

The Effect of Zinc Supplementation on Pneumonia In Hospitalized Patients Aged 1-60 Months

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Abstract

Background: -One of the important causes of pediatric deaths in underdeveloped countries is Pneumonia and to reach the fourth Millennium Development Goal which aimed at reducing the under-five mortality rate. Study the effect of zinc as optional therapy on duration until normalization of respiratory rate, temperature, oxygen saturation, feeding, chest auscultation, and duration of hospitalization in Babylon Teaching Hospital for Gynecology and Pediatrics.

Objectives: To evaluate the effect of zinc supplementation as an adjunctive therapy on the outcome of pneumonia.

Patients and Methods: In a hospital-based cross-sectional study in Babylon Teaching hospital for Gynecology and Pediatrics, two hundreds children aged between one month and 60 months with pneumonia had been followed, one hundred patients received zinc in addition to their treatment (10 mg for patients their ages six months or below, and 20 mg for those who were older than 6 months of age) during the days of hospitalization, and the other one hundred received their treatment without zinc. The clinical symptoms and signs of pneumonia had been detected and documented at time of admission, after 24 hours, 72 hours, and after 120 hours.

Results: From the medical history there were significant differences (p value ≤ 0.05) regarding duration of pneumonia, but there were no significant differences regarding type of feeding or body weight. Females benefited more than males. There were clinical and statistically significant difference (p. value ≤ 0.05) in the patient's clinical condition regarding duration of hospitalization, improvement of temperature, chest in drawing, audible wheeze, feeding, and fate (discharge or ICU admission), but there were no significant differences regarding consciousness level, SpO₂, and chest auscultation.

Conclusions: Zinc supplementation in patients with pneumonia reduces the number of admission to the hospital and hastens the improvement regarding temperature, chest indrawing, audible wheeze, feeding, and reduces ICU admission. Females benefit was more than males'.

Key words:

Pneumonia, Zinc, Pediatric

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Introduction

One of the significant and common diseases affecting children, is acute lower respiratory tract infection, associated with high death rate, especially in young age group. It is significant cause of death in age groups under five years old in underdeveloped countries and constitute one-third of the cases. ^[1-4]

One of the significant implications of lower respiratory tract involvement is pneumonia. Approximately four million deaths per year due to pneumonia according to the World Health Organization, fifty percent of the cases occurred below one year of age ^[2,3,5]. Malnutrition has a valuable role in the increased prevalence, severity, and prognosis of pneumonia, particularly in young age group. ^[3]

One of the essential nutritional element is Zinc and has a vital biological activities in humans. It plays significant role in the appropriate function of the gastrointestinal tract and the immunity. Its low level can cause impairment of growth and elevated risk of infections (pneumonia, gastroenteritis) in pediatric due to impairment of the immune system function, neural and behavioral actions. ^[1,6]

The deficiency of zinc is a worldwide trouble influencing individuals of low income populations. ^[7]

Many studies on prophylactic and therapeutic effects of zinc administration in infectious diseases indicate that ingestion of zinc medications significantly reduces the incidence of pneumonia and gastroenteritis, and its deficiency could cause alterations in the immune system functions and increase the risk of serious infectious diseases such as gastrointestinal infections and malaria ^[1,8-10]

The inadequate intakes of zinc in the diet is the main cause of zinc deficiency. The World Health Organization has advised to supplement the diet with zinc. Acute or chronic gastrointestinal infections with undernutrition, psychiatric diseases and behavioral changes are considered the clinical symptoms of zinc deficiency during early childhood. Alopecia, impaired growth, cutaneous rash, and common pediatric infections such as pneumonia could be caused by chronic zinc deficiency. ^[11]

However, zinc's treatment role in respiratory infections is less clear. Studies that evaluated the clinical role of zinc in therapy of lower respiratory tract infections in children have shown conflicting results, with some studies that showed a better role on the severity and duration of recovery, ^[5,12,13] while other studies advice that zinc has no therapeutically advantage. ^[14,15]

More information is needed to determine whether zinc has an effect in the therapy of children hospitalized for lower respiratory tract infection before treatment regime can be made. Also, the earlier studies did not assess the influence of zinc in pediatric patients with very severe pneumonia. Zinc administration, possibly has an action only on very severe pneumonia but not on milder forms of it.

Objective of the study

To evaluate the effect of zinc supplementation in patients with pneumonia (1-6 months) regarding the effect on the duration of hospitalization, and the clinical course of disease.

