## Original Article
# Serum zinc levels in children of 0-24 months diagnosed with pneumonia admitted to our clinic

Seçil Arıca[1], Vefik Arıca[2], Hüseyin Dag[3], Ayşen Kaya[4], Sami Hatipoglu[5], Aysen Fenercioglu[6], Güner Karatekin[7]

[1]Mustafa Kemal University Medical Faculty, Family Medicine Department, Asisst Proff.Dr, Hatay-Turkey; [2]Mustafa Kemal University Medical Faculty, Pediatric Clinic, Asisst Proff Dr, Hatay-Turkey; [3]Okmeydani Training and Research Hospital, Pediatric Clinic, MD, İstanbul,Turkey; [4]Istanbul University Institutes of Cardiology, Biochemistry Department, İstanbul, Turkey; [5]Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Pediatric Clinic, MD, İstanbul,Turkey; [6]Yeditepe University Medical Faculty, Family Medicine Department, Asisst Proff.Dr, İstanbul-Turkey; [7]Zeynep Kamil Training and Research Hospital, Pediatric Clinic, Asossicate Proff Dr, İstanbul, Turkey.

**Abstract:** Aim: We have planned to study the relationship between zinc (Zn) plasma levels, as well as pneumonia criteria, and zinc in healthy children younger than 2 years of age compared to pediatric patients diagnosed with pneumonia and admitted to a hospital. Materials and methods: The study enrolled 25 patients of 0-24 months referring to our hospital's pediatric clinic, who were then diagnosed with bronchopneumonia based on the World Health Organization diagnostic criteria and admitted to suckling children clinic due to inability to receive out-patient treatment, and 10 healthy children of the same age group, whose physical examinations revealed no pathological findings. Results: There was no difference between the groups in terms of age and gender distribution (p> 0.05). The control group included in the study showed a significantly higher mean duration of breast milk intake compared to the patient groups (p<0.001). WBC values obtained from the patient group was significantly higher than that of the control group (p<0.001). Zn and iron (Fe) values as determined in the control group enrolled in the study were significantly higher compared to the patient group (p<0.01). Mean total protein in the control group was found to be significantly higher versus that of the patient groups (p<0.05). With regard to the r values of correlation coefficients of the subjects enrolled in the study, a slightly positive correlation was observed between Zn levels and iron levels (r=0.457). Conclusion: It was concluded that infections, particularly pneumonia, which present a serious issue both in our country and developing countries, may be developed more commonly among children with zinc deficiency.

**Keywords:** Breast milk, zinc, pneumonia

## Introduction

Pursuant to data published by World Health Organization, 10.5 million children under the age of 2 across the world lose their lives due to preventable and curable 5 diseases every year. Respiratory tract infections are responsible for 28% of all these deaths [1, 2]. In child ages, 23% of the patients receiving outpatient treatment and 29-38% of the patients hospitalized have been diagnosed with pneumonia [2, 3]. In our country, in conformity with data published by the Ministry of Health, pneumonia is held responsible of the reason for death of 48.4% of infants aged 0-1 and of 42.1% of infants aged 1 -4 [4–6].

Zinc is included in the structure of the essential proteins and functions in the active domains of enzymes. Even a mild and moderate deficiency of Zinc impairs the function of the immune system, thus resistance against the infections is reduced and T-lymphocytes could not exhibit sufficient effectiveness.

In a study conducted with ODTU under the guidance of Ankara University, the amount of Zinc intake received by 5 out of 6 children has been found to be below the recommended amount [7]. Analyses of plants and soils give rise to thought of very low level of Zn being included in the soils and plants in Turkey and of our insufficient intake of Zn by the foods we have been

receiving. There are no adequate number of studies conducted in our country that investigate the relationship between zinc and pneumonia. Yet, no sufficient numbers of studies have been conducted in our country related to the adjuvant administration of zinc in the treatment of pneumonia. In our study, zinc will not be administered to the patients with pneumonia, but if their level of zinc is found low, this finding will guide us in performing a supportive treatment in further studies. This study is conducted with intent to investigate the relationship between pneumonia and Zn and to discuss the role of zinc in the treatment of pneumonia and the importance with regard to the preventive medicine.

