

Relationship between Vitamin D Level and Recurrent Wheezy Chest in Pediatric Patients

Ikram Ullah, Sabir Khan, Zia Muhammad, Muhamamd Shabir, Aimal Khan, Arooj Khan

Abstract

Objective: To determine the association between serum vitamin D deficiency and recurrent wheezy chest in children aged 6-36 months.

Study Design and Setting: This case-control study was conducted at the Department of Paediatrics, Khyber Teaching Hospital, Peshawar, from August 2024 to February 2025.

Methodology: Seventy children (35 cases with ≥ 3 wheezing episodes in the last year; 35 age-matched controls without wheeze) were evaluated. They were enrolled after excluding those with chronic lung disease, allergies, or recent vitamin D supplementation. Serum 25-OH-vitamin D <20 ng/mL defined deficiency. The sample size was calculated to have 80% power and an $\alpha = 0.05$. Data was analysed with IBM SPSS 25.0; an independent t-test and χ^2 test were applied; association was quantified by odds ratio (OR) with CI 95%.

Results: Mean age was 16.7 ± 7.0 D in cases (18.8 ± 5.9 ng/mL) was lower than in controls (23.6 ± 5.8 ng/mL; $p = 0.001$). Vitamin D deficiency was present in 66% cases versus 37% controls ($p = 0.017$). Children with deficiency had 3.24-fold higher odds ratio of recurrent wheeze (95% CI 1.28-8.21; $p = 0.013$).

Conclusion: Vitamin D deficiency is significantly associated with recurrent wheezy chest in early childhood. Screening and supplementation may decrease the wheezing burden in this age group.

Keywords: Paediatrics, Vitamin D deficiency, wheezing

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INTRODUCTION:

Childhood respiratory diseases caused by viruses can be classified in many ways depending on the primary

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manifestations, like acute bronchocholitis, viral infections of the lower respiratory tract (LRTA), acute viral bronchitis, viral pneumonia, persistent, transient, or nonspecific and/or virally induced wheezing, and asthma exacerbation.¹ Wheezing in children is an acute breathing symptom marked by whistling during breathing, which most usually occurs while exhaling.² Wheezing is usually caused by obstruction or narrowing of the respiratory passages and can be related to a variety of conditions, including mild viral infections and long-term diseases such as asthma.³ Wheezing in children is most usually caused by viral infections in the form of colds, but wheezing can be caused by environmental factors such as allergies to compounds in the environment, parental smoking, and atmospheric pollution.⁴ Repeated wheezing over time is known as recurrent wheezing, and it is particularly concerning because wheezing can be a sign of developing asthma or other long-term respiratory difficulties in children. To effectively treat wheeze and prevent recurring episodes, it is vital to identify the underlying conditions that cause wheezing.⁵ Recurrent wheeze in children has been linked to an interaction of genetic, environmental, and immunologic factors.⁶ Wheezing is more common in children from allergic or asthmatic families, implying an underlying propensity.⁷ Allergens in the environment, like dust mites, cat dander, and pollen, irritants such as secondhand smoking, and indoor pollutants

cause wheezing by inflaming and hyperreactivity of tissues in the respiratory tract.⁸

The epidemiological data show that wheezing is reported in nearly 30% of children 3 years of age and significantly affects their overall health status.⁹

The pathophysiology of recurrent wheezy chest is complex, and its mechanism is related to multiple immunological and environmental factors. The common causes of wheezing are asthma, viral bronchiolitis, and allergic airway diseases; however, acute respiratory tract infections are the most frequent cause. In infancy and early childhood, viruses can trigger various respiratory conditions, including viral bronchitis, bronchiolitis, pneumonia, and asthma exacerbations.¹⁰

While working on recurrent wheezy chest, nutritional status has been given attention as a leading risk factor. The researchers have more specifically focused on the significance of vitamin D as a modulator of immune response and respiratory health and found it as a pivotal immunoregulatory molecule.¹¹

