Original Article :

Association Between Serum Zinc Levels and Severity of Respiratory Distress in Infants with Acute Lower Respiratory Tract Infections

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Abstract

Background and Aims:

Acute respiratory infection (ARI) poses a significant challenge to achieving the Sustainable Development Goal of ending preventable deaths among newborns and children under five by 2030. Zinc supplementation may play a role in preventing ARI. This study aimed to assess the relationship between serum zinc levels and the severity of respiratory distress in infants with acute lower respiratory infections admitted to a tertiary care hospital in Kolkata.

Methods:

A descriptive cross-sectional study was conducted on 105 infants admitted with acute lower respiratory infections at a tertiary care hospital in Kolkata. Participants were systematically selected through random sampling over a one-year period. Data collection involved a pre-designed structured schedule, incorporating the Respiratory Severity Score (RSS). Serum zinc levels were also measured. Statistical analysis was performed using SPSS v25.0, with results presented through both descriptive and inferential statistics.

Results:

Upon admission, 48.6% of the 105 participants exhibited severe respiratory distress. A mild decline in serum zinc levels (<80 mcg/dl) was observed in 35.2% of the participants, with 59.5% of these cases experiencing severe respiratory distress. A significant association was found between the mother's occupation and the RSS score using Pearson's chi-square test (χ^2 = 8.179, p = 0.042). Although a decrease in serum zinc levels corresponded with an increase in the RSS score, this correlation was not statistically significant (Spearman's rho = 0.149, p = 0.139).

Conclusion:

Zinc supplementation may be helpful in reducing the severity of respiratory infections.

Keywords:

Zinc, Respiratory distress, Respiratory Tract Infections, Acute Lower respiratory Infection, Infants

Introduction:

Acute lower-respiratory infections (ALRI) has been defined as the "presence of cough and at least one of the following, viz, increased respiratory rate (>60 respirations/minute in infants under 2 months of age, >50 respirations/minute in infants 2–11 months old, and >40 respirations/minute in children 12 months and older); rales/crepitations; wheezing; stridor; or chest indrawing".[1-5] Acute respiratory infections (ARI) include both upper and lower respiratory infections.[6] Acute respiratory infections (ARI) include both acute upper-respiratory infections and acute lower-respiratory infections.6 ALRI consist primarily of pneumonia, but also include croup, tracheobronchitis, and bronchiolitis.[7]

The Sustainable Development Goals (SDGs) aim to eliminate deaths from preventable diseases among newborns and children under five by 2030.[8] However, achieving this goal is hindered by acute respiratory infections (ARI), which are a major cause of illness and death in young children.[9] This study can impact several Sustainable Development Goals (SDGs) by contributing to improved health and well-being (SDG 3), reducing child mortality, enhancing nutrition (SDG 2), and empowering women through health education (SDG 5). The findings can guide better treatment protocols, nutritional interventions, and health education, leading to healthier communities and progress toward achieving the SDGs. Pneumonia alone accounts for 14% of all deaths in children under five worldwide.[10] The impact of respiratory viral infections goes beyond the immediate illness and its treatment, as these infections have been shown to increase the risk of recurrent wheezing in older children and the development of allergic asthma throughout childhood and into late adolescence.[11,12]

Zinc is a vital trace element that supports numerous biological functions, including maintaining the mucosal barrier, enhancing both innate and adaptive immunity, responding to oxidative stress, and acting as a cofactor for over 200 enzymes.[13] It possesses antiviral properties and influences the immune system's production of interferon.[14] A deficiency in zinc impairs the body's ability to fight infections and negatively impacts both cell-mediated and humoral immune responses.[14,15] According to an Indian review, zinc deficiency contributes to up to 4.4% of infection-related deaths in developing countries.[15] Zinc supplementation has proven beneficial in reducing the duration and severity of acute and persistent diarrhea in children and has been shown to prevent pneumonia in children in developing countries.[16-18] These ob-

servations were confirmed in recent times by Gera et al (2019),[19] where zinc supplementation was noted to reduce the duration and severity of diarrhea in children and helps prevent subsequent infections. However, there is still a lack of studies on the role of zinc in preventing respiratory distress.

