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Serum zinc level in pneumonia and its correlation to severity of pneumonia in children

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Abstract

Background: Acute respiratory tract infections are the most common cause of morbidity and deaths in children. Pneumonia is responsible for 18% of under-five mortality as a result of an estimated 151 million new episodes each year occurring mostly in the marginalised and malnourished children in the developing countries who are often zinc-deficient. Low zinc levels not only impairs the immunity but it also enhances the infection along with a reduction in the clearance of infectious agents.

Aim & Objectives: To analyse zinc level in children with pneumonia and to correlate it with severity of pneumonia.

Method: All the children aged 6 months to 5 year admitted to the ward and PICU with pneumonia according to WHO definition were included. A detailed history including age, sex, immunization history, socioeconomic status, chief complain, nutritional history was taken. All the children were subjected to the investigation of serum zinc. Descriptive and analytical statistics were done.

Results: A total of 46 children were included in the study. A statistically significant relation of serum zinc level with severity of pneumonia was found. In pneumonia and severe pneumonia, only 25.0% and 50.0% of the patients respectively had low serum zinc level, while in very severe pneumonia patients 87.5% had low serum zinc levels.

Conclusion: Lower serum zinc levels are significantly associated with pneumonia and the more is the severity of disease, lower is the serum zinc level. Lack of exclusive breastfeeding (54.3%), partial immunization

(62.5%), overcrowding (60.8%) and malnutrition (73.9%) were found to be contributing factor.

Keywords: serum zinc level, pneumonia, severity of pneumonia, children

Introduction

Acute respiratory tract infections are the most common cause of morbidity and deaths in children less than five years of age. They account for 10 to 30% of all childhood deaths and are thus a hindrance to attaining the fourth Millennium Development Goal[1]. The burden of acute lower respiratory tract infections is 2 to 10 times more common in developing than in developed countries[2].

Zinc is an essential trace element, which plays an important role in many important biological functions. These include mucosal barrier function, innate and adaptive immunity, oxidative stress responses and a cofactor for various enzymes [3]. Trace elements, especially zinc is a cornerstone of the antioxidant defence in acute systemic inflammatory response syndrome (SIRS). SIRS is known to be associated with redistribution of zinc to the tissues involved in protein synthesis and immune cell proliferation and this leads to decrease in its serum level [4]. Acquired critical illness stress-induced immune suppression (CRISIS) plays an important role in the development of nosocomial infection and sepsis. CRISIS has been shown to be associated with deficiencies in zinc, selenium, amino acids and hypoprolactinemia [5]. Zinc deficiency has been responsible for up to 4.4% of deaths attributable to infection in developing countries. Various studies from India demonstrated that prevalence of zinc deficiency in apparently healthy children and adolescents ranged from 44% to 72% [6]. Acute respiratory infection (ARI) is a leading cause of morbidity and mortality among young children in low- and middle-income countries especially pneumonia with approximately 81% of pneumonia deaths occur during the first 2 years of life [7]. Also, pneumonia is responsible for 18% of under-five mortality as a result of an estimated 151 million new episodes each year occurring mostly in the marginalised and malnourished children in the developing countries who are often zinc-deficient [8]

The present study was conducted to analyse zinc level in children with pneumonia and to correlate zinc level with severity of pneumonia. This study might throw a light on need for prophylactic zinc supplementation in under five children. This study will provide base line data and could aid in formulation of guidelines for zinc supplementation as a part of management of pneumonia.

Methodology:

This prospective analytical hospital based study was conducted in the Department of Paediatrics, D. Y. Patil Hospital, Nerul, Navi Mumbai. Informed consent was taken from parents or guardians of the children who satisfy the inclusion criteria. An information sheet was given to all the parents or guardians of the participating patients. The research procedure followed was in accordance with the approved ethical standards of the institution.

