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EFFECTIVENESS OF ZINC AS AN ADJUNCT TO ANTIBIOTICS IN THE MANAGEMENT OF SEVERE CHILDHOOD PNEUMONIA: A PROSPECTIVE COMPARATIVE STUDY

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ABSTRACT

BACKGROUND: Pneumonia remains a leading cause of morbidity and mortality in children under five, particularly in low-resource settings. Zinc, an essential micronutrient with immunomodulatory properties, may enhance recovery when used alongside standard antibiotic therapy. However, evidence regarding its therapeutic efficacy remains inconclusive.

OBJECTIVE: :To assess the effectiveness of adjunctive zinc supplementation compared to standard antibiotic therapy alone in reducing symptom resolution time and improving treatment outcomes in children aged 6–59 months with severe pneumonia.

METHODOLOGY: :This prospecv e compara e study was conducted over seven months. A total of 160 children diagnosed with WHO-defined severe pneumonia were divided into two groups: Group I received standard antibiotics plus oral zinc (2 mg/kg twice daily for 7 days), and Group II received antibiotics alone.Clinical parameters were monitored,and the primary outcome was time to symptom resolution. Secondary outcomes included treatment success rate and duration of hospital stay.

RESULTS: Children in Group I showed significantly faster symptom resoluon (23.3±4.6 hour Vs. 43.2±7.3 hours; $p < 0.001$) and higher treatment success (93.8% vs. 68.8%). Subgroup analysis by gender, age, nutritional status, and vaccination history consistently favored the zinc group ($p < 0.001$).

CONCLUSION; Adjunctive zinc and supplementation significantly was associated with recovery and treatment success in children with Severe pneumonia. Its use may reduce healthcare burden in resource-limited settinngs. Further large-scale randomized controlled trails recommended to validate these findings and explore pathogen-specific responses.

KEYWORDS: :Zinc, Pneumonia, Pediatrics, Antibiotics, Adjuncv e Therapy,

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INTRODUCTION

The World Health Organisation (WHO) reports that childhood pneumonia continues to be one of the leading causes of death for children under five, accounting for an astounding 2.4 million deaths annually. The pathophysiology of pneumonia, which comprises an overwhelming inoculum, invasion by pathogenic organisms, and/or a compromised host defence system, results in high rates of morbidity and mortality. These variables alter ventilation-perfusion ratios and impair lung function. With an emphasis on supportive measures like antipyretics, analgesics, respiratory support, hydration, and chest physical therapy, as well as vitamin A supplementation and protein energy status optimisation, children's community-acquired pneumonia (CAP) is commonly treated empirically in clinical practice.

Zinc has been found as a potential regulator of pneumonia morbidity and death. Zinc is believed to be able to boost the host's response to infection by increasing cytokine expression, leukocyte activity, and the barrier function of skin and mucosal membranes.[1] As a cofactor, signalling molecule, and structural element that regulates leukocyte and lymphocyte proliferation, differentiation, and maturation as well as inflammatory responses and nutritional immunity, zinc is an essential part of many biological processes.[2,3] Changes in zinc status have been linked to increased susceptibility to inflammatory and infectious diseases, including pneumonia, because zinc deficiency is linked to inflammatory lung changes that predispose to fibrosis and compromised phagocyte killing activity in pneumococcal infection.[4,5] According to research, children with severe pneumonia frequently have low serum zinc levels. On the other hand, in children, zinc supplementation may help lessen the incidence of acute lower respiratory tract infections, such as pneumonia.[6]

Nonetheless, there is still debate in the literature about zinc's efficacy in treating paediatric pneumonia.[7] While some studies have found benefits, like a decrease in the frequency of chest wall indrawing and quicker resolution times, other studies have found no discernible benefits, particularly in terms of fewer hospital admissions.[8,9] This variant highlights the need for additional investigation to elucidate the role of zinc supplementation in the management of paediatric pneumonia. Therefore, this study aims to ascertain the efficacy of zinc supplementation as an adjunct to traditional antibiotic therapy by assessing the mean time to resolution of CAP. This study may provide useful details regarding the potential advantages of zinc supplementation in our neighborhood. We hypothesized that adjunctive zinc would shorten symptom resolution time compared with antibiotics

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alone.

METHODOLOGY:

This prospective comparative study was conducted in the Department of Pediatrics, Federal Government Polyclinic Hospital, Islamabad, from 1st December 2020 to 30th June 2021 (seven months).

