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ORIGINAL RESEARCH

The Effect of Vitamin D Levels on Asthma Exacerbation in Asthmatic Patients in a Tertiary Hospital: Retrospective Study

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Background: Asthma is a major global health issue, affecting over 260 million individuals and causing more than 450,000 deaths annually. A growing body of international and local research has investigated the link between Vitamin D levels and asthma outcomes. These studies suggest that Vitamin D may play a role in modulating immune responses, potentially influencing asthma control, the frequency of exacerbations, hospital visits, and overall disease severity. However, evidence remains contradictory, where other studies did not establish a direct link between vitamin D levels and asthma development given the limited real-world data from Saudi Arabia.

Objective: This study aims to investigate the effect of serum Vitamin D levels and asthma exacerbations among adults, adolescents, and children within a Saudi population.

Methods: A single-center retrospective cohort study was conducted at the National Guard Hospital in Riyadh, Saudi Arabia, involving 379 asthma patients with documented Vitamin D deficiency within the past 6 to 12 months. The primary outcome was the effect of serum Vitamin D levels and asthma exacerbations. The secondary outcome is defining the correlation between Vitamin D levels and asthma severity.

Results: A significant difference in asthma exacerbation frequency was observed between the Vitamin D–deficient and adequate groups during both the 6- and 12-month periods, with the adequate group experiencing more frequent exacerbations ($p = 0.030$). Furthermore, significant associations were found between Vitamin D levels and emergency room visits ($p < 0.001$), as well as the need for rescue medication ($p = 0.004$).

Conclusion: Interestingly, the results revealed that individuals with adequate vitamin D had a significantly higher frequency of exacerbations compared to those in the deficient group. These findings could be due to several confounding factors. Although vitamin D may contribute to overall respiratory health, its impact on severe asthma events may be overshadowed by other critical factors, such as Age and BMI, comorbidities, adherence to controller medications, and exposure to environmental triggers.

Keywords: asthma, asthma exacerbation, asthma severity, vitamin D deficiency

Background

Despite advances in therapies and management strategies, asthma remains a significant global and national health challenge, affecting individuals across all age groups.[1,2] Asthma exacerbations, defined as acute or sub-acute worsening of respiratory symptoms with a decline in lung function, continue to contribute to morbidity, hospitalizations, and healthcare burden.[3] Among the multiple factors implicated in asthma pathophysiology, vitamin D deficiency (serum levels <30 nmol/mL) has gained attention due to its potential role in modulating immune responses and airway function.[4,5] Several observational studies and randomized trials have demonstrated that low vitamin D levels are

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associated with increased asthma severity, impaired lung function, and higher exacerbation rates.[6–11] However, evidence remains inconsistent, with some studies reporting no direct effect of vitamin D status and asthma outcomes.[12–15] Notably, recent research, including a study published in the *World Journal of Pediatrics*, highlights the need for region-specific data to clarify this relationship.

In Saudi Arabia, asthma prevalence remains considerable, and the contribution of modifiable factors such as vitamin D deficiency to exacerbations is not well characterized. This knowledge gap is particularly relevant given the high prevalence of vitamin D deficiency reported in the region and its potential implications for disease control. Therefore, this study was designed to investigate the effect of serum vitamin D levels and asthma exacerbations in adults, adolescents, and children attending a Saudi tertiary hospital, with the aim of providing locally relevant evidence to inform management strategies and guide future research.

Methods

Study Design and Setting

This retrospective cohort study was conducted at a single tertiary care center, the National Guard Hospital in Riyadh, Saudi Arabia. The primary objective was to examine the effect of serum vitamin D levels and asthma exacerbations, while the secondary objective was to evaluate the relationship between vitamin D levels and asthma severity.

Sample Size Calculation

The minimum required sample size was calculated using Raosoft® (Sample Size Calculator; Raosoft Inc., Seattle, WA, USA), based on standard formulas for estimating proportions. Assuming a 95% confidence level, a 5% margin of error, and an expected population proportion of 50% (selected to maximize sample size in the absence of prior prevalence data), the estimated minimum sample size was 377 participants. The achieved sample size exceeded this threshold, ensuring sufficient precision and statistical power to address the study objectives.

