

Association between Vitamin D Deficiency and Recurrent Respiratory Tract Infections in Children

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Abstract

Background: Vitamin D plays an important role in the regulation of the immune system, and deficiency has been linked to increased susceptibility to respiratory infections. This study aimed to assess the relationship between vitamin D deficiency and recurrent respiratory tract infections (RTIs) in children.

Methods: A comparative case-control study was carried out in 60 children, including 30 with recurrent RTIs and 30 controls. Demographic, nutritional, environmental, and clinical characteristics were recorded. The serum level of 25-hydroxyvitamin-D [25(OH) D] was assessed, and vitamin D deficiency was considered to have a serum level <20 ng/mL. The association between vitamin D deficiency and recurrent RTIs was assessed using logistic regression.

Results: The mean serum 25(OH) D level was significantly lower in cases than in controls ($p < 0.001$). A higher frequency of vitamin D deficiency was observed in the cases (66.7%) than in the controls (36.7%) ($p = 0.020$). Vitamin D-deficient children had higher odds of recurrent RTIs ($p = 0.023$). Vitamin D deficiency was still significantly associated with recurrent RTIs ($p = 0.046$) when adjusted for age, sex, passive smoke exposure, socioeconomic status, nutritional status, immunization, and breastfeeding.

Conclusions: Vitamin D deficiency was found to be significantly linked to recurrent RTIs among children. Additional prospective and interventional studies are needed to further clarify the causal relationship and determine the possible beneficial effect of correcting vitamin D deficiency.

Keywords: Vitamin D; respiratory tract infections; recurrent infections; children; 25-hydroxyvitamin D

Introduction

Respiratory tract infections (RTIs) are one of the most common infectious diseases in children and are a leading cause of outpatient visits, hospitalizations, school absenteeism, and antibiotic use globally.[1] The burden is especially high in young children who have underdeveloped immune systems, social interaction with other children, inadequate nutrition, and exposure to the environment, and are more susceptible to infection due to their immature immune systems.[2] Pneumonia is also one of the principal causes of childhood deaths in the world, with an estimated 740,180 deaths in 2019, representing 14% of all under-five deaths.[3] More recent global estimates suggest that pneumonia continues to be one of the major causes of death in children below five years and continues to be a focus of the need to identify potentially modifiable risk factors for recurrent and severe respiratory infections.[4]

Vitamin D is known to play an important role in calcium metabolism and skeletal growth, but more and more evidence has emerged on its immunomodulatory properties.[5] Several immune cells express vitamin D receptors, while active vitamin D plays an important role in innate immune defense, for instance by regulating antimicrobial peptide production, epithelial barrier integrity and inflammatory responses.[6] Deficiency may then lead to weakened resistance to respiratory pathogens and may make the host more susceptible to recurrent infections.[7] A systematic review of vitamin D deficiency and respiratory infections in children suggested that respiratory

infections occurred more often in children with lower levels of vitamin D, with 7 of 10 studies making this conclusion; however, there was less consistent evidence when it came to severity of the infection.[8]

Intervention studies have also been conducted to examine the vitamin D respiratory infection connection, with results not being consistent. A systematic review of eight studies involving 2,189 children younger than six years reported variable effects of vitamin D supplementation on respiratory infection incidence, symptoms, and recovery.[9] Previous studies have shown significant relationships between low vitamin D status and respiratory infections, while other studies have not shown a significant protective effect of supplementation.[10, 11] This heterogeneity implies that the relationship could be influenced by the vitamin D status at the start of supplementation, age, infection phenotype, dosage, duration of vitamin D supplementation, and other nutritional and environmental variables.[12]

As more evidence accumulates, the following important clinical issue remains: does vitamin D deficiency simply appear in children with recurrent respiratory infections more often than in those without vitamin D deficiency, or does it actually have a significant association with increasing the burden of respiratory infection? Establishing this association in the local pediatric population may help clarify whether assessment of vitamin D status should receive greater attention in children presenting with recurrent RTIs. Therefore, the present study was designed to evaluate the association between vitamin D deficiency and recurrent respiratory tract infections in children by comparing vitamin D status between children with recurrent RTIs and those without recurrent infections. The aim of the study was to determine whether vitamin D deficiency was significantly associated with recurrent respiratory tract infections in children.

