



## THE ROLE OF VITAMIN D IN PREVENTING ACUTE RESPIRATORY TRACT INFECTIONS IN CHILDREN: LITERATURE REVIEW

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### ABSTRACT

Acute Respiratory Tract Infections (ARI), particularly pneumonia, are a leading cause of death in children under five years of age globally and in Indonesia. Vitamin D, in addition to its important role in bone health, has immunomodulatory functions by increasing the production of antimicrobial peptides such as cathelicidin and defensin, and suppressing excessive inflammatory responses. This literature review aims to explore the potential role of vitamin D supplementation in preventing ARI in children, focusing on innate and adaptive immune mechanisms, factors influencing its effectiveness, and current clinical evidence. Literature searches were conducted using PubMed, Scopus, the Cochrane Library, and Google Scholar with the following keywords “acute respiratory tract infection”, “children”, “pediatric”, “pneumonia”, “vitamin D”. The search was limited to publications from 2015–2025. A total of 356 articles were identified, of which 72 were screened based on title and abstract. After full-text eligibility assessment, 6 articles met the inclusion criteria and were included in this review. Articles were critically appraised by examining study design, sample size, intervention (dose and duration of vitamin D), and outcomes measured. Data were synthesized narratively to compare findings across studies. This review shows that vitamin D supplementation, especially in children with low baseline levels (<25 ng/mL), can reduce the incidence and duration of ARI, with a more pronounced protective effect in high-risk groups. Effectiveness is influenced by baseline vitamin D status, dose, duration of administration, age, and sunlight exposure. Clinically, these findings support the recommendation of monitoring vitamin D levels and providing supplementation as a significant preventive strategy to reduce the burden of acute respiratory infections (ARI) in children.

Keywords: acute respiratory infection; children; pediatric, pneumonia; vitamin D

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## INTRODUCTION

Acute Respiratory Tract Infections (ARI), especially pneumonia, are one of the leading causes of death in children under five. In 2015, the number of global pneumonia cases reached approximately 138 million, with the highest mortality rate in developing countries, with approximately 920,000 children under 5 years of age dying from pneumonia. In Indonesia, the prevalence of ARI in 2019 was very high, reaching 52.9% in children under five (0–5 years), although this figure declined to approximately 34.2% in 2023 (Kementerian Kesehatan RI, 2018; McAllister et al., 2019). Globally, pneumonia is a leading cause of infection and a contributor to child morbidity and mortality. Approximately 15% of deaths in children under five are caused by pneumonia, making it the most deadly infectious disease in this age group. In Indonesia, pneumonia is a major contributor to infant and toddler mortality; for example, in the age group 29 days–11 months, pneumonia accounted for 15.9% of total deaths (World Health Organization, 2021).

Vitamin D is not only important for bone health but also plays a role in the immune system. Vitamin D receptors are found on immune cells, and this vitamin has anti-inflammatory and antimicrobial effects that aid in the production of antimicrobial peptides such as cathelicidin and suppress excessive immune responses. This suggests that vitamin D supplementation could

potentially prevent ARI (Wang et al., 2024). Although numerous studies have explored the relationship between vitamin D and ARI, the results have been mixed. Given the high morbidity and mortality of ARI in children (particularly in Indonesia and other developing countries), it is important to strengthen current findings and examine factors that influence the effectiveness of vitamin D supplementation. This review will help clarify the potential role of vitamin D in ARI in children.

**METHOD**

This study used a literature review approach to explore the role of vitamin D in preventing acute respiratory tract infections (ARI) in children. Literature searches were conducted in PubMed, Scopus, the Cochrane Library, and Google Scholar. The following keywords were applied “acute respiratory tract infection”, “children”, “pediatric”, “pneumonia”, “vitamin D”. The search was limited to publications from 2015 to 2025. Inclusion criteria were children aged 0-18 years, randomized controlled trials (RCTs), cohort studies, and case-control studies, as well as studies examining the relationship between vitamin D and the incidence or prevention of acute respiratory infections. From the database search, a total of 356 articles were identified. After screening by title and abstract, 72 articles were selected, and following full-text eligibility assessment, 6 articles met the inclusion criteria and were included in this review. Critical appraisal was performed by assessing study design, sample size, intervention characteristics, and measured outcomes. The selected studies were then analyzed narratively to compare findings and identify consistencies in the effect of vitamin D supplementation on ARI in children.

**RESULT**

A total of 18 eligible studies were included in this review after the screening and selection process. The majority of the studies demonstrated a beneficial role of vitamin D in reducing the incidence or severity of acute respiratory tract infections (ARI) in children. Randomized controlled trials (RCTs) and cross-sectional studies provided direct clinical evidence, while narrative and comprehensive reviews supported the immunological mechanisms underlying this effect. However, some variations in results were observed, which could be attributed to differences in study design, population characteristics, and baseline vitamin D status.

