

Original Research Article

Vitamin D status of children with recurrent lower respiratory tract infection: a comparative observational study

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Received: 02 May 2025

Revised: 17 June 2025

Accepted: 18 June 2025

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ABSTRACT

Background: Lower respiratory tract infections (LRTIs) are one of the major causes of morbidity and mortality in children under five. Recurrent LRTIs which is defined as three or more episodes in one year or two or more in six months pose a significant health burden. Emerging evidence suggests that vitamin D deficiency in may increase susceptibility of children to such infections.

Methods: This comparative observational study was conducted over one year (January 2024 to December 2024) in the pediatric department of Bidar Institute of Medical Sciences, Karnataka, India. The study was undertaken to assess the association between vitamin D status and recurrent LRTIs in children aged 6 months to 5 years. The study included 80 children with recurrent LRTIs (group A) and 80 age matched healthy controls (group B). Detailed demographic details, clinical findings and nutritional status of cases was collected using a structured questionnaire. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured using chemiluminescent immunoassay and categorized as deficient (<20 ng/ml), insufficient (20–30 ng/ml) or sufficient (>30 ng/ml). Statistical analysis was performed using statistical package for the social sciences (SPSS) version 21.0 with significance set at $p < 0.05$.

Results: No significant differences were noted between groups regarding age and gender distribution. Bronchiolitis and pneumonia were the most common types of LRTIs observed. The mean serum vitamin D level in group A (18.7 ± 7.3 ng/ml) was significantly lower than in group B (26.1 ± 8.5 ng/ml) ($p < 0.0001$). Vitamin D deficiency was observed in 47.5% of children with recurrent LRTIs compared to 27.5% in controls ($p = 0.0002$).

Conclusions: Children with recurrent LRTIs were found to have significantly lower serum vitamin D levels compared to healthy counterparts. These findings suggest that vitamin D deficiency may be a modifiable risk factor for recurrent respiratory infections.

Keywords: Vitamin D deficiency, Respiratory tract infections, Pediatrics, Immunity, Bronchiolitis

INTRODUCTION

Lower respiratory tract infections (LRTIs) in children include conditions such as bronchitis, bronchiolitis and pneumonia. These conditions are usually diagnosed on the basis of clinical and radiological evidence of infection of the airways and lung parenchyma below the larynx. Recurrent LRTIs are commonly defined as three or more episodes of clinically diagnosed LRTI within a

twelve-month period or two or more episodes within six months. Globally, LRTIs remain the leading cause of childhood morbidity and mortality accounting for approximately 13% of all deaths in children under five years of age with an estimated 120 million new episodes of pneumonia each year.¹ The etiology of recurrent LRTIs is multifactorial and involve factors such as pathogenic microorganisms, host immune defences and environmental exposures. Common viral agents causing

LRTI include respiratory syncytial virus, rhinovirus and influenza. Bacterial pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae* type b and atypical organisms contribute to bacterial pneumonia. Anatomical abnormalities, immunodeficiency states (congenital or acquired), malnutrition and environmental factors (indoor air pollution, tobacco smoke exposure) further increase susceptibility of children for development of recurrent LRTI.²

Clinically, children with recurrent LRTIs present with symptoms ranging from persistent cough, tachypnoea, chest retractions, wheezing and fever. In neglected cases signs of systemic involvement such as poor feeding, lethargy and failure to thrive may also be present.³ Assessment of children with recurrent LRTI involves careful history taking to document the frequency, duration, severity of episodes and evaluation of perinatal history as well as vaccination status. Clinical examination for assessment of presence of respiratory distress in the form of tachypnoea and nasal flaring is usually done. Defining “recurrent” requires exclusion of persistent infections (e.g., tuberculosis) and confirmation of resolution between episodes. This often makes it necessary to undertake serial clinical and radiological evaluations of children presenting with recurrent LRTIs.⁴

Investigation of recurrent LRTIs extends beyond chest radiography and microbiological cultures and include assessment of immunological profile and nutritional assessments. In majority of the cases Chest X-Ray will be sufficient however in some cases high-resolution computed tomography may help particularly in children suspected to be having structural lung disease.⁵ Laboratory workup in these cases include complete blood counts, inflammatory markers (C-reactive protein, and procalcitonin), sweat chloride testing and immunoglobulin levels.

