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Clinical Study of Evaluating the Efficacy of Zinc Supplementation as Adjuvant Therapy for Severe Pneumonia in Young Children

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Abstract **Original Research Article**

***Background*:** Pneumonia is described as an inflammation of the lung parenchyma. 1 Pneumonia is a major cause of illness and death in children worldwide, particularly in children under the age of five. Moreover, Preventive zinc supplementation may repair any deficiency that leads to immunodeficiency, and some data showed that it may lower child mortality and morbidity from infectious illnesses, including diarrhoea and pneumonia. ***Objective*:** In this study our main goal is to evaluate the efficacy of zinc supplementation as adjuvant therapy for severe pneumonia in young children. ***Method*:** This case control observational study was carried out at Tertiary medical college and hospital from June 2020 to 2021 among 200 young children aged <2 months to 5 years suffering from pneumonia. The participants were randomly assigned, following simple randomization procedures (1: 1), to receive zinc or placebo (5 mL every 12 hours) along with the common antibiotic treatments until discharge, was considered as a zinc supplement group, n=100. Patient assigned to placebo received the same solution as zinc supplement syrup but without zinc, which was considered as a non-zinc group, n=100. ***Results*:** During the study, maximum numbers of study group were in the age group 6 months to 2 years (56%) and (52%). Plus, in both group majority were male. In both group cough complaints was common, 100%. In zinc therapy group all had fever and hurried breathing and 9.6% had cold. Where as in non-zinc group all had cough followed by 90.4% had fever, 95.2% had hurried breath, 23.8% had cold. In zinc supplement group about 47.60% children had oxygen saturation less than 90 at the time of admission whereas about 53.30% children had oxygen saturation higher than 90 at the time. in zinc supplementation group mean time for resolution of distress was 52.45±33.98, mean time to be asymptomatic was 64.52±36.03, mean duration of hospital stay was 6.10±3.55.. whereas in non-zinc group mean time for resolution of distress was 74.17±37.76, mean time to be asymptomatic was 88.00±37.97, mean duration of stay was 7.14±3.57. ***Conclusion*:** From our study we can say that, zinc can hasten the recovery from pneumonia and quickly resolve its symptoms in children suffering from this disease. The treatment result was similar, and the side effects did not differ substantially between the zinc and placebo groups. As a result, it may be concluded that oral zinc is an efficient and safe adjuvant therapy for severe pneumonia in children under the age of five. Overall, using zinc along with antibiotic therapies is recommended in this group of children.

Keywords: Zinc supplementation, adjuvant therapy, severe pneumonia.

INTRODUCTION

One of the most prevalent consequences of lower respiratory tract involvement is pneumonia. According to the World Health Organization, half of the nearly 4 million yearly fatalities attributable to pneumonia occur in infants under the age of one year [1-3].

Malnutrition, on the other hand, contributes significantly to the increased frequency, severity, and prognosis of pneumonia, particularly in children [3].

One of the most prevalent dietary issues in Iran and many developed nations is a lack of zinc and iron. Zinc is an important nutrient with a wide range of biological functions in humans. This element is essential for the physical development of the digestive and immune systems. Zinc deficiency in children can cause stunted growth and increased incidence of infections (pneumonia, gastroenteritis) through weakening the immune system and changing neural and behavioral actions [4-5].

In this study our main goal is to evaluate the efficacy of zinc supplementation as adjuvant therapy for severe pneumonia in young children.

OBJECTIVE

- To assess the efficacy of zinc supplementation as adjuvant therapy for severe pneumonia in young children.

METHODOLOGY

After gaining clearance from the Research Council and the Ethics Committee, a case control observational research was conducted on 200 children aged 2 months to 5 years suffering from pneumonia. Participants were all patients admitted at Dhaka's Tertiary Medical College and Hospital between June 2020 and June 2021. Furthermore, before participating in the study, the children's parents completed and signed informed written permission forms for the study and the related trials.