Numerous immune cells have vitamin D receptors. When 1, 25-dihydroxyvitamin D attaches to its receptor, it starts an immunological cascade and preserves the delicate equilibrium between humoral (Th2) and cellular (Th1) immune responses. Thus, Vitamin D boosts innate immunity (through macrophage function) by promoting bacterial elimination and regulating adaptive immunity (through lymphocyte regulation) to reduce inflammation. Vitamin D deficiency can, thereby, affect the Th1/Th2 cytokines balance and increase autoimmunity. Enhancing the immune defence of Vitamin D by enabling macrophages to produce antimicrobial peptides, particularly cathelicidin, ultimately helps to fight respiratory pathogens.¹²

Vitamin D appears essential for good lung function, while recent studies have repeatedly shown a robust connection between it and overall respiratory well-being, especially in children worldwide. The implications of this deficiency have now been mentioned, extending beyond skeletal health, and it is linked to a range of chronic and acute illnesses related to respiration, including infections, asthma exacerbations, and recurrent wheezy chest.¹³

Considering these results, the study on the protective effect of vitamin D levels in recurrent wheezing of the chest is an area of interest for further research. This is particularly crucial in our area where vitamin D deficiency is widespread among children, and there is a significant number of pediatric patients presenting with wheezing chest. The purpose of this study was to look at the connection between vitamin D insufficiency and recurrent wheezy chest in children, with a particular emphasis on the relationship between vitamin D levels and recurrent wheezy chest. The results of this study will help our paediatricians treat children who frequently have chest wheezing episodes.

METHODOLOGY:

This case-control study was conducted over 6 months from August 2024 to February 2025 at the Department of Paediatrics, Khyber Teaching Hospital, Peshawar, Pakistan. The study protocol was reviewed and approved by the Institutional Review Board (IRB) of the hospital with Reference No. 747/DME/KMC, ensuring compliance with ethical standards for human research.

The sample size was calculated using OpenEpi software, based on anticipated proportions of vitamin D deficiency among pediatric patients aged 6 months to 3 years with and without recurrent wheeze. Assuming a prevalence of vitamin D deficiency of 73.8% in children with recurrent wheeze (Group 1) and 39.34% in those without in Group 2, with a two-sided $\alpha = 0.05$ and 80% statistical power, the minimum required sample size was calculated to be 35 participants in each group.

A total of 70 children aged 6 months to 3 years were included using consecutive sampling.

Formula:

$$N = (Z_{1-\alpha/2}v(2p(1-p)) + Z_{\text{power}}v(p1(1-p1)+p2(1-p2))^2/(p1-p2)^2$$

In this formula

$$p^- = (0.738 + 0.3934)/2 = 0.5657$$

$$Z_{1-\alpha/2} = 1.95$$

$$Z_{\text{power}} = 0.841$$

After computing the values, 31.3 study participants per group were found. Sample size should be a whole number; we rounded it up to 32 per group (total 64). 35 per group is conservative and reasonable, which is why we selected 35 per group (70).

The case group comprised 35 children with a history of recurrent wheezing, defined as three or more wheezing episodes in the past year, each lasting longer than 24 hours. Diagnosis was confirmed through clinical examinations and parental or medical history. The control group consisted of 35 children, age-matched with no prior history of wheezing. Children with pre-existing pulmonary conditions, documented allergic diseases, or recent vitamin D supplementation (within the past 3 months) were excluded from the study. Written informed consent was taken from the parents or legal guardians of all study participants before enrollment.

In the study, detailed demographic and clinical data were collected for each study participant, including age, sex, nutritional status, and relevant medical history. A comprehensive physical examination was performed, with special attention to respiratory outcomes.¹⁴ Venous blood samples (2mL) were collected under aseptic conditions to measure serum 25-hydroxyvitamin D [25(OH)D] levels using chemiluminescent immunoassay. Vitamin D deficiency was defined as serum 25(OH)D levels <20 ng/mL, in accordance with the Endocrine Society guidelines.¹⁵

Data was analysed using IBM SPSS 25.0. Normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed data were presented as mean and standard deviation (SD), while non-normally distributed data were presented as median and interquartile range (IQR). Frequencies and percentages were found for categorical variables. Differences between groups were assessed using the independent samples t-test for continuous variables. The association between vitamin D deficiency and recurrent wheeze was quantified using odds ratios with 95% CI. A p-value of less than 0.05 was considered statistically significant.

