Vol 7| Issue 2| 2017 | 53-56.

e-ISSN 2248 – 9142
print-ISSN 2248 – 9134

International Journal of
Current Pharmaceutical & Clinical Research

www.ijcpcr.com

# A CASE CONTROL STUDY ON ROLE OF ZINC LEVELS IN ACUTE LOWER RESPIRATORY INFECTIONS

**Param joythi GE[1*] and Anki Reddy K[2]**

[1]Associate Professor, Department of Pediatrics, Government Medical College/G.G.H, Mahaboob Nagar, Telangana, India.
[2]Associate Professor, Department of Pediatrics, Narayana Medical College, Nellore-524001, Andhra Pradesh, India.

**ABSTRACT**

A case control study was conducted in a referral and teaching hospital in North India on children aged 6 months to 4 years, to compare blood zinc levels in 75 cases of severe pneumonia and 75 age, sex and nutritional status matched controls. In logistic regression model severe pneumonia was associated with lower blood zinc level, use of biomass fuel and isolation of H. Influenza from nasopharyngeal swab. Pediatric respiratory disease remains an important cause of morbidity in both the developing and the developed world. It has become the most common reason parents cite for taking their children to see the general practitioner, and nutritional factors are a major reason for ALRI. Objective: Acute respiratory infection is a leading cause of morbidity and mortality in fewer than five children worldwide especially in developing countries. Hence, the present study was undertaken to identify the serum zinc level in children's hospitalized with acute lower respiratory tract infections (ALRI) in children aged 6 months to 4 years. Methods: 75 cases fulfilling WHO criteria for pneumonia, in the age group 6 months to 4 yr were interrogated for potential nutritional risk factors as per a predesigned proforma and serum zinc level was measured. 75 healthy control children in the same age group were also interrogated and zinc level measured. Results: Significant low serum zinc level (p value <0.05 in all) were identified. Socio demographic factors like low socioeconomic status and partial immunized status were found to be significant. Conclusion: The present study has identified low levels of zinc in ALRI children's and we focus on role of zinc in the treatment of pneumonia.

**Key words:** Micro nutrients, Zinc, Respiratory infections, Nutritional factors.

## INTRODUCTION

Zinc is an essential trace element important for almost all biological systems. Zinc is a vital micronutrient in humans and is essential for protein synthesis, cell growth, and differentiation and thus is important for functioning of the immune system [1]. Zinc nutritive is likely to be suboptimal in many children of developing countries and may contribute to their impaired growth, increased susceptibility to infections and possibly to the high mortality. A large proportion of childhood deaths in developing countries are caused by diarrhea and pneumonia. Impaired zinc nutritive seems to play a role in the increased incidence and severity of these infections [2]. Strong evidence for a causal relationship between zinc deficiency and childhood infections has come from randomized controlled trials of zinc supplementation [3].

Acute respiratory infections (ARIs) especially acute lower respiratory infections (ALRIs), are among the leading causes of death in children under the age of 5 years [4-6]. Zinc deficiency is projected to be responsible for 118,000 thousand deaths in children less than 5 years in developing countries [7]. Recent trials and meta analyses have demonstrated that zinc supplementation both therapeutic and prophylactic reduces the duration, severity and incidence of ARIs [8, 9]. Most of environmental risk factors require multispectral coordination for modification. In contrast, some of the childhood risk factors can be

Corresponding Author :- **Param joythi G.E.** Email:- drgeparamj9@gmail.com

modified by simple interventions like vitamin A or zinc supplementation. Recent works have provided conflicting [9, 10, 11] evidence on the role of zinc against ALRI. The study hypothesis was that there is no difference in blood zinc levels in cases of severe pneumonia as compared to controls.

The primary objective of this study was to compare blood zinc levels in cases of severe pneumonia with age, sex and nutritional status matched controls was taken. Secondary objectives were to assess antimicrobial resistance in nasopharyngeal isolates of *S. pneumoniae* and *H. influenzae* and to assess the association of use of biomass fuels with severe pneumonia.

