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# Effect of Zinc Sulphate as Adjuvant Therapy in the Treatment of Severe Pneumonia in Children Aged Under 2 years

*Dr.Ahmed F. Raheem Al-juboory[1*], Dr.Luay Abdulraheem Hasani Alnassrawi[2]*

***Authors' Information***
*1.M.B.Ch.B, D.C.H, Alduloiyah General Hospital, Iraq*
*2.M.B.Ch.B.,F.I.C.M.S.(Ped.), C.A.B.P., Iraq*

***Corresponding author:***
***Dr. Ahmed F. Raheem Al-juboory***
*al_jubooryafr28@gmail.co*

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## Abstract

*Background: Pneumonia is an inflammation of the lungs caused by an infection. It is the leading cause of morbidity and mortality in children less than five years old. Worldwide, about 20% of deaths in children aged 4 years are attributable to pneumonia, two-third of these death happen during infancy. Zinc is one of the essential micronutrients, it's used the prevention and treatment of diarrhea was documented while in pneumonia it still need further evaluation. Objective: To evaluate if there is a beneficial effect of zinc sulphate in the treatment of pneumonia. Patients and method: Multicenter study with double blinded, randomized, controlled placebo trial to evaluate the role of zinc Sulphate in the treatment of severe pneumonia in children two years who required hospital admission. Results: In (GP 1) patients, the mean of hours at which the respiratory rate being less than or equal to 50 (RR < 50), WAS (31.44 + 12.8) while in (GP2) it was (34.68+ 11.37). Also, in (GP1) the mean of hours at which the arterial oxygen saturation being more than or equal to 95% (Spo2 >95) was (37.68+11.62) while in (GP2) it was (36.63+13.65), these results were statistically non- significant. Also on comparison of (RR<50) and (Spo2>95) between GP(A1) and GP(A2) the result were statistically non-significant. The same result was obtained on comparison of (RR<50) and (Spo2>95) between GP(B1) and GP(B2).Conclusion: No beneficial effect of zinc sulphate as adjuvant therapy in the treatment of severe pneumonia in children between under 2 years.*

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***Pneumonia, zinc sulphate, adjuvant therapy, children***

# 1 INTRODUCTION

Pneumonia is an inflammation of the parenchyma of the lunge. Although most cases of pneumonia are caused microorganisms like bacteria. Viruses, fungi, Rickettsia, and parasites; noninfectious causes include aspiration of food, gastric acid, foreign bodies, hydrocarbons and lipoid substances; hypersensitivity reaction, and drug- or radiation-induced pneumonitis are included in the causes of pneumonia.(1)

Worldwide, pneumonia is the leading cause of pediatric morbidity and mortality. It is estimated that pneumonia is responsible for about 2 million death each year in children <5 y old, which represents 19% of the annual death in this age group.(2) Approximately 95% of the pneumonia-related occur in developing countries, and the youngest age groups have the highest risk of death.(3)

Pneumonia case management, which relies on early diagnosis and prompt empiric antibiotic therapy, has been effective measure in reducing pneumonia- related death by 47%.(4) However, the efficacy of this strategy may be diminished by poor nutritional status.(5.6) Under nutrition is known to be associated with grater severity of pneumonia, a higher frequency of complications, longer episodes of infection, and greater case fatality rates.(7.8)

In southern Asia, macronutrient malnutrition and micronutrient deficiencies, especially deficiencies of iron, zinc and vitamin A, are common in young children this problem is attributed to dietary insufficiency, limited nutrient bioavailability from local diets, and consumption of nutrients during recurrent episodes of infection. (9)

One of the essential micronutrients is zinc which is associated with many biological function. It plays a critical role in immunomodulation and in maintaining the integrity of the immune system. It can influence several components of innate immunity. Its immune-enhancing activities include regulation of T lymphocytes, natural killer cells, and interleukin (IL). (10) In addition to immunity , Zinc influence tissue regeneration, promote protein synthesis. Play a role in wound healing especially following burns or surgical incisions. (11) The immunological consequences of zinc deficiency may be responsible for decreased cell mediated immune function and inflammatory reactions in zinc deficient subjects.(12)

