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Evaluation of serum zinc levels in hospitalized children with bacterial pneumonia, Urmia, Iran

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ABSTRACT

Background: Pneumonia in children causes 30% of deaths worldwide, and the role of zinc as a micronutrient in treating pneumonia is unclear. Zinc improves immune system function and deficiency increases infectious disease risk and growth. This study aims to determine zinc serum levels in children hospitalized with pneumonia and compare them with those without pneumonia.

Methods: A case-control study was conducted on 100 children aged 1 to 59 months between January and July 2022. 50 children were admitted to Urmia Motahari Hospital in Iran with pneumonia, while 50 other children were studied as a control group. Zinc levels were measured in two groups, and the data was analyzed using SPSS software.

Results: The study found that the average zinc level in the case group was 67.35 ± 42.03, while in the control group it was 93.26 ± 41.80. The control group had a significantly higher zinc level. Hospitalization for more than 10 days was significantly lower than hospitalization for less than 10 days. Patients with complications had lower serum zinc levels, with significant differences in empyema, pleural effusion, and ventilation. Patients with wheezing, stridor, cyanosis, sleep disorder, and lethargy also had lower zinc levels.

Conclusion: The average level of zinc in children with pneumonia was significantly lower than the control group.

Kewwors: Serum zinc levels, Hospitalized children, Pneumonia, Urmia

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1. Introduction

Pneumonia is an infection of the lung parenchyma, which is one of the most common lower respiratory tract infections (LRTIs). It is associated with high mortality in young children. The World Health Organization defines it as rapid breathing, coughing, and subcostal retraction. Most deaths occur during infancy and in low-income countries. Based on the World Health Organization, of the 4 million annual deaths caused by pneumonia, half occur in children less than 1 year of age (1-4). Also, malnutrition plays a significant role in increasing the prevalence, severity, and prognosis of pneumonia, especially in children (5). Zinc is an essential trace element that plays a vital role in human nutrition and health. It also plays a vital role in cell division, protein synthesis, wound healing, and immune function (6). The results of the clinical trials show. Zinc supplementation significantly reduces the incidence of pneumonia in children. (7). Daily intake of zinc is especially needed during childhood, adolescence, and pregnancy since the body has no special storage system for zinc (8). Overall, initial statistics suggest that about 25% of the world's population suffers from zinc deficiency (9).

According to the studies, zinc deficiency varies from 79% in South Asia to 5% in developed countries. Its prevalence is 46% in the Middle East and North Africa, 7% in East Asia and the Pacific, and 33% in Latin America and the Caribbean. Zinc deficiency is associated with a weak immune system, diarrhea, pneumonia, growth retardation, and weight loss (10, 11). Pneumonia, diarrhea, malaria, and neuropsychological function respond significantly to improved zinc levels. It also protects the integrity of respiratory cells during lung inflammation and injury. It has been proven that the measurement of zinc concentration in plasma can help identify the severity of the disease and predict the response to treatment (8, 12, and 13).

As stated, zinc and iron deficiency is one of the most common nutritional problems in Iran and developing countries. Based on the statistics, almost 50% of common nutritional problems are caused by a combined deficiency of these two elements. However, less attention has been paid to identifying zinc deficiency and its preventive treatment compared to iron in Iran (1, 14). Zinc deficiency in children can cause infection and exacerbate its complications by weakening the immune system, delaying growth, and disrupting the repair mechanism and function of respiratory cells.

Several studies indicate the therapeutic and preventive impacts of zinc administration in infectious diseases. Prescribing zinc compounds and correcting their deficiency can reduce the risk of severe infections and the complications of lower respiratory infections through various mechanisms, including improving the function of the immune system and respiratory mucosal cells (1, 15–17). Another study revealed that the serum zinc level in children with pneumonia and gastroenteritis is lower than in children of the same age (18). Insufficient intake of zinc in the diet is the primary cause of zinc deficiency, and consumption of foods such as legumes, eggs, red meat, white meat, and bread can be useful sources of zinc. The 2003 annual report of the World Health Organization emphasized the significance of adding zinc to the diet as a food supplement. Clinical signs of zinc deficiency in childhood include acute or chronic diarrhea with malnutrition, psychiatric disorders, and behavioral problems. Chronic zinc deficiency can cause alopecia, stops of growth, skin lesions, and common childhood infections such as pneumonia. Zinc supplementation can reduce the incidence of

pneumonia. It can also shorten periods of diarrhea and eliminate them (17, 19, 20, and 21).