Patients and methods :

3.1: Study Design and Setting

Hospital-based cross-sectional study was carried out during the period from 1st of January 2018 till the 31st of December 2018 at Babylon Teaching hospital for Maternity and Pediatrics. This hospital receives referral cases from private clinics, primary health care centers and other peripheral hospitals . It has four inpatients wards and twenty-four rooms.

3.2: Study Sample

Two hundred patients from one to sixty months had been diagnosed with pneumonia were collected from Babylon Teaching hospital for Maternity and Pediatrics during the time of study application.

One hundred patients were given zinc (10 mg for those < sex month, and 20 mg for those >sex month of age) during the days of hospitalization in addition to their antibiotic treatment, the other one hundred received their treatment without zinc.

The Inclusion and exclusion criteria were as follows:

- **Inclusion criteria:** Patients with pneumonia from 1-60 months of age who were presented to the ward either from the emergency department or from a private clinic and need hospital admission (impaired consciousness, toxic, ill-looking, fast breathing, poor feeding, low Spo₂).
- **Exclusion criteria:** Patients with the following conditions were excluded from the study:
 1. Inborn errors of metabolism.
 2. Congenital anomalies.
 3. Chronic disorders:(chronic renal failure, seizure disorder, severe malnutrition, cerebral palsy, and congenital heart disease).
 4. Patients with recurrent wheeze.
 - 5.

3.3: Questionnaire

A structured questionnaire has been done to collect data from the study patients. The questionnaire composed of patients' socio-demographic characteristics (age, gender, birth order, mother's and father's age and education, economic status and residence. Patients' medical history has been collected by (body weight, type of feeding, history of previous pneumonic attack as well as duration of staying in hospital). However, patients' clinical condition has been assessed by progress of disease, level of consciousness, temperature, level of SPO₂, auscultation as well as CXR findings. Other questions related to feeding of patients and fate of pneumonic patients. These findings recorded on admission, after 24 hrs , after 72hrs , and after 120 hrs.

3.4: Pilot study

Before starting to collect information, a pilot study was carried out for 2 weeks. The pilot study done in Babylon Teaching hospital for Gynecology and Pediatrics in January 2014 aimed at:

1. Testing the reliability and validity of questionnaire form to reveal any modification needed.
2. Estimating the time needed to collect the required data.
3. Finding out potential difficulties.

The pilot sample consisted of 20 cases and was excluded from the study sample.

3.5: Data Analysis

In this study statistical analysis was carried out using SPSS version 20. The variables were presented as frequencies and percentages. Continuous variables were presented as (Means \pm SD). Pearson's chi square (X^2) test was used to find out the possible association between the variables. *P-value* of ≤ 0.05 was considered as significant.

Results

The distribution of Patients with Pneumonia by Socio-Demographic Characteristics and the overall mean age of patients was (11.26 \pm 13.16) months old, majority (77.0%) of the patients aged younger than one year (Figure 1).



Figure : 1 The patients age distribution .

In the distribution of patients by gender, the majority (56.5%) of patients were males, as shown in figure 2.

