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ORIGINAL ARTICLE

Effect of adjuvant zinc therapy on recovery from pneumonia.

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ABSTRACT… Objective: To study the effect of zinc supplementation as an adjuvant therapy on the outcomes of pneumonia. **Study Design:** Randomized Controlled Trial. **Setting:** Department of Pediatrics, National Institute of Child Health, Karachi, Pakistan. **Period:** November 2024 to April 2025. **Methods:** A total of 50 patients (25 in each group) children, aged 2 months to 5 years, and admitted with pneumonia were randomly allocated to either Group-A (Zinc + standard treatment) or Group-B (standard treatment only). In Group-The primary outcome was recovery rate, assessed by the resolution of tachypnea, chest indrawing, hypoxemia, and fever within 48 hours. Secondary outcomes included hospitalization duration and symptom recovery time. **Results:** In a total of 50 children, the mean age in Group-A was 2.8±1.2 years, and in Group B, 2.9±1.3 years (p=0.582). Gender distribution was statistically similar among study groups (p=0.827. Recovery rates were significantly higher in Group-A for fever (88% vs. 64%, p=0.001), tachypnea (84% vs. 56%, p=0.005), chest indrawing (72% vs. 48%, p=0.011), and hypoxemia (76% vs. 52%, p=0.009). The median duration of hospitalization in Group-A was 4.0 days (3.0–5.0 days), significantly shorter than the 6.0 days (5.0–7.0 days) observed in Group B (p=0.003). **Conclusion:** Zinc supplementation significantly improved recovery rates, reduced hospitalization duration, and accelerated the resolution of clinical symptoms, providing important clinical benefits.

Key words: Fever, Length of Stay, Pneumonia, Tachypnea, Zinc.

INTRODUCTION

Pneumonia represents a significant burden on global health, particularly affecting the lower respiratory system, with substantial morbidity and mortality, especially among children under 5.[1,2] Pneumonia claims over 700,000 lives among children annually worldwide.[3-5] In Pakistan, the incidence of pneumonia is escalating, contributing to approximately 15 million cases of acute respiratory infections annually among children under five.[6,7] Mortality due to childhood pneumonia is closely linked to poverty-related factors including malnutrition, inadequate sanitation, and exposure to indoor and outdoor pollutants.[6,7]

Micronutrient deficiencies play a crucial role in immune function and susceptibility to severe infections.[8-10] Priya et al., noted that zinc supplementation (ZS) in children with pneumonia significantly reduced recovery time. (66.4±34.8 hours vs. 87.2±38.7 hours, p=0.055). Other studies have similarly highlighted the beneficial impact of ZS in pneumonia management.[12,13] ZS is emerging as a promising adjunctive treatment to enhance recovery from pneumonia, addressing a critical need in public health strategies aimed at reducing childhood mortality from infectious diseases.

ZS in children with pneumonia seems beneficial but the results of published trials are conflicting regarding the impact of treatment on improving symptoms and hospital stay. Some researchers have documented relatively reduced disease severity and duration of hospital stay with ZS[14,15], while some others have not reported significant benefits.[16] In Pakistan, the role of ZS in children with pneumonia is not much explored, considering it as an important and effective option for the management of the disease. This study was performed to determine the effect of ZS as an adjuvant therapy on the outcomes of pneumonia.

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METHODS

This randomized controlled trial was conducted at the indoor pediatric department of the National Institute of Child Health, Karachi, Pakistan, during November 2024 to April 2025. A sample size of 50 (25 in each group) was calculated through OpenEpi sample size software used for calculating sample size, considering the expected rate of recovery from pneumonia in the ZS group as 66.4% and in the non-zinc group as 24.0%[13], taking the confidential interval as 95%, the power of the study as 80%. A consecutive non-probability sampling technique was utilized for participant selection. The inclusion criteria consisted of children, regardless of gender, aged between 2 months and 5 years, who were admitted with pneumonia. Exclusion criteria included children with significant congenital abnormalities, chronic medical conditions, signs of severe acute malnutrition, or a current episode of asthma or allergic disease. Additionally, children experiencing respiratory or cardiovascular failure, or requiring mechanical ventilation or inotropic support, were excluded. Pneumonia was diagnosed based on the WHO criteria.[3] Approval from the institutional ethical review board was obtained (letter number: IERB-47/2023). Parents/ caregivers were briefed about the objective and safety of the study to obtain informed and written consent for the study.