Vitamin D traditionally known for its role in calcium homeostasis and bone metabolism, has emerged as a critical modulator of innate and adaptive immunity. Its active form, calcitriol is reported to enhance the expression of antimicrobial peptides in respiratory epithelial cells and macrophages, supports regulatory T-cell function and is known to dampens excessive pro-inflammatory cytokine release.⁶ Vitamin D status is assessed by measuring serum 25-hydroxyvitamin D [25(OH)D] concentrations which is the best indicator of overall vitamin D status. The levels below 20 ng/ml are commonly classified as deficient, 20–30 ng/ml as insufficient and above 30 ng/ml as sufficient. Interpretation of vitamin D levels in children must account for seasonal variation, latitude, dietary intake, skin pigmentation and sun-exposure patterns.⁷

Emerging evidence suggests that there is a significant association between low serum vitamin D levels and increased risk of LRTIs in children but the relationship remains incompletely understood. Some studies have reported that children with vitamin D deficiency are more

likely to develop recurrent pneumonia or bronchiolitis and tend to have more severe and prolonged episodes. Randomized trials of vitamin D supplementation have shown mixed results. Some studies reported reduced incidence or severity of respiratory infections while others show no significant benefit.⁸ With this perspective this comparative observational study was conducted to assess vitamin D status of children presenting with recurrent LRTIs.

METHODS

This comparative observational study was conducted over one year (January 2024 to December 2024) in the pediatric department of Bidar Institute of Medical Sciences, Karnataka, India. The aim of the study was to assess vitamin D status of children presenting with history of recurrent LRTI in children. The study duration was 1 year extending from January 2024 to December 2024. Since the study was purely observational ethical clearance was waived. The data was anonymised before analysis to protect personal details of participants. Children aged between 6 months and 5 years presenting with clinical diagnosis of recurrent LRTIs, defined as three or more episodes of LRTI within 12 months or two episodes within six months were included in this study after obtaining consent from parents or legal guardian of the children. Children were excluded if their parents or guardians refused to give consent for participation. Those with congenital heart diseases, congenital lung malformations, or any chronic systemic illnesses were also excluded. In addition, children who had received vitamin D supplementation or any pharmacological doses of vitamin D within the preceding four weeks were excluded from study.

Based on previous studies with a 95% confidence interval and 90% power to detect a significant difference in vitamin D levels between healthy children and those with recurrent LRTIs minimum sample size was found to be 75 patients. Considering potential drop outs a total of 80 children were included in this study. Children aged between 6 months and 5 years attending the outpatient and inpatient services of the pediatric department and meeting the criteria for recurrent LRTIs were included in this study as cases (group A). 80 healthy children between the age group of 6 months to 5 years were included as control group (group B).

Detailed demographic information including age, sex, residence, socioeconomic status, maternal education, dietary habits, and exposure to sunlight were systematically collected from the parents or caregivers of enrolled children using structured questionnaires. A detailed history regarding previous episodes of LRTIs, including their frequency, severity and duration as well as need for hospitalization and treatments received was documented. Additionally, information about the current episode, its onset, duration, clinical progression as well as associated symptoms such as fever, cough, tachypnoea and

respiratory distress was recorded. A comprehensive clinical examination was performed for each child. Vital signs, respiratory rate, presence and severity of respiratory distress (such as chest indrawing, nasal flaring, and grunting), oxygen saturation, auscultatory findings and general condition assessment was done to evaluate the severity of LRTI. Chest imaging (X-ray) was done to document radiological evidence of lower respiratory tract involvement, assess the extent and severity of lung involvement and to rule out underlying anatomical anomalies or chronic lung conditions.

A total of 3 ml of venous blood was collected from each child under all aseptic precautions. Vitamin D levels were measured by chemiluminescent immunoassay (CLIA) method. Vitamin D status was categorized as sufficient, insufficient or deficient on the basis of serum level of 25 (OH) vitamin D as following - deficient: <20 ng/ml (50 nmol/l), insufficient: 20–30 ng/ml (50–75 nmol/l), and sufficient: >30 ng/ml (>75 nmol/l).

