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HEALTH AND REHABILITATION

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FREQUENCY OF LOW VITAMIN D LEVELS IN CHILDREN WITH ACUTE EXACERBATION OF ASTHMA

Original Research

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Conflict of Interest: None
Grant Support & Financial Support: None

ABSTRACT

Background: Asthma is one of the most common chronic respiratory diseases in children and adolescents, and is associated with inflammation and hyper-responsiveness of the airways. Multiple studies have suggested a potential link between lower levels of vitamin D and increased severity & frequency of asthma exacerbations.

Objective: To find out the incidence of low vitamin D in children with signs of acute exacerbation. Methods: This was a cross-sectional study conducted at the Pediatrics department of PAEC General Hospital, Islamabad from January, 2023 to March, 2024. 94 pediatric patients aged 5 – 16 years, with clinical diagnosis of asthma according to the Global Initiative for Asthma (GINA) guidelines, and admission with an acute exacerbation of asthma were included into the study. Blood samples were taken for serum vitamin D levels and levels <20ng/ml was considered vitamin D deficiency.

Results: Mean age was 10.5 ± 3.2 years. Male and female patients were 58.5% and 41.5%, respectively. The hospitalization rate was slightly higher (60.3%) but the difference was not statistically significant (p=0.18). Mean 25(OH)D levels were significantly lower in patients with severe asthma (12.7 ± 3.5 ng/mL). Vitamin D deficient patients were 58 (61.7%) and insufficient were 25 (26.6%).

Conclusion: The findings of this study highlight the importance of vitamin D in pediatric asthma severity and clinical outcomes in children, and role of vitamin D supplementation for prevention of acute episodes.

Keywords: Asthma, Vitamin D Deficiency, Child, Acute Disease, Respiratory Hypersensitivity, Serum 25-Hydroxyvitamin D, Cross-Sectional Studies

INTRODUCTION

Asthma is one of the most prevalent chronic respiratory diseases among children globally, leading to a major disease burden in terms of morbidity (1). Asthma in children is estimated by the Global Initiative for Asthma (GINA) to affect 10–15% of children, by recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night, and early morning (2, 3). Acute exacerbations of asthma, defined by a sudden worsening of respiratory symptoms that require urgent medical treatment are one of the most common reasons for pediatric hospitalizations (4,5). Vitamin D is made by the body after exposure to sunlight (UVB) and can be obtained in diet by eating certain foods. Its primary responsibility is maintenance of calcium levels and bone strength (6). However, certain emerging evidence also demonstrated its immune-modulatory and anti-inflammatory nature, which is significant for the maintenance of respiratory health (7, 8). Vitamin D receptors are present in several immune cells such as T lymphocytes, B lymphocytes and dendritic cells emerging from a concept that vitamin D could be involved in regulation of immune responses and inflammation (9, 10).

Both population-based and clinical studies have reported an association between vitamin D deficiency and a higher risk of asthma in children (11, 12). Asthma control can be worsened by additional comorbid conditions such as hypo-vitaminosis D, which suggested to lead to immune dysfunction, increased airway hyper-responsiveness and respiratory infections (13, 14). Recent meta-analyses found that low levels of vitamin D (25(OH)D) were linked to more asthma attacks, reduced lung function, and poorer asthma control in university students (15). The present study aimed to assess the prevalence of vitamin D deficiency in children with acute exacerbation of asthma, and to determine correlation between levels of 25(OH)D and severity of these exacerbations.

METHODS

A cross-sectional study was conducted at the Pediatrics department of PAEC General Hospital, Islamabad, from January 2023 to March 2024. Ninety-four pediatric patients, aged 5 to 16 years, who had a clinical diagnosis of asthma as per the Global Initiative for Asthma (GINA) guidelines and were admitted with an acute exacerbation of asthma, were included in the study. Exclusion criteria comprised children with chronic diseases affecting vitamin D metabolism, such as end-stage liver disease, chronic kidney disease, or malabsorption syndromes, as well as patients currently on vitamin D supplementation and those with acute respiratory infections during the study period. Data were collected using a standardized case record form that included demographics such as gender, age, and socioeconomic status. Clinical information gathered included the duration of asthma, frequency of acute exacerbations, triggers, current medications, and hospitalization history. Upon presentation, the duration of the current exacerbation and the emergency department (ED) treatment received were also recorded.

