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Zinc Supplementation as an Adjunctive Therapy in Children with Acute Respiratory Tract Infections: A Literature Review

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KEYWORDS
acute respiratory infection; zinc; adjunct therapy; children

ABSTRACT
Acute respiratory infection (ARI) is one of the leading causes of morbidity and mortality among children worldwide, particularly in low- and middle-income countries. Children are more vulnerable to ARI because their respiratory defense mechanisms, including mucociliary clearance and immune responses, are not yet fully developed. This condition increases the risk of infection and the severity of respiratory illnesses. Zinc is an essential micronutrient that plays a crucial role in various enzymatic processes, cellular metabolism, and the regulation of the immune system. Zinc deficiency has been associated with impaired immune function, making children more susceptible to infectious diseases, including ARI. Therefore, zinc supplementation has been proposed as a potential adjunct therapy to improve clinical outcomes in children with ARI. This literature review aimed to evaluate evidence from clinical trials regarding the effectiveness of zinc supplementation as an adjunct therapy in pediatric ARI. A systematic search was conducted using the PubMed, Cochrane Library, and ScienceDirect databases, and study selection and synthesis followed the PRISMA approach. A total of 11 clinical trials were included in this review. The findings demonstrated inconsistent results in terms of symptom duration, severity reduction, and recovery time among children receiving zinc supplementation. Based on the current evidence, zinc supplementation cannot yet be recommended as a routine adjunct therapy for the management of ARI in children, and further high-quality, well-designed clinical trials are needed to clarify its potential benefits.

INTRODUCTION

One of the main contributors to morbidity and mortality in children worldwide is acute respiratory infection. Respiratory infection is a disease caused by pathogenic microorganisms that infect and disrupt the upper and lower respiratory systems, ranging from the nasal cavity and pharynx to the bronchi, bronchioles, and alveoli. Acute respiratory infections (ARI) have a wide range of clinical manifestations, from asymptomatic to severe, life-threatening infections (Boracchini et al., 2024; Wulandari et al., 2024; Xu et al., 2025). The severity is influenced by environmental factors, pathogen characteristics, and the condition of the infected individual. Common clinical manifestations include fever, cough, sore throat, nasal discharge, shortness of breath, wheezing, and so on. Examples of respiratory tract infections include the common cold, pharyngitis, otitis media, bronchiolitis, and pneumonia (Calderaro et al., 2022; Velmurugan & Thangamani, 2024; Vos et al., 2021).

According to the WHO, pneumonia is the leading cause of infectious death in children worldwide. In 2019, pneumonia caused the deaths of 740,180 children under five years of age,

accounting for 14% of all deaths in this age group and 22% of all deaths in children aged 1-5 years. Based on the 2023 Indonesian Health Survey, the prevalence of ARI among toddlers in Indonesia is 4.8%, with the highest prevalence in the 12-23 month and 24-35 month age groups, each with the same percentage of 5.7%. The highest prevalence of ARI in Indonesia was found in Central Papua (11.8%), Papua Pegunungan (10.7%), East Java (8.8%), and Banten (8.7%).

Children's immune systems have different characteristics from those of adults because their immune systems and respiratory tract defense mechanisms are not yet fully developed, increasing their risk of respiratory infections (Sitanggang et al., 2025). In infants and toddlers, innate immunity such as neutrophils, macrophages, and natural killer (NK) cells acts as the first line of defense, but their effectiveness and phagocytosis ability in eliminating pathogens are not as optimal as in adults. Meanwhile, the adaptive immune system, such as T cells and B cells, is still maturing, so the response to new antigens causing respiratory tract infections is less effective. If exposure to pathogens is high, but immune maturation is incomplete, coupled with unfavorable nutritional and environmental factors, children, especially toddlers, will be more susceptible to recurrent respiratory tract infections and more severe clinical manifestations (Lambert & Culley, 2017).