A few studies have been conducted until recently to elucidate the role and relationship of zinc with morbidity and mortality in community-acquired pneumonia. Some researchers have found that patients with normal serum zinc levels are less likely to suffer from infections such as acquired pneumonia and need fewer antibiotics (22). However, the results of studies concerning its administration as adjunctive therapy for pneumonia have been more limited. In a study in Bangladesh, zinc plus antimicrobial therapy for young children with pneumonia was associated with a significant reduction in the duration of pneumonia compared to a control group that received the same antimicrobial therapy but not zinc (23). A study by Ehsanipour et al. (2009) investigated the serum zinc level in children with pneumonia. The results revealed that serum zinc levels are significantly lower in children with pneumonia compared to healthy children (P = 0.0075) (24–30). Since there are different opinions in the studies about the beneficial effects of administering zinc compounds for the prevention or treatment of pneumonia in children and since only a few studies have been conducted in this regard, especially in Iran, the present study evaluated the serum levels of zinc in children hospitalized with a diagnosis of pneumonia in Shahid Motahari Hospital.

2. Materails and Methods

This case-control study was conducted on 100 patients aged 1 to 59 months between January 2021 and July 2022. In this regard, 50 children hospitalized in Motahari Hospital in Urmia, Iran, with a diagnosis of pneumonia based on WHO criteria were included in the case group, and 50 other children referred to the pediatric infectious disease clinic were also included in the control group.

According to Rajasekaran's study in 2020 (25), the average zinc level in the case group was 60.36 ± 29.23 and in the control group was 80.54 ± 25.70 with α = 90% and B = 80% calculated with the following formula: In accordance with that and the probability of 15% dropout, at least 45 children were considered in each group, and finally 50 children were studied in each group. Demographic information was collected through patient records.

The inclusion criteria for the case group include:

2-1. Age one to 59 months

2: Pneumonia based on the WHO criteria according to the diagnosis of a pediatric infectious disease specialist

2-2. The inclusion criteria for the control group include:

1. Age one to 59 months

2: Not having bacterial pneumonia

2-3. The exclusion criteria for patients in both groups include:

1. Underlying diseases such as heart disease, kidney disease, liver disease, neurological disease, immunodeficiency, cystic fibrosis (CF), FTT, and G/E disease

2-4. Treatment with Zinc

The patients of the control group were selected after adaptation and matching in terms of age and gender with the case group.

The pneumonia diagnosis was based on the WHO definition and clinical, radiological, and paraclinical findings on the first day of hospitalization. The rapidity of breathing is one of the significant factors in the diagnosis of the disease based on the age of the patient. For the age of 1 month to 12 months, more than 50 breaths per minute were considered tachypnea, and in 1 to 5 years, more than 40 breaths per minute were considered tachypnea. The severity of pneumonia was defined based on respiratory distress, cyanosis, lethargy, impaired consciousness, need for oxygen, and a sat o2 drop of less than 93%. Pneumonia was defined as the involvement of more than two lung lobes. Complications of the disease include pleural effusion, pneumatocele, empyema, and pneumothorax. The studied children were also examined in terms of their nutritional status. For this purpose, the weight-for-height Z score was used. Accordingly, children with a Z score greater than -2 were considered normal, and those with a score those with a score less than -2 were considered malnourished. The clinical information of the patients and other information such as age, gender, education level of the parents, and the duration of hospitalization were also extracted and recorded for all patients. The serum zinc level of the patients was also recorded at the first patient visit. The way to evaluate the weight-to-height score in this study was calculated by a nutritionist according to the global health standard.

2-5. Zinc measurement method

We used 5-Br-PAPS method for zinc measurement. This zinc measurement kit allows zinc to form a stable color complex with chromogen (5-Br-PAPS) specifically. Its color intensity is proportional to the amount of zinc in the sample and is measured at a wavelength of 546.575. The tested sample is serum or plasma without hemolysis or anticoagulant. Normal value in children is 64–110 µg/Dl. Each kit can be used for 50 people. Our sample was kept in the refrigerator, and the tests were performed by one person.

