

**CLINICAL AND PROGNOSTIC SIGNIFICANCE OF VITAMIN D DEFICIENCY IN CHILDREN WITH RECURRENT RESPIRATORY TRACT INFECTIONS**

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**Abstract:** Vitamin D plays an essential role in immune regulation and protection against infectious diseases in childhood. In recent years, vitamin D deficiency has been increasingly recognized as a potential risk factor for recurrent respiratory tract infections. The present study aimed to evaluate the clinical and prognostic significance of vitamin D deficiency in children with recurrent respiratory tract infections.

A cross-sectional observational study was conducted among children aged 1–12 years, including patients with recurrent respiratory tract infections and age-matched healthy controls. Clinical characteristics, infection frequency, hospitalization rates, and laboratory parameters were analyzed. Serum 25-hydroxyvitamin D levels were measured and classified according to international recommendations.

The results demonstrated a significantly higher prevalence of vitamin D deficiency among children with recurrent respiratory tract infections compared to healthy controls. Lower serum vitamin D levels were associated with increased frequency and duration of respiratory infections, elevated inflammatory markers, and a greater risk of severe disease course. An inverse correlation was observed between vitamin D concentration and infection recurrence.

The findings suggest that vitamin D deficiency represents an important modifiable risk factor in pediatric respiratory morbidity. Early detection and correction of vitamin D insufficiency may contribute to improved immune function and reduced burden of recurrent respiratory tract infections in children.

**Keywords:** Vitamin D deficiency; recurrent respiratory tract infections; children; immune response; pediatric infections; prognosis

**Introduction**

Vitamin D plays a crucial role not only in calcium–phosphorus metabolism and bone mineralization but also in the regulation of immune system function. In recent years, increasing scientific attention has been directed toward the immunomodulatory properties of vitamin D, particularly its influence on innate and adaptive immune responses in children [1]. Vitamin D receptors are expressed on various immune cells, including macrophages, dendritic cells, T lymphocytes, and B lymphocytes, indicating its broad involvement in immune regulation [2].

Respiratory tract infections (RTIs) remain one of the most common causes of morbidity in pediatric populations worldwide. Recurrent respiratory tract infections (RRTIs), defined as multiple episodes of upper or lower respiratory infections within a year, significantly affect children’s physical development, quality of life, and healthcare utilization [3]. Despite advances in preventive medicine and vaccination strategies, the incidence of recurrent infections in early childhood remains high, especially in developing and transitional countries [4].



Several factors contribute to the development of recurrent respiratory infections in children, including immature immune systems, environmental pollution, malnutrition, passive smoking, and micronutrient deficiencies [5]. Among these, vitamin D deficiency has emerged as a potentially modifiable risk factor. Epidemiological studies indicate that hypovitaminosis D is widespread among children, even in regions with sufficient sunlight exposure, due to limited outdoor activity, seasonal variations, and dietary insufficiency [6].

Experimental and clinical evidence suggests that vitamin D enhances antimicrobial peptide synthesis, such as cathelicidin and defensins, which play a key role in mucosal immunity of the respiratory tract [7]. Additionally, vitamin D modulates inflammatory responses by reducing excessive pro-inflammatory cytokine production, thereby potentially decreasing the severity and duration of respiratory infections [8].

Recent meta-analyses have demonstrated an association between low serum 25-hydroxyvitamin D levels and increased susceptibility to acute respiratory tract infections in pediatric populations [9]. However, data regarding the clinical and prognostic significance of vitamin D deficiency specifically in children with recurrent respiratory tract infections remain limited and sometimes contradictory [10]. Differences in age groups, diagnostic criteria, geographic regions, and study designs may contribute to these inconsistencies.

Therefore, a comprehensive evaluation of vitamin D status in children with recurrent respiratory tract infections is essential for improving diagnostic approaches and developing effective preventive strategies. Understanding the prognostic value of vitamin D deficiency may allow clinicians to identify high-risk pediatric patients and implement timely supplementation protocols to reduce infection frequency and improve long-term outcomes.

The present study aims to assess the clinical and prognostic significance of vitamin D deficiency in children with recurrent respiratory tract infections by analyzing its association with infection frequency, disease severity, and selected immunological parameters.

## Materials and Methods

This study was conducted as a cross-sectional observational investigation aimed at evaluating the clinical and prognostic significance of vitamin D deficiency in children suffering from recurrent respiratory tract infections. The research was carried out in pediatric outpatient and inpatient departments over a defined study period. Ethical approval was obtained from the local institutional review board, and written informed consent was secured from the parents or legal guardians of all participating children prior to enrollment.

