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Research Article

Clinical Outcome of Pneumonia with Zinc as an Adjuvant Therapy in Children: An Interventional Study in Bangladesh

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Abstract

Background: Severe pneumonia remains a leading cause of morbidity and mortality in undernourished young children across the globe and Zinc may have role in treatment of pneumonia as it contributes to the body immunity. It was aimed to find out the role of zinc supplementation along with antibiotic therapy in treatment of pneumonia of children under 5 years of age.

Methods: The interventional study was conducted from April 2012 to September 2012 in a tertiary care hospital in Dhaka city. A total 70 Children of 2 months to 5 years of age with pneumonia were included in the study. Enrollment of the study population was done by randomized sampling on the basis of inclusion and exclusion criteria. After that all patients was randomized into two groups, A and group B by lottery method. Group A was got zinc along with antibiotic and Group B was got only antibiotic therapy. Data was collected by interview, physical examinations and laboratory investigations using a structured questionnaire and analyzed using computer software SPSS.

Results: The mean age was found 12.4 ± 9.1 months in group A and 12.0 ± 8.3 months in group B. Chest indrawing and cough improvement were early start in group A. In 6th days at night all patients improved crepetation on auscultation of lungs in group A but 17.1% had crepetation on auscultation of lungs in group B, that was significantly ($p < 0.05$) higher in group A. Over all difference regarding the feeding and sleeping difficulty were not statistically significant ($P > 0.05$) between two groups. Early improvement of respiratory rate was observed in group A.

Conclusion: Children receiving zinc had a shorter duration of chest indrawing, crepetation on auscultation of lungs. Further multicentred studies would help to generalize the result.

Keywords: *Pneumonia; Zinc; Bangladesh; Children*

Background

Pneumonia continues to be the biggest single cause of childhood death, accounting for approximately 20% of the 10 million annual deaths globally [1]. Consequently, death from pneumonia is the leading single contributor to under 5 mortality globally, and Bangladesh is not an exception [2]. The etiologic agents for pneumonia include: *Streptococcus pneumonia, Haemophilus influenzae*, Respiratory Syncytial Virus (RSV) and a range of other bacteria and viruses which suggests that both intra and extra cellular immune responses are important for the disease process as well as treatment [3-8]. Malnutrition tolls a significant role in regards to the death caused by pneumonia [9]. In low-income countries, under nutrition is associated with a greater severity of pneumonia, a longer duration of illness and an increased case fatality rate [10]. While much emphasis is placed on protein- energy status and vitamin A, it has been proposed that zinc has a real potential in the prevention of pneumonia morbidity and mortality [11]. Two distinctive potential roles for zinc in modulating pneumonia burden exist; firstly as a preventive element when administered prior to pneumonia disease; secondly, zinc may change the course of pre-existing pneumonia when added as an adjunct to conventional antibiotic treatment potentially to reduce the severity and duration of pneumonia in sufferers [12]. Zinc plays a critical role in the development and maintenance of host defenses against infectious diseases [13,14]. Results from preventive trails show that zinc supplementation significantly reduces the incidence of pneumonia and chronic diarrhea in children living in areas of endemic zinc deficiency [15,16]. Although zinc as adjuvant therapy for hospitalized children with pneumonia was found to be beneficial in 1 clinical trial in Bangladesh, the benefit of zinc in the treatment of pneumonia is, however, unclear [17]. It was aimed to find out the role of zinc supplementation along with conventional antibiotic therapy in treatment of pneumonia of children under 5 years of age in regards to it would improve the outcome of pneumonia and thereby reduce the length of hospital stay.