DISCUSSION

Vitamin D is crucial for immune system regulation and pulmonary health conditions, and deficiency has been associated with causing wheezing in children under five. A study conducted in Pakistan by Naseem and her team revealed that an increased prevalence of deficiency of vitamin D and deficiency in wheezing children, with 27.4 percent deficient and 30.5 percent insufficient. This was most probably attributed to improvement in outdoor games and sunlight exposure in young children, which resulted in greater vitamin D production. His gender variation, in which males had a higher proportion of adequate vitamin D while females had a higher proportion of insufficient vitamin D, can be attributed to differences in outdoor games, clothing and exposure to sunlight. Socioeconomic factor status was a distinct variable of status in vitamin D, with pediatrics in poorer families having the highest proportion of deficiency due to inadequate dietary intake, minimal exposure to light, and limited access to medical centers.¹⁶

Naseem et al.'s¹⁶ study outcomes revealed that a mean vitamin D concentration of 26.93 ± 9.36 ng per mL, with 27.4 percent deficient, 30.5 percent insufficient, and 42.1 percent sufficient. This study was recommended by Pechanha et al.,¹⁷ finding that pediatric patients who wheeze have a higher prevalence of 57.3 percent of vitamin D deficiency or insufficiency. Another study, Khan et al.¹⁸, found that 73.8 percent of pediatric wheezers had insufficient vitamin D levels, with a mean concentration of 16.87 ± 4.9 ng per

mL, considerably lower than controls 27.23 ± 3.1 ng per mL, with a p-value of 0.001. A study conducted by Prasad et al.¹⁹ found that wheezing in children with vitamin D deficiency was more severe, with only 23 percent having levels below 5 ng per mL. This can be attributed to variation in geographic regions, exposure to sunlight, dietary patterns, and vitamin D metabolism among people. Contrary to this study, where 42.1 % of pediatrics had an optimal vitamin D concentration, Pechanha et al.¹⁷ observed lower rates in children who are not wheezing. This can be caused by differences in the criteria applied to define deficiency in these studies, as well as differences in the concentration calculation techniques.

Our study found that low socioeconomic status was a strong predictor of recurrent wheezing condition, showing that those children who are from economically not good backgrounds are far more likely to have recurring episodes than those children who belong to higher socioeconomic family backgrounds. Contrary to this, the breastfeeding period, when categorised as less than 1 year vs. one year or more than one year, did not demonstrate a statistically meaningful association with recurrent wheeze within this study, indicating that variables other than infant feeding habits may play a more crucial role in this condition. In the study conducted by Naseem et al.¹⁶, children from low-income families had the highest prevalence of vitamin D deficiency, 55.9%, while children from high-income families had better vitamin D status, 87.5 % with a significant p-value of 0.001. This study is comparable to a study conducted by Pecanha et al.¹⁷ who found that vitamin D deficiency was substantially associated with environmental pollution and lower socioeconomic status of children. Furthermore, a study conducted by Prasad et al.¹⁹ emphasised that exclusive breastfeeding after 6 months, as well as delayed initiation to complementary feeding after 6 months, predicted vitamin D insufficiency and higher wheeze risk indirectly. Low consumption of vitamin D-containing foods, as well as reduced access to health-based services in low-income households, can help explain these outcomes.