Marginal zinc deficiency states are common among children living in poverty where they may exposed to low zinc diets. These children are at increased infections. significant reduction in acute and persistent diarrhea morbidity were observed in zinc supplemented children in therapeutic trials but consensus as to whether zinc supplementation provides a similar therapeutic benefit to children with severe pneumonia requires further clarification. (13)

## 2 | PATIENTS AND METHODS

A randomized, double-blind, placebo controlled clinical trial conducted for 2 years in our hospital. Children aged between 2 to 23 months who admitted to the pediatric wards of were assessed by the researcher and considered eligible for enrollment in the trial as they fulfilled the WHO criteria for diagnosis of sever pneumonia (tachypnea plus lower chest wall indrawing), the WHO respiratory rate thresholds of tachypnea according to age were (>60 breaths/ minute among children aged <2 months, > 50 breaths/ minute among children aged 2-11 months and >40 breaths/minute among children aged 12-59 months), The total no. of the enrolled cases were 88 cases. Children were excluded if they had history of chronic cardiac or renal disease, severe malnutrition, illness requiring hospitalization in the previous 21 days, history of recurrent chest infection or current zinc supplementation. At the time of enrollment, the demographics, current illness, and history of respiratory diseases information's were collected for each subject. All physical findings including measuring of (SPO2) and (RR), chest X-ray finding were recorded and blood sample for baseline serum zinc concentrations were recorded to be measured later on. Before intervention permission of the responsible senior and the parents was taken. children with severe pneumonia were divided into two groups:

(GP1) those who taking zinc. (GP2) those who taking placebo.

(GP1) were subdivided into two subgroups according to baseline serum zinc level:

GP(A1) those who were with normal baseline serum zinc, GP(B1) those were with low baseline serum zinc.

(GP2) were also subdivided into two subgroups according to baseline serum zinc level:

GP(A2) those who were normal baseline serum zinc, GP(B2) those who were with low baseline serum zinc.

The capsule was dissolved in a teaspoon of distilled water or with milk before being administered. All enrolled children were treated according to the standard treatment of infants and children with pneumonia and they were assigned to be treated parenterally for 5 days unless the responsible senior have had another idea.

Statistical Analysis

The results of this study were represented by using tables, pie and Bar charts. Statistical analysis of the result in this study were done by using version 7.5 computer software Statistical Package for Social Sciences (SPPSS). T- test, paired T-test and P- value were used to test the significance of the result of the present study.

## 3 | RESULTS

Among the studied group, 49 (56%) of patients presented with low level of serum zinc and 39 (44%) with normal level of zinc, (Figure 1). Patient with normal baseline serum zinc level (39 cases) were divided into two subgroups: The normal taking zinc group (A1) they were (26 cases) and the normal taking placebo group (A2) were (13 cases) and when compare the mean of hours of improvement in (RR) and (spO2) the results were non-significant, (Table 1).

Patients with low base line serum zinc level (49 cases) were divided into two subgroups: The low taking zinc group(B1) were (23 cases) and the low taking placebo group (B2) were (26 cases) and when compare the mean of hours of improvement in (RR) and (spo2) the result was non-significant, (Table 2).

The Gp1 (50 cases) was subdivided into two subgroups to the level of baseline serum zinc; the 1st group (A1) was of normal baseline serum zinc level (27 cases), the 2nd one (B1) was of low baseline serum zinc level (23 cases). When compare the mean of hours of improvement in (RR) and (spo2), the result was non-significant, (Table 3).

The Gp2(38 cases) was also subdivided into two subgroups: according to the level of baseline serum zinc; The 1st group (A2) was of normal serum zinc level (12 cases), the second one (B2) was of low serum zinc level (26 cases). When compare the mean of hours of improvement in (RR) and (spo2), the results were non-significant, (Table 4). Also, there was no significant

relation between the gender and the clinical improvement of pneumonia in Gp1 according to (RR≤50) and (SpO2≥95), (Table 5).

