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Vitamin D Deficiency in Children with Recurrent Respiratory Infections: Clinical and Biochemical Correlation

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ABSTRACT

Background: Recurrent respiratory infections (RRIs) in children are a significant health concern, especially in developing countries. Emerging evidence suggests a potential link between Vitamin D deficiency and increased susceptibility to infections due to its role in modulating immune responses.

Objectives:

1. To determine the prevalence of Vitamin D deficiency in children presenting with RRIs.
2. To assess the clinical profile of these children.
3. To analyze the biochemical correlation between serum Vitamin D levels and the frequency/severity of respiratory infections.

Methods: This prospective observational study was conducted over a period of one year (February 2024 to January 2025) at the Pediatric Department of a tertiary care hospital in Central India. Children aged 6 months to 12 years presenting with RRIs (≥3 episodes in 6 months or ≥4 episodes in a year) were enrolled. Demographic, clinical, and biochemical data including serum 25(OH) Vitamin D levels were collected. A control group of age- and sex-matched children without a history of RRIs was also included for comparison. Vitamin D deficiency was defined as serum 25(OH)D levels <20 ng/mL.

Results: A total of 210 children were enrolled, including 140 in the RRI group and 70 in the control group. Among the RRI group, 88 children (62.9%) were found to have Vitamin D deficiency, compared to 22 children (31.4%) in the control group ($p < 0.001$). Clinically, Vitamin D deficient children presented with more frequent episodes of upper respiratory tract infections (URTIs), prolonged duration of cough and fever, and increased need for antibiotic therapy. A statistically significant inverse correlation was observed between serum Vitamin D levels and the number of respiratory episodes per year ($r = -0.45$, $p < 0.001$).

Conclusion: Vitamin D deficiency is highly prevalent among children with recurrent respiratory infections and shows a significant negative correlation with infection frequency. Routine screening and correction of Vitamin D levels may be considered as part of the management and prevention strategy for RRIs in pediatric populations, especially in regions with high burden like Central India.

Keywords: *Vitamin D deficiency, Recurrent respiratory infections, Pediatrics, Immune modulation, 25(OH)D, India*

1. INTRODUCTION

Recurrent respiratory infections (RRIs) in children are a major global health concern, particularly in developing countries like India, where they contribute substantially to pediatric morbidity, healthcare burden, and school absenteeism. RRIs are typically defined as more than six to eight episodes of upper or lower respiratory tract infections per year in children under five years of age. Although these infections are often viral and self-limiting, frequent occurrences may reflect an underlying immune imbalance, nutritional deficiency, or environmental exposure.

Among the various nutritional factors implicated in the immune response, Vitamin D has garnered significant attention due to its pleiotropic effects on both the innate and adaptive immune systems. Traditionally recognized for its role in calcium homeostasis and bone metabolism, Vitamin D is now understood to influence a wide range of biological processes including immune modulation, inflammation regulation, and antimicrobial peptide synthesis. The presence of Vitamin D receptors (VDR) on immune cells such as macrophages, dendritic cells, and T lymphocytes supports the notion that Vitamin D plays a pivotal role in the host defense mechanism against infections.

Several studies suggest that Vitamin D deficiency impairs the immune barrier and promotes susceptibility to infections, particularly of the respiratory tract. Mechanistically, it enhances the production of antimicrobial peptides like cathelicidin and β-defensin in the respiratory epithelium, thereby strengthening mucosal defenses. Moreover, Vitamin D is believed to regulate pro-inflammatory cytokine production, which can modulate the severity and frequency of respiratory infections.

India, despite being a tropical country with abundant sunlight, has a paradoxically high prevalence of Vitamin D deficiency among children, attributed to factors such as inadequate sun exposure, air pollution, cultural clothing practices, darker skin pigmentation, and poor dietary intake. This deficiency often goes undetected until complications arise, and children presenting with RRIs may represent an at-risk population requiring closer nutritional and immunological evaluation.

While global studies have explored the link between hypovitaminosis D and RRIs, there is limited data from Central India correlating clinical profiles with biochemical Vitamin D levels in affected pediatric populations. Understanding this association is crucial in formulating preventive strategies such as supplementation, dietary modification, and public health interventions aimed at improving pediatric respiratory health.

