A normal range of serum zinc levels was seen in children with an average zinc level of 79.07 µg/dL, who did not require antibiotics. Consequently, the requirement for antibiotics is significantly related to serum zinc levels.

Table 5: Antibiotics and level of serum zinc

Sr. No.	Antibiotic	Number	Mean of Serum Zinc
1.	Not given	12	80.02
2.	IV	18	54.01
3.	Oral	20	61.12
	Total	50	60.32

Cases with an extended hospital stay had a lower mean serum zinc level. In children whose hospital stays were less than seven days, the average zinc level dropped into the normal zinc status. Zinc deficiency was also more common in the patients compared to the controls. Zinc levels were normal in a larger proportion of children with bronchiolitis. A higher percentage of children with pneumonia and lobar pneumonia were zinc deficient. Additionally, a higher percentage of children with severe acute lower respiratory tract infections were zinc deficient, in comparison to those with mild or moderate infections.

Discussion

Acute lower respiratory tract infections are a significant contributor to both death and illness in children under the age of 5. Hence, it is imperative to implement measures aimed at preventing and mitigating the intensity of respiratory tract infections. Multiple risk factors contribute to the development of acute lower respiratory tract infections. Several risk factors have been identified, including limited educational attainment, low socioeconomic position, environmental influences, substandard living conditions, inadequate access to healthcare services, insufficient immunization rates, malnutrition, deficiencies in essential micronutrients, and demographic factors [11-13].

Micronutrient zinc has been identified as a potential contributor to the pathogenesis of acute lower respiratory tract infections. It can either directly affect the respiratory tract or play a role in the body's immunological system. Additionally, it exhibits an anti-oxidant action. This intervention has the potential to mitigate respiratory tract inflammation, hence facilitating the healing process and expediting the recuperation from various ailments. The prevalence of zinc deficiency in developing nations can be attributed to either inadequate consumption of zinc-rich food or the presence of phytate in food items, which hinders zinc absorption. Additionally, the reduced zinc level in soil could potentially contribute to the diminished zinc content observed in food [14-16].

Hence, it may be imperative to administer zinc supplementation in order to mitigate and reduce the intensity of acute lower respiratory tract infections. Numerous studies have demonstrated the efficacy of zinc supplementation in reducing the incidence of acute lower respiratory tract infections. Zinc deficiency or a diminished zinc status has been observed in certain research pertaining to acute lower respiratory tract infections or pneumonia. There were 33 males and 17 females in this study. The findings of this study indicate that children diagnosed with acute lower respiratory tract infections exhibited reduced serum zinc levels in comparison to a control group that was matched in terms of age, sex, and nutritional condition [17-19]. Children with bronchiolitis had the highest average serum zinc levels, while children with lobar pneumonia had the lowest average. There was an inverse relationship observed between the mean blood zinc level and the severity of acute lower respiratory tract infections, indicating that as the severity increased, the zinc level decreased. The cases requiring intravenous antibiotics exhibited the lowest mean serum zinc level. There was no observed disparity in zinc levels between children requiring oxygen and those not requiring oxygen. Prolonged hospital stay was associated with a reduction in mean serum zinc levels. The average zinc concentration decreased within the range of normal zinc levels in children who were hospitalized for a duration of less than 7 days [20-22].

In 76% of cases and 19% of controls, zinc insufficiency was observed. A zinc deficit was observed in 33.3% of children diagnosed with bronchiolitis. Among children with pneumonia, 80.4% tested positive for zinc deficiency, while in ALRI without any radiological abnormalities, 90.4% tested positive for zinc deficiency. Among individuals with mild ALRI, 71.8% exhibited zinc deficiency. Zinc deficiency was observed in 70.4% of those with mild ALRI, while in 91.6% of those with severe ALRI. Among ALRI cases where antibiotics were not administered, 26.6% had zinc deficiency. Zinc deficit was observed in 81.4% of children who were administered oral antibiotics, whereas 86.2% of children who received intravenous antibiotics exhibited zinc deficiency. Zinc deficiency was observed in 82.5% of cases with a hospital stay ranging from 7 to 14 days, whereas in cases where the hospital stay exceeded 14 days, zinc insufficiency was found in 100% of cases [23-27].

Conclusion

Zinc deficiency was found in all cases of children whose hospital stays were more than 14 days, in 82.5% of children whose stays were from 7 to 14 days, and in 48.8% of cases where the hospital stays were less than 7 days. Compared to healthy children, those with acute lower respiratory tract infections had low serum zinc levels. Malnutrition was associated with low serum zinc levels. Zinc serum levels were decreased in children with PEM and acute otitis media infections. Acute lower respiratory tract infection severity and length of hospital stay were also correlated with serum zinc level. In comparison to moderate and mild cases of acute lower respiratory tract infections, severe cases had significantly lower serum zinc levels. Additionally, children requiring an extended hospital stay exhibited a low serum zinc level.

Funding

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Conflict of Interest

None.

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