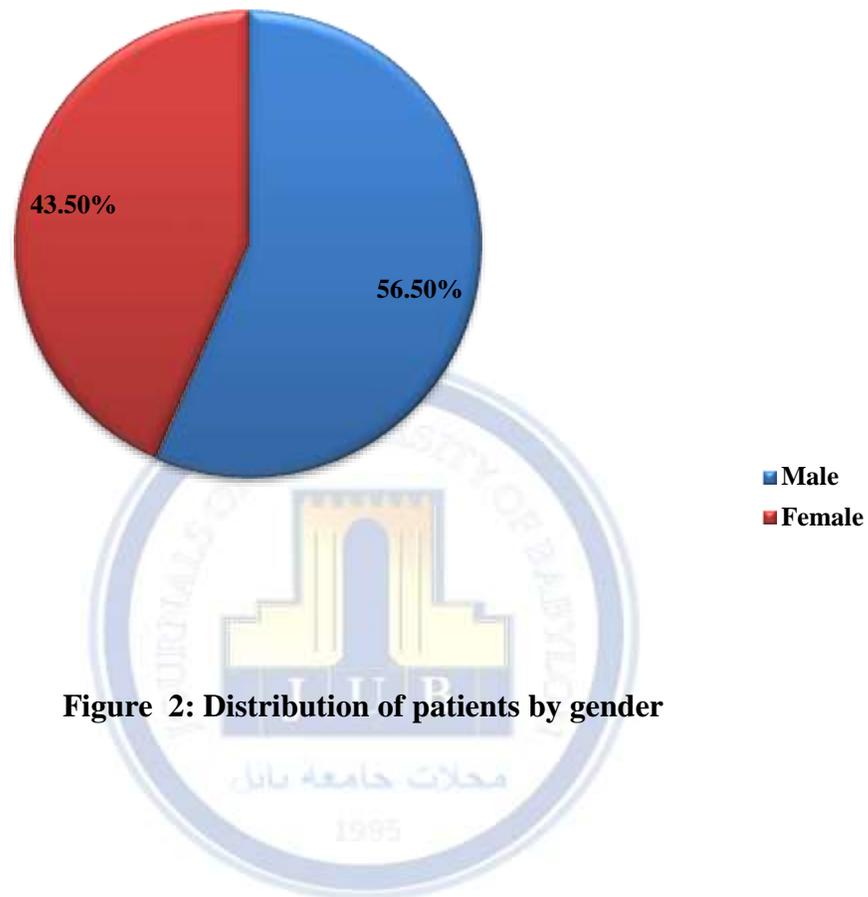


Figure 2: Distribution of patients by gender

Table1: Distribution of patients by socio-demographic characteristics .

Variable	Frequency (%)
Birth order	
1 st baby	50 (25.0%)
2 nd baby	78 (39.0%)
More	72 (36.0%)
Mother's age	
< 18 years	20 (10.0%)
18-35 years	160 (80.0%)
> 35 years	20 (10.0%)
Father's age	
<35 years	149 (74.5%)
> 35 years	51 (25.5%)
Mother's education	
Illiterate	34 (17.0%)
Primary school	120 (60.0%)
Secondary school	39 (19.0%)
Higher education	7 (3.5%)
Father's education	
Illiterate	25 (12.5%)
Primary school	93 (46.5%)
Secondary school	72 (36.0%)
Higher education	10 (5.0%)
Socio-economic status	
Good	30 (15.0%)
Moderate	137 (68.5%)
Poor	33 (16.5%)
Residence	
Urban area	104 (52.0%)
Rural area	96 (48.0%)

Table 2: Distribution of patients by medical history

Variable	Frequency (%)
Type of feeding	
Breast feeding	68 (34.0%)
Bottle feeding	45 (22.5%)
Mix feeding	61 (30.5%)
Other	26 (13.0%)
Body weight	
< 5 kg	60 (30.0%)
5-10 kg	102 (51.0%)
> 10 kg	38 (19.0%)
History of previous attack	
Yes	42 (21.0%)
No	158 (79.0%)
Duration of Pneumonic attack	
< 3 days	71 (35.5%)
3-5 days	61 (30.5%)
> 5 days	68 (34.0%)

The distribution of pneumonic patients by medical history shows that (34.0%) of the patients had breast feeding and (51.0%) weighted between 5-10 kg. The majority (79.0%) of the patients did not have history of previous pneumonic attack. Only (34.0%) of the patients have been stayed more than 5 days in hospitals as shown in table 2.

4.3: In the association of Patients with Socio-Demographic Characteristics, there is significant association between type of pneumonia treatment and patients' gender, P value ≤ 0.05 as shown in Table 3.

Table 3: Association of patients with Socio-Demographic Characteristics

Variable	Treatment of Pneumonic Patient		χ^2	P Values
	With Zinc (%)	Without Zinc (%)		
Age (years)				
< One year	72 (72.0)	82 (82.0)	4.619	0.099
Year-3 years	21 (21.0)	10 (10.0)		
> 3 years	7 (7.0)	8 (8.0)		
Gender			4.577	0.032*
Male	64 (64.0)	49 (49.0)		
Female	36 (36.0)	51 (51.0)		
Birth order			1.707	0.426
1 st baby	29 (29.0)	21 (21.0)		
2 nd baby	37 (37.0)	41 (41.0)		
More	34 (34.0)	38 (38.0)		
Mother's age			1.600	0.449
< 18 years	12 (12.0)	8 (8.0)		
18-35 years	80 (80.0)	80 (80.0)		
> 35 years	8 (8.0)	12 (12.0)		
Father's age			0.237	0.626
< years	73 (73.0)	76 (76.0)		
> 35 years	27 (27.0)	24 (24.0)		
Mother's education			4.025	0.259
Illiterate	12 (12.0)	22 (22.0)		
Primary school	63 (63.0)	57 (57.0)		
Secondary school	22 (22.0)	17 (17.0)		
Higher education	3 (3.0)	4 (4.0)		
Father's education			2.471	0.481
Illiterate	11 (11.0)	14 (14.0)		
Primary school	47 (47.0)	46 (46.0)		
Secondary school	39 (39.0)	33 (33.0)		
Higher education	3 (3.0)	7 (7.0)		
Socio-economic status			1.538	0.463
Good	18 (18.0)	12 (12.0)		
Moderate	67 (67.0)	70 (70.0)		
Poor	15 (15.0)	18 (18.0)		
Residence			2.003	0.157
Urban area	57 (57.0)	47 (47.0)		
Rural area	43 (43.0)	53 (53.0)		