Demographic details of each eligible child were obtained either from parents or from medical files, which included gender, age, weight, and height. The weight of the child was measured by using the standard weighing machine and the weight was measured using the standard stadiometer. Fever (axillary temperature ≥ 37.8°C, RR, chest indrawing, and O_2 saturation were recorded. An SpO_2 of < 95% was classified as hypoxemia. The selected participants were then split into two groups through randomization, with 25 patients in each group. Group-A included those patients who were given 10mg of elemental zinc/day in children <6 months old, and 20mg elemental zinc / day in children 6-59 months old as a single oral dose for 7 days, along with the standard treatment, while the Group-B were given standard treatment only (O_2 support, IV fluids, bronchodilators, and parenteral antibiotics).

The collected data was analyzed using "IBM-SPSS Statistics" version 26.0. The qualitative variables were expressed in the form of frequency and percentage. For the representation of quantitative variables, means and standard deviations (SD) or medians and interquartile ranges (IQR) were computed. A stratified table was constructed to see the effect of effect modifiers on outcomes (recovery rate, and duration of hospitalization). Post-stratification, chi-square test or fisher's exact test, and independent sample t-test or Mann-Whiteny U test were applied (as appropriate), taking $p<0.05$ as significant.

RESULTS

In a total of 50 children, the mean age of children in Group-A was 2.8±1.2 years, and in Group B, it was 2.9 ± 1.3 years ($p=0.582$). The gender distribution was statistically similar between the groups ($p = 0.827$). Baseline clinical characteristics such as height ($p=0.631$) and weight ($p=0.506$) did not exhibit any significant associations between the groups. At admission, all children were diagnosed with pneumonia according to WHO criteria, based on the presence of tachypnea, chest indrawing, and/or hypoxemia. The clinical features at admission, such as fever (100% of participants), chest indrawing (68% overall), and hypoxemia (90% overall), were comparable between the two groups. The median RR was 52 breaths per minute in Group A and 54 breaths per minute in Group B, indicating similar severity of illness at baseline ($p=0.612$), as shown in Table-I.

Fever resolved in 22 (88.0%) children in Group-A, compared to 16 (64.0%) in Group-B ($p=0.001$). Tachypnea resolved in 21 (84.0%) children in Group-A, compared to 14 (56.0%) in Group-B ($p=0.005$). Chest indrawing resolved in 18 (72.0%) children in Group-A, compared to 12 (48.0%) in Group-B ($p=0.011$). Hypoxemia was corrected in 19 (76.0%) children in Group-A, compared to 13 (52.0%) in Group-B ($p=0.009$). Table-2 is showing comparison of primary outcomes in terms of rate of recovery across study groups.

The median duration of hospitalization in Group-A

was 4.0 days (3.0–5.0 days), significantly shorter than the 6.0 days (5.0–7.0 days) observed in Group B (p=0.003). Fever resolved after a median of 1.0 day (1.0–1.5) in Group-A, compared to 2.0 days (1.5–2.5) in Group-B (p=0.002). Tachypnea resolved in a median of 1.5 days (1.0–2.0) in Group-A, compared to 2.5 days (2.0–3.0) in Group-B (p=0.005). Chest indrawing was corrected after a median of 2.0 days (1.5–3.0) in Group-A, compared to 3.0 days (2.5–4.0) in Group-B (p = 0.011). Hypoxemia resolved after a median of 2.0 days (1.5–3.0) in Group-A, compared to 3.0 days (2.5–4.0) in Group-B (p = 0.009), as shown in Table-III.

DISCUSSION

In children given ZS, a significantly higher proportion showed resolution of fever (p=0.001), tachypnea (p=0.005), chest indrawing (p=0.011), and hypoxemia (p=0.009) compared to standard treatment alone. Qasemzadeh et al.[17], in their trial conducted at Ayatollah Golpaygani Hospital, Iran, found that ZS significantly reduced the duration of clinical symptoms (p=0.044), and the length of hospitalization (p=0.004). A local study by Ayub et al.[18], focused on the duration of treatment with and without ZS, showed a marked improvement in the recovery times for pneumonia symptoms with ZS, particularly in the resolution of tachypnea and fever (p<0.05). These studies reinforce the idea that ZS can significantly expedite the recovery process in children with pneumonia.[17,18]

Characteristic		Group-A (n=25)	Group-B (n=25)	P-Value
Age (years)		2.8±1.2	2.9±1.3	0.582
Gender	Male	13 (52.0%)	14 (56.0%)	0.827
	Female	12 (48.0%)	11 (44.0%)	
Height (cm)		85.0 (77.0-95.0)	87.0 (78.0-96.0)	0.631
Weight (kg)		12.0 (10.0-14.0)	12.5 (11.0-14.5)	0.506
Fever (≥37.8°C)		25 (100%)	25 (100%)	-
Chest Indrawing		16 (64.0%)	18 (72.0%)	0.453
Respiratory Rate (breaths/min)		52.0 (49.0–55.0)	54.0 (51.5–57.0)	0.612
Hypoxemia (SpO2 < 95%)		22 (88.0%)	23 (92.0%)	0.735