Written informed consent was obtained from parents or legal guardians. For illiterate guardians, thumb impressions were taken after a verbal explanation of the study in the native language. Participation was voluntary, and refusal or withdrawal did not affect patient care.

160 patients, both male and female children between the ages of 6 and 59 months who had symptoms typical of severe pneumonia as described by the World Health Organization (WHO) were eligible and added to the study while taking the anticipated overall frequency of pneumonia to be 14% in Pakistan[19]. Clinical features such as coughing for less than 30 days or having trouble breathing for more than 7 days, chest indrawing, crepitations on auscultation, and rapid breathing (≥50 breaths/minute in children under 12 months or ≥40 in children over 12 months) were used to diagnose severe pneumonia.

Children with significant congenital defects or metabolic disorders, chronic illnesses like renal failure or seizure disorders, active measles, incapacity to tolerate oral intake, children who needed mechanical ventilation or inotropic support, or any other critical condition impacting the study parameters were all excluded. Children who had taken multivitamins or zinc supplements within the previous two weeks were also not included.

Group Allocation

Children were enrolled and divided into two treatment groups (80 in each) according to standard clinical management patterns following informed permission. Children in Group II received conventional antibiotic therapy alone, while patients in Group I received normal antibiotic therapy plus supplementary zinc supplementation.

An internal quasi-randomization strategy was used to lessen allocation bias despite the observational study design. A computer-generated list that was created beforehand and used successively when patients were admitted was used to create group assignments. To reduce observer bias, clinicians and researchers evaluating results were blinded to group assignment.

Intervention Details

The institutional antibiotic protocol was followed for treating each individual. Cefotaxime 150 mg/kg/day (given every 8 hours) and amikacin 15 mg/kg/day (given once daily) were administered to children less than 12 months. Cefotaxime monotherapy at the same dosage was administered to children 12 months of age or older.

Additionally, for seven days, patients in Group I received oral zinc sulphate at a dose of 2 mg/kg, diluted in 3 mL of distilled water, given every 12 hours. After enrolment, zinc supplementation was started within two hours.

Clinical Monitoring and Assessment

Clinical monitoring was performed on all recruited patients at intervals of three hours or more frequently as required. A digital pulse oximeter was used to measure vital indicators, such as oxygen saturation (SpO_2) and respiration rate. The respiratory rate was recorded, and if an infant's or older child's breathing rate exceeded 50 breaths per minute or 40 breaths per minute, additional measures were made.

Patients whose oxygen saturation was less than 90% on room air were given oxygen. Throughout hospitalisation, close monitoring was done on the patient's temperature, food status, sensorium, and chest indrawing. Escalation to second-line or third-line antibiotics was started if symptoms of severe pneumonia, such as tachypnea, hypoxaemia ($SpO_2 < 92\%$), or persistent fever, continued after 48 hours.

Laboratory Investigations

Every kid had baseline tests, including as blood culture, serum zinc levels, C-reactive protein (CRP), differential leukocyte count, and complete blood count (CBC). Both at the time of clinical recovery and 48 hours after enrolment, these were conducted again. At baseline and as clinically needed, chest X-rays were taken.

Atomic absorption spectrophotometry was used to evaluate serum zinc amounts in a hospital laboratory under controlled conditions. A nephelometric assay with great sensitivity was used to quantify CRP.

Outcome Measures

The primary outcome of the study was the time to resolution of pneumonia, defined as the duration (in hours) from hospital admission until disappearance of chest indrawing, fast breathing, fever, and hypoxemia, sustained for at least 12 hours.Treatment failure was defined as the persistence or worsening of clinical signs 48 hours post-treatment initiation.

Data Collection Procedures

At enrolment, demographic information such as age, sex, and vaccination history were noted. Standard methods were used to collect anthropometric measurements. A calibrated digital weighing scale with a 100-gram precision was used to measure weight, and an infantometer (for children under 24 months) or a stadiometer (for older children) was used to measure height. WHO growth reference tables were used to construct the weight-for-age and height-for-age Z-scores.

According to the Expanded Programme on Immunisation (EPI) schedule, vaccination status was confirmed using vaccination cards and categorised as fully, partially, or unvaccinated.

Data were analyzed in SPSS version 23. Quantitative variables

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were expressed as mean ± standard deviation and compared using the Mann Whitney U test. categorical variables were presented as frequencies/percentages and analyzed using the chi-square. Subgroup analyses were conducted for gender, age group, nutritional status (divided into moderate and severe malnutrition based on stunting protocol), and immunization status. A p-value <0.05 was considered statistically significant. No missing data were encountered.