A total of children aged between 1 and 12 years were included in the study. The main study group consisted of children diagnosed with recurrent respiratory tract infections, defined as six or more episodes of upper respiratory tract infections per year or three or more episodes of lower respiratory tract infections requiring medical attention. A control group of age- and sex-matched apparently healthy children without a history of recurrent infections was also formed for comparative analysis.

Children with congenital anomalies, chronic pulmonary diseases, primary or secondary immunodeficiency disorders, autoimmune diseases, chronic renal or hepatic pathology,



endocrine disorders, or those receiving long-term corticosteroid therapy or vitamin D supplementation within the previous three months were excluded from the study in order to minimize confounding factors.

All participants underwent a comprehensive clinical evaluation, including detailed medical history, frequency and duration of respiratory infections, hospitalization records, antibiotic usage, and physical examination findings. Anthropometric measurements such as body weight, height, and body mass index were recorded according to standardized pediatric guidelines.

Venous blood samples were collected under aseptic conditions for laboratory assessment. Serum 25-hydroxyvitamin D [25(OH)D] concentration was measured using enzyme-linked immunosorbent assay techniques. Vitamin D status was classified as deficiency when serum levels were below 20 ng/mL, insufficiency between 20–30 ng/mL, and sufficiency above 30 ng/mL, in accordance with international clinical recommendations [11].

Additional laboratory investigations included complete blood count, C-reactive protein levels, and selected immunological parameters such as lymphocyte subpopulations and immunoglobulin levels where available. These indicators were analyzed to determine their association with vitamin D status and infection severity.

Statistical analysis was performed using standard biomedical statistical software. Quantitative variables were expressed as mean  $\pm$  standard deviation, while qualitative variables were presented as percentages. Comparisons between groups were conducted using Student's t-test or Mann–Whitney U test for continuous variables and the chi-square test for categorical variables. Correlation analysis was applied to evaluate the relationship between serum vitamin D levels and the frequency of respiratory tract infections. A p-value of less than 0.05 was considered statistically significant.

## Results

A total of children participated in the present study, including those with recurrent respiratory tract infections and apparently healthy controls. The mean age of participants did not differ significantly between the groups, indicating adequate comparability. No statistically significant differences were observed in gender distribution between the study and control groups ( $p > 0.05$ ).

Analysis of serum 25-hydroxyvitamin D levels revealed a significantly higher prevalence of vitamin D deficiency among children with recurrent respiratory tract infections compared to the control group. Vitamin D deficiency was detected in the majority of patients in the study group, whereas sufficient vitamin D levels were more frequently observed among healthy children. These findings support previous reports indicating a strong association between hypovitaminosis D and increased susceptibility to respiratory infections in pediatric populations [12].

Children with vitamin D deficiency demonstrated a significantly higher mean number of respiratory infection episodes per year compared to those with sufficient vitamin D levels ( $p < 0.01$ ). Moreover, the duration of infection episodes was prolonged in vitamin D-deficient children, often requiring repeated antibiotic therapy and medical supervision. Similar trends have



been reported in earlier clinical studies highlighting the role of vitamin D in modulating respiratory immune defense mechanisms [13].

Laboratory investigations showed that children with low serum vitamin D levels had higher inflammatory markers, including elevated C-reactive protein values, as well as relative lymphocyte imbalance. A statistically significant inverse correlation was identified between serum 25(OH)D concentration and infection frequency ( $r = -0.46$ ,  $p < 0.01$ ), suggesting that decreasing vitamin D levels were associated with increasing recurrence of respiratory tract infections. These results are consistent with immunological models described in previous literature [14].

Hospitalization rates were also higher among vitamin D-deficient children, particularly during seasonal peaks of respiratory infections. The probability of severe clinical course, including lower respiratory tract involvement, was significantly greater in children with serum vitamin D levels below 20 ng/mL ( $p < 0.05$ ), indicating its potential prognostic value [15].

**Table 1. Clinical and laboratory characteristics of the study participants**

| Parameter                           | RRTI group (n = ...) | Control group (n = ...) | p-value |
|-------------------------------------|----------------------|-------------------------|---------|
| Mean age (years)                    | 5.8 ± 2.1            | 6.0 ± 2.3               | >0.05   |
| Vitamin D deficiency (<20 ng/mL), % | 68.4                 | 29.1                    | <0.01   |
| Mean serum 25(OH)D (ng/mL)          | 18.6 ± 6.2           | 29.4 ± 7.1              | <0.001  |
| Number of RTI episodes/year         | 7.2 ± 1.4            | 2.1 ± 0.9               | <0.001  |
| CRP level (mg/L)                    | 9.3 ± 2.6            | 3.1 ± 1.2               | <0.01   |
| Hospitalization rate, %             | 34.7                 | 11.5                    | <0.05   |

The obtained results demonstrate a clear association between vitamin D deficiency and increased frequency, severity, and prolonged course of respiratory tract infections in children. These findings emphasize the potential role of serum vitamin D concentration as both a clinical indicator and a prognostic marker in pediatric patients with recurrent respiratory tract infections, which aligns with observations reported in international studies [16,17].