Table 1.  
Presents a summary of the included studies

Author (Year)	Study Design	Population/Sample	Intervention/Focus	Main Findings
Ghaseminejad-Raeni A, et al. (2023)	Comprehensive review	Studies on immune-related disorders	Immunomodulatory mechanisms of vitamin D	Vitamin D enhances antimicrobial peptide production and regulates inflammation
Hamza FN, et al. (2023)	Narrative review	Respiratory and intestinal systems	Role of vitamin D in mucosal immunity	Vitamin D strengthens mucosal defense and reduces infection susceptibility
Wecke Clerico J, et al. (2025)	Randomized Controlled Trial (RCT)	Children aged 6-8 years, Germany	Vitamin D supplementation	Supplementation reduced the incidence of ARI
Sarau OS, et al. (2024)	Cross-sectional study	Preschool children	Vitamin D status and ARI incidence	Children with low vitamin D levels ARI risk, especially in deficient groups
Wang CH, et al. (2024)	Systematic review & meta analysis	Multiple RCTs on vitamin D	Dose, regimen and supplementation effect	Vitamin D supplementation reduced ARI risk, especially in deficient groups
Malawisya (2024)	SJ Narrative review	Disease prevention context	Role of vitamin D in prevention	Vitamin D plays an important role in immune modulation and infection prevention

## DISCUSSION

Vitamin D is a lipophilic prohormone that plays a crucial role in calcium-phosphate homeostasis and immune system modulation. In humans, vitamin D is obtained from two main sources: endogenous synthesis in the skin through exposure to ultraviolet B (UVB) light and dietary intake or supplementation. The primary form synthesized in the skin is vitamin D<sub>3</sub> (cholecalciferol), which then undergoes two hydroxylation stages: first in the liver to 25-hydroxyvitamin D [25(OH)D], the primary circulating form used as an indicator of vitamin D status; and second in the kidney to the active form, 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D or calcitriol]. Calcitriol works by binding to the vitamin D receptor (VDR) found on various cells, including immune cells. The calcitriol-VDR complex regulates gene transcription related to the immune response, calcium metabolism, and cell differentiation. These activities make vitamin D important not only for bone health but also for protection against respiratory infections (Wimalawansa, 2024).

The mechanism of Vitamin D in the immune system includes effects on the innate immune system, namely vitamin D increases the ability of innate immune cells such as macrophages, monocytes, and epithelial cells to recognize and destroy pathogens. Activation of TLR (Toll-like receptors) in macrophages will increase the expression of VDR and the enzyme CYP27B1, thereby accelerating the conversion of 25(OH)D into its active form within the cell. This process increases phagocytosis and the production of antimicrobial mediators as well as effects on the adaptive immune system. Vitamin D modulates the adaptive immune response by inhibiting the proliferation of T helper 1 (Th1) cells and the production of pro-inflammatory cytokines such as IL-2 and IFN- $\gamma$ , while increasing regulatory T cells (Treg) that play a role in maintaining immune tolerance. In addition, vitamin D reduces B cell differentiation and excessive antibody production, thereby preventing tissue damage due to excessive inflammation (Ghaseminejad-Raeini *et al.*, 2023).

One of the main roles of vitamin D is to induce the production of antimicrobial peptides such as cathelicidin (LL-37) and  $\beta$ -defensins in airway epithelial cells. These peptides have a direct effect on killing bacteria, viruses, and fungi, as well as disrupting pathogenic biofilms. Vitamin D reduces the expression of pro-inflammatory cytokines (IL-6, TNF- $\alpha$ ) and increases anti-inflammatory cytokines (IL-10), thereby reducing the risk of lung tissue damage caused by excessive inflammation. This is important in preventing the worsening of ARI, especially those caused by viral infections (Hamza *et al.*, 2023).

The ARI prevention response is more significant in children with low baseline 25(OH)D levels (<25 nmol/L). Deficiency increases susceptibility to infection due to low antimicrobial peptide production and impaired inflammatory regulation. Daily or weekly doses in the range of >600 IU/day (or higher for deficiencies) provide a more sustained effect than a single large bolus dose. A minimum duration during the high-risk ARI season is necessary to maintain optimal levels. Infants and toddlers are at higher risk of deficiency due to limited sunlight exposure and relatively greater needs. Supplementation in this age group provides more significant protective benefits than in older children (Sarau *et al.*, 2024).

One recent study showed that children receiving vitamin D supplementation had 17% fewer days of illness due to ARI (RR 0.83; 95% CI 0.76–0.90;  $p < 0.001$ ) and 43% fewer days of illness due to ARI with fever (RR 0.57; 95% CI 0.48–0.67;  $p < 0.001$ ) compared to placebo (Weeke Clerico *et al.*, 2025). These findings are consistent with the hypothesis that vitamin D strengthens the respiratory mucosal barrier by increasing the production of antimicrobial peptides and modulating the inflammatory response. This protective benefit was particularly evident in populations with low baseline vitamin D levels and with regular supplementation. Clinically, these results support the recommendation of vitamin D supplementation as part of a strategy for preventing ARI in children, particularly in high-risk groups.

## **CONCLUSION**

Vitamin D plays a crucial role in preventing acute respiratory infections (ARI) in children by modulating the innate and adaptive immune systems. In the innate immune system, vitamin D increases the expression of antimicrobial peptides such as cathelicidin and defensins, which directly kill pathogens. In the adaptive immune system, vitamin D regulates T and B cell differentiation, suppresses excessive pro-inflammatory responses, and supports a more controlled immune response. This regulation helps reduce the risk and severity of ARI. The effectiveness of vitamin D supplementation is influenced by the child's initial vitamin D status, dose and duration of administration, age, and sunlight exposure. A meta-analysis of studies has shown that vitamin D supplementation can reduce the duration and frequency of ARI, especially in children with initial deficiency. Therefore, monitoring vitamin D status and appropriate interventions have the potential to be a significant preventive strategy to reduce the incidence of ARI in the pediatric population.

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