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Serum Vitamin D Profiles of Children with Asthma in Southwest Saudi: A Comparative Cross-Sectional Study

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Background: Evidence suggests a strong association between vitamin D status and asthma, with individuals exhibiting vitamin D deficiency demonstrating increased prevalence and severity of asthma symptoms. This study aimed to determine the prevalence of vitamin D deficiency among asthmatic children, assess the association between vitamin D status and asthma severity/control, and identify potential predictors of vitamin D deficiency in this population.

Patients and Methods: This comparative cross-sectional, hospital-based study was conducted at Abha Maternity and Children's Hospital, a tertiary care and teaching institution in southwestern Saudi Arabia, between January 2023 and May 2024.

Results: A total of 331 asthmatic children and 101 non-asthmatic children were analyzed. Children with asthma had significantly lower serum vitamin D levels than those without asthma (21.5 ± 8.8 ng/mL vs 33.3 ± 13.2 ng/mL, $p < 0.001$). Significantly higher proportions of asthmatic children exhibited vitamin D deficiency (51.1%) and insufficiency (34.7%) compared to non-asthmatic children (19.8% and 29.7%, respectively). Serum vitamin D levels among asthmatic children showed significant negative correlations with age ($r = -0.332$, $p < 0.001$), weight ($r = -0.292$, $p < 0.001$), height ($r = -0.298$, $p < 0.001$), and BMI ($r = -0.274$, $p < 0.001$). These findings were further supported by univariate linear regression analysis. Multivariable analysis additionally confirmed age ($\beta = -0.66$, $p < 0.001$) and BMI ($\beta = -0.25$, $p = 0.05$) as independent predictors of vitamin D status, with older age and higher BMI associated with lower vitamin D levels. For each additional year of age, serum vitamin D decreased by an average of 0.66 ng/mL ($p < 0.001$) and a one-unit increase in BMI was associated with a decrease of 0.25 ng/mL in serum vitamin D ($p = 0.05$).

Conclusion: This study found a strikingly high prevalence of vitamin D deficiency among asthmatic children in southwestern Saudi Arabia, significantly exceeding rates in controls. These findings underscore the need for widespread vitamin D screening and supplementation in this population, particularly among older, overweight asthmatic children.

Keywords: children, asthma, vitamin D deficiency, Saudi Arabia, obesity

Introduction

Asthma, a widespread chronic disease affecting an estimated 300 million individuals globally,[1,2] is particularly prevalent in Saudi Arabia, with approximately 10–30% of school-age children experiencing symptoms.[3] The pathogenesis of asthma involves a complex interplay of genetic predisposition, host factors, and environmental exposures.[1–4] Vitamin D deficiency has become a critical factor in developing chronic extra-skeletal diseases, including asthma and respiratory infections.[5–7] Beyond its functions in bone health, vitamin D plays a pivotal role in regulating innate and adaptive immune systems.[8] Overall, evidence suggests a strong association between vitamin D status and asthma, with individuals having vitamin D deficiency demonstrating increased prevalence and severity of asthma symptoms,[5,9–11] particularly among those with obesity-related asthma.[12]

The underlying mechanism by which vitamin D impacts asthma involves its immunomodulatory properties, which significantly influence the inflammatory responses central to asthma pathogenesis. However, while evidence has highlighted vitamin D's potential role in asthma, their relationship's precise nature is not yet fully understood, particularly

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within specific populations and geographical regions. Several mechanisms have been proposed, such as reducing airway inflammation, enhancing epithelial barrier function, and modulating innate immunity. Vitamin D can suppress inflammatory responses mediated by T-helper 2 cells, which is crucial in atopic asthma development. In addition, vitamin D can strengthen the epithelial barrier of the airways, reducing the entry of allergens and irritants. Furthermore, vitamin D can influence the function of innate immune cells, such as dendritic cells and macrophages, which contribute to asthma pathogenesis.[5,6,8] A recent study concluded that Serum 25-hydroxyvitamin D (25(OH)D) deficiency was associated with increased inflammation and airway obstruction in both T2-high and T2-low asthma endotypes, with more pronounced effects observed in the T2-low phenotype.[13] These findings necessitate further investigation to elucidate the mechanisms underlying these changes and to explore potential therapeutic interventions targeting specific asthma endotypes. This knowledge could lead to the development of more precise and effective therapies beyond the current phenotype-based approaches.

Vitamin D deficiency remains a significant health problem in Southwest Saudi Arabia, despite being one of the sunniest areas of the world and located at 18°N latitude. Indeed, the high prevalence of vitamin D deficiency among Saudi children and adolescents,[14–17] including asthmatic individuals, is of particular concern. While several studies have highlighted an overall increased prevalence of vitamin D deficiency in asthmatic children,[16,18] data specific to the Southwest region of Saudi Arabia are lacking. Hence, this study aimed to determine the prevalence of vitamin D deficiency among asthmatic children in Southwest Saudi Arabia, assess the association of vitamin D status with asthma severity/control, and identify potential predictors of vitamin D deficiency in this population.