Study Participants

Patients were included if they met the following criteria: a confirmed diagnosis of asthma, a recent measurement of serum vitamin D levels, and a history of asthma exacerbation requiring a short course of oral corticosteroids (≥3 days), an ED visit, or hospitalization due to worsening asthma symptoms.

Exclusion criteria included absence of a recent vitamin D measurement, pregnancy, asthma episodes triggered primarily by anxiety attacks, and other respiratory conditions such as pneumonia, upper or lower respiratory tract infections, COPD, acute bronchitis, allergic rhinitis, and non-asthmatic allergic respiratory diseases, as detailed in Figure 1.

Data Collection

Demographic and clinical data were extracted from electronic health records and managed using Microsoft Excel. Collected variables included age, gender, body mass index (BMI), vitamin D supplementation status, and comorbidities such as diabetes, hypertension, heart disease, gastroesophageal reflux disease (GERD), and dyslipidemia.

Patients were categorized into three groups based on serum vitamin D levels (Deficient, Insufficient, and Adequate; Table 1). For each group, we assessed the frequency of asthma exacerbations within the past 6 and 12 months, including episodes requiring oral corticosteroids, ED visits, or hospitalization. Asthma severity was classified as mild, moderate, or severe according to GINA guidelines, and lung function measurements, including FEV_1 and FEV_1/FVC ratio, were recorded when available. We also collected data on the use of rescue medications such as short-acting beta agonists (SABA) and systemic corticosteroids, hospital-based interventions related to asthma exacerbations, vitamin D supplementation status, and the use of maintenance asthma medications, including inhaled corticosteroids (ICS), leukotriene receptor antagonists (LTRA), and long-acting beta agonists (LABA).