Materials and Methods

The interventional study was conducted from April 2012 to September 2012 in a tertiary care hospital in Dhaka city. A total 70 Children of 2 months to 5 years of age with pneumonia admitted in Department of Pediatrics were included in the study. Enrollment of the study population was done by randomized sampling on the basis of inclusion and exclusion criteria. After that all patients was randomized into two groups, A, B by lottery method. Group A was got zinc along with antibiotic and Group B was got only antibiotic therapy. At the end of the study group A was taken as a case and group B was as control. Data was collected by interview, physical examinations and laboratory investigations using a structured questionnaire. Data was processed and analyzed using computer software SPSS (Statistical package for Social Science).

Inclusion Criteria:

i) Age: 2 months to 5 years
ii) Fast breathing (50 per minute or more if infant 2 months upto 12 months; 40 per minute or more if child 12 months upto 5 years).
iii) Chest indrawing.
iv) Fever (axillary temperature > 37.5°C)
v) Crepetation on auscultation of lung fields.
vi) X-ray Chest: Lobar or Patchy segmental opacity

Exclusion Criteria:

i) Age less than 2 months, more than 5 years.
ii) Wheezing at presentation.
iii) Severe malnutrition (weight for height medium < 70% or Z score < -3SD according to WHO).
iv) Congenital heart disease having murmur.
v) Severe anemia (defined as hemoglobin <7 gm/dL).
vi) Concurrent diarrhoea receiving zinc therapy.
vii) Tuberculosis in any form including pulmonary tuberculosis

Main outcome variable:

i. Time of resolution of Fast breathing, Chest indrawing, Fever and Crepitation on auscultaion.
ii. Time of recovery from feeding/ sleeping difficulty, restlessness, inconsolable crying or nasal flaring.
iii. Duration of hospital stay.
iv. Duration of hypoxemia (SpO_2 < 90%) Number of patient develop complication (pleural effusion, empyema, pneumothorax).

Procedures of collection data:

Children aged 2 months to 5 years who was diagnosed as a case of pneumonia was enrolled in this study. Chest radiograph was done to confirm the diagnosis. Patient was randomized into two groups by lottery method: Group A and Goup B. Group A was received zinc (10 mg in 2 to 11 months old and 20 mg in older children) along with standard antibiotic treatment (Intravenous Inj. Ampicillin and Inj. Gentamycin) and Group B was received only antibiotic (Intravenous Inj. Ampicillin and Inj. Gentamycin) treatment until discharge. Data for respiratory rate, chest indrawing, auscultation finding (crepitation), fever, cyanosis and general well being was obtained at admission, and every 8 hourly by four trained physician on a structured sheet. The day of recovery from severe pneumonia was defined as the beginning of the first 24 hour period without Lower Chest Indrawing. Patients who were fail to improve after 48 hours of antibiotics or whose condition was worse, their antibiotic was changed to ceftriaxone. Treatment failure, was defined as a requirement for change in antibiotics, development of complications such as pleural effusion, empyema or pneumothorax requiring surgical intervention or admission to the ICU for ventilator or inotropic support. Children was discharged from hospital once respiratory rate will fall to less than 50 per min (2 - 12 months) and 40 per min (12 month to 5 years) for 24 consecutive hours with no recurrence of respiratory distress, other danger signs or fever. Duration of clinical signs of pneumonia and duration of hospital stay was compared in both groups.

Ethical consideration

The researchers were properly concerned about the ethical issues relate to the study. Formal ethical clearance was taken from the proper ethical review committee for conducting the study. Participation was fully volunteered and informed written consent was taken. Confidentiality of the persons and the information was maintained and observed and unauthorized persons did not have any access to the collected data.

Results

A total of 70 patients were included in this study, in group A maximum 18 (51.4%) patients age belonged to 2 - 6 months and in group B 12 (34.3%) and 12 (34.3%) patients age belonged to 7 - 12 months and 13 - 18 months respectively. The mean age was found 12.4 ± 9.1 months in group A and 12.0 ± 8.3 months in group B. The mean age difference, gender, body weight, and income of the family was not statistically significant (P > 0.05) between two groups (Table 1). Mean body weight was found 8.75 ± 4.68 kg in group A and 9.52 ± 3.24 kg in group B (Table 1).