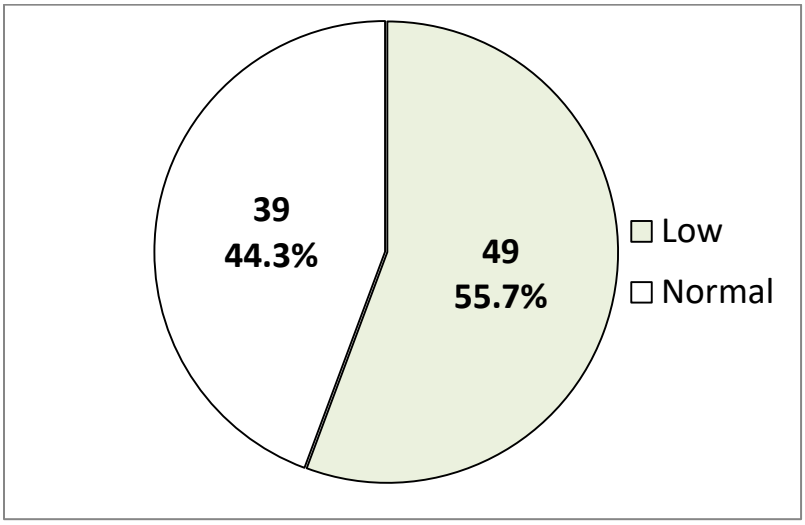


Figure 1. Distribution of the studied sample according to the level of serum zinc.

Table 1. The Relation Between Zinc Administration in Patients with Normal Baseline Serum Zinc and the Improvement of Pneumonia.

| Normal Serum Zinc | No. of cases | RR ≤50 (mean± SD) | SpO2 ≥95 (mean± SD) |
|---|---|---|---|
| A 1 | 26 | 31.84 ± 12.67 | 37.38 ± 11.42 |
| A 2 | 13 | 34.15 ± 10.87 | 37.84 ± 14.57 |
| Total | 39 | 32.99 ± 11.77 | 37.61 ± 12.99 |
| P> 0.05 non-significant. | | | |

Table 2. The Relation Between Zinc Administration Patient with Low Baseline Serum Zinc Level and Improvement of Pneumonia.

| Normal Serum Zinc | No. of cases | RR≤50 (mean ± SD) | SpO2≥95 (mean ± SD) |
|---|---|---|---|
| B 1 | 23 | 30.78 ± 13.45 | 37.56 ± 12.16 |
| B 2 | 26 | 35.0 ± 11.6 | 36.4 ± 13.3 |
| Total | 49 | 32.89 ± 25.35 | 36.98 ± 25.46 |
| P> 0.05 non-significant | | | |

Table 3. Relation Between Baseline Serum Zinc Level and Improvement in (RR) and (SPO2) Level Gp1.

| Gp 1 | No. of cases | RR≤50 (mean ± SD) | SPO2≥95 (mean ± SD) |
|---|---|---|---|
| A 1 | 27 | 32 ± 12 | 38 ± 11.3 |
| B 1 | 23 | 30.7 ± 13.4 | 37.5 ± 12 |
| Total | 50 | 31.4 ± 12.8 | 37.6 ± 11.6 |
| P. value | | 0.700 | 0.900 |

Table 4. Relation between Serum Zinc level and Improvement in Respiratory Rate and SPO2

| Gp2 | No. of cases | RR≤50 (mean ± SD) | SpO2≥95 (mean ± SD) |
|---|---|---|---|
| A 2 | 12 | 34.0 ± 11.24 | 37.56 ± 12.16 |
| B 2 | 26 | 35.0 ± 11.36 | 36.4 ± 13.3 |
| Total | 38 | 34.68 ± 11.36 | 36.63 ± 13.65 |
| P Value | | 0.800 | 0.900 |

Table 5. Relation Between Gender in Gp1 and the Mean of Hours of Improvement in Respiratory Rate and SPO2 Level.