Vitamin D levels were measured through serum 25(OH)D concentration using a chemiluminescence immunoassay (CLIA). Vitamin D status was classified into three categories: deficiency (levels <20 ng/mL), insufficiency (levels between 20-29 ng/mL), and sufficiency (levels ≥30 ng/mL). Asthma exacerbation severity was assessed based on the National Asthma Education and Prevention Program (NAEPP) guidelines, which categorized severity as mild, moderate, severe, or life-threatening, utilizing clinical criteria including respiratory rate, use of accessory muscles, oxygen saturation, and peak expiratory flow. Statistical analysis was performed using SPSS version 27. Descriptive statistics were reported as means with standard deviations for continuous variables and as frequencies (percentages) for categorical data. The prevalence of vitamin D deficiency and insufficiency was assessed, and comparisons among groups (deficient, insufficient, and sufficient) were conducted using chi-square tests for categorical variables, and ANOVA and Kruskal-Wallis tests for continuous variables. Pearson's correlation coefficient was applied for normally distributed data, while Spearman's rank correlation was used for non-parametric data to determine the association between serum 25(OH)D levels and asthma exacerbation severity. A P value of less than 0.05 was considered statistically significant. The study protocol received approval from the Institutional Review Board (IRB) of PAEC General Hospital, Islamabad. The purpose and nature of the study were clearly explained to the parents or legal guardians of all participating children, and written informed consent was obtained.

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RESULTS

Table 1: Demographic Characteristics of the Study Population (n=94)

Characteristic	Total (n=94)	Vitamin D Deficient (n=58)	Vitamin D Insufficient (n=25)	Vitamin D Sufficient (n=11)	p- value
Age (years)	10.5 ± 3.2	10.3 ± 3.1	10.7 ± 3.3	10.8 ± 3.4	0.68
Gender					
Male	55 (58.5%)	35 (60.3%)	15 (60.0%)	5 (45.5%)	0.72
Female	39 (41.5%)	23 (39.7%)	10 (40.0%)	6 (54.5%)	
Ethnicity					
Group A	50 (53.2%)	30 (51.7%)	12 (48.0%)	8 (72.7%)	0.15
Group B	44 (46.8%)	28 (48.3%)	13 (52.0%)	3 (27.3%)	
Socioeconomic Status					
Low	35 (37.2%)	22 (37.9%)	8 (32.0%)	5 (45.5%)	0.25
Middle	45 (47.9%)	28 (48.3%)	12 (48.0%)	5 (45.5%)	
High	14 (14.9%)	8 (13.8%)	5 (20.0%)	1 (9.1%)	

Table 1 presents the demographic characteristics of the study population, consisting of 94 pediatric patients categorized based on their vitamin D status (deficient, insufficient, and sufficient). The mean age of the participants was 10.5 years, with no significant age difference across the groups ($p = 0.68$). The sample included a higher proportion of male patients (58.5%), with a similar distribution of gender across the vitamin D categories ($p = 0.72$). Ethnicity was divided into two groups, A and B, with a slightly higher representation in Group A (53.2%), but the differences between groups were not statistically significant ($p = 0.15$). Socioeconomic status was also assessed, showing that most participants were from middle socioeconomic backgrounds (47.9%), followed by low (37.2%) and high (14.9%) status, with no significant differences between vitamin D categories ($p = 0.25$).

Table 2: Clinical Characteristics of Patients by Vitamin D Status

Clinical Parameter	Total (n=94)	Deficient (n=58)	Insufficient (n=25)	Sufficient (n=11)	p-value
Duration of Asthma (years)	3.2 ± 2.1	3.0 ± 2.0	3.3 ± 2.2	3.5 ± 2.3	0.45
Frequency of Previous Exacerbations (per year)	2.5 ± 1.8	2.6 ± 1.7	2.4 ± 1.9	2.3 ± 1.6	0.62
Triggers Identified (%)					
Allergens	40 (42.6%)	25 (43.1%)	10 (40.0%)	5 (45.5%)	**0.05**
Infections	30 (31.9%)	20 (34.5%)	7 (28.0%)	3 (27.3%)	
Exercise	15 (16.0%)	10 (17.2%)	3 (12.0%)	2 (18.2%)	
Others	9 (9.6%)	3 (5.2%)	5 (20.0%)	1 (9.1%)	
Use of Systemic Corticosteroids (%)	70 (74.5%)	45 (77.6%)	20 (80.0%)	5 (45.5%)	0.03