## Materials and methods

Our study was a case-control study and 25 patients aged between 0-24 months were enrolled, who had applied to the Polyclinic of Pediatrics, diagnosed with Bronchopneumonia and found to be suitable for being hospitalized in the clinic without receiving an outpatient treatment.

Bronchopneumonia diagnosis was established according to anamnesis and physical examination, AP chest x-ray and laboratory results, and diagnostic criteria of WHO and pneumonia criteria of WHO were questioned and recorded daily. Control group consisted of 10 healthy children with no pathological findings having been recorded in their physical examinations and being within the same range of age. Besides carrying out routine examinations for the patients included in the study as they were hospitalized in the clinic, having obtained 2 ml of citrated blood from the healthy children for the study, these were separated from the plasma as soon as possible and kept in glass tubes at 70ºC until the beginning of the study. Quantitative determination of zinc was performed by WAKO Zn test applying colorimetric method.

Study project was approved by the Ethical Committee of Dr. Sadi Konuk Training and Research Hospital. Data obtained from the study were studied using SPSS 11.0 statistical program. Anova and Tukey's b and Kruskal Wallis, Student's t, Mann Whitney U, Fisher Exact and Chi-square tests were used in the comparison of data, whereas Pearson correlation test was performed in the correlation calculation. In the statistical evaluation, p value < 0.05 was accepted as significant. Correlation analyses were performed by Pearson test.

## Results

Twenty-five diseased (10 female, 15 male) and 10 healthy (10 female, 15 male) suckling infants were included in the study (p > 0.05). Mean age of the study group was (month: 6.340±4.498, mean ± SD) and (age-month: 6.050±0.599, mean ± SD) for the control group and there was no statistically significant difference between groups (p > 0.05, **Table 1**).

No statistically significant difference was found between the study and control groups regarding the gestational week at delivery and birth weight (p > 0.05), but weight of the patient group at hospitalization was statistically lower compared to the control group (p < 0.05). However, no significant difference was recorded between both groups with regard to the head circumference (p: 0.060). No statistically significant difference was noted among the groups regarding the number of siblings and consanguinity (p > 0.05). There was a significant difference between the pneumonia group (3.06 ± 1.9 months) and control group (4.35 ± 0.82 months) only with respect to period of lactation (p < 0.001). Fully vaccinated children rate and application rate of Devit-3 in the patient group were found to be significantly lower compared to the control group (p < 0.01 and p < 0.001, respectively). Features of the cases are shown in **Table 1**.

No statistically significant difference was observed between groups regarding consanguinity (p > 0.05). As is seen, educational background of the mothers and fathers in the study group was statistically lower compared to the control group (p < 0.01; p < 0.05, respectively). 6 (24%) of the mothers and 19 (76%) of the fathers in study group and 1 (10%) of the mothers and 4 (40%) of the fathers in control group were smoking. No significant difference could be found between the pneumonia group and control group with regard to rent status of apartments and social security (p > 0.05). Features of the cases are shown in **Table 1**.

Twenty-one (84%) of the cases included in our study defined the pneumonia case as a first attack, 3 (12%) of those as a second attack and 1 (4%) of those as a third attack. Among the