| Gender | No. of cases | RR≤50 (mean ± SD) | SpO2≥95 (mean ± SD) |
|---|---|---|---|
| Male | 23 | 31.1 ± 13 | 37.9 ± 10.7 |
| female | 27 | 31.5 ± 12.7 | 37.2 ± 13.3 |
| Total | 50 | 31.4 ± 12.8 | 37.6 ± 11.6 |
| P Value | | 0.900 | 0.800 |

## 4 DISCUSSION

The current study did not show a clinically or statistically significant reduction in the severity or duration of pneumonia or a reduction in duration of hospital stay for children aged (2-23 months) given daily zinc supplementation along with standard treatment of pneumonia. There was no significant difference between the zinc and placebo group in the mean of hours of recovery from pneumonia clinical outcome was assessed, also the mean length of hospitalization (in hr.) did not differ significant between the zinc and placebo groups.

No significant difference in the recovery from severe pneumonia was observed in the cases of normal baseline serum zinc given or placebo which means that there was no effect of zinc as adjuvant therapy in the treatment of pneumonia.

There was no observed significant difference in the recovery from pneumonia in the taking zinc cases of normal or low baseline serum zinc. There was no observed significant difference in the recovery from pneumonia in the taking placebo cases normal or low baseline serum zinc show that there was no significant relation between gender in taking zinc group and the improvement of pneumonia.

These finding are consistent with Bose et al (14) where they evaluate efficacy of zinc in the treatment of severe pneumonia in hospitalized children <2 y old and found that there were no clinical or statistically significant differences in the duration of tachypnea, hypoxia, chest in drawing, inability to feed, lethargy, severe illness and hospitalization when mean of the time of improvement of these dependent criteria was compared between the placebo and zinc taking groups.

The results of our study also consistent with results of Dr.Dilip Mahalanabis et al the study did not show a clinically worthwhile benefit from or statistically significant of the administration of zinc as an adjunct therapy in children with measles accompanied by pneumonia(15). The same results were obtained worldwide e.g. Long KZ et al(16) in Mexico, Richard SA et al(17) in Peru, Luabeya KK et al (18) in south Africa and Tielsch JM et al (19) in Nepal.

In the other hand the results of our study were in consistent with the results of Dr. Abdullah Brook et al the results showed that the children who received zinc had a shorter duration of severe pneumonia symptoms and signs ( in drawing of the chest when breathing severely

raised respiratory rate and low oxygen saturation in the blood) compared to children who received the placebo.(20)

The results of our study also were inconsistent with the results of Dilip mahalanabis et al (21). They concluded that zinc treatment significantly reduces duration of fever and very ill status.

This inconsistency with our study was due to the short period of hospital staying, as 54 cases (61.4.%) of enrolled cases discharge at 48 hours, 22 cases (25%) discharge at 60 hours and only 12 cases (13.6%) reached 72 hours of admission. This early hospital discharging may be related to many causes, of them , most of cases included in the current study were already exposed to outpatient antimicrobial therapy for about five days before admission and they admitted impending to recover from the illness, or the responsible senior who admit the patient to the pediatric ward decided to discharge him/her early in the course of the treatment, or the parents insisted to discharge their child from hospital on their responsibility just their child started to improve or even earlier. The benefit from zinc seems to increase after 100 hours of illness, this lag period in the onset of effect might be inherent in the mechanism of zinc effect (22) and in the face of the previously mentioned early discharging there was no enough time for zinc to show its effect.

## 5 CONCLUSIONS

No beneficial effect of zinc sulphate as adjuvant therapy in the treatment of severe pneumonia in children under 2 years. Therefore, we recommend that arterial oxygen saturation had to be measured when assess severity of pneumonia. Further researches including larger sample size for long period should be carried out to assess the real role of oral Zinc administration in the treatment of pneumonia

**Ethical Issue:**

All ethical issues were approved by the author, in accordance with Ethical Principles of Declaration of Helsinki of the world Medical Association, 2013, for research involving human subjects

# 6 BIBLIOGRAPHY

1-Behrman RE, Kleigman RM Jenson HB. Nelsons text book of pediatric 18th edition Philadelphia, Theodore C, 2008; 397: 1795-600.