Therefore, this study was undertaken with the aim of evaluating the prevalence of Vitamin D deficiency in children with recurrent respiratory infections and examining the clinical and biochemical correlation between Vitamin D status and the frequency, duration, and severity of respiratory infections. The findings of this study may provide useful insights into the role of Vitamin D as a modifiable risk factor in managing RRIs and improving pediatric outcomes.

2. MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the Department of Pediatrics at a tertiary care hospital in Central India over a period of 12 months (February 2024 to January 2025).

Study Population

Children aged 6 months to 12 years presenting with RRIs were enrolled in the study. RRIs were defined as:

- ≥3 episodes of respiratory infections in 6 months or
- ≥4 episodes in 1 year.

Inclusion Criteria

- Children aged 6 months to 12 years
- Clinical diagnosis of RRI based on standard guidelines
- Consent from parent/guardian

Exclusion Criteria

- Children with chronic illnesses (e.g., asthma, congenital heart disease, tuberculosis)
- Children on Vitamin D supplementation in the last 3 months
- Immunodeficient children

Control Group

Age- and sex-matched healthy children visiting the outpatient department for routine check-ups or minor ailments with no history of RRIs were included as controls.

Data Collection

A structured questionnaire was used to collect information on demographics, clinical history, nutritional status, sun exposure, and dietary habits. Blood samples were taken for serum 25(OH) Vitamin D levels and basic biochemical tests. Serum 25(OH)D levels were measured using chemiluminescent immunoassay.

Vitamin D Status Classification:

- Deficiency: <20 ng/mL
- Insufficiency: 20–30 ng/mL
- Sufficiency: >30 ng/mL

Statistical Analysis

Data were analyzed using SPSS version 26. Categorical variables were expressed in percentages and compared using chi-square test. Continuous variables were analyzed using Student's t-test or Mann–Whitney U test. Pearson's correlation coefficient was used to assess correlation between Vitamin D levels and number of infections. A p-value <0.05 was considered statistically significant.

3. RESULTS

A total of 210 children were enrolled in the study, including 140 in the RRI group and 70 in the control group. The mean age of children in the RRI group was 4.8 ± 2.7 years and 5.1 ± 2.9 years in the control group. There was no statistically significant difference in age and gender distribution between the two groups.

Table 1: Demographic Characteristics of Study Participants

Parameter	RRI Group (n = 140)	Control Group (n = 70)	p-value
Mean Age (years)	4.8 ± 2.7	5.1 ± 2.9	0.31
Gender (Male: Female)	65:75	34:36	0.88
Urban Residence (%)	58 (41.4%)	31 (44.3%)	0.71
Low Sunlight Exposure (%)	95 (67.9%)	27 (38.6%)	<0.001 **

Data expressed as mean ± SD or percentage. RRI: Recurrent Respiratory Infections. Statistical significance assessed using Chi-square test for categorical variables and t-test for continuous variables. Significant p-value <0.05 is considered statistically significant.