Materials and Methods

Study Design, Setting, and Population

A comparative cross-sectional, hospital-based study was conducted at Abha Maternity and Children's Hospital (AMCH), a tertiary care and teaching institution in southwestern Saudi Arabia, between January 2023 and May 2024. This setting provided access to a substantial pediatric population. A total of 432 children were recruited via a convenience sampling approach. The study cohort comprised two groups: an asthma group (n = 331) of children aged 3–12 years with physician-diagnosed asthma and a control group (n = 101) of age-matched children without asthma. Asthma diagnosis was confirmed by a pediatric pulmonologist and aligned with the Global Initiative for Asthma (GINA) guideline; that is, the condition was characterized by recurrent episodes of wheezing, breathlessness, cough, and chest tightness triggered by various stimuli, including viral infections and allergens.[19] Informed written consent was obtained from all participants. Exclusion criteria were applied to both the asthma and non-asthma groups. Children with a history of recurrent wheezing before the age of three years and those with coexisting medical conditions, including prematurity, cystic fibrosis, sickle cell disease, or other pulmonary disorders, were excluded. Participants with diabetes mellitus type 1, bone disorders, parathyroid disease, malabsorption syndromes, or liver disease were excluded from the study.

Data Collection and Vitamin D Assessment

Data were collected through structured face-to-face interviews conducted by treating physicians. Clinical and demographic data, including age, sex, age at first wheezing episode, allergic history, asthma severity, family history of asthma, asthma control within the preceding four weeks, school absences during the previous year, emergency department visits, hospital admissions, intubation history, and pediatric intensive care unit admissions were recorded. Participants' height, weight, asthma severity, and control were also assessed. Body mass index (BMI, weight in kilograms divided by height in square meters) was obtained from the body measurements. Children with a BMI in the >95th percentile were considered to be obese; those with a BMI between the 85th and 95th percentile were considered to be overweight. These definitions were based on the corresponding age and sex reference groups. Asthma severity was determined based on the dosing of inhaled corticosteroids and the worsening of symptoms with treatment discontinuation. This is consistent with the GINA criteria for managing mild, moderate, and severe childhood asthma.[19] Asthma control was likewise assessed based on the GINA guidelines; control was determined by the presence or absence of diurnal or nocturnal symptoms, short-acting beta-agonist use, and activity limitations within the preceding four weeks. Patients were categorized as well-controlled (no symptoms), partially controlled (one or two symptoms), or uncontrolled (three or more symptoms). Asthma control levels were reported as frequencies and percentages.

Vitamin D status was determined based on serum 25(OH)D, considered the primary indicator of vitamin D status. This parameter was measured by radioimmunoassay using the Wallac 1470 Gamma Counter (Wallac Inc, Gaithersburg, MD). Blood samples (4 mL) were collected and analyzed at the hospital laboratory.[20] Participants were categorized based on 25(OH)D level into three groups of vitamin D status: deficient (<20 ng/mL), insufficient (20–30 ng/mL), and sufficient (>30 ng/mL).[7,21]

Statistical Analysis

Statistical analyses utilized the SPSS software program version 29 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp). Descriptive statistics were used to summarize participant characteristics. Normally distributed continuous variables were presented as mean ± standard deviation, while non-normally distributed variables were reported as median (interquartile range). Categorical variables were summarized as frequencies and percentages. Independent samples *t*-tests were used to compare means of continuous variables among two groups, and one-way analysis of variance (ANOVA) was used for multiple groups. Mann–Whitney U assessed group differences tests for non-normally distributed continuous variables. Categorical variables were compared using Pearson's chi-square test (> 5 cell count) or Fisher's exact test (< 5 cell count).

Bivariate correlations between continuous variables and vitamin D levels were assessed using Pearson's correlation coefficient. Univariate and multivariate linear regression models were used to identify predictors of vitamin D levels. Before model building, assumptions of linearity, normality of residuals, and homoscedasticity were assessed and met for age, weight, height, and BMI. Multicollinearity was assessed using variance inflation factors, with values exceeding 10 indicating multicollinearity. Height and weight were excluded from the final model due to multicollinearity. Finally, univariable and multivariable binary logistic regression models were employed to identify the factors associated with vitamin D deficiency/insufficiency among the studied population. Results were reported as odds ratios (OR) and their associated 95% confidence intervals (CIs). Having vitamin D deficiency/insufficiency was considered the dependent variable. Independent variables included age > 6 years and being overweight/obese (BMI percentile > 85%). Statistical significance was set at $p < 0.05$.

Ethical Statement

The study was approved by the Research Ethics Committee at King Khalid University (HAPO-06-B-001) via approval number (ECM# 2023–3319). It was carried out according to the Declaration of Helsinki. Patients' informed consent was taken prior to data collection. Informed consent was obtained from all parents or legal guardians of the patients involved in the study.

Results

Population Characteristics and Prevalence of Vitamin D Deficiency

A total of 331 asthmatic children and 101 non-asthmatic children were analyzed. Table 1 presents the demographic and clinical characteristics of the study participants. There were no significant differences between the asthma and non-asthma groups regarding age, weight, height, or BMI. However, a significantly higher proportion of males were found in the asthma group compared to the non-asthma group (62.5% vs 44.6%, $p < 0.005$). Notably, children with asthma had significantly lower serum vitamin D levels than those without asthma (21.5 ± 8.8 ng/mL vs 33.3 ± 13.2 ng/mL, $p < 0.001$). Figure 1 illustrates the distribution of vitamin D status according to the sample group. Vitamin D status was categorized as sufficient (≥30 ng/mL), insufficient (21–29 ng/mL), or deficient (<20 ng/mL).[20] A significantly higher proportion of asthmatic children exhibited vitamin D deficiency (51.1%) and insufficiency (34.7%) compared to non-asthmatic children (19.8% and 29.7%, respectively). The combined deficiency and insufficiency rate was substantially more significant in the asthma group (85.8%) than in the non-asthma group (49.5%). Conversely, the prevalence of vitamin D sufficiency was notably higher in the non-asthmatic group (50.5%) than in the asthmatic group (14.2%).