Ethical approval was obtained from the Ethical Committee of the Federal Government Polyclinic Hospital (Reference No. FGPC.1/12/2020).

RESULTS:

Participants in this trial were 160 children who were presented with pneumonia. In contrast to Group II patients, who only got standard antibiotic therapy, Group I patients received zinc supplementation twice daily at a level of 2 mg/kg. Table 1 provides a summary of the patients in each groups' demographics, growth metrics, nutritional status, and vaccination history.

The distribution of participants in both groups by gender, age, growth characteristics, nutritional condition, and vaccine coverage is displayed in Table 1. Both groups' mean ages (24.8 ± 13.6 months in Group I and 26.4 ± 16.1 months in Group II) and male-to-female ratios were similar. The majority of the children had moderate malnutrition, and each group's vaccination status was equal.

Table 1: Demographics, growth anthropometric malnutrition and vaccination status of all patients included in the study

Variable	Group I (Zinc + Antibiotics)	Group II (Antibiotics only)	Total
Gender			
Male	42 (52.5%)	52 (65.0%)	94 (58.8%)
Female	38 (47.5%)	28 (35.0%)	66 (41.2%)
Age (months)	24.8 ± 13.6	26.4 ± 16.1	-
6–24 months	48 (60.0%)	46 (57.5%)	94 (58.8%)
25–59 months	32 (40.0%)	34 (42.5%)	66 (41.2%)
Growth metrics			
Height (cm)	85.8 ± 14.6	87.2 ± 17.1	-
Weight (kg)	9.5 ± 3.0	9.9 ± 0.7	-
Malnutrition status			
Moderate nutrition	67 (83.8%)	69 (86.3%)	136 (85.0%)
Severe malnutrition	13 (16.3%)	11 (13.8%)	24 (15.0%)
Vaccination status			
Fully vaccinated	43 (53.8%)	42 (52.5%)	85 (53.1%)
Partially vaccinated	25 (31.3%)	24 (30.0%)	
Unvaccinated	12 (15.0%)	14 (17.5%)	

Table 2 shows the results of treatment for both groups. With a treatment success rate of 93.8%, Group I outperformed Group II, which had a rate of 68.8%. This suggests that giving children with severe pneumonia an adjuvant zinc supplement may increase the overall effectiveness of their treatment

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Table 2: Treatment outcomes in Group I and Group II

Outcome	Group I (Zinc + Antibiotics)	Group II (Antibiotics only)
Treatment success	75 (93.8%)	55 (68.8%)
Treatment failure	5 (6.2%)	25 (31.2%)

Table 3 indicates that the time to clearance of pneumonia symptoms, the main end measure, was considerably shorter in Group I than in Group II. The zinc-supplemented group saw a mean time to symptom relief of 23.3 hours, while the usual therapy group experienced a mean time to symptom resolution of 43.2 hours ($p < 0.001$).

Table 3: Mean time to resolution of pneumonia symptoms

Group	Mean Time (hours)	Standard Deviation	p-value
Zinc + Antibiotics (Group I)	23.3	4.6	
Antibiotics only (Group II)	43.2	7.3	< 0.001

Symptom resolution times were categorised by age group, gender, nutritional status, and immunisation status in order to further investigate the variables affecting therapy response. Patients treated with zinc in addition to antibiotics experienced considerably faster symptom recovery than those treated with antibiotics alone in all subgroups, as indicated in Table 4 ($p < 0.001$ in all comparisons).

Table 4: Symptom resolution time stratified by gender, age, malnutrition, and vaccination status

Stratification Factor	Group I (hours)	Group II (hours)	
Gender			
Male	22.7 ± 10.3	42.5 ± 10.7	< 0.001
Female	24.1 ± 9.8	44.1 ± 9.5	< 0.001
Age group			
6–24 months	22.4 ± 9.7	41.7 ± 9.9	< 0.001
25–59 months	24.7 ± 10.4	44.9 ± 10.2	< 0.001
Malnutrition			
Moderate	23.2 ± 10.2	43.0 ± 10.3	< 0.001
Severe	24.0 ± 9.9	44.3 ± 10.0	< 0.001
Vaccination status			
Fully vaccinated	22.5 ± 9.6	42.1 ± 9.8	< 0.001
Partially vaccinated	24.6 ± 10.5	44.2 ± 10.4	< 0.001
Unvaccinated	25.2 ± 10.0	45.3 ± 10.1	< 0.001