Zinc is an essential micronutrient that plays an important role in the body's enzymatic processes. Zinc-containing enzymes are involved in cell metabolism, membrane stability, proliferation, DNA and protein synthesis, oxidative stress regulation, and gene expression. In the immune system, zinc also plays an important role in the maturation and activation of innate immunity, such as neutrophils, macrophages, NK cells, and dendritic cells, and helps differentiate and regulate the function of T and B lymphocytes as part of adaptive immunity. Zinc deficiency has been shown to reduce phagocytosis, inhibit cytokine and interferon production, and decrease antiviral responses, thereby increasing children's susceptibility to infections, including ARI (Kinash et al., 2021). Several studies show that children with zinc deficiency have a higher risk of developing ARI, and zinc supplementation can reduce the incidence and severity of lower respiratory tract infections, including pneumonia. According to some literature, zinc can protect the integrity of the respiratory tract epithelium, support mucosal barrier function, and reduce excessive inflammatory responses, thereby potentially accelerating clinical recovery in children with respiratory tract infections (Khera et al., 2020), (Kumari et al., 2022).

To date, most literature related to zinc in children has focused on the prevention of infection or its impact on growth, while literature that specifically and comprehensively discusses the effectiveness of zinc supplementation as an adjunct therapy in children with ARI is still limited. Therefore, this literature review aims to examine clinical trials on the effectiveness of zinc supplementation as an adjunct therapy in children with ARI, particularly in relation to clinical symptom improvement. This study is expected to serve as a comprehensive reference and consideration in daily clinical practice in the management of ARI in children.

RESEARCH METHOD

This literature review was conducted by searching three databases, namely PubMed, Cochrane Library, and ScienceDirect, without specifying publication years. The literature was searched using keywords such as “zinc,” “zinc supplementation,” “respiratory tract infection,” “acute respiratory infection,” “pneumonia,” and “child.” The inclusion criteria included primary studies with a population of children aged 0-18 years, which discussed the relationship or effectiveness of zinc supplementation and ARI in children, and were published in English or Indonesian. Exclusion criteria for this literature review were irrelevant titles and abstracts, research subjects with other comorbidities, articles in the form of literature reviews, systematic

reviews, meta-analyses, letters to the editor, case reports, studies with unclear clinical outcomes, and those without full-text availability.

The process of identifying and selecting studies used the PRISMA flow, starting from collecting all articles found in the search, removing duplicates, to selecting based on relevant titles and abstracts. Next, studies that met the requirements were reviewed.

RESULTS AND DISCUSSION

A literature search and selection using the PRISMA approach yielded 11 clinical trials (randomized controlled trials) that met the inclusion criteria, with varying sample sizes. The acute respiratory infections studied included the common cold, moderate pneumonia, severe pneumonia, and very severe pneumonia. Most of these studies showed the benefits of zinc supplementation, especially in studies with subjects diagnosed with pneumonia and lower respiratory tract infections. Several studies reported that zinc administration can accelerate symptom improvement, such as shortening the duration of fever, improving oxygenation, and accelerating resolution.

Several studies also report that the length of hospital stay for children with pneumonia is shorter in the zinc supplementation group compared to the placebo group. However, more than half of the studies found no significant benefits from zinc supplementation. Several studies reported that zinc did not significantly reduce the duration of clinical signs such as tachypnea or hypoxemia, nor did it reduce the risk of pneumonia treatment failure. Studies on zinc supplementation for the common cold also showed no significant reduction in the duration of symptoms, but one study reported a possible improvement in the severity of nasal congestion symptoms.

Overall, the results of 11 studies showed varying results, with some studies showing clear benefits or effectiveness of zinc, while others showed no improvement compared to standard therapy or placebo.

Table 1. Study results of selection using the PRISMA approach

Title	Researcher	Study design	Sample	Results	Conclusion
A randomized controlled trial of zinc supplementation in the treatment of acute respiratory tract infection in Thai children	Rerksuppaphol S, dkk. 2019	A randomized, double-blind, placebocontrolled trial	64	Lower respiratory tract infections improve more quickly in children with zinc supplementation.	Zinc supplementation improves recovery in Thai children with lower respiratory tract infections and shortens the length of hospital stays.