Correlation between vitamin D status and recurrent LRTIs was assessed by comparing serum vitamin D concentrations among children with and without history of recurrent lower respiratory infections. Statistical analysis was done using the statistical package for social sciences (SPSS) software version 21.0. A p value of less than 0.05 was considered statistically significant.

RESULTS

The analysis of the gender distribution of the studied cases showed that boys constituted 60.00% (48 cases) of group A and 56.25% (45 cases) in group B, while girls made up 40.00% (32 cases) in group A and 43.75% (35 cases) in group B. The proportion of boys was slightly more in group A as compared to group B. However, the difference was not statistically significant ($p=0.8717$) (Table 1).

Majority of children in group A (cases) and group B (controls) were in the 1–3 years age group, with 32 cases

(40.00%) and 38 controls (47.50%), respectively. This was followed by the age group above 3 years, comprising 30 (37.50%) children in group A and 26 (32.50%) children in group B. The mean age was slightly higher in group A (2.41 ± 1.36 years) as compared to group B (2.35 ± 1.28 years). However, the difference in age distribution between the two groups was not statistically significant ($p=0.7742$) (Table 2).

The analysis of the LRTI types among the studied cases showed that bronchiolitis was slightly more common, accounting for 42 (52.50%) cases while pneumonia was observed in 38 (47.50%) cases (Figure 1).

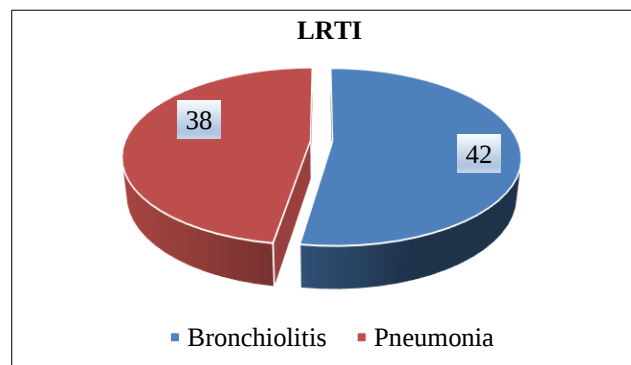


Figure 1: Type of LRTI in cases of recurrent LRTI.

The analysis of the vitamin D status among the studied groups showed that vitamin D deficiency (<20 ng/ml) was significantly more common in the LRTI group (47.50%) as compared to only 12 cases (27.50%) in the control group. Vitamin D insufficiency (20–30 ng/ml) was noted in 26 LRTI cases (32.50%) and 29 controls (37.50%), while sufficient levels (>30 ng/ml) were found in 16 cases (20.00%) and 39 controls (22.50%). Children in Recurrent LRTI group were found to have lower level of vitamin D as compared to healthy control and the difference was found to be statistically highly significant ($p=0.0020$) (Table 3).

Table 1: Gender distribution of studied cases.

Gender	Cases (group A)		Control (group B)		P value
	No. of cases	Percentage	No. of cases	Percentage	
Boys	48	60.00	45	56.25	0.8717 (not significant)
Girls	32	40.00	35	43.75	
Total	80	100.00	80	100.00	

Table 2: Comparison of age distribution of studied cases.

Age (years)	Cases (group A)		Control (group B)		P value
	No. of cases	Percentage	No. of cases	Percentage	
<1	18	22.50	16	20.00	0.7742
1-3	32	40.00	38	47.50	
Above 3	30	37.50	26	32.50	
Total	80	100.00	80	100.00	
Mean age	2.41±1.36		2.35±1.28		

Table 3: Comparison of vitamin D status of studied groups.

Vitamin D status (ng/ml)	LRTI group (n=80)		Control group (n=80)		P value
	No of cases	Percentage	No of cases	Percentage	
Deficient (<20)	38	47.50	12	27.50	0.0002
Insufficient (20–30)	26	32.50	29	37.50	
Sufficient (>30)	16	20.00	39	22.50	

The analysis of the mean 25 (OH) vitamin D levels among the studied groups showed that the recurrent LRTI group had a significantly lower mean 25 (OH) vitamin D level of 18.7 ± 7.3 ng/ml compared to the control group, which had a mean level of 26.1 ± 8.5 ng/ml. The difference in mean 25 (OH) vitamin D was statistically highly significant (Table 4).

Table 4: Comparison of mean vitamin D levels in studied groups.