## SUBJECT AND METHODS

### Study design

This was a hospital based case control study conducted in Department of Pediatrics, S.V. Medical College Tirupathi, India between August 2014 to May 2015. Included were children between ages of 6 months to 4 years, admitted in the indoor pediatric ward and satisfying the World Health Organization (WHO) case definition of severe pneumonia [14, 15]. Healthy children attending pediatric outdoor for immunization were controls. Informed and written consent of the parents of cases and controls were taken. Excluded were children less than 6 months or more than 4 years, with an associated clinical diagnosis of diarrhea, allergic diseases or asthma, or known zinc supplementation and documented parenteral antibiotic intake prior to indoor admission for current illness (16).

### Sample size

72 cases of severe pneumonia and 75 sex, age and nutritional status matched controls were taken. Age was matched within 6 months. For matching nutritional status weight for height "Z" score were used. This sample size was adequate to assess a difference of 100 µg/dL in mean of blood zinc level in cases and controls with a power of 0.8 and an alpha error of 0.05 with a standard deviation.

### Variables for data collection and definitions

Data was collected on age, sex, anthropometry, family characteristics, environ-mental exposures and immunization status. Patients were examined clinically. In cases, data on investigations ordered by the treating physician was abstracted. Record of the treatment given and outcome of the disease was also maintained.

### Zinc estimation

For this 2 mL of whole blood was collected using 22 gauge steel needle in preheparized Eppendoff's tube through Venepuncture using aseptic precautions. Samples were stored at –20ºC, 1 mL of blood was mixed with 5 mL of deionized water, glass beads and 2 mL of 1:1 mixture of concentrated HN03 and HCIO. Samples were digested at 120-150ºC in a fuming chamber over hot plate for approximately 2 hours, until a clear solution was obtained which was re-diluted to 5 mL with de-ionized water(20). A sample blank was always prepared with each set of samples in order to control for possible contamination by external zinc. Estimation of zinc levels was done by atomic abosorption spectrophotometry (20).

## RESULTS

There were 75 cases, each of severe pneumonia and age, sex and nutritional status matched controls. Seventy four percent of cases and controls were 12 months of age and 26% in each group were between 12 months to 4 years. There were 75% males in cases and controls. Among cases and controls 78% were adequately nourished while 38% were malnourished. Mean weight was 5.08 kg ± 2.54 and 5.19 kg ± 2.15 in cases and controls, respectively ($p = 0.73$). Mean height was 64.14 cm ± 11.43 and 66.6 cm ± 7.33 in cases and controls, respectively ($p = 0.22$). Use of biomass fuels emerged as a significant risk factor (Odd's ratio = 1.67; 95% CI: 2.19 - 4.95, $p = 0.057$) for cases of severe pneumonia. Immunization status, family type, availability of separate cooking space, maternal education and smoking status of father was not significantly associated with case control status (*Table I*).

Fever and difficulty in breathing (*pasli chalna)* were the most common complaints found in 76% and 95% of cases respectively. All cases had intercostals retractions and increased respiratory rate. Mean respiratory rate, in cases, was 83.32 ± 16.38 per minute (range 70-190). 10% had cyanosis. While duration of symptoms among cases from ruralareas was more by 2-3 days when compared to those from urban areas, the differences were not statistically significant (data not was not showed). Mean blood zinc levels among cases and controls by place of residence and nutritional status is given in *Table II*.

**Table 1. Blood Zinc levels**

| Blood Zinc levels | Cases | | Control | | |
|---|---|---|---|---|---|
| | N0 | Mean Value | No | Mean value | P value |
| Overall | 75 | 246±215.63 | 75 | 529± 238.0 | 0.0002 |
| Urban subjects | 32 | 237±149.77 | 45 | 411±313.35 | 0.17 |
| Rural subjects | 24 | 256± 151.06 | 20 | 302±242.25 | 0.0001 |
| Malnourished subjects | 24 | 302± 176.03 | 29 | 258±174.67 | 0.02 |
| Adequately nourished subjects | 51 | 405± 256.03 | 46 | 571±232.69 | 0.06 |