*P value ≤ 0.05 is significant

4.4: Association of patients with Medical History

There are significant associations between type of pneumonia treatment with the duration of disease. Only (21.0%) of pneumonic patients on zinc treatment have been stayed for 5 days in hospital, P value ≤ 0.05 as shown in Table 4..

Table 4.: Association of Patients with Medical History

Variable	Treatment of Pneumonic Patient		χ^2	P Values
	With Zinc (%)	Without Zinc (%)		
Type of feeding				
Breast feeding	26 (26.0)	42 (42.0)	6.755	0.080
Bottle feeding	28 (28.0)	17 (17.0)		
Mix feeding	32 (32.0)	29 (29.0)		
Other	14 (14.0)	12 (12.0)		
Body weight				
< 5 kg	23 (23.0)	37 (37.0)	5.304	0.071
5-10 kg	54 (54.0)	48 (48.0)		
> 10 kg	23 (23.0)	15 (15.0)		
Duration of Pneumonic attack				
< 3 days	48 (48.0)	23 (23.0)	18.760	<0.001*
3-5 days	31 (31.0)	30 (30.0)		
> 5 days	21 (21.0)	47 (47.0)		

*P value ≤ 0.05 is significant.

4.5: Association of Patients with Clinical Condition

There were significant associations between types of pneumonia treatment with progress of disease, only (35.0%) of pneumonic patients on zinc treatment stayed for four days in hospital.

Nine percent of patients on zinc free treatment complained from fever, meanwhile, (19.0%) patients with zinc free treatment had chest in drawing on physical examination. However, (8.0%), (48.0%) and (45.0%) on patients with zinc free treatment had audible wheezing, crepitation on chest auscultation as well as patching on CXR, respectively. Majority (97.0%) and (99.0%) of patients with zinc treatment had good feeding and have been discharged, respectively. Meanwhile, (11.0%) of pneumonic patients on zinc free treatment has been admitted to ICU, p value ≤ 0.05 as shown in table 5.

Table 5: Association of Patients with Clinical Condition

Variable	Treatment of Pneumonic Patient		χ^2	P Values
	With Zinc (%)	Without Zinc(%)		
Progress of disease (hours)				
24 hours	20 (20.0)	7 (7.0)	32.376	<0.001*
72 hours	45 (45.0)	18 (18.0)		
120 hours	35 (35.0)	75 (75.0)		
Consciousness			3.046	0.385 ^a
Alert	99 (99.0)	96 (96.0)		
Lethargic	0 (0.0)	2 (2.0)		
Irritable	1 (1.0)	1 (1.0)		
Drowsy	0 (0.0)	1 (1.0)		
Temperature			9.424	0.002*^a
Normal	100 (100.0)	91 (91.0)		
High	0 (0.0)	9 (9.0)		
SPO2			3.046	0.081 ^a
Normal	100 (100.0)	97 (97.0)		
Low	0 (0.0)	3 (3.0)		
Respiratory Rate			1.220	0.269
Normal	79 (79.0)	85 (85.0)		
Low	21 (21.0)	15 (3.0)		
Chest in drawing			18.000	<0.001*
Present	1 (1.0)	19 (19.0)		
Absent	99 (99.0)	81 (81.0)		
Audible wheezing			5.701	0.017*
Present	1 (1.0)	8 (8.0)		
Absent	99 (99.0)	92 (92.0)		
Chest auscultation			2.956	0.086
Crepitation	36 (36.0)	48 (48.0)		
Clear chest	64 (64.0)	52 (52.0)		
CXR finding			4.800	0.028*
Findings	30 (30.0)	45 (45.0)		
No findings	70 (70.0)	55 (55.0)		
Feeding			10.064	0.007*^a
Good	97 (97.0)	85 (85.0)		
Moderate	3 (3.0)	8 (8.0)		
Poor	0 (0.0)	7 (7.0)		
Fate of pneumonia			8.865	0.003*
Discharge	99 (99.0)	89 (89.0)		
ICU admission	1 (1.0)	11 (11.0)		

*P value ≤ 0.05 is significant

^a: Fisher Exact test

4.6: Association of Fate of Pneumonia with Type of Treatment among patients .