Kit brand: Ziestchem-Diagnostics

It should be noted that this study has been presented to the ethics committee of Ravmia University of Medical Sciences and has received a code of ethics. Finally, the collected data were analyzed in SPSS-22 software. In this study, an independent t-test and analysis of variance (ANOVA) were used at a significance level of 0.05.

3. Resutls

In the present study, a total of 100 children (50 in the control group and 50 in the case group) were examined. Thirty people (30.0%) were in the age group of 1–12 months, 42 people (42.0%) were in the age group of 13–36 months, and 28 people (28.0%) were in the age group of 37–59 months. Regarding gender, 52 (52.0%) were male and 48 (48.0%) were female. Also, regarding the father's education level, 10% were illiterate, 39% had less than a diploma, and 51% had more than a diploma. Regarding the mother's education level, 22% were illiterate, 51% had less than a diploma, and 27% had more than a diploma.

In the present study, smoking in parents was not reported in 41% of cases, and in 59% of cases, the father was smoking. The mean zinc level in the studied population was 80.17 ± 43.69, with a minimum value of 4.30 and a maximum value of 164.0. The mean zinc level in the case group was 67.35 ± 42.03 and 93.26 ± 41.80 in the control group. Based on the results of the independent t-test, the zinc level in the control group was significantly higher ($p = 0.003$).

Table 1. Measurement and comparison of serum zinc levels based on groups (case and control groups) and demographic characteristics

P-value	Mean ± S.D	Variable	
0.003	67.35 ± 42.03	Case	*Groups
	93.26 ± 41.8	control	
0.71	80.71 ± 40.7	Male	*Gender
	78.48 ± 47.16	female	
0.47	84.02 ± 47.14	1-12	**age
	73.92 ± 41.8	13-36	
	85.62 ± 43.01	37-59	

T-test *- ANOVA**

Table 2. Measurement and comparison of serum zinc level based on the length of hospitalization, severity of pneumonia, and nutritional status

P-value	Mean ± S.D	Frequency	Variable	
0.003	81.2 ± 36.87	15	1-5	**Length of hospitalization
	76.41 ± 42.61	23	6-10	
	32.66 ± 27.61	12	>10	
0.07	53.02 ± 38.96	17	severe	*Severity of pneumonia
	74.72 ± 42.2	33	not severe	
0.18	65.53 ± 42.13	20	<-2	*Nutritional status
	83.12 ± 43.84	80	>-2	

T-test *- ANOVA**

Table 3: Measurement and comparison of zinc serum level based on the presence and absence of complications

P-value	Mean ± S.D	Frequency	Variable	
0.66	49	1	Yes	*Pneumatocele
	67.72 ± 42.38		No	
0.5	39	1	Yes	*Pneumothorax
	67.92 ± 42.27		No	
0.25	33.85 ± 21.42	2	Yes	*Involvement of more than one lobe
	68.74 ± 42.21		No	
0.02	26.86 ± 20.12	5	Yes	*Empyema
	71.84 ± 41.51		No	
0.02	26.86 ± 20.12	5	Yes	*Pleural effusion
	71.84 ± 41.51		No	
0.01	23.6 ± 19.79	5	Yes	*Ventilation
	72.21 ± 41.11		No	

T-test *- ANOVA**

Based on the results of the independent t-test, there was no statistically significant difference between the two genders regarding the zinc level ($p = 0.71$). Additionally, based on the results of the ANOVA test, there was no statistically significant difference between the age groups regarding mean zinc level ($p = 0.47$). Based on the data of this study, 15% of patients were hospitalized for 1 to 5 days, 23% were hospitalized for 6 to 10 days, and 12% were hospitalized for more than 10 days. Based on the information in Table 10, to compare the mean zinc level based on the duration of hospitalization, ANOVA and Tukey's post-HOC tests were used. Based on the results of the test, the zinc level in a hospitalization of more than 10 days is significantly lower than that of a hospitalization of less than 10 days (1–5 and 6–10 days) ($P > 0.05$). Also, 17% of children had severe pneumonia, and 33% had non-severe pneumonia.