**Table 2. Family characteristics and Environmental conditions of Cases and controls**

| Characteristics | Cases(N=75) | | Control (N=75) | | Odd ratio | P value |
|---|---|---|---|---|---|---|
| | N0 | % Cases | NO | % Cases | | |
| Un immunized | 75 | 22 | 15 | 15 | 1.48 | 0.40 |
| Urban Subjects | 61 | 61 | 75 | 75 | 0.69 | 0.4 |
| Joint Family | 61 | 61 | 40 | 40 | 0.43 | 0.39 |
| Separate cooking space | 40 | 40 | 35 | 35 | 1.10 | 0.78 |
| Biomas fuel | 64 | 64 | 30 | 30 | 1.57 | 0.037 |
| Mother uneducated | 40 | 40 | 30 | 30 | 1.5 | 0.57 |
| Father nonsmoking | 80 | 80 | 75 | 75 | 1.58 | 0.64 |

## DISCUSSION

Childhood pneumonia clearly represents one of the most common infective illnesses in developing countries and is of great importance as a cause of preventable mortality in children. To attack this global problem, WHO shaped strategy for early diagnosis and effective case management that had remarkable impact on mortality due to childhood pneumonia in developing countries. Even after these measures the burden caused by childhood pneumonia in terms of both mortality and morbidity is very high. It is necessary to identify other causes which contribute to the severity of pneumonia. Influence of demographic, socioeconomic and nutritional factors has been a matter of debate for quite few years. Among the nutritional factors, vitamin A deficiency, anemia, rickets, and zinc level is considered important.

In the present study, we found lower blood zinc level of cases when compared to age, sex and nutritional status matched controls. One explanation for lower zinc level in severe pneumonia can be pre-existing zinc deficiency, making the child susceptible to pneumonia due to impaired immunity [10]. In addition, respiratory tract infections are also known to result in lower zinc levels [14, 15]. A decline in plasma zinc concentration has been reported after a broad range of febrile illnesses [10]. It has also been suggested that lowered zinc level is mediated by interleukins and tumor necrosis factor alpha (TNFa) and is a part of predictable set of metabolic reactions to infection or tissue injury known as acute phase reaction [12]. Use of biomass fuels (coal, wood, dung and kerosene) was significantly associated with severe pneumonia. (Tables I & II). Previous studies have also associated use of biomass fuels with respiratory tract infections [11, 12]. This was a hospital based case-control study. We have not used radiological confirmation as an inclusion criteria for cases as this has not been recommended by the WHO and national ARI control programs. We did not perform blood or lung aspirate cultures to confirm invasive bacterial isolates [17]. We conclude that cases of severe pneumonia have a significantly lower blood zinc level as compared to age, sex and nutritional status matched controls. Role of zinc in the treatment of severe pneumonia should be investigated. Use of biomass fuels must be phased out. Incorporation of vaccination against *H. influenzae* in national ARI program can be considered (17,18). Since a high resistance to cotrimoxazole has been found in *S. pneumoniae* and *H. influenzae* in the present study, a surveillance system should be instituted to monitor changes in antimicrobial resistance with time and the pattern of bacterial isolates from the community [19, 20].

## CONCLUSION

The present study identified many nutritional risk factors for ALRI. The significant nutritional risk factors were malnutrition, anemia and low serum zinc level. Socio demographic factors like partial immunization status and SES which were taken into study didn't have any significant association with ALRI. The interesting fact is nutritional factors which were found to be significant in this study are actually either preventable or curable. The above risk factors should be tackled with effective health education of the community and appropriate initiatives should be taken by the government which can lead to a healthy community and a healthy nation as a whole. Limitations of the study should be considered while interpreting the results. The total number of cases taken for the study, i.e. which satisfied the WHO criteria for ALRI is less compared to the incidence of ALRI. Moreover zinc values were estimated only at the time of admission. A follow up estimation of zinc level at the time of discharge or after 2 weeks of infection would have given more detailed results. A randomized controlled trial study with zinc supplementation would have been an ideal study method.