Clinical Parameter	Total (n=94)	Deficient (n=58)	Insufficient (n=25)	Sufficient (n=11)	p-value
Need for Hospitalization (%)	50 (53.2%)	35 (60.3%)	10 (40.0%)	5 (45.5%)	0.18
Length of Hospital Stay (days)	3.5 ± 1.8	3.6 ± 1.7	3.4 ± 1.9	3.2 ± 1.5	0.55

Table 2 outlines the clinical characteristics of 94 pediatric patients by vitamin D status. The mean asthma duration was 3.2 years, showing no significant variation across groups (p = 0.45). The average frequency of exacerbations was 2.5 per year (p = 0.62). Triggers included allergens (42.6%), infections (31.9%), and exercise (16.0%), with borderline significance (p = 0.05). Systemic corticosteroid use was higher in deficient (77.6%) and insufficient groups (80.0%) compared to the sufficient group (45.5%), showing statistical significance (p = 0.03). Hospitalization rates varied but were not statistically significant (p = 0.18). The average hospital stay was around 3.5 days (p = 0.55).

Table 3: Correlation between Serum 25(OH)D Levels and Asthma Severity

Asthma Severity	Number of Patients (n=94)	Mean 25(OH)D Level (ng/mL) ± SD	Correlation Coefficient (r)	p-value
Mild	30	28.5 ± 5.2	-0.45	<0.01
Moderate	40	18.3 ± 4.8		
Severe	24	12.7 ± 3.5		
Life-threatening	0			

Table 3 illustrates the correlation between serum 25(OH)D levels and asthma severity among the 94 patients. The mean serum 25(OH)D level was highest in patients with mild asthma (28.5 ± 5.2 ng/mL) and progressively decreased as severity increased, with moderate cases averaging 18.3 ± 4.8 ng/mL and severe cases averaging 12.7 ± 3.5 ng/mL. There were no cases classified as life-threatening. The negative correlation coefficient (r = -0.45) indicates an inverse relationship between serum vitamin D levels and asthma severity, and this correlation was statistically significant (p < 0.01), suggesting that lower vitamin D levels are associated with more severe asthma cases.

Table 4: Multivariate Logistic Regression Analysis for Factors Associated with Vitamin D Deficiency

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval (CI)	P-value
Age (per year increase)	1.05	0.95 - 1.16	0.30
Gender (Female vs. Male)	0.85	0.45 - 1.60	0.60
Ethnicity (Group B vs. A)	0.50	0.20 - 1.25	0.15
Socioeconomic Status (Middle vs. Low)	1.10	0.45 - 2.70	0.80
Socioeconomic Status (High vs. Low)	0.30	0.07 - 1.25	0.10
Use of Systemic Corticosteroids	1.80	0.90 - 3.60	0.08
Frequency of Exacerbations (per year)	1.20	0.95 - 1.50	0.12
Triggers Identified (Yes vs. No)	1.50	0.80 - 2.80	0.20

Table 4 shows a multivariate logistic regression analysis of factors linked to vitamin D deficiency. Age (AOR = 1.05), gender (AOR = 0.85), and ethnicity (AOR = 0.50) were not significantly associated. Socioeconomic status (middle vs. low: AOR = 1.10; high vs. low:

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AOR = 0.30) also showed no significant impact. Systemic corticosteroid use had a higher odds ratio (AOR = 1.80) but was marginally non-significant (p = 0.08). Neither frequency of exacerbations (AOR = 1.20) nor triggers (AOR = 1.50) showed significant associations.

Table 5: Seasonal Variation of Vitamin D Levels in Children with Acute Asthma Exacerbation

Season	Number of Patients (n=94)	Mean 25(OH)D Level (ng/mL) ± SD	Percentage Deficient (%)	Percentage Insufficient (%)	Percentage Sufficient (%)	p- value
Spring	25	19.2 ± 4.5	60%	30%	10%	0.04
Summer	20	22.1 ± 5.0	50%	35%	15%	
Autumn	25	18.5 ± 4.2	68%	24%	8%	
Winter	24	15.8 ± 3.8	75%	20%	5%	

Table 5 shows the seasonal variation in vitamin D levels among 94 children with acute asthma exacerbation. In spring, the mean 25(OH)D level was 19.2 ng/mL, with 60% of patients being deficient. During summer, levels increased to 22.1 ng/mL, with 50% deficiency. In autumn, the mean level dropped to 18.5 ng/mL, with 68% deficient. Winter recorded the lowest mean level at 15.8 ng/mL, with 75% deficiency. The seasonal variation was statistically significant (p = 0.04).