Table 4: Measurement and comparison of serum zinc level based on clinical symptoms

P-value	Mean ± S.D	Frequency	Variable	
0.13	60.86 ± 43.51	33	Yes	*crackle
	79.94 ± 36.98		No	
0.02	49.28 ± 23.72	12	Yes	*Wizzing
	73.05 ± 45.09		No	
0.04	26.75 ± 19.42	4	Yes	*stridor
	70.88 ± 41.7		No	
0.01	22.76 ±19.04	5	Yes	*cyanosis
	72.3 ± 41.03		No	
0.05	45.9 ± 40.6	11	Yes	*hypoxia
	73.39 ± 40.91		No	
0.001	47.88 ± 31.91	23	Yes	*sleep disorder
	83.93 ± 42.97		No	
0.04	44.57 ± 36.9	11	Yes	*lethargy
	73.77 ± 41.56		No	
0.08	55.6 ± 42.91	22	Yes	*feeding problem
	76.57 ± 39.66		No	
0.2	68.89 ± 42.2	48	Yes	*Cough
	30.25 ± 2.47		No	
0.3	68.55 ± 42.46	48	Yes	*Fever
	38.5 ± 9.19		No	

T-test *- ANOVA**

According to the independent t-test results, although the zinc serum level was lower in children with severe pneumonia, this difference was not statistically significant (P = 0.07). Additionally, 20% had a Z-score below -2, and 80% had a Z-score above -2. Based on the independent t-test results, there was no statistically significant difference between zinc serum and nutritional status (p = 0.18).

Based on the information in Table 3, 2% of patients had pneumatocele, 2% had pneumothorax, 4% had more than one involved lobe, 10% had empyema, 10% had pleural effusion, and 10% were under ventilation. Based on the information in Table 3, the mean serum zinc level was lower in patients with complications, and this difference in empyema (P = 0.02), pleural effusion (P = 0.02), and ventilation (P = 0.01) was statistically significant. Based on the information in Table 4, the most common clinical symptoms among children with pneumonia were tachypnea, cough, and fever, respectively. The mean serum zinc level was significantly lower in patients with wheezing (P = 0.02), stridor (P = 0.04), cyanosis (P = 0.001), sleep disorder (P = 0.001), and lethargy (P = 0.04).

4. Discussion

Pneumonia is the single largest infectious cause of death in children worldwide. Pneumonia killed 740,180 children under the age of 5 in 2019, accounting for 14% of all deaths of children under 5 years old but 22% of all deaths in children aged 1 to 5 years (1-4). Pneumonia in children is the cause of about 30% of deaths in the world. Despite an approximate reduction in the incidence and mortality caused by it over the last two decades, it is still the primary cause of death after the infancy period (31). The results of recent reviews indicate that the rate of occurrence of this disease is 0.22 per child every year in low-income countries, and 11.5% of them occur as severe pneumonia (32). There is ambiguity regarding the role of zinc as an important micronutrient in the treatment of

pneumonia. This substance improves the function of the immune system, and its deficiency is associated with an increased risk of infectious diseases and impaired growth and development (33). Thus, the present study measures the serum zinc level of children hospitalized with pneumonia in Shahid Motahari Hospital and compares it with that of people without pneumonia.

In the present study, 30% were in the age group of 1–12 months, 42.0% were in the age group of 13–36 months, and 28.0% were in the age group of 37–59 months. In a study by Ehsanipour et al. (24), 74% of children were in the 3–12 month group, and 26% were in the 1–5 year group. The age distribution in the mentioned study is different from ours. In the study by Jayashree Rajasekaran et al. (25), 34% of children were in the age group of 1–12, 26% were in the age group of 13–36 months, and 40% were in the age group of 12–16 months. No significant difference was found between the two genders or between different age groups in this study. Our results were in line with those of a study conducted by Jayashree Rajaskaran et al. (25).

In the present study, the mean zinc level was 67.35 ± 42.03 in the case group and 93.26 ± 41.80 in the control group. Based on the results of the statistical test, the zinc level in the control group was significantly higher ($p = 0.003$). In the case-control study by Ehsanipour et al. (24), conducted to investigate serum zinc levels in children with pneumonia, in line with the present results of our study, the results showed that the zinc level in children with pneumonia was significantly lower. Additionally, in the study by Strand et al. (34) in 2004 in Bangladesh, results revealed that zinc levels in children with pneumonia are significantly lower than in the control group.