All the children aged 2 months to 5 year admitted to the ward and PICU with complain of fever, cough, rapid breathing and /or radiological evidence of opacity in chest were included in the study. Those children who were on zinc supplementation or received zinc supplements within last 3 month were excluded. Those patients who had congenital malformation of lung, congestive cardiac failure, metabolic acidosis, neurogenic hyperventilation, non-infective pneumonia (aspiration pneumonia, chemical pneumonia, persistent

pneumonia) or with coexisting illness / chronically ill patients were also excluded.

This study was conducted with a detailed history including age, sex, immunization history, socioeconomic status, chief complain, nutritional history. Complete physical examination of the child was performed and anthropology findings were recorded in a predesigned performa. The diagnosed children were categorized according to severity as pneumonia. Venous blood samples were obtained from each subject and transferred to normal tubes. Serum was obtained by centrifugation of blood samples taken without anticoagulant and stored at 20°C until analysis date. All chemicals and reagents used in this study were of analytical grade. All the children were subjected to the investigation of serum zinc measured by Inductively Coupled Plasma Mass Spectrometry method. The normal serum zinc level was considered 54-151 µg/dl.

Statistical Analysis

Descriptive and analytical statistics were done using SPSS (Statistical Package for Social Sciences) Version 24.0 for Mac (IBM Corporation, Chicago, USA). The data is represented in number and percentages and mean with standard deviation. The chi-square test with fishers exact test was used to understand relations between categorical data. The level of significance was kept at $p<0.05$.

Results

A total of 46 children were included in the study. There were 27 males and 19 female children with mean age of 25.45 months. (Table 1) There were 21 (45.5%) children with a history of low birth weight. Over-crowing was present in 28 (60.8%) the study subjects. Only 5 (10.9%) children were given additional immunization, 8 (17.4%) had primary immunization and more than two-third of the study population 31(69.5%) were partially immunized and 1 (2.17%) child was un-immunized. Exclusive breast feeding was present in 21 (45.7%) children. (Table 2) The general physical examination showed that around three fourth of children (73.95%) had protein energy malnutrition. Eighteen children (39.1%) had severe pneumonia and 8 (17.4%) had very severe pneumonia .Twenty-one children (45.7%) had low serum zinc level.

Table 1: Demographic details of the study population (n=46)

Age (Months)	Mean	S.D.	RANGE
	25.45	17.90	6-60
Sex	n	Percentage	
Male	27	58.7%	
Female	19	41.3%	

Table 2: Birth history, over-crowding, immunization, Exclusive Breast Feeding and General Physical Examination of the study population (n=46)

Variables	N	Percentage
Birth history		
Low birth weight	21	45.7
Normal	25	54.3
Overcrowding		
Present	28	60.8
Absent	18	39.1
Immunization		
Primary Immunization	8	17..4
Additional Immunization	5	10.9
Partially immunized	32	69.5
Un-immunized	1	2.17
Exclusive breast feeding		
Exclusively breastfeed	21	45.7
Not exclusively breastfeed	25	54.3

Protein energy malnutrition		
Present	34	73.9
Absent	12	26.1

The correlation of serum zinc level with severity of pneumonia was analysed. The chi-square test showed statistically significant (**p=0.010**) relation of serum zinc level with severity of pneumonia. In pneumonia patients, only 25.0% of the patients had low serum zinc level, while in severe pneumonia 50.0% patients had low serum zinc level. In very severe pneumonia patients 87.5% had low serum zinc levels. This signifies a strong relation between serum zinc level with severity of pneumonia. (Table 3).

Table 3: Correlation of serum zinc level with severity of pneumonia

Type of Pneumonia		Zinc	
		Low	Normal
Pneumonia	n	5	15
	%	25.0%	75.0%
Severe Pneumonia	n	9	9
	%	50.0%	50.0%
Very Severe Pneumonia	n	7	1
	%	87.5%	12.5%