**Table 1.** Features of the patient and control groups

| | Pneumonia group | Control group | p |
|---|---|---|---|
| Age (months): (mean ± SD) | 6,3±4,5 | 6,0±0,6 | 0,840 |
| Weight at Hospitalization (g) (mean ± SD) | 6341,7±1724,8 | 7824,0±440,2 | 0,009* |
| Gender ( n; % ) | | | |
|     Female | 10 ( 40) | 5 ( 50 ) | |
|     Male | 15 ( 60 ) | 5 ( 50 ) | 0.273 |
| Birth Weight g (mean± SD) | 2775,60±726,70 | 3106,00±212,40 | 0,599 |
| Gestational Week at Delivery | 37,84±3,16 | 39,40±1.71 | 440,18 |
| DEVIT-3: | | | |
|     Yes | 11 ( 44,0 ) | 10,0 (100 ) | |
|     No | 14 (56,0) | | 0,000* |
| Iron | | | |
|     Yes | 4 (16.0) | 3 (30) | |
|     No | 21 (84.0) | 7 (70) | 0,000* |
| Breast milk only ± months (mean±SD) | 3,06±1.94 | 4,35±0 .82 | 0,001* |
| Educational Background of Mother (years) (mean±SD) | 2,68±3.34 | 6,80±2.53 | 0,007* |
| Educational Background of Father (years) (mean±SD) | 5,48±2.71 | 7,50±3.63 | 0,044* |
| Consanguinity (n; %) | 9 (36) | 1 (10) | 0.272 |
|     Available | 16 (64) | 9 (90) | |
|     N/A | | | |
| Smoking in Mother (n; %) | 6 (24) | 1 (10) | |
|     Yes | 19 (76) | 9 (90) | |
|     No | | | |
| Smoking in Father (n; %) | | | |
|     Yes | 19 (76) | 4 (40) | |
|     No | 6 (24) | 6 (60) | |
| | | 0,123 | |

*$p < 0.05$ then it is statistically significant

findings of Physical Examination recorded in our case group, 25 (100%) of cases had cough, 21 (84%) of those wheezing, 25 (100%) of those shortness of breath, 7 (28%) of those nasal flow, 20 (80%) of those nasal congestion, 2 (2%) of those bruising, 25 (100%) of those groaning, 25 (100%) of those withdrawal, 23 (92%) of those fever, 25 (100%) of those crepitation, and 12 (48%) of those had expiration length. Mean length of stay in the hospital was 9.12±1.72 days in our case group. Groaning continued for 4.36±1.04 days, whereas withdrawal continued 3.24±1.20 days in average in the patients.

Blood count and some biochemical values of our cases are given in **Table 2** and **3**. As is seen, mean Hematocrit (Htc) and Mean Corpuscular Volume (MCV) values in the control group were significantly higher compared to the patient group, whereas values for White Blood Cells (WBC) were found significantly lower ($p < 0.001$).

Mean values of total protein and iron (Fe) in the control group were recorded to be significantly higher when compared to the pneumonia group ($p < 0.05$, $p < 0.01$, respectively; **Table 3**). However, no statistically significant difference was observed among the groups regarding glucose, urea, ALT, AST, Ca, Na, and K values, which were not shown in the table ($p > 0.05$). Zn and Fe values of the control group included in our study were found significantly higher compared to the patient group ($p < 0.01$; **Table 3**).

Considering r values of correlation coefficients of the cases included in our study, a weak positive correlation was recorded between levels of Zn and Fe (r=0.457; **Table 4**).

**Table 2.** Blood count values of our cases

|  | Pneumonia group | Control group | p |
|---|---|---|---|
| HB(gr/dl) | 10,868±1,453 | 11,890±0,70 | 0,051 |
| HTC(%) | 31,24± 3.05 | 35,70±1,896 | 0,000* |
| WBC(10³/ul) | 18258,80±9991,1 | 7074±2001,06 | 0,000* |
| PLT(10³/ul) | 440600±201539,7 | 254000±89003 | 0,005* |
| MCV(μ) | 71,48±7,47 | 78,20±3,61 | 0,010* |
| RDW(%) | 18,24±3,05 | 14,90±1,45 | 0,004* |

*p < 0.05 then it is statistically significant.