In two studies by Mahalanabis (23) and Brooks (22), results showed that the consumption of zinc during the treatment of pneumonia leads to a reduction in the duration of fever and infection recovery time. In the study by Salim et al. (35) in India, results showed that children suffering from zinc deficiency are at higher risk of lung infection. Also, in the study by Jayashree Rajaskaran et al. (25), results showed that the zinc level in children with pneumonia is significantly lower than that in the control group (60.3 vs. 80.5). The study by Seçil Arca et al. (29) investigated serum zinc levels in children 0–24 months with pneumonia. Results showed that the serum zinc level in children with pneumonia was significantly lower than that in the control group. Kumar et al. (36) also measured the zinc level in 50 children aged 2–5 with pneumonia. They concluded that the zinc level in children with pneumonia is significantly lower than that of children without pneumonia.

The study by Dr. Soleimani et al. evaluated the zinc level in children with pneumonia and gastroenteritis. Results showed that the zinc level in children with pneumonia and gastroenteritis was significantly lower than that in the control group. However, no significant difference was found between the patients with pneumonia and gastroenteritis regarding serum levels. In the present study, 20% had a Z-score below -2, and 80% had a Z-score above -2. In the study by Jayashree Rajasekaran et al. (25), in line with the results of our study, 78% had a Z-Score above -2, and 22% had a Z-Score below -2. In this study, the most common clinical symptoms among children with pneumonia were tachypnea, cough, and fever, respectively, and the mean serum zinc level was lower in patients with complications, and this difference was statistically significant in empyema ($P = 0.02$), pleural effusion ($P = 0.02$), and ventilation ($P = 0.01$). Also, the mean serum zinc level was

significantly lower in patients with wheezing (P = 0.02), stridor (P = 0.04), cyanosis (P = 0.001), sleep disorder (P = 0.001), and lethargy (P = 0.04).

In the study by Jayashree Rajaskaran et al. (25) et al., in line with the results of our study, the most common clinical symptoms were fever, cough, tachypnea, and loss of appetite. In the study by Seçil Arca et al. (29), the most common clinical symptoms of children with pneumonia were cough, fever, wheezing, and a stuffy nose. In the present study, the zinc level during hospitalization for more than 10 days was significantly lower than hospitalization for less than 10 days (1–5 and 6–10 days), and the serum zinc level was lower in children with severe pneumonia. However, this difference was not statistically significant.

The study by Gauri S. Shah et al. (28) evaluated the role of zinc in patients with pneumonia, and its results revealed that administration of zinc simultaneously with routine antibiotic treatment does not reduce the duration of hospitalization or the severity of the disease. Several studies have investigated the effect of zinc on controlling infectious diseases such as diarrhea and colds. For example, a study in Ethiopia showed that children who received zinc had higher height, weight, appetite, lower diarrhea and fever, and more vomiting than children who did not receive zinc (37). Also, the study by Ninh et al. (38) in Vietnam revealed that zinc supplementation causes a 44% reduction in the incidence of diarrhea and pneumonia in children. In the study by Sazawa et al. in India, it was found that zinc supplementation caused an 8% reduction in diarrhea, a 44% reduction in pneumonia, and a 68% reduction in child mortality. The study by Gardner et al. (39) in Jamaica also revealed that zinc supplementation reduces diarrhea and pneumonia in children by 8% and 88%, respectively.

Conclusion

The mean zinc level was 67.35 ± 42.03 in the case group and 93.26 ± 41.80 in the control group. Based on the independent t-test, the zinc level in the control group was significantly higher (p = 0.003). The results revealed that the zinc level in hospitalization for more than 10 days was significantly lower than in hospitalization for less than 10 days (1–5 and 6–10 days). Also, the mean serum zinc level was lower in patients with complications, and this difference was statistically significant in empyema (P = 0.02), pleural effusion (P = 0.02), and ventilation (P = 0.01). The mean serum zinc level was significantly lower in patients with wheezing (P = 0.02), stridor (P = 0.04), cyanosis (P = 0.001), sleep disorder (P = 0.001), and lethargy (P = 0.04).

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