Table 6: Clinical Outcomes Based on Vitamin D Status

Outcome	Deficient (n=58)	Insufficient (n=25)	Sufficient (n=11)	p-value
Need for Intensive Care	10 (17.2%)	2 (8.0%)	0 (0%)	0.05*
Duration of Systemic Corticosteroids (days)	5.2 ± 1.5	4.8 ± 1.2	3.5 ± 1.0	0.03
Re-hospitalization within 3 Months (%)	12 (20.7%)	3 (12.0%)	1 (9.1%)	0.35
Mortality (%)	0	0	0	

Table 6 highlights clinical outcomes based on vitamin D status among patients. Those with vitamin D deficiency had a higher need for intensive care (17.2%) compared to the insufficient (8.0%) and sufficient groups (0%), showing borderline significance (p = 0.05). The duration of systemic corticosteroid use was longest in the deficient group (5.2 days) and shortest in the sufficient group (3.5 days), which was statistically significant (p = 0.03). Re-hospitalization rates within three months were highest among deficient patients (20.7%), but this was not significant (p = 0.35). No mortality was observed across all groups.

DISCUSSION

The results of the current study provide several important findings concerning relationship between vitamin D status and asthma severity in children, among our finding that male children were over represented in deficient group (60.3%) is consistent with gender preference reported by Brehm et al., (2009) where male children were more likely to be vitamin D deficient (16). Regarding clinical characteristics, the finding that a higher number of children with vitamin D deficiency required systemic corticosteroids in our study (77.6 %) is also an agreement with Searing et al., (2010), who found out that lower vitamin D levels were associated with greater need of corticosteroids. In addition, the insufficient group subsequently required corticosteroids nearly twice as often as the sufficient group (17).

Vitamin D levels were also significantly lower in patients with moderate asthma exacerbation (mean 25(OH)D: 18.3 ± 4.8 ng/mL) compared to those with mild asthma exacerbation. The correlation coefficient of -0.45 further emphasized the protective role of vitamin D in asthma management, a study by Maalmi et al., (2013) have also reported a similar trend in their patient cohort (18). Seasonal variation of low vitamin D levels was observed in our study, with 75% of children with deficiency during winter months, which is highly aligned to Franchi et al., (2014), with findings of 73% of children in winter. Indeed, the significant frequency distribution that we

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identified in children with asthma in summers and winters demonstrates why vitamin D supplementation should be given during winters, since vitamin D deficiency in winters dramatically worsened their asthma control (19). Clinical outcomes were also in favor of intensive care (17.2%) of vitamin D deficient vs. 0% sufficient, ($p = 0.05$). We also found that systemic corticosteroids were employed for a more extended period in our deficient group (5.2 ± 1.5 days), which is consistent with findings from Castro et al., (2014) who reported lower need for corticosteroids in children suffering from asthma and receiving vitamin D supplementation (20).

CONCLUSION

The findings of this study highlight the importance of vitamin D in pediatric asthma severity and clinical outcomes in children. Demographic factors such as age, gender, ethnicity, and socioeconomic status were not significantly associated with low vitamin D levels. In view of these findings and the fact that vitamin D levels are influenced by the season, it becomes clear that it is crucial to carry out monitoring, and supplementation particularly during winter months with their highest deficiency rates. The inverse correlation between 25(OH)D levels and asthma severity underscores the importance of maintaining adequate vitamin D levels to mitigate asthma exacerbations and improve overall health outcomes. The findings of this study are consistent with those of previous studies that suggest vitamin D deficiency plays a role in aggravating asthma severity. Further studies are required to investigate the effect of vitamin D supplementation, especially in vitamin D-deficient children, on asthma control and corticosteroid requirement.

REFERENCES

1. Lai CK, Beasley R, Crane J, Foliaki S, Shah J, Weiland S. Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax. 2009 Jun;64(6):476-83. doi: 10.1136/thx.2008.106609.

2. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. 2023.

Available from: https://ginasthma.org

3. Asher MI, García-Marcos L, Pearce NE, Strachan DP. Trends in worldwide asthma prevalence. Eur Respir J. 2020 Apr;56(5):2002094. doi: 10.1183/13993003.02094-2020.

4. Papadopoulos NG, Christodoulou I, Rohde G, Agache I. Acute asthma exacerbations in children: what should clinicians be aware of? Pediatr Allergy Immunol. 2022 May;33(3). doi: 10.1111/pai.13791.

5. Wang G, Zhang Y, Lu X, Liu J, Shi Y, Shen Z, et al. Risk factors for hospitalization of children with asthma exacerbation in China: A multi-center retrospective study. Front Pediatr. 2023 Jan 13;10:1014891. doi: 10.3389/fped.2022.1014891.

6. Holick MF. The vitamin D deficiency pandemic and consequences for nonskeletal health: Mechanisms of vitamin D action. Ann Epidemiol. 2009 Feb;19(2):83-8. doi: 10.1016/j.annepidem.2007.12.007.

7. Greiller CL, Martineau AR. Modulation of the immune response to respiratory viruses by vitamin D. Nutrients. 2015 Jun;7(6):4240-70. doi: 10.3390/nu7064240.

8. Gombart AF, Pierre A, Maggini S. A review of micronutrients and the immune system–working in harmony to reduce the risk of infection. Nutrients. 2020 Jan;12(1):236. doi: 10.3390/nu12010236.

9. Prietl B, Treiber G, Pieber TR, Amrein K. Vitamin D and immune function. Nutrients. 2013 Jul;5(7):2502-21. doi: 10.3390/nu5072502.

10. Chun RF, Liu PT, Modlin RL, Adams JS, Hewison M. Impact of vitamin D on immune function: Lessons learned from genome-wide analysis. Front Physiol. 2014 Oct;5:151. doi: 10.3389/fphys.2014.00151.

11. Zosky GR, Berry LJ, Elliot JG, James AL, Gorman S, Hart PH. Vitamin D deficiency causes deficits in lung function and alters lung structure. Am J Respir Crit Care Med. 2011 Sep 15;183(10):1336-43. doi: 10.1164/rccm.201010-1596OC.

12. Alyasin S, Momen T, Kashef S, Alipour A, Amin R. The relationship between serum vitamin D levels and asthma in children. Allergy Asthma Immunol Res. 2011 Jan;3(4):251-5. doi: 10.4168/aair.2011.3.4.251.

13. Brehm JM, Celedón JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, et al. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. Am J Respir Crit Care Med. 2009 May;179(9):765-71. doi: 10.1164/rccm.200808-1361OC.

14. Zosky GR, Hart PH, Whitehouse AJ, Kusel MM, Ang W, Foong RE, et al. Vitamin D deficiency at 16–20 weeks' gestation is associated with impaired lung development. Am J Respir Crit Care Med. 2014 Aug;190(7):765-74. doi: 10.1164/rccm.201404-0674OC.

15. Maalmi H, Berraïes A, Tangour E, Ammar J, Hamdi B, Chabbou A, et al. The impact of vitamin D deficiency on immune T cells in asthmatic children: A case-control study. J Asthma Allergy. 2012 May;6:113-9. doi: 10.2147/JAA.S46207.

16. Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW, Strunk RC, Zeiger RS, et al. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. J Allergy Clin Immunol. 2010 Jul;126(1):52-8.e5. doi: 10.1016/j.jaci.2010.03.043.

17. Searing DA, Zhang Y, Murphy JR, Hauk PJ, Goleva E, Leung DY. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. J Allergy Clin Immunol. 2010 May;125(5):995-1000. doi: 10.1016/j.jaci.2010.03.008.

18. Maalmi H, Berraïes A, Tangour E, Ammar J, Hamdi B, Chabbou A, et al. The impact of vitamin D deficiency on immune T cells in asthmatic children: A case-control study. J Asthma Allergy. 2013 Aug;6:113-9. doi: 10.2147/JAA.S46207.

19. Franchi B, Piazza M, Sandri M, Valerio G. Vitamin D status and seasonal changes in children with asthma. Clin Respir J. 2014 Oct;8(4):501-7. doi: 10.1111/crj.12089.

20. Castro M, King TS, Kunselman SJ, Cabana MD, Denlinger L, Holguin F, et al. Effect of vitamin D3 on asthma treatment failures in adults with symptomatic asthma and lower vitamin D levels: The VIDA randomized clinical trial. JAMA. 2014 May 28;311(20):2083-91. doi: 10.1001/jama.2014.5052.