**Table 3.** Zn and biochemical values of our cases

|  | Pnömoni grubu | Kontrol grubu | p |
|---|---|---|---|
| Zn (μg/dl) | 24,472 ± 12,419 | 54,960±29,999 | 0,004* |
| T.Protein(gr/dl) | 6,840 ± 0,883 | 7,110 ± 0,401 | 0,018* |
| ALB(gr/dl) | 4,568 ± 0,551 | 4,510 ± 0,363 | 0,299 |
| MG(mg/dl) | 2,24 ± 0,25 | 2,23 ± 0,23 | 0,589 |
| FE(μg/dl) | 13,80 ± 6,64 | 50,90 ± 16,58 | 0,000* |
| FEBK(μg/dl) | 328,36 ± 72,03 | 351,00 ± 104,26 | 0,079 |

*p < 0.05 then it is statistically significant

**Table 4.** Serum Zn and Fe values and r values of correlation coefficients

|  | Zn |
|---|---|
| HTC | 0,123 |
| WBC | -0,138 |
| PLT | -0,154 |
| MCV | 0,165 |
| RDW | 0,022 |
| T.Protein | 0,029 |
| MG | -0,216 |
| Fe | 0,457* |

*p < 0.05 then it is statistically significant

## Discussion

With many factors being involved in the etiology of pneumonia, out of those of being preventable, it has been known that zinc has an important role especially in developing countries. Also in our study, serum zinc levels of patients diagnosed with pneumonia and received inpatient treatment in suckling period were statistically and significantly lower compared to their healthy peers. Additionally, administration of Vitamin D, lactation period, educational background of mothers and mean level of serum total protein in the patient group diagnosed with pneumonia were detected to be lower com-

pared to the our control cases.

It has been known that zinc affects immuno-modulators, immunoregulators and epithelium of the respiratory tract, protects children from infections and improves T-lymphocytes [8]. Furthermore, zinc is an important antioxidant and zinc received by diet is extremely essential in the healthy functioning of the body [8, 9]. In a study conducted, it has been demonstrated that zinc is a cytoprotective agent also against toxins and inflammatory mediators as seen in the respiratory epithelium [10].

Numerous studies investigating the effects of zinc on many infections such as diarrhea and common cold have been conducted in our country as well as in other countries and positive results have been obtained. However, few numbers of studies have been conducted in various countries, which may reveal the relationship between pneumonia and zinc, and a single study has been found in our country regarding this issue, which may count as a reference [11]. However, numerous studies on the various effects of zinc have been conducted both in Turkey and abroad and these studies still continue to be performed [12, 19]. To date, 3 major studies have been carried out in Ethiopia, India and Bangladesh due to the importance of zinc and

zinc deficiency in developing countries.

In Ethiopia, Umeta et al. [13] studied the effects of zinc fortification on sufficiently-developed and underdeveloped children aged between 6-12 months. As the result of the study, height increase, weight gain, increased appetite, very low rate of developing cough, and significant decrease in diarrhea, fever and vomiting were observed to be statistically higher in zinc-received group compared to the placebo-received group.

In Bangladesh, Brooks et al. [14], in addition to the antimicrobial treatment, administered 20 mg zinc to the patients under the age of 2 with severe pneumonia, whereas they gave placebo to a certain group. As the result of the study, they indicated that shortening of the recovering period from severe pneumonia and its components and of length of stay at hospital by adjuvant treatment of zinc might have been related to the role of zinc in acute infections as a acute phase reactant, that children with higher level of zinc in tissues probably had a more stronger immune system, and that another probable effect of zinc was to recover inflammation.

In India, Kumart et al. [15], blood levels of zinc were 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.

Similar results with our study were obtained. These studies demonstrated that adjuvant treatment of zinc speeded up the recovery from severe pneumonia in children, that it might help to reduce the development of antibiotic resistance by decreasing administration of multiple antibiotics, and that it might reduce complications and mortality depending on infections. In these three studies, no adverse effect of administered zinc was observed. This is significant for the reliable administration and application of the drug in the studies.