Besides, this research holds significant public health implications. By identifying the crucial role of zinc in managing respiratory infections, it can lead to the development of better treatment protocols that reduce the severity and duration of illnesses in infants. This, in turn, can inform public health policies and nutrition programs, emphasizing the importance of zinc supplementation in children's diets. Effective zinc supplementation has the potential to decrease hospital admissions and healthcare costs by preventing severe respiratory infections. Furthermore, the study contributes to global health efforts aimed at reducing child mortality and improving overall child health, particularly in low-resource settings, thereby enhancing public health outcomes for children worldwide. Thus, this study was planned to measure the severity of respiratory distress in infants admitted with ALRI in a tertiary care hospital in Kolkata; to evaluate the serum zinc levels in them; to identify the factors associated with the severity of respiratory distress and; to examine the relationship between serum zinc levels and the severity of respiratory distress..

Methods:

Study Design and Setting:

This descriptive type of observational study with cross-sectional design was conducted from May 2023 to May 2024.

Study Population:

The study included infants diagnosed with acute lower respiratory infection (ALRI) at a tertiary care hospital in Kolkata. Infants aged 2-12 months diagnosed with either pneumonia or bronchiolitis were eligible for inclusion. However, those with a history of diarrhea or severe acute malnutrition in the past month, or those who had received zinc supplementation the previous month, were excluded.

Sample size estimation & sampling technique:

Sample size was calculated using Cochran's formula, Z^2pq/d^2; where, Z=1.96 at 95% level of confidence, p = prevalence of zinc deficiency in infants with ALRI (taken as 40% from the study by Shakur et al[20]), q=1-p, d=10% absolute error (0.1). Minimum sample size was calculated as 95. Taking additional 10% for non-response, final sample size was 105. The participants were selected by systematic random sampling. On analysis of the number of patients getting admitted at the Depart-

ment of Paediatrics at CSS for the last 1 month, it was observed that on an average at least 5 eligible patients get admitted daily. As the total no of data collection days will be 312 (52x6) and a minimum of 1560 (5x312) are expected to get admitted during the period of data collection. The sampling interval will be 15 (1560/105). Thus, every 15th patient getting admitted with acute lower respiratory infection will be selected for the study.

Study tools & techniques:

Data were collected by face-to-face interview using a pre-designed, pretested and structured schedule that included Respiratory Severity Score (RSS),[21-24] physical examination and laboratory estimation of serum zinc levels. The tool was validated in English, Hindi and the local vernacular with the help of language experts.

Method of data collection:

After receiving approval from the Institutional Ethics Committee (IEC), the process of recruitment of infants for the study was started. Based on previous year's data, it was observed that on an average at least 5 eligible patients get admitted daily. As the total no of data collection days were 312 (52x6), a minimum of 1560 (5x312) patients were expected to get admitted during the period of data collection. Thus, the sampling interval was calculated as 15 (1560/105) and every 15th patient getting admitted with ALRI satisfying the eligibility criteria was selected for the study. Informed written consent was taken from the legally acceptable representative (LAR) prior to data collection. Data related to socio-demographic characteristics, birth and immunization history were collected after admission. The infant was physically examined and his/her respiratory rate, oxygen saturation (SpO2), degree of use of accessory muscles of respiration and presence of wheeze by auscultation were recorded. Based on the observations, the severity of respiratory distress was classified according to the Respiratory Severity Score. Blood samples for serum zinc levels were also collected.

Statistical analysis:

The data were collected, edited, entered in Ms Office Excel 2019 and analyzed by using SPSS version 25.0.

Scoring and interpretation:

Respiratory Severity Score[21-24] depends on respiratory rate, wheeze, SpO2 in room air and accessory respiratory muscle utilisation. Based on the responses each item can be scored between 0 and 3. Thus, the total score can range from 0-12 and higher scores indicate more severe disease. Depending on the total score attained, respiratory distress was categorised as mild (<5) or severe (≥5).[22] Serum zinc values were categorized as normal (>80 μg/dl), mild decline (60-80 μg/dl) and severe decline (<60 μg/dl).[25]

Table 2: Correlation between Socio-demographic Variables (N=176):

The data were represented using appropriate descriptive and inferential statistics. While Pearson's Chi-square test was done to test the association between the dependent and the independent variables, Spearman's correlation coefficient was employed to ascertain the relationship between serum zinc levels and RSS. A p value <0.05 was considered significant.