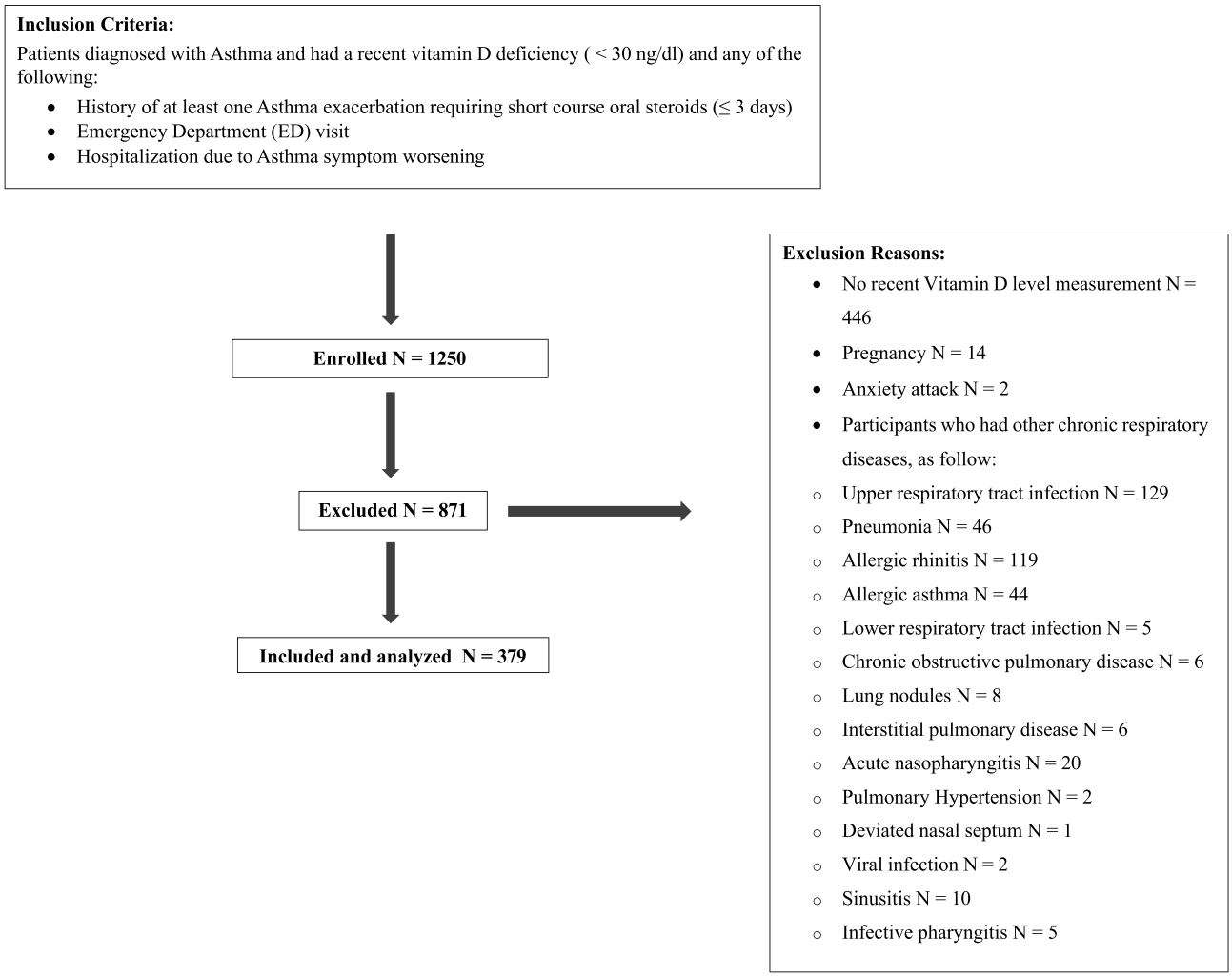

Figure 1 Participants follow diagram.

Ethical Approval

The study was approved by the Institutional Review Board (IRB) of King Abdullah International Medical Research Center (KAIMRC) (IRB/1192/24). The ethics committee exempted the requirement for informed consent because the study involved a retrospective analysis of anonymized data using existing records without any personal identifiers. All procedures were conducted in accordance with relevant ethical guidelines and regulations, including the Declaration of Helsinki.

Statistical Analysis

All analyses were conducted using SPSS software. The Shapiro–Wilk test assessed the normality of continuous variables (age, weight, height, BMI), all of which were non-normally distributed ($p < 0.05$). Consequently, non-parametric tests

Table 1 Categories of Serum Vitamin D Levels

Category	25-Hydroxyvitamin D (25OHD) Levels
Adequate	(> 50 nmol/L)
Insufficient	(30–50 nmol/L)
Deficient	(< 30 nmol/L)

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were applied. Continuous variables were presented as medians with interquartile ranges (IQR), and categorical variables were reported as frequencies and percentages.

The Kruskal–Wallis test was used to compare continuous variables across vitamin D categories. For clinical interpretation, asthma exacerbations were categorized as <2 versus ≥2 episodes, and their association with vitamin D levels was assessed using the Chi-square test. Ordinal logistic regression was performed to evaluate the effect of vitamin D levels and asthma severity, adjusting for age and BMI as primary confounders based on biological plausibility, prior evidence, and baseline differences across vitamin D categories.

Results

Study Population and Baseline Characteristics

A total of 379 patients were included in the final analysis (Figure 1). Excluded participants were those with non-asthmatic respiratory diseases (eg, upper respiratory tract infections, pneumonia, COPD) or pregnant/lactating women. Baseline characteristics are presented in Table 2, with patients categorized into three groups based on serum vitamin D levels: Deficient (<30 nmol/L), Insufficient (30–50 nmol/L), and Adequate (>50 nmol/L). Participants in the Adequate