Socio-demography N		Group A		Group B	
		%	N	%	
Age in Months	2 – 6	18	51.4	8	22.9
	7 – 12	8	22.9	12	34.3
	13 – 18	7	20	12	34.3
	> 18	2	5.7	3	8.6
	Mean ± SD	12.4 ± 9.1		12 ± 8.3	
	Range(min-max)	(2 - 53)		(2 - 34)	
Sex	Male	15	42.9	20	57.1
	Female	20	57.1	15	42.9
Weight	weight (kg)	8.75 ± 4.68		10 ± 3.24	
	Range(min-max)	(4 - 15)		(3 - 14)	
Income	(5,000 - 15,000 BDT)	24	68.6	21	60
	(< 5,000 BDT)	11	31.4	14	40

Table 1: *Socio-demographic distribution of the study patients (n = 70).*

Chest indrawing was improved during 3rd days in both groups, which was 60.0% and 60.0% at morning. No statistically significant (p > 0.05) between two groups. In 4th days at night all patients were improved in group A, but 6 (17.1%) patients had chest indrawing in group B. In 5th days at night all patients were improved in group A but 3 (8.6%) patients had chest indrawing in group B. The difference was not statistically significant (P > 0.05) between two groups (Table 2).

Chest indrawing	Group A (n = 35)		Group B (n = 35)		P value
	n	%	n	%	
Days 1	No Change				
Day 2	No Change				
Day 3					
TIME (6:00 AM)					
Present	21	60.0	21	60.0	0.100ns
Absent	14	40.0	14	40.0	
TIME (2:00 PM)					
Present	13	37.1	21	60.0	0.055ns
Absent	22	62.9	14	40.0	
TIME (10:00 PM)					
Present	13	37.1	18	51.4	0.228ns
Absent	22	62.9	17	48.6	
Day 4					
TIME (6:00 AM)					
Present	9	25.7	9	25.7	1.000ns
Absent	26	74.3	26	74.3	
TIME (2:00 PM)					
Present	4	11.4	9	25.7	0.124ns
Absent	31	88.6	26	74.3	
TIME (10:00 PM)					
Present	0	0.0	6	17.1	0.012s
Absent	35	100.0	29	82.9	
Day 5					
TIME (6:00 AM)					
Present	0	0.0	3	8.6	0.119ns
Absent	35	100.0	32	91.4	
TIME (2:00 PM)					
Present	0	0.0	3	8.6	0.119ns
Absent	35	100.0	32	91.4	
TIME (10:00 PM)					
Present	0	0.0	3	8.6	0.119ns
Absent	35	100.0	32	91.4	

Table 2: *Distribution of the study patients according to chest indrawing during baseline and follow-up (n = 70).*

Crepetation on auscultation of lungs improved during 2 days in group B, which was 5.7% at night. No statistically significant ($p > 0.05$) between two groups. In 3rd days at night 16 (45.7%) patients improved crepetation on auscultation of lungs in group A and 3 (8.6%) in group B. The difference was statistically significant ($p < 0.05$). In 4th days at morning 24 (68.6%) patients in group A and 14 (40.0%) patients in group B improved crepetation on auscultation of lungs. The difference was statistically significant ($p < 0.05$) (Table 3). In 5th days at night all patients were improved crepetation on auscultation in group A but 6 (17.1%) patients had crepetation on auscultation in group B. The difference was statistically significant ($p < 0.05$). In 6th days at night all patients improved crepetation on auscultation of lungs in group A but 6 (17.1%) patients had crepetation on auscultation in group B. The difference was statistically significant ($P > 0.05$) between two groups (Table 3).