Table 1 Study Participant Characteristics Overall and by Group

Variable	Total (n=425)	Asthma (n=331, 76.6%)	Non-asthma (n=101, 23.4%)	p-value
Age, median (IQR), y	8 (5–10)	8 (5–12)	8 (5–12)	0.110
Sex, male, No. (%)	252 (58.3)	207 (62.5%)	45 (44.6%)	0.005
Weight, kg (mean ± SD)	28.0 (14.8)	28.2 (14.9)	27.2 (14.6)	0.285
Height, cm (mean ± SD)	124 (19.1)	124.4 (18.9)	123.7 (19.7)	0.389
BMI, kg/m2 (mean ± SD)	16.8 (4.5)	16.9 (4.6)	16.5 (4.0)	0.188
Vitamin D, ng/mL (mean ± SD)	23.9 (10.9)	21.5 (8.8)	33.3 (13.2)	<0.001

Abbreviations: IQR, interquartile range; y, year; No, number; kg, kilogram; SD, standard deviation; cm, centimeter; BMI, Body mass index; m2, square meter.

Vitamin D Status and Asthma

Table 2 presents the characteristics of asthmatic children stratified by vitamin D status. Children with vitamin D insufficiency/deficiency were significantly older, had higher weight, and had higher BMIs than those with normal vitamin D levels (all $p < 0.001$). No significant differences between the two groups were found regarding sex, family history of asthma, asthma severity, hospitalizations, PICU admissions, school absences, or asthma control.

Association of Vitamin D Status with Asthma Severity/Control

Figure 2 illustrates the observed significant differences in serum vitamin D level among non-asthmatic children and asthmatic children stratified by asthma severity (mild, moderate, severe; $p < 0.05$). Post-hoc analyses revealed significant differences between the non-asthmatic group and each asthma severity group (all $p < 0.05$). Exploration of the association between vitamin D status and asthma severity/control (Table 3) revealed a trend towards a higher proportion of children with vitamin D insufficiency/deficiency in the moderate/severe asthma and uncontrolled asthma groups. However, these differences did not reach statistical significance ($p = 0.255$ and $p = 0.099$, respectively).

Correlation and Univariate Analysis of Serum Vitamin D3 Association with Asthma Characteristics

Table 4 and Figure 3 present the significant negative correlations identified between serum vitamin D level and age ($r = -0.332$, $p < 0.001$), weight ($r = -0.292$, $p < 0.001$), height ($r = -0.298$, $p < 0.001$), and BMI ($r = -0.274$, $p < 0.001$)

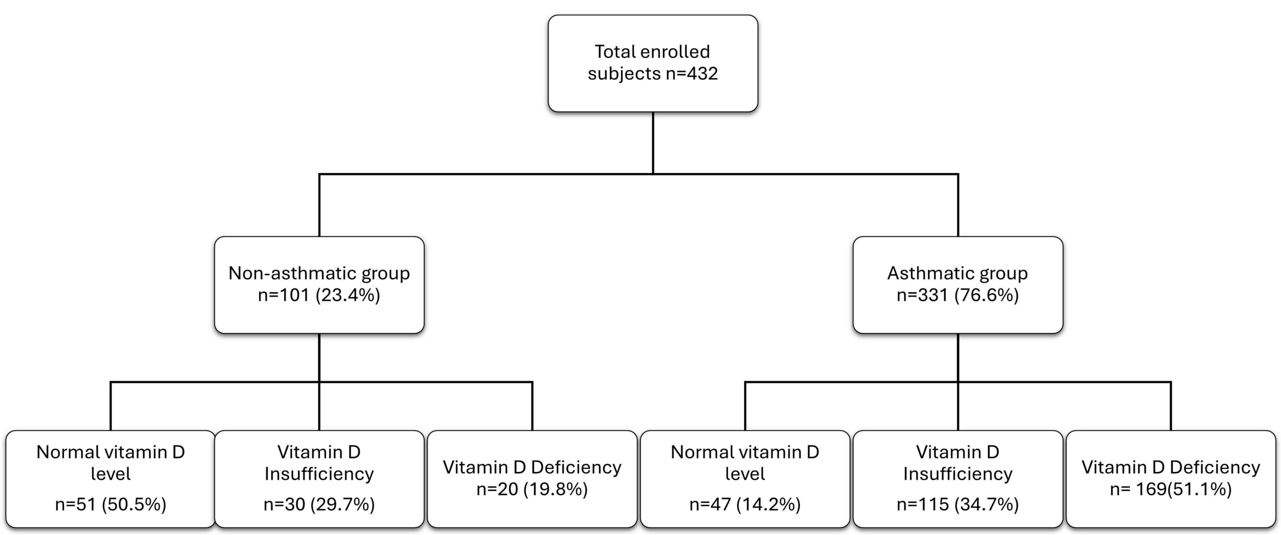

Figure 1 Flowchart of vitamin D status in asthmatic and non-asthmatic study participants.