Table 2 Baseline Characteristics

Variable	Deficiency < 30 nmol/ L N (271) (71.50%)	Insufficiency 30–50 nmol/ L N (63) (16.62%)	Adequate > 50 nmol/ L N (45) (11.8%)	P-value
Gender No. (%) Female Male	 180 (66.4) 91 (33.6)	 41 (65.1) 22 (34.9)	 35 (77.8) 10 (22.2)	 0.289
Age, yr, median (IQR)	35 (17–50)	43 (22–52)	51 (40–59)	**p<0.001**
Weight, kg, median (IQR)	74 (55–89)	75 (66–93)	82 (71–92)	0.062
Height, cm, median (IQR)	156 (149–163)	160 (151–166)	157 (150–164)	0.095
BMI, (Kg/m2), median (IQR)	29 (23–34)	29 (25–35)	31 (27–37)	**0.040**
Vitamin D supplementation No. (%)	79 (29.2)	24 (38.1)	22 (48.9)	**0.021**
Smoker No. (%)	21 (7.7)	2 (3.2)	0 (0)	0.075
Comorbidities No. (%)				
Had at least one comorbidity	163 (60.1)	40 (63.5)	35 (77.8)	0.076
DM	55 (20.3)	11 (17.5)	16 (35.6)	-
COPD	3 (1.1)	0 (0)	0 (0)	-
CKD	6 (2.2)	0 (0)	0 (0)	-
HTN	46 (17)	7 (11.1)	16 (35.6)	-
OP	2 (0.7)	0 (0)	1 (2.2)	-
Heart diseases	17 (6.3)	2 (3.2)	4 (8.9)	-
GERD	16 (5.9)	0 (0)	4 (6.3)	-
DLP	71 (26.2)	21 (33.3)	15 (33.3)	–
H. Pylori	3 (1.1)	0 (0)	1 (1.6)	
Vaccination No. (%)				

(*Continued*)

Table 2 (Continued).

Variable	Deficiency < 30 nmol/ L N (271) (71.50%)	Insufficiency 30–50 nmol/ L N (63) (16.62%)	Adequate > 50 nmol/ L N (45) (11.8%)	P-value
COVID-19	9 (3.3)	2 (3.2)	1 (2.2)	-
Influenza	1 (0.4)	2 (3.2)	1 (2.2)	-
Pneumonia	0 (0)	0 (0)	0 (0)	-
Pertussis (Whooping cough)	0 (0)	0 (0)	0 (0)	-
TB	0 (0)	0 (0)	0 (0)	-
Respiratory Syncytial Virus (RSV)	0 (0)	0 (0)	0 (0)	-
Death	1 (0.26)	0 (0)	0 (0)	-

Note: Bold p-values indicate statistically significant differences ($p < 0.05$).
Abbreviations: yr, years; IQR, interquartile range; kg, kilograms.

vitamin D group were significantly older (median [IQR] 51 [40–59] years) than those in the Deficient group (35 [17–50] years; $p < 0.001$), with post hoc analysis confirming this difference ($p < 0.001$). BMI was also higher in the Adequate group compared to the Deficient group ($p = 0.048$), whereas the Insufficient group did not differ significantly from either group. Gender distribution was similar across groups, with most participants being female ($p = 0.289$).

The prevalence of comorbidities was highest in the Adequate group, although this difference was not statistically significant ($p = 0.076$). Hypertension and diabetes were more frequent in the Adequate group than in the Deficient group (35.6% vs 17% and 35.6% vs 20.3%, respectively). No cases of COPD or chronic kidney disease were reported in the Insufficient and Adequate groups. Smoking prevalence was low across all groups and did not differ significantly ($p = 0.075$).

Vitamin D supplementation rates differed significantly among the groups ($p = 0.021$), with 48.9% of the Adequate group, 38.1% of the Insufficient group, and 29.2% of the Deficient group receiving supplementation. Vaccination history, including pneumonia, pertussis, tuberculosis (TB), respiratory syncytial virus (RSV), COVID-19, and influenza, showed no significant differences across the groups.

Study Outcomes

Effect of Vitamin D Levels on Asthma Exacerbations

The primary outcome assessed the effect of vitamin D levels on the frequency of asthma exacerbations. The Kruskal–Wallis test revealed a statistically significant difference in exacerbation frequency across the vitamin D groups ($p = 0.025$; Figure 2). Post hoc pairwise comparisons over the past 6 months showed that participants in the Adequate group experienced more exacerbations than those in the Deficient group ($p = 0.026$), whereas no significant differences were observed between the Deficient and Insufficient groups ($p = 0.770$) or the Insufficient and Adequate groups ($p = 0.527$). Over the past 12 months, the difference between the Deficient and Adequate groups remained statistically significant ($p = 0.002$). Exacerbations requiring oral corticosteroids were also significantly effected by vitamin D levels ($p = 0.005$).