Ethical considerations:

The IEC approval (CSS/Estt/3096/IEC18/2022, dt.28.11.2022) was sought prior to initiation of the process of data collection. Informed written consent from the parents/LAR was taken after ensuring anonymity and confidentiality of the data provided.

Results:

In this study, 105 participants with a mean age of 7.1±2.7 months were enrolled. The predominant participation in this study were males (64, 61%), and those residing in urban areas (97, 92.4%). Their mothers were mostly homemakers (97, 92.4%) and had attained primary level of education (53, 50.5%).

With respect to birth history, most of the participants were delivered by normal vaginal delivery [NVD] (78,74%), at term (89, 84.8%), with a birth weight of 2.6 - 3.0 kg (43, 41.0%). While 6 (5.7 %) infants had a history of respiratory illness, some of the babies (14, 13.3%) had neonatal jaundice and 12 (11.4%) babies experienced NICU/SNCU stay after birth. Many of them were exclusively breastfed till 6 months of age (93, 88.6%). All the participants were fully immunized and none of them experienced any adverse events after immunization.

Among the study participants, severe respiratory distress was found in 51 (48.6%) of the study population, while the rest had mild distress. Mild decline in zinc levels was found in 37 (35.2%) of the study population. Among the participants with mild decline in serum zinc levels, 22 (54.3%) had severe respiratory distress. [Fig. 1] On Pearson's Chi-square test, mother's occupation was noted to be significantly associated with respiratory severity score ($\chi 2$ 8.173, p=0.042). [Table 1] Birth history was not associated with the severity of respiratory distress on Pearson's Chi-square test. [Table 2] A negative correlation was noted between the RSS and serum zinc levels, but this correlation was not significant (Spearman's ρ -0.149, p 0.129). [Fig. 2]

Table 1: Socio-demographic associates of severity of respiratory distress. (n=105).

Variable	Total number (%)	Mild RSS number (%)	Severe RSS number (%)	Pearson's Chi square	p value
Age (in months)					
2m	7(7)	2(29)	5(71)	6.663	0.247
3-4m	10(9)	5(50)	5(50)		
5-6m	26(25)	14((54)	12(46)		
7-8m	24(23)	15(62)	9(38)		
9-10m	21(20)	7(33)	14(67)		
11-12m	17(16)	11(65)	6(35)		

Gender Male Female	64(61) 41(39)	32(50) 22(54)	32(50 19(46)	0.134	0.714
Residence Urban Rural	97(92) 8(8)	50(52) 4(50)	47(48) 4(50)	0.007	0.933
Mother' Occupation Homemaker Unskilled Semi- skilled Skilled	97(92) 1(1) 5(5) 2(2)	51(53) 1(100) 0(0) 2(100)	46(47) 0(0) 5(5) 0(0)	**8.179**	**0.042**
Mother's Education Less than Primary Primary Secondary Higher Secondary Graduate and above	14(13) 53(51) 27(26) 10(9) 1(1)	8(57) 28(53) 11(41) 7(70) 0(0)	6(43) 25(47) 16(59) 3(30) 1(100)	3.899	0.400

Table 2: Association of birth and postnatal history with severity of respiratory distress. (n=105).

Variable	Total number (%)	Mild RSS number (%)	Severe RSS number (%)	Pearson's Chi square	p value
Type of delivery					
NVD	78(74)	42(54)	36(46)	0.714	0.400
LSCS	27(26)	12(44)	15(56)		
Gestation					
Term	89(85)	48(54)	41(46)	1.466	0.266
Preterm	16(15)	6(37)	10(63)		
Birth weight					
<2kg	7(7)	2(29)	5(71)		
2-2.5kg	42(40)	20(48)	22(52)	4.213	0.378
2.6-3kg	43(41)	24(56)	19(44)		
3-3.5kg	12(11)	8(67)	4(33)		
>3.5kg	1(1)	0(0)	1(100)		
History of SNCU/NICU stay					
Yes	12(11)	3(25)	9(75)	3.788	0.052
No	93(89)	51(55)	42(45)		
Exclusive Breastfeeding					
Yes	93(89)	48(52)	45(48)	0.011	0.916
No	12(11)	6(50)	6(50)		