Title	Researcher	Study design	Sample	Results	Conclusion
Efficacy of Adjunctive Zinc in Improving the Treatment Outcomes in Hospitalized Children with Pneumonia: A Randomized Controlled Trial	Rerksuppaphol L, dkk. 2019	A randomized, double-blind, placebo-controlled trial was conducted	96	Zinc supplementation accelerates the resolution period of pneumonia, normalizes oxygen levels and body temperature. The length of hospital stay for children receiving zinc is shorter than those receiving a placebo. The resolution time for severe pneumonia is slightly shorter in children receiving zinc.	Zinc supplementation accelerates the resolution period, normalizes oxygen levels and body temperature, and shortens the length of hospital stay for children with pneumonia.
A randomized controlled trial of zinc as adjuvant therapy for severe pneumonia in young children	Basnet S, dkk. 2011	Double-blind, randomized, placebo-controlled trial	500		Clinical improvement in children with severe pneumonia who were treated and a reduction in the risk of treatment failure with zinc supplementation were not significant.
Role of zinc in severe pneumonia: a randomized double bind placebo-controlled study	Shah GS, dkk. 2012	A double blind randomized, placebo-controlled clinical trial	110	Respiratory rate, chest wall retractions, cyanosis, stridor, nasal flaring, wheezing, and fever upon admission to the hospital did not differ significantly between the zinc and placebo groups.	Zinc supplementation during the acute phase does not aid in the short-term clinical recovery from severe pneumonia.

Title	Researcher	Study design	Sample	Results	Conclusion
Zinc as an adjunct to the treatment of severe pneumonia in Ecuadorian children: a randomized controlled trial	Sempertegui F, dkk. 2014	A randomized parallel group, double-blind, placebo-controlled clinical trial	450	There were no significant differences between the zinc and placebo groups in terms of primary outcomes. In addition, there were no significant differences in the duration of respiratory signs and symptoms or the prevalence of treatment failure.	Zinc does not affect the time to resolution of pneumonia or treatment failure.
Efficacy of zinc in the treatment of severe pneumonia in hospitalized children <2 y-old	Bose A, dkk. 2006	Randomized double-blind, placebo-controlled clinical trial	300	There were no clinically or statistically significant differences in the duration of tachypnea, hypoxemia, chest wall retractions, inability to feed, lethargy, severe illness, or length of hospital stay.	Zinc supplementation had no overall effect on the length of hospital stay or clinical signs of severe infection in young children hospitalized for severe pneumonia.
The efficacy of zinc supplementation on outcome of children with severe pneumonia. A randomized double-blind placebo-controlled clinical trial	Valavi E, dkk. 2011	A randomized double-blind placebo-controlled trial	128	The time required for complete resolution of symptoms in the group given zinc supplementation was significantly shorter than in the placebo group.	The results of the study show that supplemental zinc therapy accelerates recovery from severe pneumonia in young children and significantly reduces the length of hospital stays.
Zinc gluconate lozenges for treating the common cold in children: a randomized controlled trial	Macknin ML, dkk. 1998	A randomized double-masked, placebo-controlled study	220	The time required for complete resolution of common cold symptoms did not differ significantly between students who received zinc and those who received a placebo.	Zinc gluconate lozenges are not effective in treating common cold symptoms in children and adolescents.

Title	Researcher	Study design	Sample	Results	Conclusion
Efficacy of zinc given as an adjunct in the treatment of severe and very severe pneumonia in hospitalized children 2-24 mo of age: a randomized, double-blind, placebo-controlled trial	Wadhwa N, dkk. 2013	Randomized, double-blind, placebo-controlled trial	550	In stratified analysis, zinc was shown to be effective in accelerating recovery time in children with severe pneumonia.	Overall, there were no significant benefits from adding zinc to antibiotic therapy in accelerating recovery from pneumonia, but there were possible benefits in the subgroup of children with very severe pneumonia.
A randomized controlled trial of oral zinc in acute pneumonia in children aged between 2 months to 5 years	Ganguly A, dkk. 2011	Randomized controlled single blind design.	98	Children receiving zinc supplementation showed no difference in clinical cure rates on day 14 compared to placebo.	Zinc supplementation did not improve the duration of symptoms or recovery rates in children under five years of age with acute bacterial pneumonia.
Effect of zinc sulfate on common cold in children: randomized, double-blind study	Kurugol Z, Bayram N, Atik T. 2007	Randomized double-blind, placebo-controlled study	150	The time to improvement of all common cold symptoms in the placebo group was the same as in the zinc group, namely 6 days. Improvement of nasal congestion symptoms was 5 days in both groups. There was no significant difference in the duration of common cold symptoms.	Zinc sulfate has no effect on the duration of common cold symptoms. However, zinc may be effective in reducing the severity of symptoms.