2-Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates the causes of death in children. Lancet 2005;365: 1147-52.

3-Mulholland K.Global burden of acute respiratory infection in children implication for intervention. Pediatric Pulmonol 2003;36: 469-74.

4-Sazawal S, Black RE. Meta-analysis of intervention trial on case management of pneumonia in community settings, Lancent 1992; 340: 528-33.

5-Scrimshaw NS, SanGiovanni JP. Synergism of nutrition and immunity an overview. Am J Clin Nutr 1997;66 (suppl) : 464S-77S.

6-Brundtland GH. Nutrition and infection: malnutrition and mortality in public health. Nutr Rev 2000: 58: S1-4.

7-Caulfield LE, de Onis M, Black RE. Undernutrition as an underlying cause of child death associated with diarrhea, pneumonia, malaria, and measles. Am J Clin Nutr 4004;80;193-8.

8-Fishman SM, Caulfield LE, de Onis M, et al. childhood and maternal underweight. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, eds. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva, Switzerland: World Health Organization, 2004:39-162.

9-Febris N, Mocchegiani E. Zinc, human diseases and Aging (Milano) 1995; 7:77-93.

10-Prasad AS. Zinc: an overview. Nutrition 1995;11:93-9.

11-Shankar AH, Prasad AS. Zinc and immune function: the biological basis of altered resistance to infection. Am J Clin Nutr 1998;68(suppl): 447S-63S.

12-Black R.E. zinc deficiency, infection disease and mortality in the developing world .J. Nutr.;133:1485S-1489S.

13-Bhutta ZA. Bird SM, Black RE, Brown KH, Gardner JM, Hidayat A, et al. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries; 72: 1516-22.

14. Bose. A., et al. Efficacy of zinc in the treatment of severe pneumonia in hospitalized children <2 y old, am. J. Clin , Nutr. 2006;83:1089-1096.

15. Mahalanabis D., et al. zinc supplementation as adjunct with measles accompanied pneumonia: a double-blind, randomized controlled trial. Am. J. Clin Nutr. 2002;76:604-607.

16-Long KZ, Montota Y, Hertzmark E, santos J. A double-blind randomized, clinical trial of the effect of viamin A and zinc supplementation on diarrheal diseas and respiratory tract infections in children in Mexico City., Mexico. Am J Clin Nutr 2009;83:693-700.

17-Richerd SA, Zavaleta N, Caulfied LE, Black RE. Witzing RS, Shankar AH, zinc and iron supplementation and malaria, diarrhea and respiratory infection in children in the Peruvian Amazon Am J Trop Med Hyg 2006;75:126-32.

18-Luabeya KK, Mpontshane N, mackay M, Ward H, Elson I, chhagan M, et al . zinc or multiple micronutrient supplementation to reduse diarrhea and respiratory dieases in South Africa children : a randomized controlled trial. PLoS ONE 2007;2;e541.

19-Tielsch JM, Khatry SK, Stoltzfus RJ, LeClerq SC, Adhikari R, et al . Effect of daily zinc supplementation on child mortality in southern Nepal: a community-based , cluster randomized, placebo-controlled trial. Lancet 2007;370:1230-9.

20-Brooks WA, Yunus M, Santosham M, Wahed MA, Nahar K, Yeasmin S, Black RE. Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. The Lancet. 2004 May 22;363(9422):1683-8.

21-Mahalanabis D, et al. Randomized , double-blind, placebo-controlled clinical trial of efficacy of treatment with zinc or vitamin A in infants and young children with severe acute lower respiratory infection . Am .J. Clin . Nutr. 2004;79:430-433.

22-Sazawal S, Black RE, Bhan MK, Bhandari A, Jalla S. zinc supplementation in young children with acute diarrhea in India. N Engl J Med 1995;333:839-44.

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