Table 2 Asthmatic Patient Characteristics by Vitamin D Status (Normal Vs Insufficient/Deficient)

Variable	Normal D (No=47, 14.2%)	Insufficient D No=284, 85.8%)	p-value
Age, median (IQR), y	5 (3–8)	8 (6–10)	<0.001
Sex, male, No. (%)	29 (61.7%)	178 (63.1%)	0.852
Weight, kg (mean ± SD)	21.5 (13.3)	29.3 (14.9)	<0.001
Height, cm (mean ± SD)	114.1 (19.2)	126.1 (18.3)	<0.001
BMI, kg/m2 (mean ± SD)	15.0 (4.0)	17.3 (4.7)	<0.001
Overweight/obese (BMI percentile ≥85%), No. (%)	6 (12.8)	78 (27.5)	0.020
Family history of asthma, No. (%)	34 (72.3)	212 (74.6)	0.506
Asthma severity, No. (%)			
- Mild	19 (40.4)	84 (29.6)	0.198
- Moderate	20 (42.6)	142 (50.0)	0.257
- Severe	5 (10.6)	38 (13.4)	0.426
≥1 hospitalization for asthma exacerbation (ever), No. (%)	27 (57.4)	157 (55.3)	0.902
Any prior PICU admission, No. (%)	8 (17.0)	71 (25.0)	0.213
School missed days last year (total=1571 days), median (IQR)	5 (0–10)	5 (0–10)	0.461
Asthma control, No. (%)			
- Well-controlled	19 (40.4)	115 (40.5)	0.873
- Partially controlled	21 (44.7)	87 (30.6)	0.057
- Uncontrolled	4 (8.5)	55 (19.4)	0.041

Abbreviations: No, number; IQR, interquartile range; SD, standard deviation; BMI, body mass index; PICU, pediatric intensive care unit.

among asthmatic children. These findings were further supported by univariate linear regression analysis (Table 5), which demonstrated each of these variables to be a significant predictor of serum vitamin D level (all $p < 0.001$). Finally, the detailed results of the univariate models indicated that age in years ($\beta = -0.33$, $p < 0.001$), weight in kg ($\beta = -0.29$, $p < 0.001$), height in cm ($\beta = -0.30$, $p < 0.001$), and BMI in kg/m2 ($\beta = -0.27$, $p < 0.001$) are negatively associated with vitamin D level among asthmatic children.

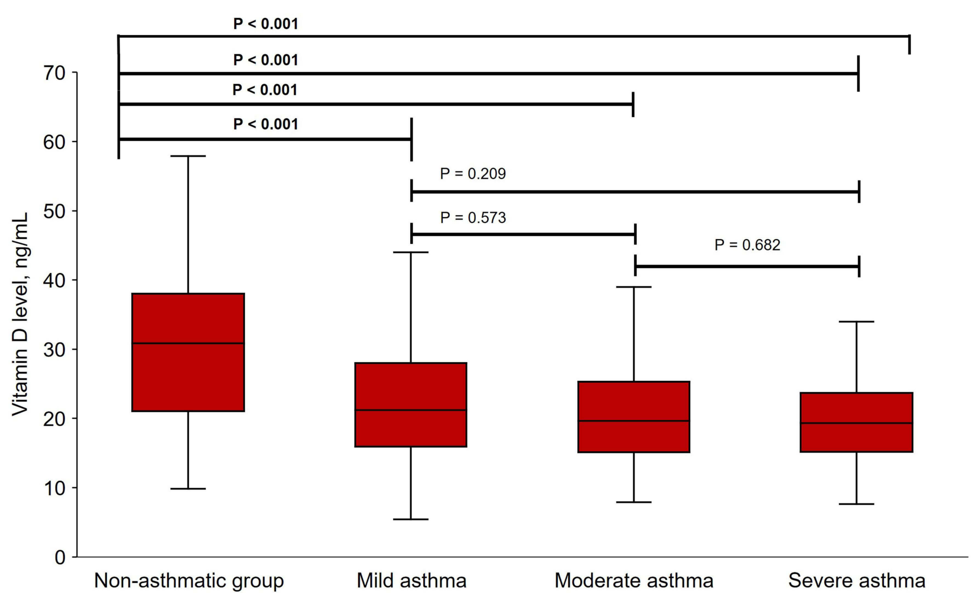

Figure 2 ANOVA of serum vitamin D levels between non-asthmatic and asthmatic groups, stratified by asthma severity (mild, moderate, severe) and with Bonferroni post hoc comparisons. Bold values indicate statistically significant differences (p < 0.05).

Table 3 Association Between Vitamin D Status and Asthma Severity/control

Variables Asthma severity/control	Vitamin D Category		
	Normal	**Insufficiency**	**Deficiency**
Mild (n=106), No. (%)	19 (17.9)	39 (36.8)	48 (45.2)
Moderate/severe (n=225), No. (%)	28 (12.4)	76 (33.8)	121 (53.8)
p-value	0.255		
Well-controlled (n=135), No. (%)	19 (14.1)	52 (38.5)	64 (47.4)
Partially controlled (n=107), No. (%)	21 (19.6)	32 (29.9)	54 (50.5)
Uncontrolled (n=58), No. (%)	3 (5.2)	21 (36.2)	34 (58.6)
p-value	0.099		

Table 4 Correlation of Serum Vitamin D3 Level with Asthma Characteristics

Variable	Pearson's Correlation Coefficient, r	p-value
Age, y	−0.332	<0.001
Weight, kg	−0.292	<0.001
Height, cm	−0.298	<0.001
Body mass index, kg/m2	−0.274	<0.001