The association of fate of pneumonia with treatment type weighted by sex is shown in table 6. There is a significant association between fate of pneumonia and type of treatment among female, p value ≤ 0.05 .

Table 6: Association of Fate of Pneumonia with Type of Treatment among Male and Female patients.

Variable	Fate of Pneumonia		χ^2	P Values
	Discharge (%)	ICU Admission (%)		
Treatment of Pneumonic Patient among Male				
With Zinc	63 (58.3)	1 (20.0)	2.859	0.091
Without Zinc	45 (41.7)	4 (80.0)		
Treatment of Pneumonic Patient among Female			5.374	0.020*
With Zinc	36 (45.0)	0 (0.0)		
Without Zinc	44 (55.0)	7 (100.0)		

*P value ≤ 0.05 is significant

Discussion

The study aimed to evaluate zinc effect on the clinical course of pneumonia in children their ages ranged from one to sixty months been admitted to Babylon Teaching hospital for Maternity and Pediatrics.

There were no statistical significance between the two groups regarding factors which has an effect the course of the disease including the age, birth order, mother's age, parental education, socio-economic status, and residence. This could be due to random allocation of the patients included in the study. There are significant difference between the two groups according to sex, females' benefit from zinc more than males' regarding ICU admission versus discharge. A study by Morris,*etal* in India found the mortality from pneumonia was 50% more in girls than in boys^[16]. Another study in India at Christian Medical College Hospital has found male children got more beneficial effect from zinc than females. In our study regarding the duration of hospitalization ,the difference between the two groups was significant while in a double-blind randomized controlled trial in Qom, they found a significant reduction in the days of admission and the period of recovery from the disease in zinc-receiving patients. This finding was consistent

with the results by Brooks , *et al*, Mahalanabis ,*et al*, N. Bhandari , *et al*, and C. L. Coles,*et al*^[5,13,17,18] .

Brooks, *et al* found that using zinc in two to twenty –three months old patients with severe pneumonia result in significant reduction in the severity of symptoms as shortness of breaths, anorexia, restlessness, and days of admission .^[5]

Also another Indian study included two hundred ninety- nine children aged 2–23 months admitted for severe pneumonia showed improvement in the symptoms of the disease and the days of admission decreased significantly in the zinc-receiving patients.^[18]

The Indian study by Mahalanabis ,*et al* was applied on one hundred fifty three children their ages ranged between two and twenty four months old been admitted due to acute lower respiratory infection and divided into two groups (one taking 10 mg of zinc plus vitamin A daily, and the other taking placebo plus vitamin A), which showed the time of clinical improvement was significantly shorter than the treatment group than in the control group. The duration of the disease and acute clinical condition , can be reduced by Zinc administration^[13] , which goes with the findings of the current study.

In a clinical trial conducted in Bangladesh by Brooks , *et al*,^[5] Zinc administration leads to a decrease of twelve hours in the period of severe pneumonia and a decrease of sixteen hours in the hospital admission with a decrease in the respiratory rate in addition to reductions in tachypnea, chest indrawing, and hypoxia. Another study in Kolkata by Mahalanabis ,*et al* ,in India found a reduction by fifty percent in the duration of severe illness and a reduction by seventy five percent in the duration of fever.^[13]

The reductions of the duration of severe pneumonia and hospitalization time might be due to zinc effect in the acute phase response ,^[19-22] mediated by cytokines during acute infection.^[23-25] The lung may be protected from the inflammatory states by the administration of Zinc , but the airway inflammation and cellular damage may potentiated by Zinc deficiency.^[26]

Another study by Valentiner-Branth P ,*et al* from Nepal found that adjuvant zinc neither reduced the risk of treatment failure nor fasten the recovery from non- severe or severe pneumonia in children their age between two and thirty-five months .^[27]

In our study there are significant differences between the two groups regarding fever, chest in drawing, audible wheeze, CXR findings, and feeding improvement, but there are no significant differences between the two groups in O₂ saturation, consciousness level, respiratory rate, and chest auscultation.

Mahalanabis ,et al , the duration of fever reduced by fifty seven percent^[13] There were no effects on respiratory rate and feeding status, and the effects of Zinc administration on chest indrawing, hypoxia, and wheeze were not recorded .