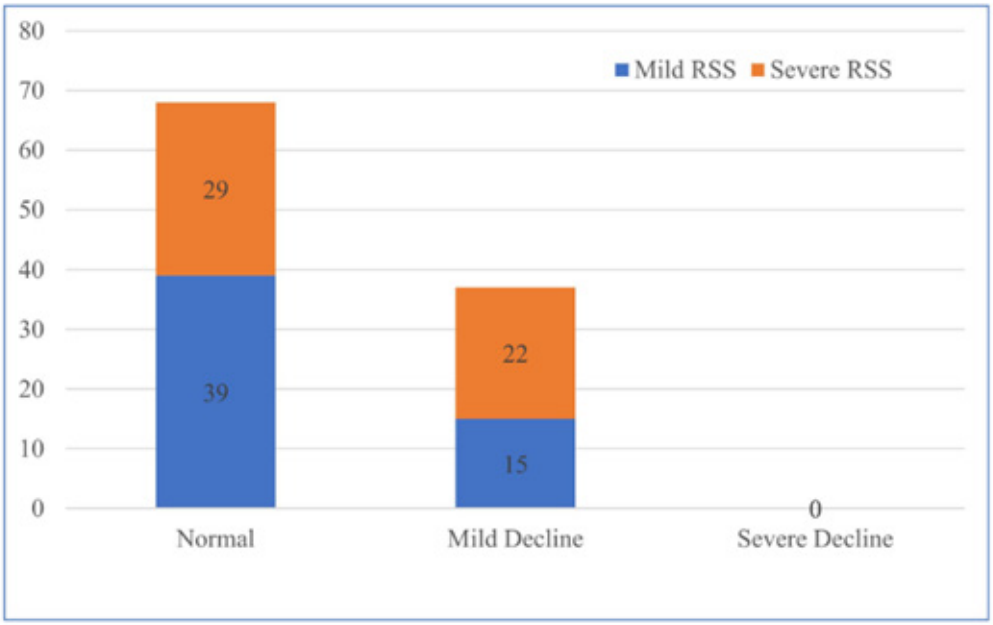


Fig. 1: Distribution of the participants as per their serum zinc levels and severity of respiratory distress. (n=105)

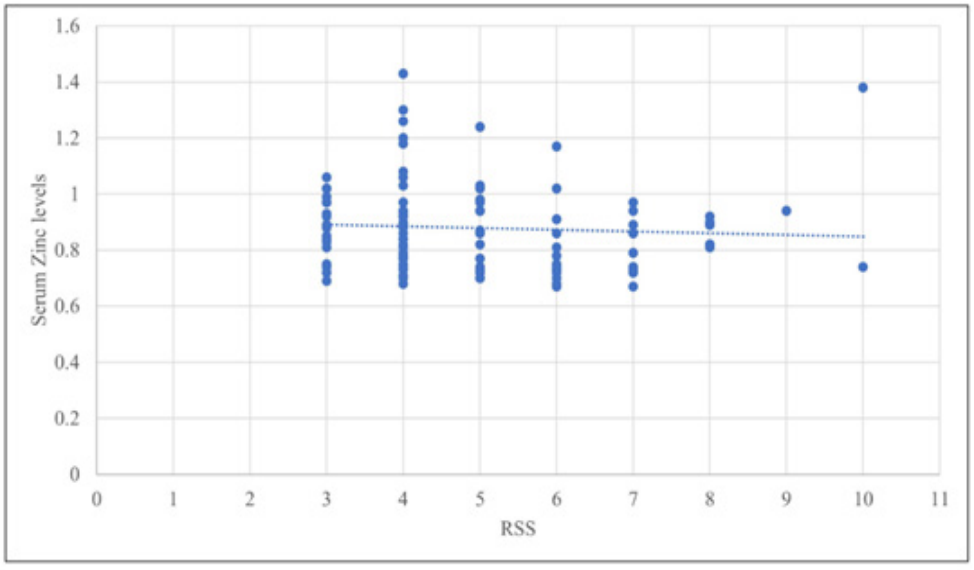


Fig. 2: Scatter plot showing the relation between Serum Zinc levels and RSS. (n=105)

Discussion

Acute lower respiratory infections (ALRI) pose a significant public health challenge.[26] Despite substantial evidence indicating that controlled zinc supplementation can prevent chronic inflammation and other illnesses related to zinc deficiency, and even alleviate symptoms in both humans and animal models, it is still not widely adopted in medical practice, even among high-risk groups.[27,28]