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DISCUSSION

When children between the ages of 6 and 59 months present with severe pneumonia, supplementary zinc supplementation dramatically improves clinical outcomes, according to this prospective comparative observational study. In comparison to children who got antibiotics alone (Group II), children who received zinc in addition to standard antibiotic therapy (Group I) had a considerably shorter mean time to resolution of symptoms (23.3 vs. 43.2 hours; $p < 0.001$) and a greater treatment success rate (93.8% vs. 68.8%). Regardless of baseline characteristics, these effects were consistently found across all subgroups stratified by age, gender, nutritional status, and vaccination history ($p < 0.001$ in all comparisons). This indicates that zinc's therapeutic impact is widely applicable.

These results are consistent with earlier studies conducted in comparable low-resource environments. Zinc supplementation reduces the length of illness and speeds up recovery in children with pneumonia, according to studies from Bangladesh and Iran.[10,11] Similar results have been noted in India, where research from Vellore and Kolkata revealed that children taking zinc have shorter hospital stays and quicker symptom clearance. Some studies differ ,however, where statistical analysis revealed no significant difference in hospitalization duration or symptom severity between the zinc-supplemented group and the control group (p-values of 0.741 and 0.402, respectively). The findings suggest that zinc supplementation does not significantly alter treatment outcomes in terms of reducing hospital stay or symptom intensity for children with pneumonia.[14] According to other research, children receiving zinc treatment saw a quicker recovery of severe clinical symptoms such hypoxia and chest indrawing.[11] Additionally, Rerksuppaphol et al. found that children who took zinc supplements had shorter fever and pneumonia durations (48 vs. 72 hours).[8]

The immunomodulatory qualities of zinc, which are crucial in malnourished children—a group that made up a sizable section of our study cohort (85% moderately and 15% severely malnourished)—may be the reason behind its beneficial effects. A zinc deficit might hinder the host's capacity to combat infections since zinc is essential for immune cell proliferation, development, and function. Children's pneumonia incidence and severity have been demonstrated to decrease with preventive supplementing,[17] and during acute bouts, therapeutic supplementation may aid in regaining immunological competence.

It has been proposed that zinc may be more beneficial for bacterial pneumonia than for viral illnesses. Children without wheezing, a clinical symptom more frequently associated with viral respiratory infections, had greater treatment results in certain studies[11]. Zinc response may also be influenced by regional and seasonal variations, with bacterial pneumonia being more common in warmer months.[13] Different studies have observed differences in clinical symptoms such hypoxemia and wheeze,[11,13,15,16] indicating that future study could benefit from classification based on aetiology and clinical phenotype.

The therapeutic response may also be impacted by the baseline zinc status. While studies involving children with greater baseline zinc levels (e.g., 22.9 µmol/L) did not show substantial benefit, children with marginal blood zinc levels (10.1–11.0 µmol/L) have clearly benefited from supplementation during pneumonia episodes.[11–13] However, because levels can drop as a result of inflammation-related redistribution, serum or plasma zinc concentrations may not correctly reflect total body zinc during acute infections.

There are various restrictions/limitations on this study. Because it is an observational study, even with measures to guarantee group comparability, residual confounding may still exist. The evaluation of the results may have been biassed due to the absence of blinding. Furthermore, the interpretation of zinc's efficacy against particular pathogens is limited because the microbiological aetiology of pneumonia was not identified. Because baseline zinc level was not assessed, it was not possible to link supplementation to dietary needs. Reason being that the specialized reagent that is used to measure zinc levels in the blood was not available in our hospital laboratory, future studies in more advanced centers with state-of-the-art equipment could address this issue while providing more convincing results. Lastly, because this study was conducted at a single location, its applicability to other contexts or demographics may be limited.

CONCLUSION

In children aged 6–59 months with severe pneumonia, adjunctive zinc supplementation combined with standard antibiotic therapy was associated with a shorter time to symptom resolution and a higher treatment success rate. These benefits were consistently observed across subgroups stratified by age, gender, nutritional status, and immunization history, indicating potential broad clinical relevance.

Given the high burden of pneumonia and malnutrition in low-resource settings such as Pakistan, zinc may serve as a valuable supportive therapy within routine inpatient care. However, as this was a comparative observational study, causal inferences should be made with caution. Further large-scale, multicenter randomized controlled trials are warranted to confirm these associations, explore underlying mechanisms, and determine optimal dosing strategies in relation to baseline zinc status and pneumonia etiology.

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