$x^2 = 9.222$; $P = 0.010$

Discussion

Zinc plays an important role in maintaining a normal immune function and participates in all major biochemical pathways. It plays multiple roles in the perpetuation of genetic material and cellular division. Studies have suggested that zinc deficiency impairs immunocompetence with reduced cell-mediated immune responses, decreased T-lymphocytes, abnormal T-helper and/or suppressor functions, impaired macrophage function, reduced killer cells and antibody dependent cytotoxicity[9,10]. Children who are living in low-income settings are often undernourished and zinc deficient. Zinc deficient children are at increased risk of restricted growth and developing diarrheal diseases, as well as respiratory tract infections such as acute lower respiratory tract infections. Diarrheal disorders and acute lower respiratory tract infections, especially pneumonia are the two most common causes of infant and child death in low-income countries. Undernutrition is considered the underlying cause of approximately half of these fatal acute lower respiratory tract infections. Pneumonia alone kills more children each year than AIDS, malaria or measles combined, with over two million deaths per year. Some research studies have suggested that zinc supplementation may reduce the number of episodes and severity of bronchiolitis and pneumonia cases in children [11].The present study was conducted to study blood zinc levels in children with community acquired pneumonia and to find the relationship between the serum zinc level and severe pneumonia.

A total of 46 subjects aged 6 to 60 months fulfilling the inclusion criteria were taken and the mean age of our patients was 25.45 ± 17.90 months. This was similar to a study done by Rady HI et[11].The age of the studied participants was higher than that found in studies undertaken by Valentiner-Branth et al[12], Basnet et al[13], Srinivasan et al[14], and lower than that reported by Shah et al[15]. This difference in mean age may be due to the wide variation in the causative organisms that led to pneumonia.

We observed that male patients were affected by pneumonia more than females which delineate our cultural preference and concern regarding male gender. This male predominance was also recorded by other studies of pneumonia [11,13,14,16].

In this study, 25%, 50%, 87.5% of patient with pneumonia, sever pneumonia and very severe pneumonia respectively had low serum zinc level. This signifies a strong negative correlation between serum zinc levels with severity of pneumonia. This was similar to results found by Shakur et al [16] and Kumar et al [17]. In India, Kumar et al [17] reported blood levels of zinc measured in 50 patients aged 2-5 years, which had been hospitalized due to pneumonia and measured amount of plasma zinc was found to be statistically and significantly lower in patients with pneumonia compared to the control cases. On the other hand, two other studies concluded that serum zinc levels were not significantly different in children having acute lower respiratory infection from those serum levels of healthy controls [18,19].

This study showed that in severe pneumonia more children were there with low level of serum zinc. Other studies demonstrated that these findings might be reduced by improving the serum zinc level of patients with pneumonia infection, which posed a serious problem in our country and in other developing countries [20,21]. Rate of children died of pneumonia ranked 1st in developing countries and in India may be due to numerous reasons such as low socioeconomic status, nutritional deficiency and increasing population and poor family planning. Zinc deficiency, which is a serious problem in our country, should be prevented by improving immunity through nutrition rich in zinc (rich in proteins but poor in carbohydrates) or external zinc fortifications.

A range of supplementation doses have also been assessed, from 15 mg to 140 mg per week, with the upper range exceeding the recommended daily intake (RDI) for children of 2 mg per day for children less than one year of age and up to 7 mg per day for children between 1 to 3 years . It is important to better understand optimal supplementation doses, especially because high dosages of zinc and long-term supplementation have been shown to be associated with the inhibition of absorption of other nutrients such as copper and iron as well as poorer survival rates for children with HIV. Dietary impacts on micronutrient absorption should also be considered, as it has been suggested that the bioavailability of zinc is greater in more refined urban diets. In addition, supplementation is not the only route to decrease nutrient deficiencies that may make children more susceptible to infection. Decreasing the consumption of absorption-inhibiting foods, dietary diversification and food fortification should also be investigated as possible alternatives [22].

A number of authors have confirmed that routine zinc supplementation for more than three months does have a positive effect on reducing the duration of acute lower respiratory tract infections among children in developing countries. These effects observed could translate into major absolute reductions in childhood morbidity and mortality rates given the numbers of children who die from acute lower respiratory tract infections every year [22]. It remains important to better understand how zinc may also work in conjunction with antibiotics in the treatment of children with severe acute lower respiratory tract infections and to reduce the number of child deaths due to pneumonia.

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