A literature review of 11 clinical trials evaluating zinc supplementation as an adjunct therapy in children with ARI showed inconsistent results. Several studies reported that zinc supplementation can accelerate clinical improvement in severe pneumonia, normalize oxygen saturation and body temperature, and shorten the length of hospital stay compared to placebo. In other studies, such as those involving severe or very severe pneumonia and the common cold, no significant differences were found in symptom duration, respiratory rate, signs of respiratory distress, treatment failure rates, or length of hospital stay between the zinc-treated group and the control group.

Zinc plays a broad role in the immune system, where it acts as a cofactor for hundreds of enzymes and proteins involved in T cell maturation and function, as well as B cell and phagocyte activation (Kumari et al., 2022). Zinc deficiency can reduce the immune system's ability to eliminate pathogens in the respiratory tract, thereby increasing susceptibility to

infection and slowing down the resolution of inflammation. In addition, zinc also plays a role in defending the integrity of the respiratory tract mucosal epithelium and repairing tissue damaged by inflammation. In children with ARI, especially if accompanied by zinc deficiency, zinc can theoretically enhance the immune response and promote faster clinical improvement (Brown et al., 2020), (Bose et al., 2006), (Islam et al., 2018), (Rerksuppaphol & Rerksuppaphol, 2019).

Not all results from the 11 studies were consistent. Some clinical trials reported the effectiveness of zinc in improving symptoms at the time of pneumonia resolution or shorter hospital stays, but several other studies showed no significant clinical differences between ARI therapy with zinc and without zinc. The varying results of these studies are likely due to several factors, such as the nutritional status and zinc levels of each child. The effectiveness of zinc supplementation is more apparent in children with zinc deficiency, while this effectiveness is not as apparent in children with adequate zinc levels (Rerksuppaphol & Rerksuppaphol, 2019). In addition, the severity and type of infection vary, ranging from the common cold to severe and very severe pneumonia, so the response to zinc cannot be directly compared. Other factors that influence the effectiveness of zinc include variations in dosage, formulation, and duration of zinc administration, as well as differences in study design and methodological quality (sample size, treatment adherence, and methods of measuring clinical outcomes), which may contribute to inconsistent results (Roth et al., 2010), (Sakulchit & Goldman, 2017), .

The studies reviewed have limitations that need to be considered because not all studies examined zinc levels and nutritional status of subjects, making it difficult to determine which groups actually had zinc deficiency and were most likely to benefit from zinc supplementation. The dosage and duration of zinc administration, as well as the clinical outcomes assessed, make it difficult to compare studies and draw uniform conclusions. Further clinical trials require a more standardized study design, adequate sample size, assessment of zinc levels, and nutritional status in subjects, and subgroup analysis based on the severity of acute respiratory tract infection, which can be specified as upper or lower acute respiratory tract infection. With this approach, it is hoped that the group of children most likely to benefit significantly from zinc supplementation can be identified. In addition, it can also provide support in the development of evidence-based clinical recommendations for the management of ARI in children.

CONCLUSION

The results of 11 reviewed or examined studies show that zinc supplementation as an adjunct therapy in children with acute respiratory tract infections has varying effectiveness. This inconsistent response suggests that the effectiveness of zinc may depend on initial nutritional status and disease severity. Therefore, zinc supplementation cannot yet be recommended as a routine adjunctive therapy for acute respiratory infections, although it may be effective in groups of children at risk of zinc deficiency. Further clinical trials with more uniform methodologies are needed to identify the populations that would most benefit from zinc supplementation interventions.

REFERENCES

Boracchini, R., Canova, B., Ferrara, P., Cantarutti, L., Giaquinto, C., Di Chiara, C., & Cantarutti, A. (2024). A silent strain: the unseen burden of acute respiratory infections in children. In *Italian Journal of Pediatrics* (Vol. 50, Issue 1). https://doi.org/10.1186/s13052-024-01754-2

Bose, A., Coles, C. L., John, H., Moses, P., Raghupathy, P., Kirubakaran, C., Black, R. E., Brooks, W. A., & Santosham, M. (2006). Efficacy of zinc in the treatment of severe pneumonia in hospitalized children< 2 y old. *The American Journal of Clinical Nutrition*, *83*(5), 1089–1096.