Chi-square analysis revealed no significant effect of vitamin D levels and the number of exacerbations over the past six months; however, a significant effect was observed over the past 12 months ($p = 0.030$), with participants in the Adequate group more likely to experience ≥2 exacerbations (Table 3). Significant effect were also observed between vitamin D levels and emergency department visits (Table 4) and the use of rescue medications (Table 5). No significant effect were observed for SpO_2 levels ($p = 0.404$), worsening symptoms ($p = 0.077$), hospitalization ($p = 0.281$), ICU admissions ($p = 0.196$), or addition/increase of ICS dose ($p = 0.245$).

Effect of Vitamin D Levels on Asthma Severity

The secondary outcome assessed the effect of vitamin D levels on asthma severity. Participants with Adequate vitamin D levels were less likely to have severe persistent asthma, although the overall effect was not statistically significant ($p =$

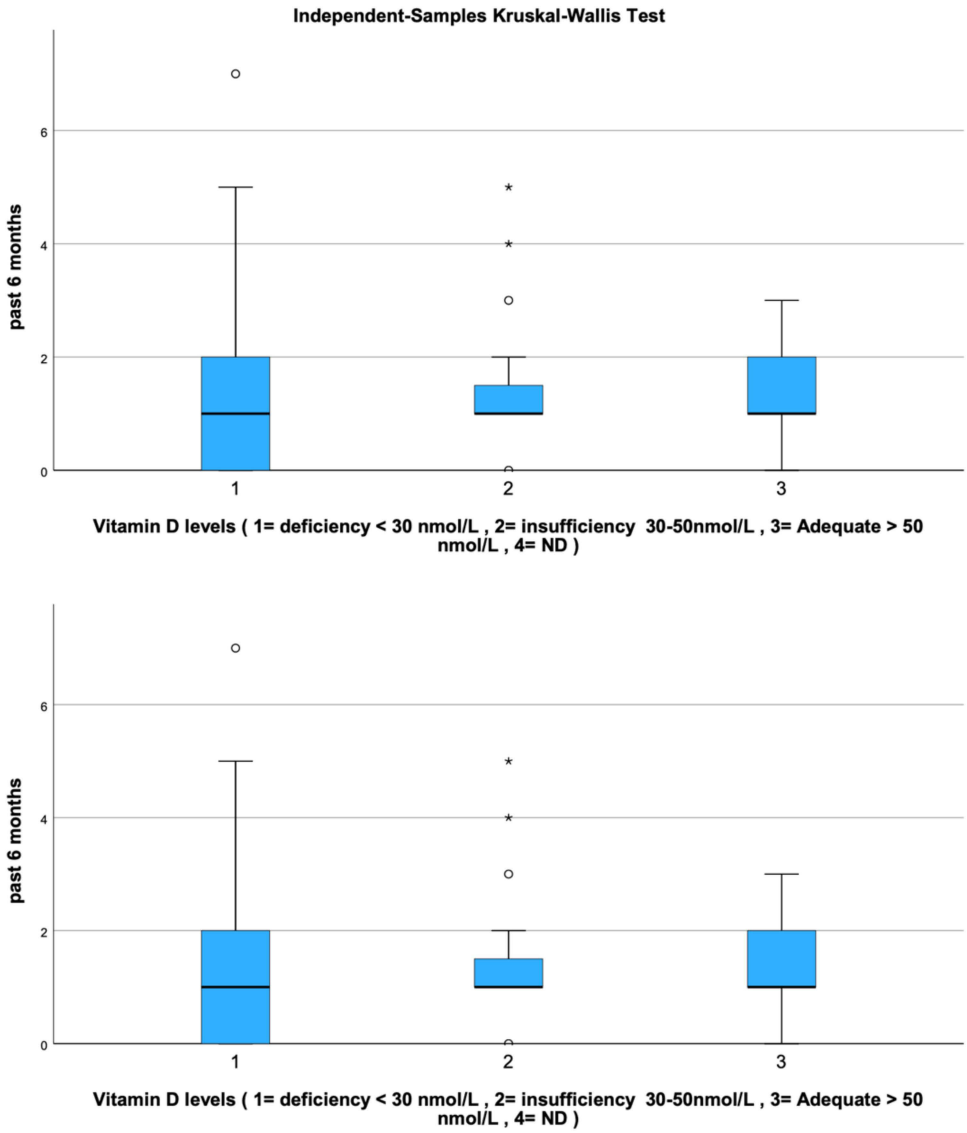

Figure 2 Frequency of exacerbations in 6-months and 12-months periods. (0) Indicate mild outliers. (*) Indicate extreme outliers.