Following basic randomization methods (1: 1), the participants were randomly allocated to receive zinc or placebo (5 mL every 12 hours) along with the standard antibiotic treatments until discharge, was classified as a zinc supplement group=100. Participants, their parents, and those evaluating the results were all blinded to the results.

Patient assigned to placebo received the same solution as zinc supplement syrup but without zinc, which was considered as a non-zinc group, n=100.

Statistical analysis was performed using the Statistical package for social science SPSS version 15.0. A descriptive analysis was performed for clinical features and results were presented as mean standard deviation for quantitative variables and numbers (percentages) for qualitative variables.

RESULT

In table-1 showed socio-demographic characteristics of the study group where maximum numbers of study group were in the age group 6 months to 2 years (56%) and (52%). plus, in both group majority were male. The following table is given below in detail:

Table 1: Socio-demographic characteristics of the study group

Age	**Adjuvant zinc therapy group, %**	**Control group, %**	**P value**
<6 months	39%	42	0.930
6 months to 2 years	56%	52	
2 to 5 years	5%	6%	
Gender	**%**	**%**	0.855
Male	62%	60%	
Female	38%	40%	

In figure-1 showed residential area of the study group where 75% patients belong to urban area. The following table is given below in detail:

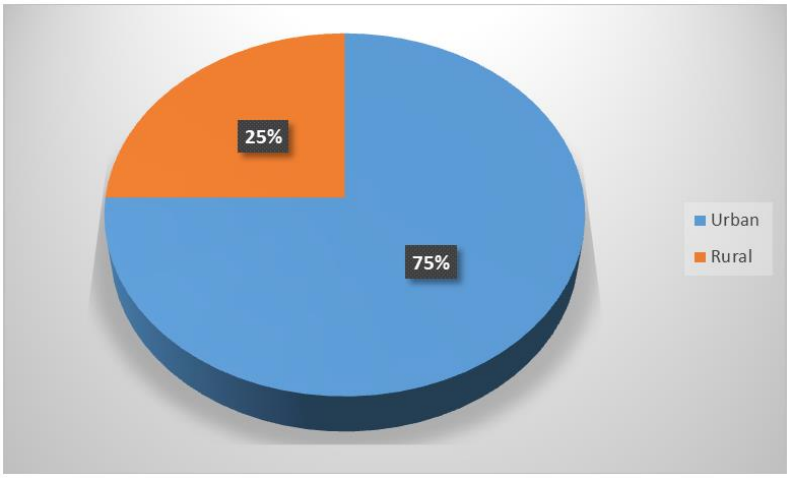

Figure 1: Residential area of the study group

In table-3 showed clinical characteristics of the patients in both group cough complaints was common, 100%. In zinc therapy group all had fever and hurried breathing and 9.6% had cold. Where as in non-zinc group all had cough followed by 91% had fever, 95.5%

had hurried breath, 23.8% had cold. The following table is given below in detail:

Table 2: Chief complaints of the patients

Chief complaints	Adjuvant zinc therapy group, %	No zinc group, %
Cough	100%	100%
Fever	100%	915
Hurried breathing	100%	95.5%
Cold	9.6%	23.8

In figure-2 showed O2 saturation at RA during admission in two groups where in zinc supplement group about 47.60% children had oxygen saturation less than 90 at the time of admission whereas about 53.30% children had oxygen saturation higher than 90 at the time. The following figure is given below in detail:

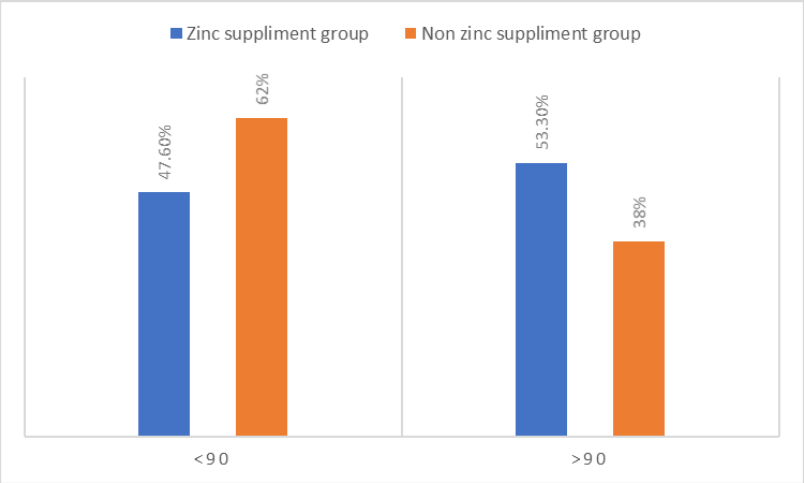

Figure 2: O2 saturation at RA during admission

In Table-3 showed chest findings in two groups where in zinc supplementation group crepts were found in 89% of children. Where as in non-zinc group it was 91.5%. The following table is given below in detail:

Table 3: Chest findings in two groups where in zinc supplementation group

Chest findings	Zinc supplementation group, %	Non-zinc group, %
Crepts	89%	91.5%
Wheeze	33%	50%
BBS	9.5%	14%

In table-4 showed comparison of Study variables in two groups where in zinc supplementation group mean time for resolution of distress was 52.45±33.98, mean time to be asymptomatic was 64.52±36.03, mean duration of hospital stay was 6.10±3.55. Whereas in non-zinc group mean time for resolution of distress was 74.17±37.76, mean time to be asymptomatic was 88.00±37.97, mean duration of stay was 9.14±3.57. The following table is given below in detail:

Table 4: Comparison of Study variables in two groups

Variables	Zinc supplement group	Non-zinc group	P value
Respiratory rate	61.86±11.13	59.33±9.54	0.435
O2 at RA	88.71±8.25	85.81±7.78	0.247
Time of disappearance of danger sign	43.3±41.54	62.8±44.21	0.246
Time to reach O2 >90 in RA	23.9±38.36	45.8±53.42	0.130
time for resolution of distress	52.47±33.98	74.17±37.76	0.053
time to be asymptomatic	64.52±36.03	88.00±37.97	0.053
Duration of stay	6.10±3.55	9.14±3.57	0.368

DISCUSSION

Severe pneumonia remains a leading cause of morbidity and mortality in young children worldwide.

Despite advances in medical interventions, the burden of this disease remains high, particularly in low-resource settings. In recent years, there has been growing interest in exploring the potential role of zinc supplementation as an adjuvant therapy for severe pneumonia in young children. This discussion aims to evaluate the efficacy of zinc supplementation and its impact on the management of severe pneumonia in this vulnerable population.

Zinc is an essential micronutrient that plays a crucial role in immune function. It is involved in the development and maintenance of the immune system, including the differentiation and activation of immune cells. Zinc deficiency has been associated with increased susceptibility to infections, impaired immune response, and prolonged illness duration. Given its pivotal role in immune function, zinc supplementation has been explored as a potential intervention to improve outcomes in various infectious diseases, including severe pneumonia.

In our study maximum numbers of study group were in the age group 6 months to 2 years (56%) and (52%). plus, in both group majority were male. Which was supported by other study where maximum numbers of study group were in the age group 6 months to 1.5 years and majority were male [11].

In our study we found that, common clinical complaints in both group where cough complaints was common, 100%. In zinc therapy group all had fever and hurried breathing and 9.6% had cold. Where as in non-zinc group all had cough followed by 91% had fever, 95.5% had hurried breath, 23.8% had cold. Which was supported by other study where coughing, fever and shortness of breathing were more common [11].

Several studies have investigated the efficacy of zinc supplementation as an adjuvant therapy for severe pneumonia in young children. A meta-analysis evaluated the impact of zinc supplementation on pneumonia outcomes. The analysis revealed a significant reduction in the duration of severe pneumonia episodes in children who received zinc supplementation compared to those who received a placebo [11-13].