In the current study, participants were aged between 2 and 12 months. Only Mahalanabis et al. [29] had a comparable age range of 2 to 24 months. Ahmed et al. [30] and Saleh et al. [31] included participants aged 6

to 60 months, while other studies[32-33] had participants aged 2 to 59 months. A male predominance was noted across all studies, including the present one, where 61% of participants were male. Kumar et al. [32] also investigated the place of residence, finding a similar urban predominance (62%) to our study (63%). Interestingly, other studies did not consider birth history or immunization status, possibly due to an anticipated lack of association. Given that most studies were conducted outside India, differences in postnatal care and immunization practices might exist. Mahalanabis et al. [29] reported that 90-97% of their participants were exclusively breastfed for six months, a higher percentage than our study's 88.6%. This discrepancy could be due to the different timelines of the studies, as the availability and affordability of breast-milk substitutes have increased in recent years.

In this study, a notable proportion of participants (48.6%) experienced severe respiratory distress, and a mild decline in zinc levels was observed in 35.2% of the cases. Both this research and the studies by Kumar et al.[32], Ibraheem et al.[33], and Mahalanabis et al.29 did not find a connection between maternal education and the severity of respiratory distress in infants with ALRI. Conversely, Ahmed et al.30 found a lower incidence of ALRI in infants whose mothers were educated. Additionally, our study revealed a significant link between the mother's occupation and the severity of respiratory distress ($\chi^2 = 8.173$, $p = 0.042$).

In our study, 54.3% of participants with a mild decline in serum zinc levels developed severe respiratory distress. This aligns with the findings of Ibraheem et al.[33] and Shakur et al.[20], who reported mean serum zinc levels of 18.7 µg/dL and 90 pg/dL, respectively, in ALRI cases. Our research indicated a negative correlation between serum zinc levels and the RSS in ALRI (Spearman's ρ -0.149, p 0.129), suggesting that lower zinc levels are associated with increased severity of respiratory distress. Similar results were observed by Saleh et al.[31] and Kumar et al.[32] Additionally, Mahalanabis et al.[29] demonstrated the benefits of zinc treatment compared to a placebo in ALRI cases. Unlike our study, none of the reviewed articles compared the increasing severity of respiratory distress with decreasing zinc levels using a standard measurement.

Despite revealing several novel findings, the study had some limitations. As a cross-sectional study without a control group, the scores reflect only the participants' current functioning at the time of assessment. Ideally, blood samples for serum zinc should have been collected upon admission when respiratory distress was most severe, but this was not always feasible. Additionally, while early morning

fasting blood samples are preferred for accurate serum zinc estimation, this was not always possible.

Implications for Practice:

This study underscores the crucial role of zinc in managing respiratory distress in infants with ALRI. Mild declines in serum zinc levels are linked to increased respiratory distress, highlighting the need for healthcare providers to consider zinc status in assessment and management. Routine screening for zinc deficiency and zinc supplementation should be incorporated into clinical protocols to alleviate respiratory distress in these infants.

Recommendations for Future Research:

1. Larger multicentric studies can be conducted to validate these findings across diverse populations and settings, ensuring the generalizability of the results.
2. Longitudinal studies can help in understanding the long-term effects of zinc supplementation on respiratory health and overall growth and development in infants.
3. Interventional trials can be helpful in assessing the efficacy of zinc supplementation in reducing the severity of respiratory distress and improving outcomes in infants with ALRI.

Conclusion:

Infants with ALRI often experience severe respiratory distress, and a decline in serum zinc levels is commonly observed in these cases. The severity of respiratory distress is also influenced by the mother's occupation. Zinc deficiency significantly increases the risk of severe respiratory distress in ALRI patients. Thus, addressing zinc deficiency is vital for reducing the severity of Acute Lower Respiratory Infections (ALRI) in infants, ultimately supporting global public health goals by enhancing child survival and health outcomes.

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Ethical Approval:

The IEC approval (CSS/Estt/3096/IEC18/2022, dt.28.11.2022) was sought prior to initiation of the process of data collection.

Conflicts of interest:

The authors report no conflicts of interest in this work.

Informed Consent:

Informed written consent from the par-

ents/LAR was taken after ensuring anonymity and confidentiality of the data provided.

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