0.423; Table 6). Spearman's analysis indicated a very weak negative relationship between vitamin D levels and asthma severity ($r = -0.043$, $p = 0.405$).

Ordinal logistic regression, adjusting for age and BMI, demonstrated that Deficient vitamin D levels were effect with a higher likelihood of severe asthma compared to Adequate levels (OR = 1.84, $p = 0.045$; Table 7), indicating that lower vitamin D is related to increased asthma severity once confounders are accounted for.

Discussion

This study investigated the relationship between vitamin D levels and asthma outcomes, including exacerbation frequency and asthma severity, across different age groups in a tertiary care hospital in Saudi Arabia. While vitamin D is widely recognized for its immunomodulatory role in respiratory diseases, our findings revealed a complex relationship with asthma outcomes, highlighting the influence of confounding factors and the need for careful interpretation.

The primary outcome of this study was the relationship between vitamin D levels and asthma exacerbations. Interestingly, patients with adequate vitamin D levels appeared to experience more frequent exacerbations compared to those with deficient levels. At first glance, this finding seems paradoxical, as the majority of existing literature suggests

Table 3 Number of Exacerbations of Bronchial Asthma Among Different Vitamin D Categories

A. Number of exacerbations of bronchial asthma in the last 6 months	**Vitamin D3 levels**			
	Deficient (No. 271)	**Insufficient (No. 63)**	**Adequate (No. 45)**	**P value**
< 2 episodes	192	47	30	0.667
≥ 2 episodes	79	16	15	
B. Number of exacerbations of bronchial asthma in the last 12 months	**Vitamin D3 levels**			
	Deficient (No. 271)	**Insufficient (No. 63)**	**Adequate (No. 45)**	**P value**
< 2 episodes	171 (75.3)	37 (16.3)	19 (8.4)	**0.030**
≥ 2 episodes	100 (65.8)	26 (17.1)	26 (17.1)	

Note: Bold p-values indicate statistically significant differences (p <0.05).

Table 4 Emergency Visit

	Vitamin D3 Levels			
Emergency Visit	**Deficient**	**Insufficient**	**Adequate**	**P value**
Yes	130	38	35	**<0.001**
No	141	25	10	

Note: Bold p-values indicate statistically significant differences (p <0.05).

Table 5 Vitamin D Levels and Need for Rescue Medications

	Vitamin D3 Levels			
Rescue Medications	**Deficient**	**Insufficient**	**Adequate**	**P value**
Yes	103	34	27	**0.004**
No	167	29	18	

Note: Bold p-values indicate statistically significant differences (p <0.05).

Table 6 Distribution of Asthma Severity Across Vitamin D Categories

	Vitamin D Category			**P-value**
Asthma Severity	**Deficiency < 30 nmol/L N (%)**	**Insufficiency 30–50 nmol/L N (%)**	**Adequate > 50 nmol/L N (%)**	0.423
Intermittent	57 (21)	13 (20.6)	9 (20)	
Mild persistent	96 (35.4)	23 (36.5)	21 (46.7)	
Moderate persistent	92 (33.9)	20 (31.7)	15 (33.3)	
Severe persistent	26 (9.6)	7 (11.1)	(0)	

Table 7 Asthma Severity Predictors

Predictor	Odds Ratio (95% CI)	P-value
Deficient Vitamin D	1.84 (1.01–3.34)	**0.045**
Insufficient Vitamin D	1.69 (0.83–2.93)	0.148
Adequate Vitamin D	**(Ref)**	**(Ref)**
Age (years)	1.02 (1.01–1.03)	**0.015**
BMI (kg/m^2)	1.02 (0.85–1.29)	0.692
Height (cm)	1.01 (0.99–1.03)	0.622
Height (cm)	1.00 (0.95–1.04)	0.892

Note: Bold p-values indicate statistically significant differences ($p < 0.05$). Ref indicates Reference.

that sufficient vitamin D may reduce exacerbation risk. Observational and interventional studies have consistently shown that vitamin D deficiency is associated with increased exacerbation frequency and poorer asthma control, and supplementation in deficient patients can improve outcomes.