In Vietnam, Ninh et al. [16] showed that zinc fortification reduced diarrhea incidence by 44% and pneumonia incidence by 44% in children. In India, Sazawal et al. [17, 18], in their two separate studies, demonstrated that zinc fortification reduced diarrhea incidence by 8%, pneumonia

incidence by 44% and mortality by 68% in children. Gardner et al [19], in their study conducted in Jamaica, indicated that the zinc administration in children decreased diarrhea incidence by 8% and pneumonia incidence by 88%. Prior to administering zinc in cases with pneumonia as an adjuvant treatment to the antimicrobial treatment, we determined that in our society, plasma level of zinc in infants especially with LRTI below the age of 2 was significantly lower compared to those levels recorded in normal healthy children.

Our study showed that the tendency to develop pneumonia was increased in our group 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 [13-15]. Rate of children died of pneumonia ranked 1st in developing countries and in Turkey may be due to numerous reasons such as low socioeconomic status, low per capita income, and nutrition rich in carbohydrates but poor in proteins, and population and family planning. Zinc deficiency, which is a serious problem in our country, should be avoided by improving immunity through nutrition rich in zinc (rich in proteins but poor in carbohydrates) or external zinc fortifications and thus people should be protected against diseases causing serious morbidity and mortality. Through the more extensive studies to be conducted in future, zinc administration as an adjuvant treatment in addition to the classical antimicrobial treatments could be routinely available in serious infections like pneumonia.

Significant difference was found between the vaccination rates of our patients and control group. This issue made a sense regarding infectious diseases and their spreading. Significantly low intake of Vitamin D in our patients is important with regard to pneumonia and improvement of the patient [20]. More than half of our patients in pneumonia group (56%) did not receive Vitamin D. Vitamin D intake, which is a great problem in developing countries, was started to be supported by providing Vitamin D and Fe preparations free of charge in Health Care Centers and Maternal and Infant Health Centers beginning from 2003 due to usage of Vitamin D and Fe preparations being around by 50% according to data published by the Ministry

of Health [11].

Significantly higher rate of lactation in our patients in control group showed the necessity of lactation regarding immunity and protection from infections. It is known that high concentration of zinc is included in colostrum. In the studies conducted, it has been demonstrated that lactation protects children from diarrhea, LRTI, otitis and malaria [12]. Our study supports the significantly low level of total protein in our patients compared to the control cases, our patients being fed with a diet poor in proteins, that is, poor in zinc, and the relationship between infections and zinc. In a study conducted in Turkey, zinc was administered to children and it was indicated that the total serum level of protein was significantly increased [12].

Educational background of mothers of our patients was lower. This gives rise to thought of the importance of the relationship between pneumonia and the educational background, and thus of conscious nutrition and care. Our findings showed once again the need for attaching importance especially to the education of girls.

Children died of pneumonia still being ranked 1st in developing countries like Turkey indicates that there are many factors taking part in developing pneumonia, but among these factors the preventable ones are important for us. Zinc deficiency, which is a serious problem in our country, should be avoided by improving immunity through nutrition rich in zinc (rich in proteins but poor in carbohydrates) or external zinc fortifications and thus people should be protected against diseases causing serious morbidity and mortality.

**Address correspondence to:** Dr. Vefik Arica, Medical Faculty of the Mustafa Kemal University, 31100, Serinyol, Antakya, Hatay, Turkey. Tel: +90 326 2291000; Mobile phone: +90 505 6797877; Fax: +90 326 2455654; E-mail: vefikarica@hotmail.com