Multivariable Analysis

Table 6 presents the results of the multivariable linear regression model examining factors associated with serum vitamin D levels. The model, adjusted for gender, asthma severity, and asthma control, explained 11% of the variance in vitamin D level ($R^2adj = 0.11$, $p < 0.001$). Age ($\beta = -0.66$, $p < 0.001$) and body mass index (BMI; $\beta = -0.25$, $p = 0.05$) emerged

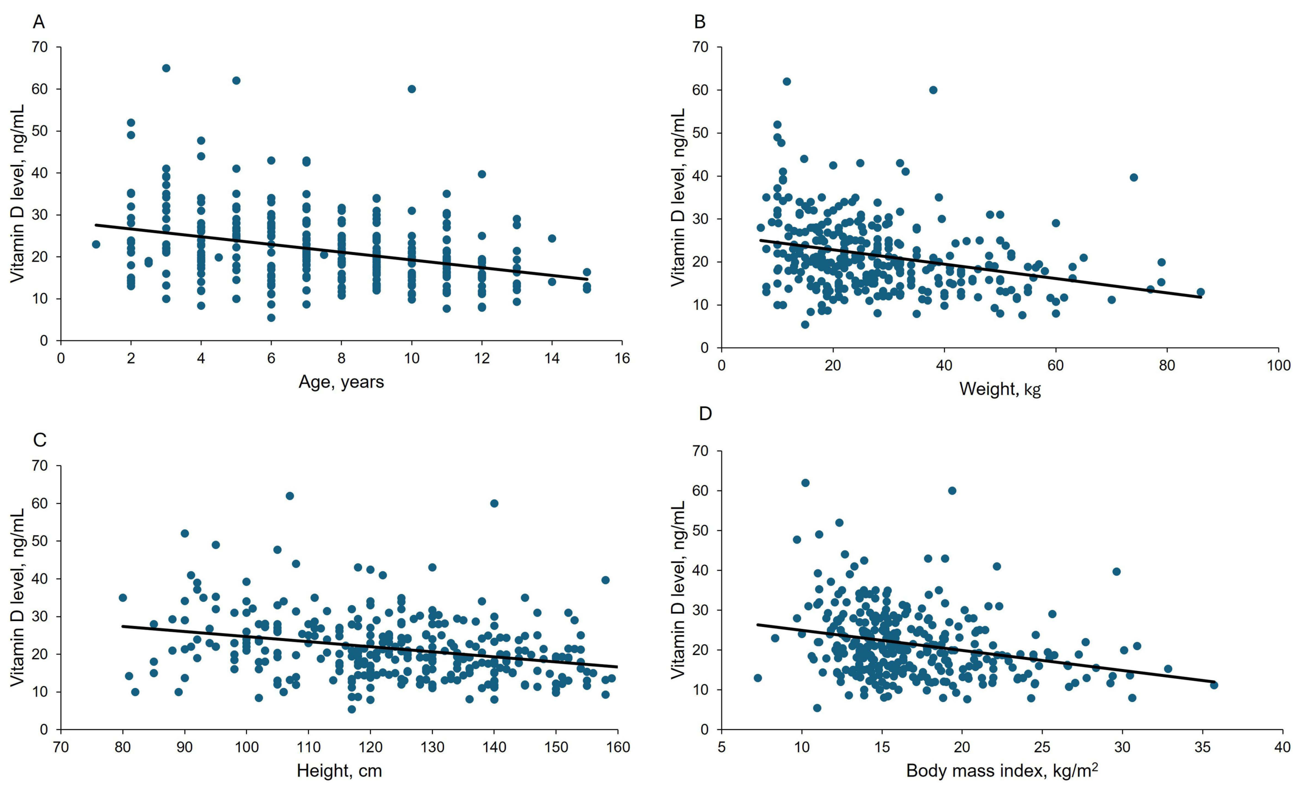

Figure 3 The scatter plot shows the relationship of vitamin D level with (**A**) age, (**B**) weight, (**C**) height, and (**D**) body mass index.

Table 5 Univariate Linear Regression Analysis of Associations Between Serum Vitamin D Level and Continuous Clinical Variables (N = 320)

Variable	B coefficient (standard error)	95% CI	β (t)	p-value
Age, y	−0.92 (1.2)	[−1.21, −0.64]	−0.33 (−6.34)	<0.001
Weight, kg	−0.17 (0.03)	[−.23, −0.11]	−0.29 (−5.45)	<0.001
Height, cm	−0.13 (0.02)	[−.18, −0.09]	−0.30 (−5.60)	<0.001
BMI, kg/m2	−0.50 (0.10)	[−.70, 0.31]	−0.27 (−5.09)	<0.001

Table 6 Multivariable Linear Regression Analysis to Identify Predictors of Serum Vitamin D Level (N = 317)

Variable	B coefficient (standard error)	95% CI	β (t)	p-value
(Constant)	30.35 (1.71)	[26.98, 33.72]	- (17.74)	<0.001
Age, y	−0.66 (0.20)	[−1.01, −0.30]	−0.24 (−3.62)	0.001
BMI, kg/m2	−0.25 (0.12)	[−.48, −0.01]	−0.13 (−1.90)	0.05

Note R^2_{adj} = 0.11 (N = 317, p < 0.001). CI: confidence interval for B. Adjusted for potential confounders (gender, asthma severity, and asthma level of control).

