

# Vitamin D3 Level in Children with Respiratory Tract Infection; A Case Control Study

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## ABSTRACT

**Objective:** To determine the Vitamin D3 Level in Children with Respiratory Tract Infection.

**Study Design:** A Case Control Study

**Place and Duration of Study:** This study was conducted at the Hospital and Research Center, Department of Pediatric, Baqai Medical University, Karachi from 6 May 2018 to 5 May 2020.

**Materials and Methods:** The present study, conducted within a hospital setting, comprised a cohort of 128 pediatric individuals, ranging in age from six months to 15 years. These participants were selected as cases and were admitted to the hospital or attended outpatient clinics due to the presence of recurrent respiratory infections. A cohort of 42 pediatric patients, all in a state of optimal health, belonging to the same age bracket, were selected as control subjects for this study. These individuals were attending the hospital for the purpose of receiving vaccinations and undergoing routine check-ups, within the designated study period. Venous blood specimens were procured from both cases and controls in order to investigate the levels of serum 25-hydroxyvitamin D.

**Results:** In this study, we compared the levels of 25-hydroxyvitamin D (25(OH)D) between healthy children (controls) undergoing normal checkups and children with recurrent respiratory infections (cases). This finding implies that a lack of vitamin D may increase a person's susceptibility to upper respiratory infections during particular seasons of the year. This data raises the possibility that vitamin D deficiency may be a significant factor in higher incidence of recurrent infectious rhinitis in children, children's vulnerability to lower airway infections and recurrent otitis media and recurrent pharyngitis or tonsillitis.

**Conclusion:** The observed study population exhibited a markedly elevated incidence of vitamin D deficiency in children presenting with recurrent respiratory infections, in stark contrast to the control group. The incorporation of vitamin D status evaluation is imperative within the comprehensive care regimen for pediatric patients exhibiting recurrent respiratory infections.

**Key Words:** vitamin d deficiency, respiratory tract infections, children, vitamin D3

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## INTRODUCTION

Respiratory tract infections frequently manifest in pediatric patients and are routinely encountered within the realm of clinical practice. Infections of this nature represent a prevalent a boost for seeking medical consultation and exert a substantial impact on the morbidity and mortality rates among pediatric populations. In the year 2013, a total of 2.65 million fatalities resulting from respiratory tract infections were documented on a global scale, encompassing

individuals of all age cohorts<sup>1-3</sup>. The acute respiratory infection mortality rate was significantly influenced by four countries, namely India, Bangladesh, Indonesia, and Nepal, collectively contributing to 40% of the global burden.<sup>4,5</sup> Based on available reports, it has been observed that children who are below the age of five experience an average of five occurrences of acute respiratory infections within a span of one year. Acute respiratory infections have been identified as a significant causative factor in the development of hearing impairment, primarily due to the occurrence of acute otitis media<sup>5</sup>. It is imperative to ascertain the identification of modifiable factors that may exert an influence on the prevalence and therapeutic management of respiratory infections in pediatric patients. Insufficient levels of vitamin D have been observed to perturb immunological processes that are intricately associated with the susceptibility of a child to respiratory infections. A notable reduction in vitamin D levels was observed among pediatric patients experiencing recurrent respiratory tract infections.

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Studies have proposed the undertaking of additional research to explore the correlation between insufficient levels of vitamin D and respiratory infections in the pediatric population.<sup>6,7</sup> a hospital-based study was conducted to assess vitamin D levels in children who frequently presented with respiratory infections at a tertiary care facility at the Baqai Medical University Area: GADAP & NEAR Vicinity.

## MATERIALS AND METHODS

This hospital-based observational study encompassed a cohort of 163 pediatric patients (referred to as cases) who presented with recurrent respiratory infections. These cases were either admitted as inpatients or received medical attention in the outpatient department of a tertiary care hospital. The pediatric population exhibited a wide age spectrum, spanning from infancy at six months to adolescence at fifteen years. The study protocol received approval from the ethics committee of the Hospital and Research Center. The investigation was conducted from the 6th of May, 2018, to the 5th of May, 2020. The inclusion criteria for the patients encompassed a frequency of three annual occurrences of lower respiratory infections affecting the lower airways, a single upper respiratory infection spanning from September to April, and a total of six respiratory infections per year involving the upper airways. (iii) The patient presents with a condition known as recurrent infectious rhinitis, characterized by the occurrence of more than five episodes per year. (iv) The patient exhibits recurrent pharyngitis or tonsillitis, with a frequency exceeding three episodes within a span of 12 months. (v) The patient displays recurrent otitis media, with a frequency of three episodes within a period of six months or four episodes within a span of 12 months.

The study excluded individuals of pediatric age who presented with congenital structural anomalies, congenital cardiac pathologies, gastroesophageal reflux disease, allergic respiratory conditions (such as asthma), or immunodeficiency disorders. A cohort of 38 pediatric patients, exhibiting sound health and

ranging in age from six months to 15 years, were selected as the control group for this study. These individuals sought routine immunizations and checkups at the outpatient department of a single hospital throughout the designated research period. Parents or guardians of both the patients and controls gave their informed consent. Serum 25-hydroxyvitamin D (25(OH)D) levels were measured using venous blood samples from both patients and controls. Patients who did not have an acute respiratory infection had their blood sampled. The Roche Elecsys Vitamin D3 (25OH) analyzer measured 25(OH)D via electrochemiluminescence immune assay. The technique detected 3 ng/mL. Serum vitamin D reference range: Vitamin D deficiency is defined by blood levels below 20 ng/mL, whereas insufficiency is 21–29 ng/mL. Serum values between 30 and 100 ng/mL indicate vitamin D sufficiency.<sup>8</sup> The chi-square test was employed to assess the proportions. A p-value less than 0.05 was deemed to possess statistical significance.

## RESULTS

**Table No. 1: Age group distribution between cases and controls**

Age (months)	Cases	Controls	Total
0-60	55 (32.4%)	40 (23.5%)	95 (55.9%)
61-120	40 (23.5%)	20 (11.8%)	60 (35.3%)
>120	33 (19.4%)	10 (5.9%)	43 (25.3%)
Total	128	42	170

In the age group of 0-60 months, which continues to be the largest proportion of the study population, there were 55 cases and 40 controls. Among cases, 32.4% were in this age group, while controls constituted 23.5% of the same range. The second age group (61-120 months) had 40 cases and 20 controls. In this age group, cases accounted for 23.5% of the total, and controls represented 11.8%. The age group above 120 months had 33 cases and 10 controls, making up 19.4% and 5.9% of cases and controls, respectively.

**Table No. 2: Comparison of 25(OH)D between cases and controls**

Group	25-hydroxy vitamin D			Total
	Sufficient	Insufficient	Deficient	
Control	25 (45.5%)	20 (36.4%)	10 (18.2%)	55
Case	5 (4.6%)	60 (55.6%)	43 (39.8%)	108
Criteria 1	1 (2.3%)	15 (34.1%)	28 (63.6%)	44
Criteria 2	0 (0%)	7 (20%)	28 (80%)	35
Criteria 3	0 (0%)	3 (42.9%)	4 (57.1%)	7
Criteria 4	0 (0%)	2 (66.7%)	1 (33.3%)	3
Criteria 5	0 (0%)	6 (42.9%)	8 (57.1%)	14
Criteria 6	4 (80%)	0 (0%)	1 (20%)	5
Total	35	113	103	170

In this study, we compared the levels of 25-hydroxyvitamin D (25(OH)D) between healthy children (controls) undergoing normal checkups and children with recurrent respiratory infections (cases). The investigation into the relationship between vitamin D level and particular inclusion criteria pertaining to the frequency and kind of respiratory infections was also expanded.

**Criteria 1:** A considerable portion (70.5%) of the cases with six or more respiratory infections annually were found to be vitamin D deficient, whereas 29.5% had inadequate levels. It is interesting to note that none of the cases had adequate vitamin D levels. This finding suggests a possible link between a vitamin D deficit and youngsters developing respiratory infections more frequently.

**Criteria 2:** Children who experienced upper airway infections at least once a month from September to April were assessed for this criterion. The bulk of the cases (77.1%) were found to have deficient vitamin D levels, whereas 22.9% had insufficient level. Once more, no instances had adequate vitamin D levels. This finding implies that a deficiency of vitamin D may increase a person's susceptibility to upper respiratory infections during particular seasons of the year.

**Criteria 3:** This criterion covered children who annually had three or more respiratory illnesses involving the lower airways. Only 14.3% of the cases in this group had insufficient levels of vitamin D, although a considerable fraction (85.7%) did. Again, none of the cases demonstrated adequate vitamin D levels. This data raises the possibility that vitamin D deficiency may be a significant factor in children's vulnerability to lower airway infections.

**Criteria 4:** Children with recurrent otitis media (middle ear infection) were evaluated in this category. Sixty-six percent (66.6%) of the cases had low vitamin D levels, while 33.3% did not. None of the instances, as was previously noted, had adequate vitamin D levels. This finding suggests a possible connection between recurrent otitis media and vitamin D deficiency.

**Criteria 5:** Children experiencing more than five episodes of recurrent infectious rhinitis (inflammation of the nasal mucous membrane) per year were evaluated. The majority of the cases (78.6%) were found to be deficient in vitamin D, while 21.4% had insufficient levels. Similar to previous criteria, none of the cases had sufficient vitamin D levels. This result implies that vitamin D deficiency might contribute to the higher incidence of recurrent infectious rhinitis in children.

**Criteria 6:** In this subgroup, children with recurrent pharyngitis or tonsillitis were analyzed. The majority (80%) of the cases were found to be deficient in vitamin D, while 20% had insufficient levels. Notably, in this criterion, a small number of cases (20%) showed sufficient vitamin D levels. This finding suggests that

vitamin D deficiency may be associated with the increased susceptibility to recurrent pharyngitis or tonsillitis, but some cases with sufficient vitamin D levels may have a different immunological profile.

## DISCUSSION

The present study's findings reveal a consistent pattern of vitamin D deficiency among children afflicted with recurrent respiratory infections, as evidenced by the evaluation of various criteria. The presence of a deficiency in vitamin D demonstrates a robust correlation with an elevated susceptibility to respiratory infections in pediatric patients, particularly those affecting the upper and lower airways, otitis media, infectious rhinitis, pharyngitis, and tonsillitis. The study conducted by Wayse et al. in 2004 elucidated the pivotal role played by subclinical vitamin D deficiency as a notable risk factor for lower respiratory tract infections in children under the age of five in India.<sup>9</sup> As per the findings of Ozdemir et al. (2016), it was observed that children presenting with recurrent respiratory infections exhibited an average vitamin D concentration of  $11.97 \pm 4.04$  ng/mL. Similarly, children suffering from chronic cough displayed an average vitamin D concentration of  $13.76 \pm 4.81$  ng/mL. In contrast, children belonging to the control group demonstrated an average vitamin D concentration of  $31.91 \pm 18.79$  ng/mL. The observed disparities exhibited statistical significance. Consequently, the presence of insufficient levels of vitamin D in pediatric patients has been associated with an elevated prevalence of recurrent respiratory infections and the presence of a persistent cough of prolonged duration.<sup>10</sup> A recent investigation conducted in the Indian state of Telangana has revealed a noteworthy association between diminished levels of vitamin D and the recurrence of respiratory infections.<sup>11</sup> A recent inquiry undertaken in the Indian state of Telangana has unveiled a notable correlation between reduced levels of vitamin D and the frequency of respiratory infections.<sup>12</sup> Extensive investigation has been conducted to elucidate the fundamental mechanism underpinning the correlation between vitamin D and respiratory infections. The immune system can potentially be modulated by the presence of vitamin D, while insulin-like growth factor 1 (IGF-1) exerts stimulatory effects on the synthesis and secretion of immunoglobulins. Furthermore, it is noteworthy that vitamin D plays a pivotal role in the promotion of growth and differentiation of T and B lymphocytes. Furthermore, scientific investigations have revealed a correlation between insufficiency of vitamin D and diminished levels of CD4+ and CD3+ cells, both of which exhibited a positive response to therapeutic intervention involving vitamin D. Furthermore, subsequent to the administration of vitamin D supplements, there was an observed elevation in the

levels of immunoglobulin. Recent findings have elucidated the role of vitamin D in augmenting humoral immunity and mitigating the incidence of respiratory tract infections.<sup>13</sup> Lack of vitamin D is thought to cause muscle weakness, particularly in the diaphragm and intercostals. This probably makes it challenging to remove the respiratory tract's secretions and encourages infections.<sup>14</sup> A comprehensive literature review was conducted by Esposito and Lelii to investigate the correlation between vitamin D insufficiency and respiratory infections. Their findings revealed an elevated susceptibility to childhood tuberculosis, bronchiolitis, and recurrent otitis media in individuals with inadequate levels of vitamin D. The researchers arrived at the consensus that the maintenance of adequate levels of vitamin D would represent a cost-effective and efficacious strategy for mitigating certain respiratory tract infections. A plethora of global literature substantiates the correlation existing between insufficiency of vitamin D and respiratory infections.<sup>15-17</sup>

Our research's conclusions highlight the significance of diagnosing and treating vitamin D deficiency in children with chronic respiratory infections. Increasing vitamin D levels through dietary supplements or sensible sun exposure may have an impact on lowering the incidence of respiratory infections in children and enhancing their general health.

**Limitations:** It is crucial to take into account the study's constraints, such as the relatively small sample size and single-center design. Additionally, this analysis did not take into account any additional potential confounding variables including food practices, UV exposure, or genetic factors. These results need to be validated by other prospective studies with bigger sample sizes and multivariate analysis to explain the underlying processes connecting vitamin D deficiency to pediatric recurrent respiratory infections.

## CONCLUSION

The observed study population exhibited a markedly elevated incidence of vitamin D deficiency in children presenting with recurrent respiratory infections, in stark contrast to the control group. The incorporation of vitamin D status evaluation is imperative within the comprehensive care regimen for pediatric patients exhibiting recurrent respiratory infections.

### Author's Contribution:

Concept & Design of Study: Tabassum Sultana  
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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