Crepetation on auscultation of lungs	Group A (n = 35)		Group B (n = 35)		P value
	n	%	n	%	
Day 1	No Change				
Day 2	No Change				
Day 3					
Time (6:00AM)					
Present	29	82.9	35	100.0	0.012[s]
Absent	6	17.1	0	0.0	
Time (2:00PM)					
Present	27	77.1	32	91.4	0.100[ns]
Absent	8	22.9	3	8.6	
Time (10:00PM)					
Present	19	54.3	32	91.4	0.001[s]
Absent	16	45.7	3	8.6	
Day 4					
Time (6:00AM)					
Present	11	31.4	21	60.0	0.016[s]
Absent	24	68.6	14	40.0	
Time (2:00PM)					
Present	9	25.7	18	51.4	0.021[s]
Absent	26	74.3	17	48.6	
Time (10:00PM)					
Present	6	17.1	15	42.9	0.018[s]
Absent	29	82.9	20	57.1	
Day 5					
Time (6:00AM)					
Present	0	0.0	9	25.7	0.001[s]
Absent	35	28.6	26	74.3	
Time (2:00PM)					
Present	0	0.0	6	17.1	0.001[s]
Absent	35	28.6	29	82.9	
Time (10:00PM)					
Present	0	0.0	6	17.1	0.001[s]
Absent	35	28.6	29	82.9	
Day 6					
Time (6:00AM)					
Present	0	0.0	3	8.6	0.119[ns]
Absent	35	100.0	32	91.4	
Time (2:00PM)					
Present	0	0.0	3	8.6	0.119[ns]
Absent	35	100.0	32	91.4	
Time (10:00PM)					
Present	0	0.0	6	17.1	0.012[s]
Absent	35	100.0	29	82.9	

Table 3: *Distribution of the study patients according to lung finding on auscultation during baseline and follow-up (n = 70).*

Inconsolable crying improved during 3rd days at morning in both groups, which was 27 (77.1%) in group A and 20 (57.1%) in group B. The difference was statistically significant ($p < 0.05$). In 4th days at morning, at lunch and at night 25 (71.4%) patients improved in group A and 11 (31.4%) patients in group B improved Inconsolable crying. The difference was statistically significant ($p < 0.05$). In 5th days at three times (6:00 AM, 2:00 PM and 10:00 PM) all patients were improved Inconsolable crying in group I and in group II 29 (82.9%) improved at morning, 32 (91.4%) at lunch and all patient improved at night (Table 4). In 5th days at morning difference was not statistically significant ($p > 0.05$) between two groups. Inconsolable crying was improved early in group A, but the over all improvement at 5th day was almost similar ($P > 0.05$) between two groups (Table 4).

Inconsolable crying	Group A (n = 35)		Group B (n = 35)		P value
	n	%	n	%	
Day 1	No Change				
Day 2	No Change				
Day 3					
Time (6:00am)					
Present	20	57.1	27	77.1	0.074ns
Absent	15	42.9	8	22.9	
Time (2:00pm)					
Present	23	65.7	29	82.9	0.100ns
Absent	12	34.3	6	17.1	
Time (10:00pm)					
Present	29	82.9	29	82.9	0.100ns
Absent	6	17.1	6	17.1	
Day 4					
Time (6:00am)					
Present	11	31.4	25	71.4	0.001s
Absent	24	68.6	10	28.6	
Time (2:00pm)					
Present	11	31.4	25	71.4	0.001s
Absent	24	68.6	10	28.6	
Time (10:00pm)					
Present	11	31.4	25	71.4	0.001s
Absent	24	68.6	10	28.6	
Day 5					
Time (6:00am)					
Present	0	0.0	6	17.1	0.010s
Absent	35	100.0	29	82.9	
Time (2:00pm)					
Present	0	0.0	3	8.6	0.119ns
Absent	35	100.0	32	91.4	
Time (10:00pm)					
Present	0	0.0	0	0.0	-
Absent	35	100.0	35	100.0	

Table 4: *Distribution of the study patients according to inconsolable crying during baseline and follow-up (n = 70).*

Cyanosis was improved during 2 days in both groups, which was 100.0% and 100.0% at lunch and night. In 3rd days at morning, lunch and night all patients were improved in group B, but 2 (5.7%) patients had cyanosis in group A. The difference was not statistically significant ($p > 0.05$) between two groups.

Cough was improved during 3rd days in both groups, which was 5.7% and 8.6% at night. No statistically significant ($p > 0.05$) between two groups. In 4th days at night 24 (68.6%) patients in group A and 14 (40.0%) patients in group B improved cough. The difference was statistically significant ($p < 0.05$). In 5th days at night all patients were improved cough in group A but 6 (17.1%) patients had cough in group B. In 6th days at night all patients improved cough in group A but only 3 (8.6%) patients had cough in group B. The difference was not statistically significant ($P > 0.05$) between two groups.

Social smile improved during 3rd days in both groups at three times (6:00 AM, 2:00 PM and 10:00 PM). In 3rd days at morning 22 (62.9%) in group A and 27 (77.1%) patients in group B improved social smile. In 4th days at morning 16 (45.7%) patients in group A and 18 (51.4%) patients in group B were improved social smile. The difference was not statistically significant ($p > 0.05$). In 5th days at three times (6:00 AM, 2:00 PM and 10:00 PM) 27 (77.1%) patients were improved social smile in group A and 23 (65.7%) improved in group B. In 6th days at three times (6:00 AM, 2:00 PM and 10:00 PM) all patients were improved in group I but 32 (91.4%) patients were improved social smile in group B. The difference was not statistically significant ($p > 0.05$).

Nasal flaring improved during 2 days at lunch in both groups, which was 15 (42.9%) in group A and 11 (31.4%) in group B at lunch. In 4th day, at morning all patients improved in group A and 29 (82.9%) improved in group B. The difference was statistically significant ($p < 0.05$). In 5th days all three times (6:00 AM, 2:00 PM and 10:00 PM) all patients were improved nasal flaring in group A and group B respectively.

Mean respiratory rate in 1 day at lunch was found 58.51 ± 5.1 per min in group A and 56.94 ± 5.69 per min in group B. The difference was statistically significant ($p < 0.05$) between two groups (Table 5). In 2 days at three times (6:00 AM, 2:00 PM and 10:00 PM) almost similar respiratory rate was found between two groups, which was statistically not significant ($p > 0.05$). In 3rd days respiratory rate was higher than group A. The difference was statistically significant ($p > 0.05$). In 4th days mean respiratory rate was almost similar between two groups. In 5th days, at morning respiratory rate was found 47.2 ± 1.03 per min in group I and 43.73 ± 3.74 per min in group B. At lunch time mean respiratory rate was found 45.2 ± 1.03 per min and 43.5 ± 3.65 per min in group A and group B respectively (Table 5). The difference was statistically significant $p < 0.05$) between two groups.