Table 7 Multivariable Logistic Regression Analysis of Associations Between Serum Vitamin D Level (Insufficiency/Deficiency) and Age > 6 and Overweight/Obese Status (N = 320)

Variables	Comparison	Univariable		Multivariable			
		OR	95% CI	p-value	aOR	95% CI	p-value
Age > 6 years	Yes vs no	3.46	1.8–6.5	<0.001	3.1	1.5–6.3	0.002*
Overweight/obese	Yes vs no	2.6	1.1–6.4	0.037	1.6	0.6–4.2	0.321

Note: The multivariable logistic regression model was adjusted for gender, asthma severity, and asthma control. Values of p < 0.05 are statistically significant.
Abbreviations: OR, odds ratio; aOR, adjusted odd ratio; CI, confidence interval.

as significant negative predictors of vitamin D status. These findings suggest that while age and BMI contribute to variations in vitamin D levels, unmeasured factors likely influence vitamin D status in this population. For each additional year of age, serum vitamin D decreased by an average of 0.66 ng/mL ($p < 0.001$), controlling for the effects of other variables in the model. Similarly, a one-unit increase in BMI was associated with a decrease of 0.25 ng/mL in serum vitamin D ($p = 0.05$). These findings suggest that older age and higher BMI are associated with lower vitamin D levels in the study population, even after accounting for other potential confounders. The predicted vitamin D level equals 30.35 + (−0.66 *age in years) + (−0.25 *BMI, kg/m2) per unit decrease in each factor. Furthermore, the logistic regression analysis indicated a significant association between vitamin D insufficiency/deficiency with age > 6 and overweight/obese status (Table 7). The multivariate analysis controlling for gender, asthma severity, and level of control further confirmed this trend.

Discussion

Prior observational studies and clinical trials have noted detrimental effects of vitamin D deficiency in pediatric asthma, both in terms of prevalence and severity, via the regulatory effects of this vitamin on the immune system.[7,22,23] The present study was designed to determine the prevalence of vitamin D deficiency in asthmatic children and evaluate the relationship of vitamin D status with asthma severity and control. A total of 331 asthmatics and 101 non-asthmatic children were included in this study. A significantly higher proportion of asthmatic children exhibited vitamin

D insufficiency or deficiency (85.8%) compared to non-asthmatic controls (49.5%). Correspondingly, mean serum vitamin D levels were significantly lower ($p < 0.001$) in the asthma group (21.5 ± 8.8 ng/mL) compared to the non-asthma group (33.3 ± 13.2 ng/mL). Significant negative correlations were observed between vitamin D level and age, weight, height, and BMI, suggesting an increased risk of vitamin D deficiency among older children with higher BMI. While a trend toward higher vitamin D deficiency rate in children with severe asthma was noted, this association did not reach statistical significance. Multivariable analysis confirmed age and BMI as independent predictors of vitamin D status, with older age and higher BMI associated with lower vitamin D levels.

The current study, conducted in southwestern Saudi Arabia, enrolled a pediatric population with asthma. Based on established vitamin D deficiency cutoffs (≤20 ng/mL),[6,20,23] 85.8% of asthmatic children had insufficient or deficient vitamin D levels, with 51.1% being deficient. In accordance with the present results, previous studies have demonstrated a prevalence of 40–80% for vitamin D deficiency among Saudi asthmatic children. Bindayel (2021),[18] in a study involving 60 asthmatic children aged 2–17 years, reported a high prevalence (52%) of vitamin D deficiency (defined as vitamin D level < 20 ng/mL). Aldubi et al[16] reported a substantial proportion (78%) of asthmatic children in Jeddah to have vitamin D deficiency (defined as level < 20 ng/mL), highlighting the high prevalence of this condition among that population. Irrespective of asthma and other pediatric health problems, vitamin D deficiency represents a substantial health risk for Saudi Arabian children.[14,15,17,24] These local findings align with previous regional research conducted in Qatar, which reported a substantial prevalence (68.1%) of vitamin D deficiency among asthmatic children.[11] Bener et al (2009) similarly observed a high incidence of vitamin D deficiency among Qatari children, with a notable increase in deficiency with advancing age.[11] Additionally, an Iranian study contrasting asthmatic and non-asthmatic children reported significantly lower mean serum vitamin D (14.53 ± 8.10 ng/mL) in the asthmatic group compared to controls (22.45 ± 13.46 ng/mL, $p < 0.001$) along with a high prevalence of vitamin D deficiency (73.6%) among the asthmatic children.[25] In contrast, the prevalence of vitamin D deficiency in the present study is higher than reports for Costa Rican and Nigerian children with asthma (3.4% and 0%, respectively).[26,27] The marked differences in vitamin D deficiency prevalence across studies are likely attributable to heterogeneity in study populations and sampling methodologies. However, caution must be applied with a cross-sectional study design, as the findings cannot prove a causal relationship between vitamin D deficiency and asthma. Therefore, a well-designed prospective cohort study is needed to answer this question clearly among the studied population. It is essential to screen children with established asthma diagnoses for vitamin D deficiency and provide vitamin D supplementation.