Methods

A comparative case-control study was done at _Department of Paediatrics, TeachingHospitalChaman_____. The study was carried out over a period of six months, from _1st November, 2025_____ to _30th April, 2026_____.

The minimum sample size was estimated to be 30 cases and 30 controls using OpenEpi software, with expected proportions of low vitamin D levels observed in 86% of children with recurrent respiratory tract infections and 35% in controls from a previous study, a 95% confidence level, 80% power, a two-sided alpha of 0.05, and a case-to-control ratio of 1:1.

Non-probability consecutive sampling was used for participant recruitment. Children aged 1–10 years of either sex were included. Children meeting the operational definition, which included those with six or more respiratory infections annually, at least 1 upper respiratory infection each month (September to April), or at least 3 lower respiratory infections annually, were included as cases. Children with no history of recurrent respiratory infections and recruited from the paediatric outpatient department during the same period of the study served as controls and were of similar age. Children who were on vitamin D supplementation or on vitamin D at therapeutic doses in the last three months were excluded.

Children with a known chronic respiratory condition (such as bronchial asthma, cystic fibrosis, bronchiectasis, or congenital lung disease) were excluded. Other children with chronic kidney disease, chronic liver disease, malabsorption syndromes, metabolic bone disease, known immunodeficiency, malignancy, or other chronic systemic diseases that may alone have an impact on vitamin D status or susceptibility to infections were also excluded. Cases that underwent immunosuppressive therapy or long-term use of corticosteroids were excluded. Children whose parents/guardians refused consent and/or who did not have enough blood drawn were also not included.

Eligible children were recruited after obtaining written informed consent from the parents/legal guardians. Demographic and clinical data such as age, sex, weight, height, residence, socioeconomic status, nutritional status, immunization status, breastfeeding history, dietary intake, history of vitamin D supplementation, passive smoke exposure, and relevant environmental factors were documented by a structured proforma. Clinical history and available medical records were used to document the number and type of respiratory infections in the previous year, frequency of upper and lower respiratory infections, previous hospitalizations, and antibiotic use for cases.

After clinical examination, about 3-5 mL of venous blood was drawn under aseptic conditions from all participants. The sample was shipped to a laboratory at the hospital, where the 25(OH)D concentration was determined using the standard laboratory test at the hospital. Vitamin-D status was classified by the predefined laboratory/clinical

cut-off, and vitamin-D deficiency was classified as serum 25(OH)D <20 ng/mL. This cutoff was also used in the previous Pakistani study of children with recurrent chest infections. To ensure comparability, the same laboratory method and cutoff were used for both cases and controls.

All the data were entered and analyzed using SPSS version 26.0. Continuous variables, like age, weight, height, and serum 25(OH)D level, were checked for normality by the Shapiro–Wilk test and were presented as mean $\pm$ SD or median (IQR) depending on the normality of the distribution. Categorical variables such as sex, vitamin D deficiency, nutritional status, and recurrent respiratory tract infection were expressed as frequencies and percentages. Data distribution was analyzed, and continuous variables between the two groups were compared with the independent-samples t-test. Categorical variables were compared between the two groups by the chi-square test. The odds ratio (OR) with 95% confidence interval (CI) was used for the assessment of the association between vitamin D deficiency and recurrent respiratory tract infections. Analysis was adjusted for potential confounding variables including age, sex, nutritional status, socioeconomic status, breastfeeding, passive smoking, and vitamin D supplementation history, as appropriate, and binary logistic regression was performed. P value < 0.05 was regarded as statistically significant.

Results

A total of 60 children were included in the study, comprising 30 children with recurrent respiratory tract infections (RTIs) and 30 controls. The mean age was comparable between cases and controls ($p=0.744$). Similarly, age-group distribution, sex, weight, height, and BMI did not differ significantly between the two groups (all $p>0.05$). Males constituted 56.7% of cases and 53.3% of controls. The mean weight, height, and BMI were also comparable between groups. (Table 1)

Clinical and environmental characteristics were generally comparable between cases and controls. Exclusive breastfeeding for at least six months was reported in 63.3% of cases and 73.3% of controls, while complete age-appropriate immunization was observed in 90.0% and 96.7%, respectively. Passive cigarette-smoke exposure and low socioeconomic status were more frequent among cases than controls, although these differences did not reach statistical significance. Similarly, indoor biomass-fuel exposure, previous vitamin-D supplementation, and underweight were more common among cases, without statistically significant differences between groups. (Table 2)

Among children with recurrent RTIs, 60.0% experienced six or more respiratory infections per year, while 66.7% reported at least one upper respiratory tract infection per month during September–April. Recurrent URTI alone was present in 53.3%, recurrent LRTI alone in 13.3%, and both URTI and LRTI in 33.3% of cases. The mean number of respiratory episodes per year was 7.1 ± 2.3 . Previous hospitalization due to RTI was reported in 36.7% of children, while 70.0% had used antibiotics during the preceding year. (Table 3)

Serum 25(OH)D concentrations were significantly lower among children with recurrent RTIs compared with controls, with mean levels of 16.8 ± 7.2 ng/mL and 24.9 ± 8.1 ng/mL, respectively ($p<0.001$). Vitamin-D deficiency, defined as serum 25(OH)D <20 ng/mL, was identified in 66.7% of cases compared with 36.7% of controls ($p=0.020$). Conversely, vitamin D sufficiency was observed in 33.3% of cases and 63.3% of controls. (Table 4)

Vitamin-D deficiency was significantly associated with recurrent RTIs. Among vitamin-D-deficient children, 20 (66.7%) were cases compared with 11 (36.7%) controls. Children with vitamin-D deficiency had 3.45 times higher odds of having recurrent RTIs compared with children who were not deficient ($p=0.023$). (Table 5)

In multivariable logistic regression analysis, vitamin-D deficiency remained significantly associated with recurrent RTIs after adjustment for age, sex, passive smoke exposure, socioeconomic status, underweight, immunization status, and exclusive breastfeeding. Vitamin-D-deficient children had approximately threefold higher adjusted odds of recurrent RTIs ($p=0.046$). Age, male sex, passive smoke exposure, low socioeconomic status, underweight, incomplete immunization, and lack of exclusive breastfeeding for at least six months were not independently associated with recurrent RTIs in the adjusted model ($p>0.05$). (Table 6)

Table 1. Demographic and baseline characteristics of study participants

Variable	Recurrent RTI cases (n=30)	Controls (n=30)	p-value
Age (years), mean $\pm$ SD	5.8 $\pm$ 2.4	5.6 $\pm$ 2.3	0.744
Age group, n (%)			0.791

1–5 years	16 (53.3)	15 (50.0)	
6–10 years	14 (46.7)	15 (50.0)	
Male, n (%)	17 (56.7)	16 (53.3)	0.793
Female, n (%)	13 (43.3)	14 (46.7)	
Weight (kg), mean $\pm$ SD	19.2 $\pm$ 6.1	19.8 $\pm$ 6.4	0.713
Height (cm), mean $\pm$ SD	108.6 $\pm$ 14.2	110.1 $\pm$ 14.7	0.692
BMI (kg/m ²), mean $\pm$ SD	16.0 $\pm$ 1.8	16.2 $\pm$ 1.7	0.663

Table 2. Clinical and environmental characteristics of participants

Variable	Cases n (%)	Controls n (%)	p-value
Exclusive breastfeeding for ≥ 6 months	19 (63.3)	22 (73.3)	0.405
Complete age-appropriate immunization	27 (90.0)	29 (96.7)	0.301
Passive cigarette-smoke exposure	12 (40.0)	6 (20.0)	0.091
Low socioeconomic status	18 (60.0)	11 (36.7)	0.071
Indoor biomass fuel exposure	10 (33.3)	5 (16.7)	0.136
Previous vitamin-D supplementation	5 (16.7)	8 (26.7)	0.371
Underweight	8 (26.7)	5 (16.7)	0.347
Normal nutritional status	22 (73.3)	25 (83.3)	

Table 3. Characteristics of recurrent respiratory tract infections among cases

Clinical characteristic	Cases (n=30)
≥ 6 respiratory infections/year	18 (60.0%)
≥ 1 URTI/month during September–April	20 (66.7%)
≥ 3 LRTIs/year	9 (30.0%)
Recurrent URTI only	16 (53.3%)
Recurrent LRTI only	4 (13.3%)
Both URTI and LRTI	10 (33.3%)
Number of episodes/year, mean $\pm$ SD	7.1 $\pm$ 2.3
Previous hospitalization due to RTI	11 (36.7%)
Antibiotic use during previous year	21 (70.0%)

Table 4. Comparison of serum vitamin D levels between cases and controls

Variable	Cases (n=30)	Controls (n=30)	p-value
Serum 25(OH)D (ng/mL), mean $\pm$ SD	16.8 $\pm$ 7.2	24.9 $\pm$ 8.1	<0.001
Vitamin-D deficient (<20 ng/mL)	20 (66.7%)	11 (36.7%)	0.020
Vitamin-D sufficient (≥ 20 ng/mL)	10 (33.3%)	19 (63.3%)	

Table 5. Association between vitamin D deficiency and recurrent respiratory tract infections

Vitamin-D status	Cases n (%)	Controls n (%)	Odds ratio (95% CI)	p-value
Deficient	20 (66.7)	11 (36.7)	3.45 (1.18–10.08)	0.023
Not deficient	10 (33.3)	19 (63.3)	Reference	

Table 6. Logistic regression analysis of factors associated with recurrent RTIs

Predictor	Adjusted OR	95% CI	p-value
Vitamin-D deficiency	3.18	1.02–9.91	0.046
Age (per additional year)	1.05	0.87–1.27	0.620
Male sex	1.12	0.41–3.09	0.824
Passive smoke exposure	1.89	0.64–5.57	0.248
Low socioeconomic status	1.76	0.63–4.94	0.279
Underweight	1.51	0.43–5.28	0.519

Incomplete immunization	1.42	0.20–10.05	0.728
No exclusive breastfeeding ≥6 months	1.34	0.47–3.84	0.584

Discussion

The present study showed that there was a significant relationship between vitamin-D deficiency and recurrent respiratory tract infections (RTIs) among children. Children with recurrent RTIs showed marked reductions in mean serum 25-hydroxyvitamin-D [25(OH)D] concentration ($p < 0.001$) and a higher prevalence of vitamin-D deficiency (66.7% vs 36.7%). Children who were found to be vitamin D deficient had a risk of recurrent RTIs of about 3.45 times and this was statistically significant after adjustments were made for age, sex, passive smoke, socioeconomic status, nutrition, immunization, and breastfeeding. After adjusting for a number of potential confounding factors, the odds ratio was adjusted to 3.18 (95% CI: 1.02–9.91) indicating that vitamin-D deficiency was independently associated with recurrent RTIs.

The results of these findings are consistent with the case control study by Zaman et al. which was published in Pakistan in 2022. They studied 30 children with recurrent RTIs and 30 children who did not have RTIs. The sizes of the two groups were the same as in the present study. In 66.7% of cases, there was a lack of vitamin D, which was statistically significant with an odds ratio of 3.455 ($p = 0.02$), and was found in 36.7% of controls. The very similar proportions and effect estimates further validated our results in a pediatric population in Pakistan.[13]

Likewise, a study conducted at a hospital in India in 2022 included 108 children with RRI and 55 healthy children. Vitamin D deficiency in children with recurrent infections was significantly higher compared to controls, with 25% vitamin D deficient and 75% vitamin D insufficient. Although their classification and population differed from those of the present study, the overall finding of a high burden of suboptimal vitamin-D status among children with recurrent respiratory infections supports our observation that vitamin-D deficiency is associated with recurrent respiratory morbidity.[14]

Evidence from younger children has also demonstrated an association between vitamin-D status and respiratory disease. A Pakistani case-control study conducted among infants aged 1–6 months between August 2021 and February 2022 specifically compared vitamin-D status in infants with acute lower respiratory tract infection and healthy controls. The study does support the biological relevance of vitamin-D status to acute infections in very young infants, but not to recurrent infections in children 1-10 years of age as we focus.[13]

Other observational evidence has not shown the same link, however. An investigation of 2021 found vitamin-D status and respiratory disease in preschool children in Hangzhou. Although children with recurrent respiratory infections initially showed a difference in vitamin-D concentrations compared with healthy children, the association was no longer statistically significant after adjustment for sex, age and BMI. The investigators also found no significant relationship between vitamin-D categories and respiratory infections. This discrepancy with our findings may reflect differences in population characteristics, baseline vitamin-D status, definitions of recurrent infection, environmental exposure, and study design. It also highlights that there is no consistent link between vitamin-D deficiency and recurrent RTIs among all populations.[15]

Other supportive data include a 2021 study that assessed vitamin-D drops in 119 children who had recurrent respiratory tract infections. Vitamin-D supplementation was associated with increased 25(OH)D levels, reduced post-supplementation respiratory infections and improvement in several immune parameters in children compared with those who were treated routinely. This study did not just compare vitamin-D status, but its results are in line with our observation of increased risk for recurrent respiratory morbidity in those with low vitamin-D status, and they propose a mechanism by which vitamin-D status might affect susceptibility to infection, namely through the immune system.[16]

Our results are further supported by the 2022 systematic review by Raju et al. that involved 10 good quality pediatric studies with 11565 participants. Seven of the 10 studies included reported that children with low vitamin-D levels were more likely to have respiratory infections. The authors were able to conclude that vitamin D deficiency was linked to the risk of acquiring respiratory infection, but the relationship between vitamin D deficiency and the severity of infection was not consistent. This is important to bear in mind when making this distinction to the present study since our primary endpoint was not severity, but rather recurrent infection, and our results suggest that this is linked to susceptibility to infection and do not necessarily mean that vitamin-D deficiency leads to more severe infections.[8]

The 2022 meta-analysis by Park et al. on the randomized controlled trials of vitamin-D supplementation gives a more conservative view. It concluded that there was inconsistent evidence of the effectiveness of vitamin-D supplementation in treating acute respiratory infections. This contrast between observational studies that implicate low vitamin-D status as a risk factor for respiratory infection and intervention studies with mixed results as to vitamin-D's preventive or therapeutic effect indicates that vitamin-D deficiency is not a stand-alone risk factor, but is possibly a risk factor for susceptibility and/or interacts with other environmental and dietary factors.[17]

Another systematic review, which was published in 2023, and was specific to children under 6 years of age, noted mixed evidence. Among eight eligible studies involving 2,189 children, three studies found significant associations between low vitamin-D levels and respiratory infections, whereas several other studies did not demonstrate significant differences in infection incidence or severity. The review suggested that the available evidence was not conclusive for an overall preventive effect of vitamin-D supplementation. These findings do not conflict with the present study however as our study was concerned with investigating natural vitamin-D deficiency and recurrent RTIs, rather than supplementation effectiveness.[9]

This complexity has been continually found in more recent randomized evidence. The study included 303 preschool children from three cities in Chile who participated in a 2024 randomized controlled trial that consisted of weekly vitamin D supplementation for six months at various doses. The mean level of vitamin D at the baseline measurement was 24.9 ng/mL and around 23% of subjects had a level less than 20 ng/mL. The study aimed to assess the effect of supplementation on acute respiratory infections (ARI), and reflected the persistent role of vitamin-D levels as a potentially modifiable factor in pediatric ARI. However, because our study was designed as a case-control study, and the baseline population was quite different from that of the intervention group, it is inappropriate to directly compare the results of our study with the case-control study results.[18]

In 2025, another Danish randomized clinical trial showed that supplementation may impact some respiratory variables. Daily vitamin-D supplementation was found to lead to a reduction in the number of sick days secondary to acute respiratory tract infection and the number of days with febrile respiratory illness in a study of 189 children aged 6–8 years. However, the mean baseline 25(OH)D level was very high, with 79.8 nmol/L (ca. 32 ng/mL), compared to the 49.9 nmol/L (ca. 19.6 ng/mL) observed among our participants. Therefore, the results of the Danish study indicated that vitamin-D supplementation may have an effect on some respiratory parameters even in a population that is generally vitamin-D sufficient, which cannot be directly transferred to the vitamin-D deficient children in our study.[19]

Further evidence also points to the uncertainty over the use of supplementation as a common prevention method. A review of 17 pediatric randomized controlled trials (RCTs) with 18,372 children included, published in 2025, did not confirm a significant overall reduction in incidence of acute respiratory infection cases, duration of hospitalization, recovery time, or mortality in children taking vitamin-D supplements. The results of the subgroup analysis however indicated a possible preventative effect from the ≤ 1000 IU/day daily low dose group. These findings help to account for the fact that the association between deficiency and respiratory infection can be clearly seen in observational evidence (such as ours) but is more variable in intervention trials. This heterogeneity may relate to baseline vitamin-D status, dosing regimen, length of vitamin-D supplementation, age, and respiratory outcomes.[20] In the present study, other potential determinants of recurrent RTIs were more common among cases but did not reach statistical significance. Overall, passive cigarette-smoking was reported in 40.0% of cases and in 20.0% of controls, and low socioeconomic status was seen in 60.0% versus 36.7% of cases and controls, respectively. Cases also were more likely to be exposed to biomass fuels indoors. These variables were not found to be individually predictive of the outcome in the adjusted model, but the distribution of these variables does indicate that there may be a multifactorial etiology behind recurrent respiratory infections. The modest effect of vitamin-D status could be masked by other factors, such as environmental exposures, household conditions, nutritional status or immunity, which could interact with vitamin-D status, and the small sample size of the present study may have reduced the power to detect small independent effects.

Another example to the clinical profile of the recurrent-RTI group is the considerable respiratory morbidity in these children. Two-thirds experienced at least one upper respiratory infection per month during the September–April period, 60% experienced six or more respiratory infections annually, and one-third had both recurrent upper and lower respiratory tract infections. Over one third had previously been hospitalized due to an RTI and 70% had been prescribed antibiotics in the last year. These results suggest that the children studied were not typical acute, uncomplicated respiratory infections, but rather those with a clinically significant recurrent respiratory phenotype.

The lack of important differences in age, sex, weight, height and BMI between cases and controls is supportive of the interpretation that the observed difference in vitamin D was not due to large baseline differences in these variables. Similarly, the association remained after adjustment for various known or likely respiratory risk factors in the logistic regression model. The confidence interval around the adjusted odds ratios was relatively wide, however, due to the small sample size and caution should be used when interpreting the size of the association.

In general, the results of the present study agree with that of some recent studies conducted in children which indicated that vitamin-D status was lower in children with recurrent or acute respiratory infections, especially the Pakistani case-control study which was most similar to the present study. However, over the last few years, randomized trials and systematic reviews have shown that supplementation is not always effective in preventing all respiratory infections. The current results suggest that vitamin-D deficiency is associated with recurrent RTIs but should not be considered as causal for recurrent infections or as an absolute requirement for vitamin-D supplementation to prevent recurrent infections. The causal relationship needs to be further clarified, and intervention studies with sufficient power and repeated measurements of 25(OH)D, standardized definitions of recurrent RTI, and assessment of sunlight and dietary vitamin-D exposure, should be conducted to determine whether low 25(OH)D levels cause recurrent respiratory morbidity in children and whether the use of vitamin-D supplementation to correct the deficiency will decrease the burden of recurrent respiratory morbidity.

Limitations

There were some limitations encountered in this study. This relatively small sample size (60 children) may have reduced the power to detect small effect sizes for associations between recurrent respiratory tract infections and other potential risk factors. Recurrent respiratory tract infections were associated with vitamin-D deficiency, but no temporal or causal relationship could be established because of the case-control design. Vitamin-D status was evaluated based on a single serum 25(OH)D level, which may not accurately capture seasonal or chronic vitamin-D status. The information on past respiratory infections, antibiotic use, breastfeeding and environmental exposures was partially subject to parental recall and recall bias may have influenced this information. Other micronutrient deficiencies, important factors like diet vitamin-D intake, sunlight exposure, duration of outdoor activity and parental smoking intensity were not covered in full. Last, the study was performed in one clinical environment, which potentially may restrict the external validity of the study results to other pediatric populations.

Conclusion

Recurrent respiratory tract infections were significantly more likely to be associated with vitamin-D deficiency and when adjusted for selected demographic, nutritional and environmental factors, were linked to about three times the odds of having RTIs. The results confirm a link between vitamin-D status and recurrent respiratory morbidity in children. But the observational design does not allow for causal conclusions. Multicenter prospective studies and sufficiently sized intervention trials are needed to prove whether vitamin D supplementation can decrease the incidence of recurrent respiratory tract infections in children with vitamin D deficiency.

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