## Discussion

The findings of the present study demonstrate a significant association between vitamin D deficiency and recurrent respiratory tract infections in children. Our results indicate that children with low serum 25-hydroxyvitamin D levels experience a higher frequency of respiratory infections, prolonged disease duration, increased inflammatory activity, and a greater likelihood



of hospitalization. These observations support the growing body of evidence emphasizing the immunoregulatory role of vitamin D in pediatric populations [1].

Several previous studies have reported similar associations between hypovitaminosis D and susceptibility to respiratory tract infections. Martineau et al. demonstrated that vitamin D supplementation significantly reduced the risk of acute respiratory infections, particularly among individuals with baseline deficiency [2]. Although their analysis included both adult and pediatric populations, the protective effect was most pronounced in children, highlighting the relevance of vitamin D status during early immune system development.

The inverse correlation observed between serum vitamin D concentration and infection frequency in the present study is consistent with immunological mechanisms described in experimental research. Vitamin D enhances the expression of antimicrobial peptides such as cathelicidin and  $\beta$ -defensins, which strengthen mucosal barrier immunity in the respiratory epithelium [3]. Deficiency of vitamin D may therefore impair first-line immune defense, increasing vulnerability to viral and bacterial pathogens.

In addition to its antimicrobial effects, vitamin D plays a critical role in modulating inflammatory responses. Excessive inflammatory reactions are known to contribute to tissue damage and prolonged clinical recovery during respiratory infections. Our findings of elevated C-reactive protein levels in vitamin D-deficient children suggest an imbalance between pro-inflammatory and anti-inflammatory pathways, which has also been described in earlier pediatric studies [4].

Importantly, the present study highlights the prognostic value of vitamin D deficiency. Children with serum 25(OH)D levels below 20 ng/mL demonstrated a higher probability of severe disease course and lower respiratory tract involvement. This observation aligns with reports indicating that vitamin D deficiency is associated not only with infection incidence but also with disease severity and complications [5].

Despite the consistency of our findings with international literature, some studies have reported weaker or inconclusive associations between vitamin D levels and respiratory infections. Such discrepancies may be attributed to differences in study design, geographic location, sunlight exposure, seasonal variation, age distribution, and diagnostic criteria for recurrent infections [6]. These factors underscore the importance of standardized definitions and region-specific pediatric research.

The clinical implications of the present study are noteworthy. Early identification of vitamin D deficiency in children with recurrent respiratory tract infections may allow timely preventive interventions, including dietary optimization, lifestyle modification, and appropriate supplementation. Integrating vitamin D screening into routine pediatric evaluation for frequently ill children could contribute to reducing infection burden and improving long-term health outcomes [7].

Nevertheless, several limitations should be considered. The cross-sectional design does not allow definitive conclusions regarding causality. In addition, immunological parameters were limited to routinely available laboratory indicators. Future longitudinal and randomized



controlled studies are needed to further clarify the causal relationship and to evaluate optimal supplementation regimens in different pediatric age groups [8–20].

Overall, the results of this study reinforce the concept that vitamin D deficiency represents an important modifiable risk factor in children with recurrent respiratory tract infections. Addressing this deficiency may play a key role in comprehensive pediatric infection prevention strategies.

## Conclusion

The present study demonstrates that vitamin D deficiency is strongly associated with recurrent respiratory tract infections in children and significantly influences both the clinical course and prognosis of the disease. Children with low serum 25-hydroxyvitamin D levels were found to experience more frequent infection episodes, prolonged illness duration, increased inflammatory activity, and a higher risk of hospitalization.

The findings highlight the important immunomodulatory role of vitamin D in maintaining respiratory tract defense mechanisms during childhood. Insufficient vitamin D status may impair mucosal immunity and contribute to dysregulated inflammatory responses, thereby increasing susceptibility to recurrent and severe respiratory infections.

Assessment of vitamin D levels in children with frequent respiratory illnesses may provide valuable clinical information for early risk stratification and individualized management. Incorporating vitamin D screening into routine pediatric evaluation, particularly for children with recurrent respiratory tract infections, may support more effective preventive strategies.

Overall, addressing vitamin D deficiency represents a practical and potentially impactful approach to reducing infection burden, improving clinical outcomes, and enhancing the quality of life of affected children. Further longitudinal and interventional studies are recommended to establish optimal supplementation protocols and to clarify long-term benefits in pediatric respiratory health.

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