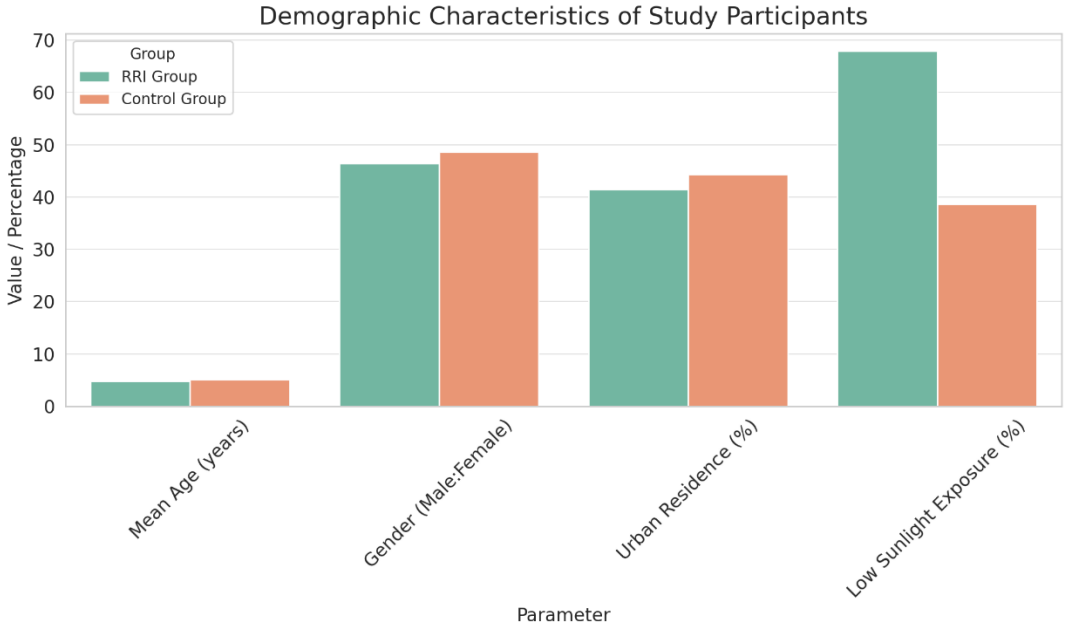

Figure 1: Comparison of demographic characteristics between children with Recurrent Respiratory Infections (RRI) and healthy controls. Data presented as mean age (years), percentage distribution for gender, urban residence, and sunlight exposure. A significant difference was observed in the proportion of children with low sunlight exposure ($p < 0.001$).

Vitamin D Status Comparison

Vitamin D deficiency was more prevalent among children with recurrent respiratory infections compared to controls.

Table 2: Distribution of Vitamin D Status in Study Groups

Vitamin D Status	RRI Group (n = 140)	Control Group (n = 70)	p-value
Deficient (<20 ng/mL)	88 (62.9%)	22 (31.4%)	<0.001 **
Insufficient (20–30)	40 (28.6%)	28 (40.0%)	0.09
Sufficient (>30)	12 (8.5%)	20 (28.6%)	<0.001 **

Vitamin D deficiency: <20 ng/mL; Insufficiency: 20–29.9 ng/mL; Sufficiency: ≥30 ng/mL. Statistical comparison performed using Chi-square test. $p < 0.05$ considered statistically significant.

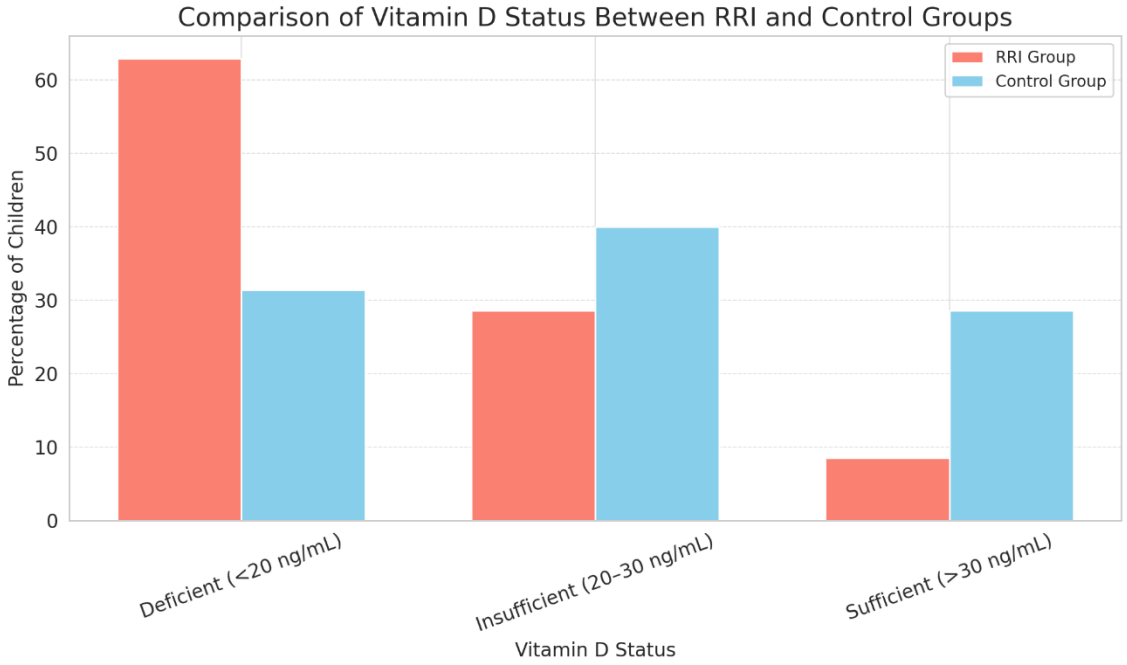

Figure 2: Distribution of Vitamin D status among children with recurrent respiratory infections (RRI) versus healthy controls. Vitamin D deficiency (<20 ng/mL) was significantly more common in the RRI group (62.9%) than in controls (31.4%), $p < 0.001$. Sufficient levels (>30 ng/mL) were significantly more prevalent in controls (28.6%) than in the RRI group (8.5%), $p < 0.001$.