Table-I. Baseline characteristics (N=50)

Group-A: Zinc + Standard Treatment; Group-B: Standard Treatment

Symptom	Group-A (n=25)	Group-B (n=25)	P-Value
Fever resolution	22 (88.0%)	16 (64.0%)	0.001
Tachypnea resolution	21 (84.0%)	14 (56.0%)	0.005
Chest Indrawing resolution	18 (72.0%)	12 (48.0%)	0.011
Hypoxemia resolution	19 (76.0%)	13 (52.0%)	0.009

Table-II. Comparison of rate of recovery across study groups (N=50)

Group-A: Zinc + Standard Treatment; Group-B: Standard Treatment

Outcome	Group-A (n=25)	Group-B (n=25)	P-Value
Duration of Hospitalization (days)	4.0 (3.0–5.5)	6.0 (5.5–7.0)	0.003
Fever Recovery Time (days)	1.0 (1.0–1.5)	2.0 (1.5–2.5)	0.002
Tachypnea Recovery Time (days)	1.5 (1.0–2.0)	2.5 (2.0–3.0)	0.005
Chest Indrawing Recovery Time (days)	2.0 (1.5–3.0)	3.0 (2.5–4.0)	0.011
Hypoxemia Recovery Time (days)	2.0 (1.5–3.0)	3.0 (2.5–4.5)	0.009

Table-III. Comparison of secondary outcomes across study groups (N=50)

Group-A: Zinc + Standard Treatment; Group-B: Standard Treatment

In contrast, Haider et al.[19], did not observe significant benefits of ZS in reducing the time to clinical recovery. This discrepancy highlights the importance of context and patient selection in determining the effectiveness of ZS.

The duration of hospitalization was significantly shorter in ZS group (p=0.003), and these results are aligned with Kazi et al.[20], who found that ZS reduced the mean duration of hospital stay by more than 23 hours. Farahat et al.[21], reported a shorter hospitalization period in children who received ZS compared to those who received a placebo (p=0.004). The reduction in hospital stay can directly impacts healthcare resource utilization and the cost of care.[22] These findings support the integration of ZS as an adjunct therapy in pneumonia management protocols, especially in settings where hospital resources are limited. The reduction in hospitalization duration observed in the present study was not universally seen as studies by Haider et al.[19], and Das et al.[23], failed to observe a significant impact of ZS on hospitalization duration. Such inconsistencies suggest that the effect of ZS on hospitalization time may be influenced by factors such as the severity of pneumonia, the timing of ZC administration, and the presence of underlying comorbidities.

In terms of clinical symptoms, the present study demonstrated that ZS accelerated the resolution of fever, tachypnea, chest indrawing, and hypoxemia compared to standard treatment alone. Padmini et al.[24], found that ZS was associated with a shorter duration of symptoms such as cough and cold in children with severe pneumonia (p=0.013). Rao et al.[23], observed that children receiving ZS had faster resolution of distress (48.42 hours vs. 60.48 hours).

The significant reduction in recovery times and hospitalization duration observed in this study suggests that ZS could be integrated into pneumonia treatment protocols to enhance the speed of recovery and reduce healthcare costs.[25,26] This is especially relevant in settings with limited access to advanced medical resources and where early discharge can facilitate better resource management. ZS could help improve the clinical outcomes in children with pneumonia by addressing nutritional deficiencies that often accompany infections.

This study only focused on children aged 2 months to 5 years, and the effects of ZS in younger or older children were not evaluated. Future studies should explore the impact of ZS in different age groups to determine if the benefits observed in this study extend to other pediatric populations. Another limitation is the short duration of the study, as the follow-up period was limited to the duration of hospitalization.

CONCLUSION

The study supports the use of zinc supplementation as an effective adjuvant therapy for pneumonia in children. Zinc supplementation significantly improved recovery rates, reduced hospitalization duration, and accelerated the resolution of clinical symptoms, providing important clinical benefits.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Hina Rashid:** Data collection, data analysis, final approval.
2	**Muhammad Ashfaq:** Conception, critical revision.
3	**Maria Kulsoom:** Methodology, proof read.
4	**Bader u Nisa:** Literature review.
5	**Muhammad Hanif:** Study design, data collection.