The current study recruited patients from a high-altitude area, Abha, at an average of 2270 meters above sea level (latitude 18°N). Despite being near the equator, this study observed elevated vitamin D deficiency prevalence, likely attributable to several factors, including dietary patterns, limited sun exposure due to traditional clothing and indoor activities, and obesity. The complex interplay of these variables, compounded by the region's high altitude and cold climate, contributes to the observed deficiency, even among healthy children.[17] There have been advancements in vitamin D food fortification, yet vitamin D insufficiency remains a significant public health concern. To elucidate the precise etiologies of this issue, particularly within the asthmatic pediatric population, further comprehensive community-based studies investigating dietary habits, sun exposure, and other relevant factors are warranted.

The age of the cases in this study ranged between 3 and 14 years, with a median of 8 and IQR of 5–10 years. Children with asthma and vitamin D deficiency exhibited significantly greater age compared to children with asthma and normal serum vitamin D ($p < 0.001$), in accordance with literature reports demonstrating that vitamin D deficiency prevalence increases with age.[18,24,26] This finding contradicts previous studies that reported no association between low vitamin D and age.[28,29] In the current study, the negative correlation between age and vitamin D level ($r = -0.332$, $p < 0.001$) persisted even after adjusting for possible confounders in a multivariate linear regression; it is, therefore, likely that age and serum vitamin D are connected. Hence, age could be a significant factor, if not the only one, contributing to vitamin D deficiency in this population of asthmatic children. Given the heterogeneous geographic distribution of the populations studied to date and the hospital-based nature of the cited studies, the generalizability of these findings to the broader asthmatic pediatric population should be interpreted with caution.

The present study also demonstrated that asthmatic children with vitamin D insufficiency or deficiency exhibit distinct characteristics compared to those with sufficient levels. Notably, vitamin D insufficiency/deficiency (defined as < 30 ng/mL) was significantly associated with weight, height, and BMI, indicating potential underlying factors that might influence both vitamin D status and asthma pathogenesis in older children. This finding is broadly supported by other studies in this area linking vitamin D deficiency with high BMI among Saudi asthmatic children.[16,18] Additionally, Brehm et al observed an inverse relationship between BMI and vitamin D levels among Costa Rican children with asthma.[26] These results likewise agree with studies from the US and Peru that reported higher BMI among asthma patients with lower serum vitamin D.[9,10] The association between asthma and obesity is complex, as both conditions are associated with inflammation and decreased serum 25(OH)D.[12,30] Given the lipophilic nature of vitamin D,[12] it seems possible that the association between vitamin D deficiency and high BMI in the current study is related to the large volume of distribution in these children and to the greater adipose tissue reservoir that can sequester large amounts of the vitamin. An alternative explanation is that the presence of asthma contributes to both high BMI and vitamin D deficiency. The final multivariable linear model in this study was adjusted for asthma severity, and the association between vitamin D and BMI remained significant; hence, it is likely that this association is present irrespective of asthma severity, particularly in this population. Finally, vitamin D deficient/insufficient children had high odds of being overweight/obese and more than six years of age. Accordingly, one can infer that asthmatic children > 6 years with high BMI (BMI percentile > 85%) should be supplemented with the recommended dosing of vitamin D (600–1000 IU/day of vitamin D3).[20]

The association of vitamin D with asthma prevalence, severity, and level of control has been an area of debate for many decades.[5] The current results showed mean serum vitamin D to be significantly higher in non-asthmatic children (33.3 ± 13.2 ng/mL) compared to asthmatic children (21.5 ± 8.8 ng/mL) ($p < 0.001$). No statistically significant differences in vitamin D status were observed among the various severity subgroups within the asthmatic population. Moreover, a trend that did not achieve significance was found between the vitamin D category and asthma control ($p = 0.099$). This finding broadly concurs with other studies in this area linking vitamin D deficiency with asthma severity. One such study was a secondary analysis of data from multicenter US clinical trials that enrolled children with established persistent asthma treated with inhaled steroids; this analysis found more significant improvement of lung function over one year in children with vitamin D sufficiency versus deficiency.[30] A temporal and causal relationship between vitamin D and asthma morbidity cannot be established from the present work, given its cross-sectional design; as such, additional research is needed to understand better the role of vitamin D in asthma morbidity among this population.

These data must be interpreted with caution because of several study limitations. Firstly, cross-sectional observational design increases the chance of bias, such as selection bias. Secondly, the study did not account for the influence of seasonal fluctuations or individual attributes such as patient ancestry, skin color, and detailed sun exposure on vitamin D levels. Thirdly, hospital-based recruitment and sampling techniques may limit the generalizability of the findings to the broader population. Therefore, further studies remain needed that take these limitations into account.

The findings of this study have significant public health implications. A nationwide recommendation for routine vitamin D screening in children with asthma, particularly obese children over six years of age, should be implemented to optimize health outcomes. The high prevalence of vitamin D deficiency among the study participants necessitates further public health research to comprehensively assess the extent of this medical problem, extending beyond individuals with asthma. Education and public health messaging are key to ensuring primary care physicians take steps to screen for vitamin D deficiency among children. In addition, a 2013–2014 survey study revealed that many commonly consumed food products in Saudi Arabia intended to be fortified with vitamin D are, in fact, either inadequately fortified or contain insufficient amounts compared to international guidelines.[31] Given the high prevalence of vitamin D deficiency and documented low intake among the Saudi population, implementing national strategies to enhance food fortification is imperative to mitigate the burden of this deficiency.