Age differences in vitamin D status were also found in a study conducted by Naseem et al. 16 study, where infants

Table 1: Demographics of the Study Participants (n=70)

Demographic Variable	Study Group (n=35)	Control Group (n=35)	p-value
Age (Mean \pm SD) months	16.23 ± 6.66	17.14 ± 7.38	0.581
Gender			
Male n (%)	16 (45.7%)	18 (51.4%)	0.814
Female n (%)	19 (54.3%)	17 (48.6%)	
Socioeconomic Status			
High n (%)	8 (22.9%)	6 (17.1%)	0.463
Medium n (%)	14 (40.0%)	13 (37.1%)	
Low n (%)	13 (37.1%)	16 (45.7%)	
Breastfeeding (Mean \pm SD) months	13.77 ± 5.48	14.54 ± 4.90	0.528

Figure 1: Gender Distribution in Study & Control Groups

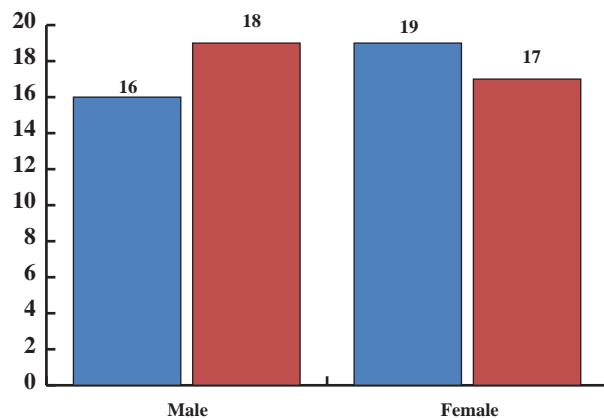


Table 2: Status of Vitamin D Levels and Deficiency (n=70)

Parameter	Study Group (n=35)	Control Group (n=35)	p-value
Vitamin D Level (Mean \pm SD) ng/mL	18.77 \pm 5.89	23.59 \pm 5.78	0.001
Vitamin D Deficiency (<20 ng/mL)			
Yes n (%)	23 (65.7%)	13 (37.1%)	
No n (%)	12 (34.3%)	22 (62.9%)	0.017

Table 3: Univariate Analysis of Factors Associated with Recurrent Wheezy Chest

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Vitamin D Deficiency	3.24	1.28 - 8.21	0.013
Low Socioeconomic Status	3.50	1.23 - 9.97	0.019
Breastfeeding <12 Months	1.17	0.47 - 2.89	0.735

and children aged from two to three years had a higher percentage, 35.4% than children aged 4-5 years, who had a higher percentage than children aged 2 to 3 years (59.6%) with $p=0.003$. Another study conducted by Hodiatska et al.²⁰ found that children aged 6 months to 3 years of age had a 75 percent prevalence of vitamin D deficiency, which was associated with an exponential rise in wheezing recurrence with an odds ratio (OR= 4.3 with a 95% confidence interval 2.75 to 6.86 and with a significant probability value. This represents that young children are more vulnerable because of less dietary intake, less outdoor activities during this duration, increased infections related to the hospital, and thus less exposure to light.

The children in our study were approximately 16.7 months old, with ages ranging from 6 to 36 months. The sample

consisted of approximately the same number of males (34) and females (36). Laboratory analysis revealed that the study group's vitamin D levels were considerably lower than those of the control groups (18.77 ± 5.89 ng/ml vs. 23.59 ± 5.78 ng/ml, $p=0.001$). In a similar vein, the study group experienced a considerably greater prevalence of vitamin D deficiency than the control group (66% vs. 37%, $p=0.017$). The authors concluded that using vitamin D supplements could help prevent COVID-19. Additionally, the data indicated a high correlation between repeated wheezy chest and vitamin D deficiency (OR = 3.24, 95% CI: 1.28-8.21, $p = 0.013$). Additionally, the data indicated a high correlation between repeated wheezy chest and vitamin D deficiency (OR = 3.24, 95% CI: 1.28-8.21, $p = 0.013$).

The likelihood of recurrent wheeze in preschoolers who needed corticosteroid dosages was connected to vitamin D insufficiency in a previous study on the subject conducted in the United States by Beigelman A. 264 children, whose average age was 35 months, participated in the study. The children who had vitamin D levels below 20 ng/ml had more frequent and severe wheezing episodes. Keeping blood vitamin D levels over 20 ng/ml may reduce the likelihood of exacerbations in young children, according to the study's findings.²¹

Khan compared children with recurrent wheeze to age-matched controls to investigate the relationship between vitamin D levels in the blood and recurrent wheezing in kids as young as three years old. Children who frequently wheezed in their chest had much lower vitamin D levels than a control group, according to an Indian study (73.8% vs. 39.34%, $p=0.001$). These results strongly showed that recurring wheezy chests in young children are associated with vitamin D insufficiency.¹⁸ Osman NS et al.²² looked at the link between the frequency and intensity of wheezing episodes and the serum vitamin D levels of preschool-aged children who reported having RWC. 53% of participants with 100 children who had at least three recorded wheezing episodes in the past year had low vitamin D levels (32% deficient, 21% insufficient). Compared to children who did not have adequate vitamin D, those who did had fewer symptoms of wheezing in their chests ($p<0.025$). Vitamin D levels, recurrent wheezing episodes, and the severity of asthma were found to be significantly inversely correlated ($r=-0.334$, $p=0.001$).

El fiki OA et al.²³ worked on the subject in preschool children with a mean age of 3.63 ± 1.1 years. The results showed that children with daytime symptoms of wheezing had significantly lower mean vitamin D levels compared to those without it (9.37 ± 2.75 ng/mL Vs 15.59 ± 6.23 ng/mL, $p<0.001$). Similarly, patients with nighttime awakenings showed markedly lower vitamin D levels than those without it (12.18 ± 5.54 ng/mL vs 21.45 ± 0.07 ng/mL, $p<0.001$). A similar strong association was also found between Vitamin D levels and recurrent wheezing in a study performed in

Pakistan by Hussain M et al (13.90±4.63 ng/mL Vs 25.90±7.57 ng/mL, p= 0.02).²⁴

In 2024, a study conducted by Feketea G. involved 40 children with wheezing and 16 individuals without any respiratory issues. The findings revealed that children with recurrent wheezing had significantly lower levels of vitamin D compared to those who had experienced wheezing for the first time and those without any wheezing. The research findings indicated that a higher prevalence of vitamin D deficiency was observed in individuals with recurrent wheezing, implying a substantial association between vitamin D and the recurrence of wheezing.²⁵ Our results are consistent with previous studies in this area and demonstrate a strong association between vitamin D levels and repeated wheezing in children under the age of 3 years. This study's limited sample size was one of its main limitations. Future studies involving more participants will validate these preliminary findings in our local population.

The case-control design indicates an association, but not causation, between vitamin D deficiency and recurrent wheeze. The single-centre sample size may restrict the applicability of the findings. The results could be affected by residual confounding from unmeasured factors such as sunlight exposure, dietary habits, and atopy history. The definition of recurrent wheezing was based on parental recall and clinical history, which is prone to reporting bias. A single measurement of serum vitamin D might not accurately represent the participants' long-term vitamin D levels.

CONCLUSION

This study highlights that a lack of vitamin D is a significant risk factor for recurring wheezy chest in early childhood. Furthermore, a low socioeconomic position was recognised as a significant contributor to the disease. These findings highlight the need to take nutritional and socioeconomic factors into account when treating pediatric respiratory health issues. Screening for vitamin D deficiency in young infants with recurrent wheeze, combined with public health initiatives that address nutritional support for at-risk populations, could be critical strategies for reducing the burden of wheezing disorders in this vulnerable age group.

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Authors Contribution:

Ikram Ullah: Conceptualization, final review, final investigation
Sabir Khan: Writing and review of manuscript
Zia Muhammad: Review and editing
Muhamamd Shabir: Data Collection
Aimal Khan: Data analysis and editing
Arooj Khan: Data acquisition and editing

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