Several factors may explain this apparent discrepancy. First, baseline characteristics indicated that patients in the adequate vitamin D group were generally older and had higher BMI. Both age and BMI are known independent risk factors for increased asthma exacerbations, which could have confounded the raw association. Second, reverse causality may have played a role: patients with frequent exacerbations are more likely to engage with healthcare services and receive vitamin D supplementation, potentially inflating the number of exacerbations observed in those with adequate levels. Third, variability in individual responses to vitamin D supplementation and the possibility of a "U-shaped" relationship, where both low and high levels may have adverse effects, could contribute to these findings. Finally, hospital-based data may overrepresent patients with more severe asthma who receive routine supplementation, further influencing observed patterns.

Despite these complexities, the secondary outcome assessing asthma severity demonstrated results more consistent with the current understanding of vitamin D biology. After adjusting for confounders such as age and BMI, vitamin D deficiency was associated with a higher likelihood of severe asthma, supporting the hypothesis that low vitamin D contributes to worse long-term disease control. This aligns with prior studies indicating that insufficient vitamin D levels may exacerbate airway inflammation, impair immune regulation, and reduce responsiveness to standard therapies. However, the weak overall effect also suggests that vitamin D is only one of multiple factors influencing asthma severity, alongside genetics, environmental exposures, and treatment adherence.

Additionally, this study highlighted a relationship between vitamin D levels and markers of asthma instability, including emergency department visits and the use of rescue medications, although no significant effect was observed with hospitalization or ICU admissions. These findings support the concept that vitamin D may influence milder acute outcomes and day-to-day asthma control, but its impact on severe or life-threatening exacerbations may be limited by other dominant clinical factors.

Overall, the results emphasize the complexity of vitamin D's role in asthma. While low vitamin D is likely a contributing factor to worse asthma outcomes, confounding variables, population characteristics, and study design intricacies can produce findings that appear contradictory to established theory. These observations underscore the importance of considering patient age, BMI, supplementation practices, and disease severity when evaluating vitamin D status in clinical practice.

Future research should aim to clarify the mechanistic pathways linking vitamin D with asthma outcomes and determine optimal supplementation strategies tailored to patient-specific factors. Well-designed prospective studies and randomized controlled trials are needed to disentangle the effects of vitamin D from confounders and to establish evidence-based clinical recommendations.

Limitations and Future Directions

This study has several limitations that should be considered. First, the observational design and reliance on electronic health records limited the ability to fully control for potential confounders, including dietary vitamin D intake, sun exposure, and adherence to asthma medications. Second, the findings may have limited generalizability to populations outside this tertiary care hospital, particularly in regions with different climates, dietary patterns, or genetic backgrounds. Third, the possibility of reverse causation cannot be excluded, as patients with more severe asthma may have been more likely to receive vitamin D supplementation, potentially contributing to the higher exacerbation rates observed in the adequate vitamin D group.

Additionally, the study lacked longitudinal follow-up, which limits the ability to determine the long-term impact of correcting vitamin D deficiency on asthma outcomes. Future research should focus on prospective, controlled studies with longer follow-up periods to clarify the causal effects of vitamin D supplementation and to identify patient subgroups that may benefit most.

Conclusion

This study highlights the complex relationship between vitamin D levels and asthma outcomes in adults, adolescents, and children. Consistent with current understanding, vitamin D deficiency was had a higher effect on likelihood of severe asthma, supporting its role as an immune modulator. However, the observed higher frequency of exacerbations in patients with adequate vitamin D appears to be influenced by confounding factors, particularly older age and higher BMI, rather than representing a direct causal effect.

These findings underscore the importance of careful interpretation of observational data, as unaccounted variables can influence outcomes and potentially lead to misinterpretation. Future research should focus on prospective, controlled studies that adjust for key confounders, including age, BMI, medication adherence, supplementation patterns, environmental exposures, and genetic factors. Such studies are needed to clarify the true effect of vitamin D on asthma exacerbations and guide evidence-based recommendations for supplementation in patients with asthma.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no competing interests to declare that are relevant to the content of this article.

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