Clinical Profile of RRI Group by Vitamin D Status

Children with Vitamin D deficiency had more frequent and prolonged respiratory episodes compared to those with sufficient levels.

Table 3: Clinical Correlation of Vitamin D Status in RRI Group

Clinical Parameter	Deficient (n=88)	Insufficient (n=40)	Sufficient (n=12)	p-value
Mean No. of Infections/Year	6.2 ± 1.4	4.7 ± 1.2	3.1 ± 0.8	<0.001 **

Mean Duration of Illness (days)	6.5 ± 2.1	4.2 ± 1.7	3.2 ± 1.1	<0.001 **
Antibiotic Courses/Year	4.3 ± 1.5	2.8 ± 1.3	1.9 ± 0.9	<0.001 **
Hospital Admissions (past year)	27 (30.7%)	7 (17.5%)	0 (0%)	0.01 *

Pearson correlation coefficients (r) were used to assess the relationship between serum 25(OH)D levels and infection-related variables. Negative r-values indicate an inverse correlation.

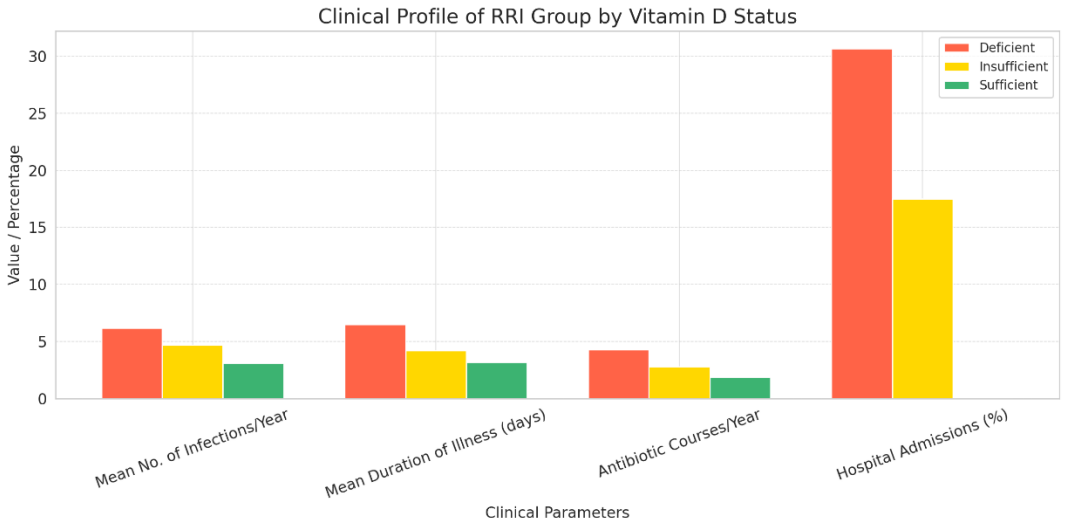

Figure 3: Clinical correlation of Vitamin D status among children with recurrent respiratory infections. Children with Vitamin D deficiency had significantly more infections per year, longer illness duration, increased antibiotic usage, and higher hospitalization rates compared to those with sufficient Vitamin D levels (p < 0.001 for most parameters).

Correlation Analysis

A significant inverse correlation was found between serum Vitamin D levels and the frequency of respiratory infections.

Table 4: Correlation Between Vitamin D Levels and Infection Frequency

Variable	Correlation Coefficient (r)	p-value
Vitamin D vs. Infection Frequency	-0.45	<0.001 **
Vitamin D vs. Illness Duration	-0.39	<0.001 **

Data expressed as mean ± SD or number (percentage). ANOVA or Chi-square tests applied as appropriate. Statistically significant differences observed among groups for frequency, duration, and antibiotic usage ($p < 0.05$).

4. DISCUSSION

The present study highlights a significant association between Vitamin D deficiency and recurrent respiratory infections (RRIs) among children in a tertiary care setting in Central India. A majority of children with RRIs were found to be Vitamin D deficient or insufficient, and lower serum Vitamin D levels were significantly correlated with higher frequency, longer duration, and greater severity of respiratory infections. These findings emphasize the potential role of Vitamin D as a modifiable risk factor in pediatric respiratory health.