Respiratory rate/per min	Group A (n = 35)	Group B (n = 35)	P value
	Mean ± SD	Mean ± SD	
Day 1			
Time (6:00am)	58.97 ± 5.43	56.63 ± 6.36	0.102ns
Range(Min-Max)	(42 - 66)	(50 - 68)	
Time (2:00pm)	58.51 ± 5.1	56.94 ± 5.69	0.001s
Range(Min-Max)	(44 - 66)	(50 - 68)	
Time (10:00pm)	57.26 ± 4.8	57.31 ± 6.3	0.970ns
Range(Min-Max)	(42 - 62)	(50 - 70)	
Day 2			
Time (6:00am)	55.89 ± 4.99	55.74 ± 5.22	0.902ns
Range(Min-Max)	(42 - 62)	(48 - 66)	
Time (2:00pm)	54.46 ± 4.3	54.97 ± 5.41	0.663ns
Range(Min-Max)	(40 - 60)	(48 - 68)	
Time (10:00pm)	52.86 ± 4.4	53.97 ± 5.76	0.368ns
Range(Min-Max)	(40 - 58)	(45 - 66)	
Day 3			
Time (6:00am)	50.57 ± 4.62	52.8 ± 4.56	0.046s
Range(Min-Max)	(36 - 56)	(46 - 62)	
Time (2:00pm)	49.11 ± 4.64	52.17 ± 5.28	0.012s
Range(Min-Max)	(34 - 55)	(44 - 62)	
Time (10:00pm)	48.69 ± 4.76	51.37 ± 5.08	0.025s
Range(Min-Max)	(36 - 59)	(44 - 62)	
Day 4			
Time (6:00am)	46.65 ± 5.43	47.71 ± 4.73	0.386ns
Range(Min-Max)	(32 - 58)	(40 - 58)	
Time (2:00pm)	45.35 ± 3.77	46.46 ± 5.04	0.300ns
Range(Min-Max)	(32 - 48)	(40 - 58)	
Time (10:00pm)	44.9 ± 4.03	45.74 ± 5.11	0.447ns
Range(Min-Max)	(32 - 48)	(40 - 58)	
Day 5			
Time (6:00am)	47.2 ± 1.03	43.75 ± 3.74	0.001s
Range(Min-Max)	(46 - 48)	(40 - 52)	
Time (2:00pm)	45.2 ± 1.03	43.5 ± 3.65	0.010s
Range(Min-Max)	(44 - 46)	(40 - 50)	
Time (10:00pm)	43.6 ± 3.1	42.88 ± 3.87	0.393ns
Range(Min-Max)	(40 - 46)	(38 - 50)	
Day 6			
Time (6:00am)	- -	43 ± 5.48	-
Range(Min-Max)	- -	(38 - 48)	
Time (2:00pm)	- -	43 ± 5.48	
Range(Min-Max)	- -	(38 - 48)	
Time (10:00pm)	- -	42 ± 4.38	
Range(Min-Max)	- -	(38 - 46)	
Day 7			
Time (6:00am)	- -	46 ± 0.0	
Range(Min-Max)	- -	(46 - 46)	
Time (2:00pm)	- -	44 ± 0.0	
Range(Min-Max)	- -	(44 - 44)	
Time (10:00pm)	- -	42 ± 0.0	
Range(Min-Max)	- -	(42 - 42)	

Table 5: *Distribution of the study patients according to respiratory rate/per min during baseline and follow-up (n = 70).*

Discussion

In current study it was observed that the mean age was 12.4 ± 9.1 months with range from 2 – 53 months in group A and 12.0 ± 8.3 months with range from 2 – 34 months in group B (Table 1). The age distribution was different from other study by Brooks., *et al*. where the authors observed the mean age was 9.5 ± 6.2 months in group I and 9.6 ± 6.0 months in group II [17] and Sazawal., *et al*. observed mean age of the patients, was 18.6 ± 8.5 months in group I and 18.6 ± 8.7 months in group II [18]. In case of chest indrawing, improvement was early start in group I but the over all difference was not statistically significant ($P > 0.05$) between two groups which was closely resembled with the other studies conducted in Bangladesh where the patients received zinc had a shorter duration of chest indrawing and the overall duration of pneumonia (Table 2) [17]. Crepetation on auscultation of lungs was observed in all patients in both groups during admission. In 3rd days at night 45.7% improved crepetation on auscultation of lungs in group A and 8.6% in group B, which was significantly ($p < 0.05$) higher in group A (Table 3) and the result was aligned with other study which mentioned early improved in zinc supplementation group [17]. The nasal flaring symptoms improves earlier in the zinc supplemented group that was statistically significant and aligned with similar study that studied the efficacy of zincum gluconicum nasal gel and found that zinc-treated patients had a significantly shorter duration of nasal flaring (4.3 days versus 6.0 days) when compared to placebo ($p < 0.001$) [19].