## REFERENCES

1. Biesel WR. Single nutrient and immunity. *Am J Clin Nutr*, 35, 1982, 417-68.
2. Black RE. Zinc deficiency, immune function, and morbidity and mortality from infectious disease among children in developing countries. *Food Nutr Bull*, 22, 2001, 155-62.
3. Baqui AH, Black RE, Walker CLF, Shams A, Yunus M. Effect of zinc supplementation started during diarrhoea on morbidity and mortality in Bangladeshi children: community randomized trial. *BMJ*. 325, 2002, 1059-65.

4. Brian G. Global action plan for prevention and control of pneumonia (GAPP). *Bull World Health Organ*, 86, 2008, 322.
5. Walker CF, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, *et al*. Global burden of childhood pneumonia and diarrhoea. *Lancet*, 381, 2013, 1405-16.
6. Roth DE, Caulfield LE, Ezzati M, Balck RE. Acute lower respiratory infections in childhood: Opportunities for reducing the global burden through nutritional interventions. *Bull World Health Organ*, 86, 2008, 356-64.
7. Rahman MM, Vermund SH, Wahed MA, Fuchs GJ, Baqui/AH, Alvarez JO. Simultaneous zinc and vitamin A supplementation in Bangladeshi children: randomized double blind controlled trial. *BMJ*, 323, 2001, 314-8.
8. Mahalanabis D, Lahiri M, Paul D, et al. Randomized, double-blind, placebo-controlled clinical trial of the efficacy of treatment with zinc or vitamin A in infants and young children with severe acute lower respiratory infection. *Am J ClinNutr*, 79, 2004, 4306.
9. Bose A, Coles CL, Gunavathi, et al. Efficacy of zinc in the treatment of severe pneumonia in hospitalized children 2 y old. *Am J ClinNutr*. 83, 2006, 1089 —96.
10. Sazawal S, Black RE, Bhan MK, Jalla S, Sinha A. Majumdar. Zinc supplementation reduces the incidence of acute lower respiratory tract infections in infants and preschool children. *Pediatrics* 102, 1998, 1-5.
11. Bahl R, Bhandari N, Hambridge KM, Bhan MK. Plasma zinc as a predictor of diarrheal and respiratory morbidity in children in urban slum setting. *Am J Clin Nut*, 68, 1998, 414-417.
12. Aggarwal R, Sentz J, Miller MA. Role of zinc administration in prevention of childhood diarrhoea and respiratory illnesses: A meta-analysis. *Paediatrics*, 119, 2007, 1120-30.
13. Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C.Estimates of world-wide distribution of child deaths from acute respiratory infections. *Lancet Infect Dis* , 2, 2002, 25-32.
14. Scott JA, Brooks WA, Peiris JS, Holtzman D, Mulhollan EK. Pneumonia research to reduce childhood mortality in the developing world. *J Clin Invest*, 118, 2008, 1291-300.
15. Behrman S. Epidemiology of acute respiratory infection in children of developing countries. *Rev Infect Dis*, (Suppl 6), 1991,S454-S462.
16. Broor S, Pandey RM, Ghosh M, Maitreyi RS, Lodha R, Singhal T, *et al*. Risk factors for severe acute lower respiratory tract infections in Under Five Children. *Indian Pediatr*, 38, 2001, 1361-1969.
17. Smith KR, Sarnet JM, Romieu I, Bruce N. Indoor air pollution in developing countries and acute lower respiratory infection in children. *Thorax*, 55, 2000, 518-532.
18. Awasthi S, Glick HA, Fletcher RH. Effect of cooking fuels on respiratory diseases in preschool children in Lucknow, India. *Am J Trop Med Hyg*, 55, 1996, 48-51.
19. Perkin Elmer Manual. Analysis of tissues determination of zinc. *In:*Analytical methods for atomic absorption spectrophotometry. Perkin-Elmer; Connecticut, USA, 1976, pp 260.
20. O'Brien KL, Bronsdon MA, Dagan R, yagupsky P, Janco J, Elliott J, *et al*. Evaluation of a medium(STGG) for transport and optimal recovery of *Streptococcus pneumoniae* from nasopharyngeal secretions collected during field studies. *J Clin Microbiol*, 39, 2001, 10211024.