In a study in Uganda' found the time of the parameters for disease severity to reach a normal level did not reduced by the administration of Zinc as adjunct treatment for pneumonia . These finding are goes with the finding two Indian studies by, Mahalanabis ,et al , Bose A,et al., and one Australian study by Chang AB ,et al.^[13,28,29]

A study by N. Bhandari ,etal, in India, on 2482 healthy children aged sex to thirty months, revealed pneumonia prevalence was lower in the treatment group than in the control group. This indicates that in addition to reducing the duration of symptoms and expediting the healing process in patients suffering from pneumonia, zinc can also prevent this disease^[17] In a study in Mashhad ,Iran conducted on two hundred early school age children, it was found that the number of respiratory infections reduced in the zinc –treated group when compared to the control group .

This showed zinc could be useful in the prevention of respiratory infection in children by improving their nutritional status.^[28]

In our study 11% of patients without zinc treatment had been admitted to the ICU, and 89% had been discharged, whereas only 1% of patients with zinc treatment had been admitted to the ICU, and 99% of patients had been discharged.

Conclusions

1. Zinc reduces the duration of hospitalization in pediatric patients with pneumonia when added to the usual pneumonia treatment.
2. Zinc hastens recovery in pediatric patients with pneumonia regarding fever, chest in drawing, audible wheeze, CXR findings, and feeding improvement.
3. Zinc supplementation reduces the need for ICU admission in pediatric patients with pneumonia.
4. Females were with better outcome than males.

Recommendations

1. Zinc should be added to any pediatric patient with pneumonia when seeking medical help.
2. Doctors should focus on those less than 1 year of age because they constitute the greater percentage of patients.
3. Further researches should be done to prove the preventive role of zinc in respiratory disease.

Conflict of interests.

There are non-conflicts of interest.

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الخلاصة

خلفية الدراسة: ذات الرئة مرض يقود الى وفيات الأطفال في الدول النامية ويعيق انجاز هدف تطوير الالفية الرابعة. هذا الهدف هو تقليل وفيات الأطفال دون سن الخامسة للثلاثين بين 1990-2015. تم تحديد تأثير اضافة الزنك لعلاج المرضى المصابين بذات الرئة على الوقت اللازم لتحسن المريض من ناحية سرعة التنفس, تحسن درجة الحرارة, نسبة تشبع الدم بالأوكسجين, تغذية المريض, فحص الصدر, ومدة رقود المريض في المستشفى في مستشفى بابل التعليمي للنسائية والأطفال.

هدف الدراسة: لبيان تأثير اضافة الزنك لعلاج المرضى المصابين بذات الرئة.

طرق العمل: في دراسة عرضية في مستشفى بابل التعليمي للنسائية والأطفال, تم تحديد 200 طفل بعمر (60-1 شهر) مصاب بذات الرئة وتم اضافة علاج الزنك (10 ملغم للأطفال ≥ 6 أشهر, و 20 ملغم للأطفال < 6 أشهر) الى 100 مريض بالاضافة الى علاج ذات الرئة أثناء فترة الرقود في المستشفى, وال 100 طفل المتبقين اخذوا علاج ذات الرئة بدون اضافة زنك. تم تسجيل الأعراض والعلامات السريرية لذات الرئة وقت الدخول, بعد 24 ساعة, بعد 72 ساعة, وبعد 120 ساعة.

النتائج: من التاريخ المرضي كان هناك اختلافات هامة (قيمة $P \leq 0,05$ في مدة ذات الرئة, لكن لم يكن هناك اختلافات هامة من ناحية وزن الجسم او نوعية التغذية. استجابة الاناث افضل من الذكور. كان هناك اختلافات سريرية وهامة بشكل احصائي (قيمة $P \leq 0,05$ في مدة العلاج بالمستشفى, تحسن درجة الحرارة, استخدام عضلات الصدر, الأزيز المسموع, التغذية, والخروج من المستشفى او دخول وحدة العناية المركزة. لكن لم يكن هناك اختلافات هامة بخصوص مستوى الوعي, نسبة تشبع الدم بالأوكسجين, وفحص الصدر.

الأستنتاجات: اضافة الزنك للمرضى المصابين بذات الرئة يقلل مدة رقود المريض في المستشفى ويزيد التحسن السريري بخصوص درجة الحرارة, استخدام عضلات الصدر, الأزيز المسموع, والتغذية. استجابة الاناث افضل من استجابة الذكور.