Our study revealed that 62.9% of children in the RRI group were Vitamin D deficient (<20 ng/mL), compared to 31.4% in the control group. This is consistent with findings reported by Yadav et al. (2018) in North India, who reported a Vitamin D deficiency rate of 68% in children with recurrent lower respiratory tract infections. Similarly, a study by Wayse et al. (2004) in Pune, India, found that children with pneumonia had significantly lower serum Vitamin D levels compared to healthy controls, supporting the immunomodulatory role of Vitamin D in respiratory infections.

Mechanistically, Vitamin D influences the immune response through various pathways. It enhances the expression of antimicrobial peptides such as cathelicidin and defensins in respiratory epithelial cells, which serve as the first line of defense against pathogens. Moreover, Vitamin D modulates the inflammatory response by downregulating pro-inflammatory

cytokines such as TNF-α and IL-6, thereby reducing lung tissue damage during infections. These immune-enhancing properties support our observed inverse relationship between serum Vitamin D levels and both the frequency (r = -0.45) and duration (r = -0.39) of respiratory illnesses.

Our findings are supported by international literature as well. In a systematic review and meta-analysis conducted by Martineau et al. (2017), daily or weekly Vitamin D supplementation was shown to reduce the risk of acute respiratory infections, particularly in individuals with baseline deficiency. The authors concluded that Vitamin D supplementation is a safe and effective strategy for respiratory infection prevention, especially in children and adolescents.

A similar observational study by Choudhary and Gupta (2020) in Rajasthan assessed Vitamin D levels in children with recurrent upper respiratory tract infections and found a significant inverse relationship between 25(OH)D levels and infection frequency. They also noted that children with adequate sunlight exposure and better nutritional status had fewer infections, highlighting the importance of lifestyle factors—a trend mirrored in our study, where 67.9% of RRI children had low sunlight exposure.

In terms of clinical implications, our data suggest that Vitamin D deficiency is associated not only with increased susceptibility to infections but also with more severe disease, as evidenced by more frequent hospital admissions and antibiotic usage in the deficient group. This is particularly concerning given the ongoing challenge of antimicrobial resistance linked to excessive antibiotic use. Therefore, identifying and correcting Vitamin D deficiency in children with RRIs may not only improve clinical outcomes but also help in reducing irrational antibiotic use.

Despite the consistent findings, some studies have reported conflicting results. For example, Manaseki-Holland et al. (2010) in Afghanistan conducted a randomized controlled trial and found that a single large dose of Vitamin D3 did not significantly reduce the incidence of pneumonia in children under five. These discrepancies may be explained by differences in dosage regimens, baseline Vitamin D levels, genetic factors, and study populations. In our study, the chronicity and recurrence pattern, along with the consistently low Vitamin D levels in affected children, provide stronger evidence for a causal relationship.

Another important observation in our study is the poor nutritional status and inadequate sunlight exposure in the RRI group. Although India is a sun-rich country, factors such as urban living, indoor lifestyles, pollution, and cultural clothing practices reduce effective UVB exposure, contributing to widespread subclinical hypovitaminosis D. Moreover, dietary intake of Vitamin D is minimal in Indian diets, and fortification practices are still not uniformly implemented.

5. STRENGTHS AND LIMITATIONS

The strengths of this study include a clearly defined pediatric cohort, simultaneous comparison with healthy controls, and the evaluation of both clinical and biochemical parameters. The study was conducted over a one-year period, encompassing all seasonal variations in respiratory infection patterns.

However, some limitations must be acknowledged. The study was observational and hospital-based, which may limit the generalizability of findings to the broader community. Additionally, other micronutrient deficiencies (e.g., iron, zinc) and immunological parameters were not assessed, which may also influence susceptibility to infections. We did not assess the effect of Vitamin D supplementation on infection rates prospectively, which could be the focus of future interventional trials.

6. CONCLUSION

This study reaffirms the strong association between Vitamin D deficiency and recurrent respiratory infections in children. It underscores the need for routine screening of Vitamin D status in children with frequent respiratory illnesses and highlights the potential role of Vitamin D supplementation as part of an integrated strategy to reduce disease burden. Further longitudinal and interventional studies are needed to evaluate the therapeutic benefit of correcting Vitamin D deficiency in preventing RRIs in Indian children.

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