## Reference

[1]     DSÖ: İntegrated Management of Childhood İllness. http://www.who.int/childadolescent - health (2008).
[2]     Thoracic society, Manual of CAP diagnosis and treatment in childhood. www.toraks.org (2002).
[3]     Henrickson KJ. Viral pneumonia in children. Sem Pediatr İnfect Dis J 1998; 9: 217-33.
[4]     Collaboration program between Government of Turkish Republic – UNICEF 2001-2005. Condition of children and women in Turkey 2003; 103-85.
[5]     http://www.hips.hacettepe.edu.tr/tnsa 2008.
[6]     Sazawal S, Black RE, Ramsan M, Chwaya HM, Dutta A, Dhingra U, Stoltzfus RJ, Othman MK, Kabole FM. Effect of zinc supplementation on mortality in children aged 1-48 months: a community-based randomised placebo-controlled trial. Lancet 2007; 17; 369: 927-34.
[7]     Kahraman R. Mineral matters, their metabolisms and importance in animal feeding. I.U. Veterinary School, Department of Animal Feeding and Diseases, Course Notes 1997; 21-35.
[8]     Valle BL, Falchuk KH. The Biochemical basis of zinc physiology. Physiol Rev 1993; 73: 79-118.
[9]     De Raeve HR, Thunnissen FB, Kaneko FT, Guo FH, Lewis M, Kavuru MS, Secic M, Thomassen MJ, Erzurum Sc. Decreased Cu, Zn-SOD activity in asthmatic airway epithelium correction by inhaled corticosteroid in vivo. Am J Physiol Lung Cell Mol Physiol 1997; 272: 148-154.
[10]    Hennig B, Wang Y, Ramasamy S, McClain CJ. Zinc deficiency alters barrier function of cultured porcine endothelial cells. J Nutr 1992; 122: 1242-1247.
[11]    Tanriverdi H, Turan E, Karadag A, Elevli M. The serum zinc level in 0-2 year old hospitalized children with bronchopneumonia. Med Res J 2010; 8: 34-39.
[12]    Zinc serum and leukocyte levels in school-age children aged 7-11 years, role of the bread including zinc in the treatment of zinc deficiency XXXIX. Summary Book of Reports of National Congress of Pediatrics 1995; 303.
[13]    Umeta M, West CE, Haidar J, Deurenberg P, Hautvast J. Zinc supplemantation and stunted infants in Ethiopia: a randomised controlled trial, Lancet 2000; 10; 355: 2021-6.
[14]    Brooks WA, Yunus M, Santosham M, Wahed MA. Zinc for severe pneumonia in very young children: double-blind placebo -controlled trial. Lancet 2004; 22; 363: 1683-8.
[15]    Kumar S, Awasthi S, Jain A, Srivastava RC. Blood Zinc Levels in Children Hospitalized with severe Pneumoniae: A case control study. Indian Pediatr 2004; 41:486-91.
[16]    Ninh X, Thissen P, Collete L, Gerard G, Khoi H, Keteislegers M. Zinc supplementation increases growth and circulating insulin-like growth factor 1 (IGR -1) in growth retarded Vietnam children. Am J Clin Nutr 1996; 63: 413 -418.
[17]    Sazawal S, Black RE, Bhan MK, Jalla S, Sinha A, Bhandari N. Efficacy of zinc supplemen-tation reduces the incidence and prevalence of acute diarrhea a communitybased, double-blind, controlled trial. Am. J Clin Nutr 1997; 66: 413-418.
[18]    Sazawal S, Black R, Jalla S, Mazumdar S, Sinha A, Bhan MK. Zinc supplementation reduces the incidence of acute lower respiratory infections

in infants and preschool children. A double - blind, controlled trial. Pediatrics 1998; 102:1-5.

[19] Meeks -Gardner J, Witter M, Ramdath D. Zinc supplementation effects on the growth and morbidity of undernourished Jamaican children. Eur J Clin Nutr 1998; 52:34-39.

[20] Karatekin G, Kaya A, Salihoglu O, Balci H, Nuhoglu A. Association of subclinical vitamin D deficiency in newborns with acute lower respiratory infection and their mothers. Eur J Clin Nutr 2009; 63: 473-7.