In this current series it was observed that the mean respiratory rate/min were 58.97 ± 5.43 /min and 56.63 ± 5.43/ min in group A and group B respectively (Table 5). During 3rd days respiratory rate significantly improved more in group A. Early improvement of respiratory rate was observed in group A and there were differences with other study result but those can be explained by different setting of the study as well as in both studies improvement was rapid in the zinc supplemented group [17]. The study was conducted in single tertiary care hospital in Dhaka. Further multicentered large scale study would help much to generalize the result and take necessary steps to use zinc on routine basis.

Conclusion

This study was undertaken to evaluate the effects of zinc in the treatment of pneumonia in children age from 2 month to 5 years. Early reductions were found in chest indrawing, crepetation on auscultation of lungs, inconsolable crying, nasal flaring, respiratory rate. However cyanosis, cough, feeding, sleeping and social smile improvement were almost similar between two groups.

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Conflict of Interest

None.

Bibliography

1. Rudan I., *et al*. "Epidemiology and etiology of childhood pneumonia". *Bulletin of the World Health Organization* 86.5 (2008): 408-416.

2. Fishman SM., *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.

3. Scott JA, *et al*. "Pneumonia research to reduce childhood mortality in the developing world". *Journal of Clinical Investigation* 118.4 (2008): 1291-1300.

4. Black RE., *et al*. "Where and why are 10 million children dying every year?" *Lancet* 361.9376 (2003): 2226-2234.

5. Garenne M., *et al*. "The magnitude of mortality from acute respiratory infections in children under 5 years in developing countries". *World Health Statistics Quarterly* 45.2-3 (1992): 180-191.

6. Mathers C., *et al*. "Global Burden of disease 2000: version 2 methods and results". Discussion Paper No. 50 (2002).

7. Mulhollan K. "Childhood pneumonia mortality- a permanent global emergency". *Lancet* 370.9583 (2007): 285-289.

8. Mulhollan K. "Global burden of acute respiratory infections in children: implications for interventions". *Pediatric Pulmonology* 36.6 (2003): 469-474.

9. Caulfield LE., *et al*. "Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria and measles". *American Journal of Clinical Nutrition* 80.1 (2004): 193-198.

10. Prasad AS. "Effects of zinc deficiency on Th 1 and Th2 eytokine shifts". *Journal of Infectious Diseases* 182.1 (2000): S62-S68.

11. Black RE. "Zinc deficiency, infectious disease and mortality in the developing world". *Journal of Nutrition* 133 (2003): 1485S-1489S.

12. Richard SA., *et al*. "Zinc and iron supplementation and malaria, diarrhoea and respiratory infections in children in the peruvian Amazon". *American Journal of Tropical Medicine and Hygiene* 75.1 (2006): 126-132.

13. Shanker AH and Prasad AS. "Zinc and immunefunction: the biological basis of altered resistance to infection". *American Journal of Clinical Nutrition* 68.2 (1998): 447S-463S.

14. Bhutta ZA., *et al*. "Prevention of diarrhea and pneumonia by zinc supplemntaion in children in developing countries: pooled analysis of randomized controlled trials. Zinc Investigators Collaborative Group". *Journal of Pediatrics* 135.6 (1999): 689-697.

15. Walker CF and Black RE. "Zinc and the risk for infectious disease". *Annual Review of Nutrition* 24 (2004): 255-275.

16. Salgueiro MJ., *et al*. "Zinc an essential micronutrient A review". *Nutrition Reviews* 20 (2000): 737-755.

17. Brooks WA., *et al*. "Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial". *Lancet* 363.9422 (2004): 1683-1688.

18. Sazawal S., *et al*. "Zinc supplementation reduces the incidence of acute lower respiratory infections in infants and pre-school children: A double-blind placebo-controlled trial". *Pediatrics* 102 (1998): 1-5.

19. Mossad SB., *et al*. "Zinc gluconate lozenges for treating the common cold. A randomized, double-blind, placebo-controlled study". *Annals of Internal Medicine* 125.2 (1996): 81-88.

Volume 3 Issue 5 February 2017