Brown, N., Kukka, A. J., & Mårtensson, A. (2020). Efficacy of zinc as adjunctive pneumonia treatment in children aged 2 to 60 months in low-income and middle-income countries: a systematic review and meta-analysis. *BMJ Paediatrics Open*, *4*(1), e000662.

Calderaro, A., Buttrini, M., Farina, B., Montecchini, S., De Conto, F., & Chezzi, C. (2022). Respiratory Tract Infections and Laboratory Diagnostic Methods: A Review with A Focus on Syndromic Panel-Based Assays. In *Microorganisms* (Vol. 10, Issue 9). https://doi.org/10.3390/microorganisms10091856

Islam, S. N., Kamal, M. M., Rahmatullah, R., Sadi, S. K. S., & Ahsan, M. (2018). Serum zinc levels in children with acute respiratory infections: Association with sociodemography and nutritional status. *Clinical Nutrition Experimental*, *22*, 11–18.

Khera, D., Singh, S., Purohit, P., Sharma, P., & Singh, K. (2020). Prevalence of zinc deficiency and the effect of zinc supplementation on the prevention of acute respiratory infections. *Turkish Thoracic Journal*, *21*(6), 371.

Kinash, M., Boyarchuk, O., & Dobrovolska, L. (2021). Zinc: its impact on immune function in children. *Pediatria Polska-Polish Journal of Paediatrics*, *96*(4), 263–269.

Kumari, D., Garg, S., & Bhawrani, P. (2022). Zinc homeostasis in immunity and its association with preterm births. *Scandinavian Journal of Immunology*, *95*(4), e13142.

Lambert, L., & Culley, F. J. (2017). Innate immunity to respiratory infection in early life. *Frontiers in Immunology*, *8*, 1570.

Rerksuppaphol, S., & Rerksuppaphol, L. (2019). A randomized controlled trial of zinc supplementation in the treatment of acute respiratory tract infection in Thai children. *Pediatric Reports*, *11*(2), 7954.

Roth, D. E., Richard, S. A., & Black, R. E. (2010). Zinc supplementation for the prevention of acute lower respiratory infection in children in developing countries: meta-analysis and meta-regression of randomized trials. *International Journal of Epidemiology*, *39*(3), 795–808.

Sakulchit, T., & Goldman, R. D. (2017). Zinc supplementation for pediatric pneumonia. *Canadian Family Physician*, *63*(10), 763–765.

Sitanggang, H. D., Lanita, U., Siregar, S. A., & Ibnu, I. N. (2025). Epidemiology of acute respiratory infection among children under five in Kenali Asam Bawah, Jambi city. *Proceedings Academic Universitas Jambi*, *1*(2), 811–818.

Velmurugan, L. S., & Thangamani, N. (2024). Antibiotics In Respiratory Tract Infections. *Indian Journal of Practical Pediatrics*, *26*(1). https://doi.org/10.1093/med/9780199588084.003.0011

Vos, L. M., Bruyndonckx, R., Zuithoff, N. P. A., Little, P., Oosterheert, J. J., Broekhuizen, B. D. L., Lammens, C., Loens, K., Viveen, M., Butler, C. C., Crook, D., Zlateva, K., Goossens, H., Claas, E. C. J., Ieven, M., Van Loon, A. M., Verheij, T. J. M., & Coenjaerts, F. E. J. (2021). Lower respiratory tract infection in the community: associations between viral aetiology and illness course. *Clinical Microbiology and Infection*, *27*(1). https://doi.org/10.1016/j.cmi.2020.03.023

Wulandari, R. A., Fauzia, S., & Kurniasari, F. (2024). Investigations on the risk factors of Acute Respiratory Infections (ARIs) among under-five children in Depok City, Indonesia. *Annali Di Igiene Medicina Preventiva e Di Comunita*, *36*(1). https://doi.org/10.7416/ai.2023.2580

Xu, M., He, W., Xie, S., Ren, Z., Chen, J., & Nuerbolati, B. (2025). Epidemiological and pathological characterization of acute respiratory infections. *APMIS*, *133*(1). https://doi.org/10.1111/apm.13484