Conclusions

This study found a strikingly high prevalence of vitamin D deficiency among asthmatic children in southwestern Saudi Arabia, significantly exceeding rates in the control group. While a causal relationship cannot be definitively established due to the cross-sectional design, the consistent association of vitamin D deficiency with asthma and its correlations with age, BMI, and asthma severity suggests a potential role for vitamin D in asthma pathogenesis. These findings underscore the need for widespread vitamin D screening and supplementation in this population, particularly among older, overweight asthmatic children.

Data Sharing Statement

On reasonable request, the corresponding author will provide the datasets used and/or analyzed during the current work.

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Author Contributions

The author 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 author declares no conflicts of interest.

References

1. Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. *Front Pediatr*. 2019;7:246. doi:10.3389/fped.2019.00246
2. Global Asthma Network. *The Global Asthma Report*. 2018.
3. Alahmadi TS, Banjari MA, Alharbi AS. The prevalence of childhood asthma in Saudi Arabia. *Int J Pediatr Adolesc Med*. 2019;6:74–77. doi:10.1016/j.ijpam.2019.02.004
4. Olivier CE, Pinto DG, Teixeira APM, et al. Evaluating Non-IgE-Mediated Allergens' Immunoreactivity in Patients Formerly Classified as "Intrinsic" Asthmatics with Help of the Leukocyte Adherence Inhibition Test. *European J Clinical Medi*. 2023;4:1–7. doi:10.24018/clinicmed.2023.4.2.238
5. Paul G, Brehm JM, Alcorn JF, Holguín F, Aujla SJ, Celedón JC. Vitamin D and asthma. *Am J Respir Crit Care Med*. 2012;185:124–132. doi:10.1164/rccm.201108-1502CI
6. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007;357:266–281. doi:10.1056/NEJMra070553
7. Demirel S, Guner SN, Celiksoy MH, Sancak R. Is vitamin D insufficiency to blame for recurrent wheezing? *Int Forum Allergy Rhinol*. 2014;4:980–985. doi:10.1002/alr.21401
8. Mora JR, Iwata M, Von Andrian UH. Vitamin effects on the immune system: vitamins A and D take centre stage. *Nat Rev Immunol*. 2008;8:685–698. doi:10.1038/nri2378
9. Han YY, Forno E, Celedón JC. Vitamin D insufficiency and asthma in a US nationwide study. *J Allergy Clin Immunol Pract*. 2017;5:790–796. doi:10.1016/j.jaip.2016.10.013
10. Checkley W, Robinson CL, Baumann LM, et al. 25-hydroxy vitamin D levels are associated with childhood asthma in a population-based study in Peru. *Clin Exp All*. 2015;45:273–282. doi:10.1111/cea.12311
11. Bener A, Ehlayel MS, Tulic MK, Hamid Q. Vitamin D deficiency as a strong predictor of asthma in children. *Int Arch All Immunol*. 2012;157:168–175. doi:10.1159/000323941
12. O'Sullivan BP, James L, Majure JM, et al. Obesity-related asthma in children: a role for vitamin D. *Pediatr Pulmonol*. 2021;56:354–361. doi:10.1002/ppul.25053
13. Zhou Y, Qiu Y, Bao W, et al. Evaluating the effects of vitamin D Level on airway obstruction in two asthma endotypes in humans and in two mouse models with different intake of vitamin D during early-life. *Front Immunol*. 2023;14:1107031. doi:10.3389/fimmu.2023.1107031
14. Al-Hussaini AA, Alshehry Z, AlDehaimi A, Bashir MS. Vitamin D and iron deficiencies among Saudi children and adolescents: a persistent problem in the 21st century. *Saudi J Gastroenterol*. 2022;28:157–164. doi:10.4103/sjg.sjg_298_21
15. Hussain AN, Alkhenizan AH, El Shaker M, Raef H, Gabr A. Increasing trends and significance of hypovitaminosis D: a population-based study in the Kingdom of Saudi Arabia. *Arch Osteo*. 2014;9:190. doi:10.1007/s11657-014-0190-3
16. Aldubi HM, Alissa EM, Kamfar HZ, Gaber O, Marzouki ZM. Bronchial asthma and hypovitaminosis D in Saudi children. *Asia Pac Allergy*. 2015;5:103–113. doi:10.5415/apallergy.2015.5.2.103
17. Al-Qahtani SM, Shati AA, Alqahtani YA, et al. Prevalence and correlates of vitamin D deficiency in children aged less than two years: a cross-sectional study from Aseer Region, Southwestern Saudi Arabia. *Healthcare (Basel)*. 2022;10:1064. doi:10.3390/healthcare10061064

18. Bindayel IA. Effect of age and body mass index on vitamin D level in children with asthma in Riyadh. *Sci Rep*. 2021;11:11522. doi:10.1038/s41598-021-91108-3
19. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention: 2023 Full Report. 2023.
20. Al-Turki HA, Sadat-Ali M, Al-Elq AH, Al-Mulhim FA, Al-Ali AK. 25-Hydoxyvitamin D levels among healthy Saudi Arabian women. *Saudi Med J*. 2008;29(12):1765–1768.
21. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96:1911–1930. doi:10.1210/jc.2011-0385
22. Bantz SK, Zhu Z, Zheng T. The role of vitamin D in pediatric asthma. *Ann Pediatr Child Health*. 2015;3:1032.
23. Wu AC, Tantisira K, Li L, Fuhlbrigge AL, Weiss ST, Litonjua A; Childhood Asthma Management Program Research Group. