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Role of Zinc Supplementation in Treating Acute Respiratory Infection in Children Under 5 Years of Age

Syeda Fatima Arif[1], Amna[2], Syeda Itrat Fatima[3], Tayyaba Farid[4]

[1] **Resident Paediatric Fauji foundation hospital Rawalpindi** fatimaarifmashwani@gmail.com
[2] **Resident paediatric Fauji foundation hospital Rawalpindi** anaa.amna@gmail.com
[3] **Resident paediatrics Fauji foundation hospital Rawalpindi** syedaitratfatima@hotmail.com
[4] **Resident paediatrics Fauji foundation hospital Rawalpindi** tayyabafarid335@gmail.com

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Abstract

Objective: To compare the efficacy of added zinc supplementation to standard treatment in improving the course of acute respiratory infections (ARI) when compared with standard treatment alone in children under 5 years of age

Study Design: Quasi-experimental study

Place and Duration of Study: Department of Pediatrics, Fauji foundation Hospital, Rawalpindi from July -Dec 2024

Methodology: 120 patients were added to the study protocol divided into Group-A (n=60) to receive zinc supplementation with standard anti-biotic therapy and Group-B (n=60) to receive only standard antibiotic therapy. Primary variables measured were mean time to resolution of ALRI and clinical signs and symptoms. Secondary outcomes were duration of hospital stay between both groups.

Results: Mean time to resolution of ALRI was 2.58±0.64 days versus 3.68±0.59 days between both groups ($p<0.001$). Mean time to resolution of clinical variables of ALRI between both groups showed that tachypnea resolved in 16.15±3.79 hours versus 24.08±3.87 hours between both groups ($p<0.001$), fever resolved in 22.08±3.72 hours versus 29.05±4.80 hours ($p<0.001$), chest findings of infection resolved in 16.58±3.82 hours versus 23.87±4.54 hours ($p<0.001$) and chest findings of infection on radiology resolved in 16.53±3.69 hours versus 23.77±4.56 hours between both groups ($p<0.001$). Mean duration of hospital admission was 3.73±0.57 days versus 5.07±0.73 days ($p<0.001$).

Conclusion: We conclude that zinc supplementation added to standard antibiotic therapy in children with acute lower respiratory infections reduces both the resolution time for infection as well as the duration of hospital stay

Key Words: Acute, children, infection, respiratory, supplementation, zinc

Introduction

Acute respiratory infections (ARIs) remain the leading cause of death in children under 5 years of age worldwide.[1] The spectrum of disease is responsible for 15% of total deaths worldwide.[2] The overall global prevalence was 36.9% in ages 2-60 months of age. A total of 17-19% of all ARI cases require hospitalization.[3] In Pakistan, the prevalence of ARI in children less than five was 14% from 2018-2020 and it increased to 21% in literature reported between 2020-2023.[4] Major risk factors identified especially in low-income countries were poor immunity, malnutrition, urbanization, increase in allergic tendencies, and male gender.[5] The role of zinc in improving immunity and protective responses in response to infections is well established. It's role in expression of interferon, activation of the cytokines pathway, promotion of leucocyte activity and promoting membrane barriers to infection have been extensively

documented.[6] In children especially below the age of 5, zinc deficiency is reported to be as high as 35-40% and majority of these cases have been reported in low-income countries including Pakistan, India and Bangladesh in our demographic area.[7] Even with an adequate nutritional status, the diet provided in these areas in inherently deficient in zinc. Literature reports that adding zinc to treatment regimens in diarrhea have concluded very conducive results decreasing not only the severity but also the duration of the disease.[8] Based on the clinical data and role of zinc in immune responses, we aim to add zinc as a standard treatment strategy in children being admitted for acute lower respiratory tract infections with age under 5 years to see patients outcomes when compared with standard therapy for lower respiratory infections in our institute without the addition of zinc.[9] This would help us identify whether addition of zinc in our standard treatment protocol would improve patient recovery and discharge times.

Methodology

This quasi-experimental study was carried out at the Department of Pediatrics, Fauji foundation Hospital Rawalpindi from July 2024-Dec 2024 after approval from the ethical review board vide letter no. The sample size for two groups was calculated keeping the confidence interval at 95%, power of test at 80% with the mean difference of in resolution of danger signs and symptoms of ARI in admitted children in the zinc supplementation group versus non-supplementation group being 24.12±3.46 hours.[10] Minimum sample size for one group came out to be 27 patients using the WHO calculator (Population variance 1000). We included a total of 60 patients in each group making the final study sample of 120 patients.

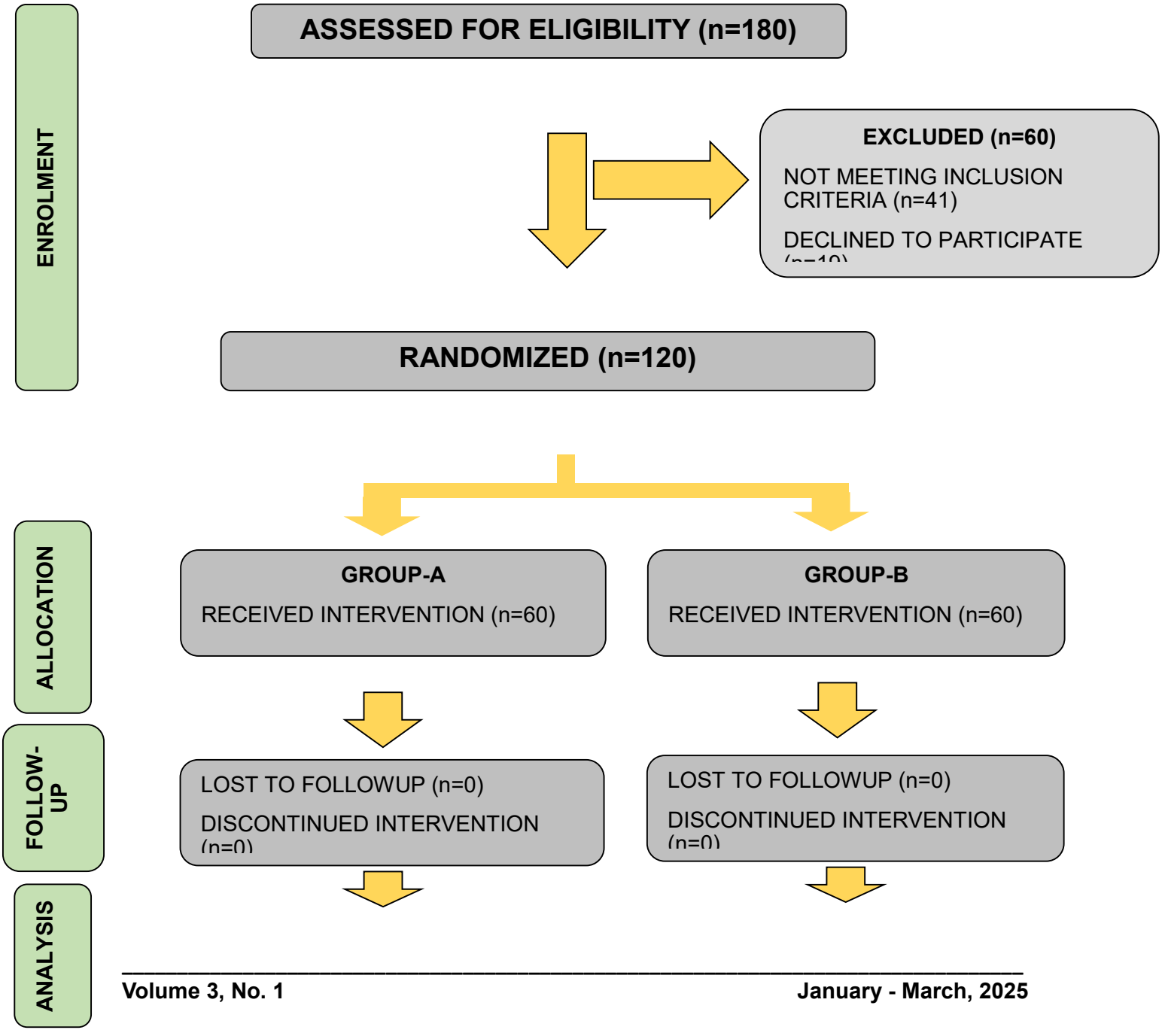
Inclusion criteria included children of both genders; age less than 5 years, admitted in the hospital with a diagnosis of lower respiratory tract infection requiring intravenous antibiotic therapy as per institutional treatment protocol

Exclusion criteria included patients with co-existing infections other than lower respiratory tract, patients already on multi-vitamin supplementation, patients who were received or went on ventilatory support, patients with severe cardiac disease, patients lost to follow-up or patients unwilling to be included in the study. The study method included all patients as per the inclusion criteria furnished. The patients were divided into two groups. Group A (n=60) to receive zinc supplementation along with standard intravenous anti-biotic therapy versus Group B (n=60) to receive standard intravenous anti-biotic therapy alone. Before addition into the study protocol, a written and informed consent was taken from the parents or next of kin. They were thoroughly counselled regarding the study type but were blinded to the group placement and study outcomes to prevent bias and ensure blinding for all patients. Acute lower respiratory infection (ALRI) was assessed clinically by a consultant pediatrician in the OPD or the emergency department having 2 or more of the following clinical findings including tachypnea (a respiratory rate of more than 50 per minute for children aged 2-12months, and more than 40 per minute for children older than 12 months), and 2)either of at least one other observed sign of ALRI [lower chest wall in-drawing, abnormal sounds on pulmonary auscultation (i.e. Bronchial breath sounds and/or crackles/crepitations), nasal flaring and fever, or one of the following danger signs(i.e. cyanosis, lethargy, irritability, inability to drink or convulsions).[11] Chest X-ray was done in all cases to assess the severity of the infection and decision to continue anti-biotic doses in patients. Antibiotic regimen in all patients included Inj Ceftriaxone 50 mg/kg given in twice daily doses. Supportive therapy included nebulization with Iptraopium bromide and Beclamethasone in all patients. Patients in Group-A received zinc in the form of zinc bis-glycinate (containing elemental zinc 15 mg) twice a day until the infection resolved, and patients were considered fit to be discharged from the hospital or up to a maximum of 10 days after admission. Patients who did not respond to therapy for more than 10 days were noted. Clinical assessment after admission in all patients included vital charting to assess the regression or severity of lower respiratory tract infection by checking fever 08 hourly, auscultation of the chest by a consultant pediatrician twice a day on ward rounds, heart rate,

respiratory rate and oxygen saturation 08 hourly. Resolution of symptoms within normal range for all parameters for two consecutive readings or within 24 hours were noted by resident pediatrics on duty blinded to the study protocol and the results were compiled in both groups. Zinc levels were measured at the start of zinc therapy in Group-A and measured at the end of therapy before discharge. Zinc levels associated with zinc deficiency in children less than 10 years of age were morning fasting levels less than 65 mg/dl.[12] Primary variables measured were resolution of ALRI defined as complete recovery with disappearance of tachypnea, chest in-drawing, abnormal pulmonary auscultation and resolution of chest X-ray changes. Secondary outcomes were duration of hospital stay between both groups.

Demographic data were statistically described in terms of mean and SD, frequencies, and percentages when appropriate. Independent samples t-test was used to compare statistically significant means. Chi-square test was used to compare frequency variables. A p value of ≤0.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for Social Sciences 26.0.

FIGURE-I: PHASES OF THE STUDY



ANALYSED (n=**60**)
EXCLUDED FROM ANALYSIS (n=0)

ANALYSED (n=**60**)
EXCLUDED FROM ANALYSIS (n=0)

Results

A total of 180 patients were assessed to be included in the study. 120 patients were added to the study protocol divided into Group-A (n=60) to receive zinc supplementation with standard anti-biotic therapy and Group-B (n=60) to receive only standard antibiotic therapy. Mean age in Group-A was 2.40±0.88 years versus 2.25±0.87 years in Group-B (p=0.353). Mean weight was 9.00±2.51 kg versus 9.15±2.60 kg between both groups (p=0.749). Gender distribution revealed 42 (70%) males and 18 (30%) females in Group-A versus 41 (68.3%) males and 19 (31.7%) females in Group-B (p=0.843). Living demographic showed that 38 (63.3%) versus 42 (70.0%) patients belonged to a rural background while 22 (36.7%) versus 18 (30.0%) belonged to a urban area of living (p=0.439) (Table-I). Mean time to resolution of ALRI was 2.58±0.64 days versus 3.68±0.59 days between both groups (p<0.001). Mean time to resolution of clinical variables of ALRI between both groups showed that tachypnea resolved in 16.15±3.79 hours versys 24.08±3.87 hours between both groups (p<0.001), fever resolved in 22.08±3.72 hours versus 29.05±4.80 hours (p<0.001), chest findings of infection resolved in 16.58±3.82 hours versus 23.87±4.54 hours (p<0.001) and chest findings of infection on radiology resolved in 16.53±3.69 hours versus 23.77±4.56 hours between both groups (p<0.001). Mean duration of hospital admission was 3.73±0.57 days versus 5.07±0.73 days (p<0.001). Mean zinc levels at the start of study were 67.90±6.86 mg/dl versus 68.10±7.02 mg/dl between both groups (p=0.875) while zinc levels at the end of the study were 102.68±9.67 mg/dl versus 68.20±7.21 mg/dl between Group-A and Group-B (p<0.001) (Table-II).