Group	Vitamin D level (ng/ml) (mean $\pm$ SD)	P value
LRTI group (n=80)	18.7 ± 7.3	<0.0001
Control group (n=80)	26.1 ± 8.5	

DISCUSSION

The age and gender distribution in our study did not show any statistically significant differences between groups. This was important to minimize potential confounding factors and strengthen the inference of a genuine association between vitamin D status and recurrent LRTIs.

A statistically significant association was found between low serum vitamin D levels and recurrent LRTIs in children aged 6 months to 5 years. Children with recurrent LRTIs were found to have significantly lower mean vitamin D levels (18.7 ± 7.3 ng/ml) compared to healthy controls (26.1 ± 8.5 ng/ml). These findings are similar to the study by Zhou et al who reported that vitamin D deficiency was significantly more prevalent in children with pneumonia than in healthy peers.⁹ These findings emphasize a possible immunomodulatory role of vitamin D in the pathogenesis of respiratory infections. Similarly, Karatekin et al demonstrated that neonates with vitamin D deficiency had a higher risk of developing acute lower respiratory tract infections suggesting that low vitamin D status early in life may predispose children to recurrent infections.¹⁰

Our data revealed that both pneumonia and bronchiolitis were common clinical manifestations in children with recurrent LRTIs. There was a slight predominance of bronchiolitis in cases who presented with history of recurrent LRTIs. The link between vitamin D and bronchiolitis has been supported by studies such as those by Belderbos et al who observed that lower umbilical cord 25(OH)D concentrations at birth were associated with

increased risk of respiratory syncytial virus (RSV) bronchiolitis during infancy.¹¹ Similar results were also reported by Roth et al who found that vitamin D deficiency contributed to increased susceptibility to both viral and bacterial respiratory tract infections in children in resource-limited settings.¹² These studies support our observation that deficient vitamin D levels may compromise mucosal immunity and weaken the respiratory epithelium's defence against pathogens thereby contributing to recurrent LRTIs.

Our study identified that children with sufficient vitamin D status were less likely to experience recurrent LRTIs as compared to those children who had vitamin D deficiency. These findings were similar to findings of meta-analysis by Martineau et al who reported that vitamin D supplementation significantly reduced the risk of acute respiratory tract infections.¹² This is particularly important in individuals with baseline 25(OH)D levels <25 nmol/l (10 ng/ml). In this study the authors highlighted the protective benefit of achieving sufficient vitamin D levels.

In contrast to these findings the VIDA trial by Manaseki-Holland et al found no significant difference in the mean number of days to recovery between the vitamin D3 (4.74 days; SD 2.22) and placebo arms (4.98 days; SD 2.89; $p=0.17$).¹³ However, the authors also reported that vitamin D supplementation reduced repeat episode of pneumonia within 90 days of supplementation in intervention group (92/204; 45%) as compared to placebo group ($p=0.01$).

The immunological rationale behind susceptibility of children having vitamin D deficiency to recurrent LRTI may be attributed to vitamin D's role in promoting antimicrobial peptide production such as cathelicidin and β -defensins. These antimicrobial peptides are essential in maintaining respiratory tract integrity and limiting pathogen invasion. Hansdottir et al demonstrated that vitamin D improves the antimicrobial response of human airway epithelial cells by inducing cathelicidin expression.¹⁴ This is important for reinforcing epithelial barrier function of airway epithelial cells. Moreover, Liu et al showed that vitamin D facilitates clearance of pathogens by enhancing macrophage function and modulating the inflammatory cytokine milieu.¹⁵

All these changes are known to reduce the risk of persistent or recurrent respiratory infections. These findings are in line with our clinical observations and emphasize the potential role of maintaining adequate vitamin D levels in preventing recurrent LRTIs.

CONCLUSION

In our comparative observational study children with recurrent LRTIs demonstrated markedly lower mean serum 25(OH)D levels and a higher prevalence of deficiency as compared to healthy peers. These findings raise the possibility that suboptimal vitamin D status may contribute to susceptibility to recurrent respiratory infections.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Patil P, Alsalloum D, Ravikant S. Vitamin D status of children with recurrent lower respiratory tract infection: a comparative observational study. *Int J Contemp Pediatr* 2025;12:1049-53.