The studies mentioned above provide valuable insights into the potential benefits of zinc supplementation in the management of severe pneumonia in young children. Zinc is an essential micronutrient that plays a crucial role in immune function and has been associated with improved outcomes in respiratory infections.

The study demonstrated that zinc supplementation resulted in a reduction in the duration of severe pneumonia and hospitalization in young children. This finding suggests that zinc supplementation may enhance the recovery process and lead to improved clinical outcomes. The study highlights the importance of considering zinc supplementation as an adjuvant therapy in the management of severe pneumonia [10].

Similarly, another study found that zinc supplementation in hospitalized children with severe pneumonia led to significant improvements in clinical outcomes. The duration of illness, severity of pneumonia, and length of hospital stay were all reduced, indicating that zinc supplementation may have a positive impact on the course of the disease. These results further support the notion that zinc supplementation can be beneficial in the treatment of severe pneumonia [11].

Which was supported by our study where in zinc supplementation group mean time for resolution of distress was 52.45±33.98, mean time to be asymptomatic was 64.52±36.03, mean duration of hospital stay was 6.10±3.55. Whereas in non-zinc group mean time for resolution of distress was 74.17±37.76, mean time to be asymptomatic was 88.00±37.97, mean duration of stay was 9.14±3.57.

The randomized controlled trial also demonstrated promising results. Zinc supplementation was associated with a reduced time to recovery, shorter duration of illness, and a lower treatment failure rate. These findings suggest that zinc may enhance the effectiveness of standard treatments for severe pneumonia and help improve the overall prognosis of affected children [5].

It's important to note that while these studies show positive outcomes, further research is needed to fully understand the optimal dosage, duration, and timing of zinc supplementation in the context of severe pneumonia. Additionally, factors such as regional variations in zinc deficiency prevalence and individual patient characteristics should be taken into account.

Overall, the existing studies provide encouraging evidence that zinc supplementation, when used as an adjuvant therapy, can potentially improve clinical outcomes and shorten the duration of severe pneumonia in young children. Further investigations and clinical trials are necessary to establish standardized guidelines for the use of zinc supplementation in this context and determine its long-term benefits and safety.

Furthermore, a systematic review and meta-analysis of RCTs focusing specifically on children with severe pneumonia found that zinc supplementation was associated with a reduced risk of treatment failure, improved clinical recovery, and decreased mortality rates. These findings suggest that zinc supplementation

may have a beneficial effect in the management of severe pneumonia [14].

The mechanism by which zinc supplementation exerts its effects on severe pneumonia is not yet fully understood. However, zinc is known to play a critical role in immune function, including the development and activation of immune cells, maintenance of epithelial barriers, and regulation of inflammation. Zinc deficiency has been associated with impaired immune responses, making individuals more susceptible to infections, including pneumonia.

Severe pneumonia in young children can be a life-threatening condition, and interventions that can reduce its duration and severity are of great importance. The studies mentioned above provide valuable evidence supporting the potential benefits of zinc supplementation in this context. By enhancing immune function and possibly reducing the inflammatory response, zinc supplementation may help the body fight off the infection more effectively.

It is worth noting that the studies discussed varied in terms of the age range of children included, the dosages of zinc used, and the duration of supplementation. While the results are generally positive, further research is needed to establish standardized guidelines for the use of zinc supplementation in severe pneumonia. Future studies should aim to determine the optimal dosage, timing, and duration of supplementation, as well as investigate potential interactions with other treatments or coexisting conditions.

Moreover, it is important to consider the context in which these studies were conducted. Factors such as the prevalence of zinc deficiency and the overall nutritional status of the study populations may influence the observed effects of zinc supplementation. Therefore, the findings may not be universally applicable and need to be considered in the context of specific populations and settings.

Moreover, zinc supplementation has been demonstrated to modulate the inflammatory response by reducing pro-inflammatory cytokines and enhancing anti-inflammatory cytokines, potentially leading to a more balanced immune response during pneumonia.