Tables

Table-I Demographic Characteristics Between Both Groups (N=120)

VARIABLE	GROUP-A (n=60)	GROUP-B (n=60)	p VALUE
MEAN AGE (YEARS)	2.40±0.88	2.25±0.87	**0.353**
MEAN WEIGHT (KG)	9.00±2.51	9.15±2.60	**0.749**
GENDER			
• **MALE**	42 (70%)	41 (68.3%)	**0.843**
• **FEMALE**	18 (30%)	19 (31.7%)	
LIVING DEMOGRAPHIC			
• **RURAL**	38 (63.3%)	42 (70.0%)	**0.439**
• **URBAN**	22 (36.7%)	18 (30.0%)	

Table-Ii Comparison of Clinical Variables (N=120)

VARIABLE	GROUP-A (n=60)	GROUP-B (n=60)	p VALUE
MEAN TIME TO RESOLUTION OF ALRI (DAYS)	2.58±0.64	3.68±0.59	**<0.001**
MEAN TIME TO RESOLUTION OF CLINICAL VARIABLES			
• **TACHYPNEA (HOURS)**	16.15±3.79	24.08±3.87	**<0.001**
• **FEVER (HOURS)**	22.08±3.72	29.05±4.80	**<0.001**
• **CHEST FINDINGS ON AUSCULTATION (HOURS)**	16.58±3.82	23.87±4.54	**<0.001**
• **CHEST FINDINGS ON RADIOLOGY (DAYS)**	16.53±3.69	23.77±4.56	**<0.001**
MEAN DURATION OF HOSPITAL ADMISSION (DAYS)	3.73±0.57	5.07±0.73	**<0.001**
MEAN ZINC LEVELS AT THE START OF STUDY (MG/DL)	67.90±6.86	68.10±7.02	**0.875**
MEAN ZINC LEVELS AT THE END OF STUDY (MG/DL)	102.68±9.67	68.20±7.21	**<0.001**

Discussion

Our study concluded that in children under 5 years of age presenting with lower respiratory tract infections requiring admission in the hospital, adding zinc supplementation not only reduces the time to resolution of symptoms, but also the duration of hospital stay which is beneficial both from the clinical as well as administrative point of view improving patient outcome and reducing admission costs especially in resource constrained setups in our demographic area. Zinc toleration was also reported to be safe with no major adverse effects reported which required cessation of therapy in patients. Critical analysis of our study with local and international literature shows that in meta-analysis assessing role of zinc in children with respiratory infections, they concluded that its role in otherwise healthy subjects in preventing infections is not significant but children especially in low income countries like India, Pakistan and others may benefit in children presenting with respiratory infections. Not only is zinc beneficial in reducing the duration of symptoms but also hospital stay.[13] Another study assessing the role of supplementation of micronutrients in both children and adults showed zinc supplementation was not associated with reducing the risk of contracting infection but it was beneficial in reducing the duration of symptoms.[14] Another study done by Sadeghsoltani et al concluded that the role in zinc in promoting immune response is well established and it has shown to improve disease progression not only in lower respiratory infections but also acute respiratory distress and children on mechanical ventilation. All these studies assert an important point that prophylactic role of zinc in reducing risk of infection has not been well established but its role in improving persisting respiratory infections is significant. Finally, international literature studying the mortality benefit of zinc supplementation in lower respiratory infections showed that given at a dose of more than 10 mg/day in children under 5 years of age, and especially in low birth weight patients, zinc supplementation was pivotal in reducing all-cause mortality as evidences by comparing various randomized controlled trials (RCTs) and meta-analyses.[15] National and local literature on the subject shows that in an RCT carried out by Khan et al in multiple cities of Khyber

Pakhtunkhwa province of the country, zinc supplementation reduced the overall duration of symptoms by a time of more than 48 hours in children especially under 5 years of age. They also concluded that it reduced morbidity when given as. A prophylactic supplement for two weeks but this was not found in international literature by the authors of our study and needs further studies for more conclusive results.[16] Another study comparing critical children ages 2 months to 5 years of age with severe type-2 pneumonia admitted at a hospital in Karachi also concluded discharge times reduced by more than 1-2 days in children receiving zinc supplementation by the intravenous route.[17] Another national study comparing children with bronchiolitis receiving zinc supplementation versus those in the placebo group showed marked improvement of symptoms within 24 hours than those in the placebo group with symptom regression seen after 2-3 days.[18]

Conclusion

We conclude that zinc supplementation added to standard antibiotic therapy in children with acute lower respiratory infections reduces both the resolution time for infection as well as the duration of hospital stay

Limitations of study

The limitations are that the study is single center only. We only included one standard antibiotic regimen to remove confounding factors that may affect disease resolution and affect results of whether zinc supplementation was beneficial or not but further studies in resistant infections and those on multiple anti-biotics need to be done for more conclusive results on the role of zinc supplementation in those cases.

Conflict of interest

None.

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