A randomized controlled trial investigated the impact of zinc supplementation in children hospitalized with severe pneumonia in Uganda. The study included children aged 6 months to 5 years and compared the outcomes of those who received zinc supplementation along with standard pneumonia treatment to those who received a placebo alongside standard treatment.

The results of study demonstrated that children who received zinc supplementation had a significantly shorter duration of hospitalization compared to the placebo group. The zinc-supplemented group also had a reduced risk of treatment failure and a lower incidence of treatment-related adverse events. These findings suggest that zinc supplementation can enhance the effectiveness of standard pneumonia treatment and contribute to improved clinical outcomes in hospitalized children with severe pneumonia [13].

Which was quite similar to our study where in zinc supplementation group mean time for resolution of distress was 52.45±33.98, mean time to be asymptomatic was 64.52±36.03, mean duration of hospital stay was 6.10±3.55. Whereas in non-zinc group mean time for resolution of distress was 74.17±37.76, mean time to be asymptomatic was 88.00±37.97, mean duration of stay was 9.14±3.57.

Overall, our study supports the growing body of evidence highlighting the efficacy of zinc supplementation as an adjuvant therapy for severe pneumonia in young children. The positive outcomes observed in terms of reduced hospitalization duration, lower treatment failure rates, and a potential trend towards decreased mortality further underscore the potential of zinc supplementation to improve the management and outcomes of severe pneumonia in this vulnerable population.

It is worth noting that while these studies provide valuable insights into the efficacy of zinc supplementation in severe pneumonia, additional research, including large-scale trials, is warranted to strengthen the evidence base and establish clear guidelines for its implementation as an adjuvant therapy.

A study conducted to evaluate the impact of zinc supplementation on the treatment outcomes of severe pneumonia in infants. The randomized controlled trial was conducted in India and included infants aged 2-11 months who were hospitalized with severe pneumonia. The study compared the outcomes of infants who received zinc supplementation along with standard treatment to those who received a placebo alongside standard treatment [14].

The findings of the study revealed that the infants who received zinc supplementation had a significantly reduced duration of severe pneumonia, improved recovery rates, and a lower risk of treatment failure compared to the placebo group. Additionally, the zinc-supplemented group showed a lower incidence of treatment-related complications. These results provide strong evidence supporting the efficacy of zinc supplementation as an adjuvant therapy for severe pneumonia in infants.

Another study aimed to assess the effect of zinc supplementation on the treatment outcomes of

severe pneumonia in children aged 2-35 months in India. This randomized controlled trial compared the outcomes of children who received zinc supplementation alongside standard pneumonia treatment to those who received a placebo along with standard treatment.

The study demonstrated that zinc supplementation significantly reduced the duration of severe pneumonia, hastened clinical recovery, and decreased the risk of treatment failure compared to the placebo group. Furthermore, the zinc-supplemented group had a lower rate of treatment-related adverse events. These findings support the notion that zinc supplementation as an adjuvant therapy can improve clinical outcomes and enhance the effectiveness of standard treatment in children with severe pneumonia [11].

These studies collectively contribute to the growing body of evidence supporting the efficacy of zinc supplementation as an adjuvant therapy for severe pneumonia in young children. The consistent findings of reduced duration of illness, improved recovery rates, and decreased treatment failure rates highlight the potential benefits of zinc supplementation in enhancing the management and outcomes of severe pneumonia in this vulnerable population. However, further research, including large-scale trials conducted in diverse settings, is necessary to confirm these findings and establish clear guidelines for the implementation of zinc supplementation in the management of severe pneumonia in young children.

CONCLUSION

The current trial of zinc adjuvant treatment in severe pneumonia found that the time for clinical recovery was substantially faster, the requirement for second line medicine was significantly lower, and the length of hospital stay was significantly shorter in the zinc group compared to the placebo group. The treatment result was similar, and the side effects did not differ substantially between the zinc and placebo groups. As a result, it may be concluded that oral zinc is an efficient and safe adjuvant therapy for severe pneumonia in children under the age of five.

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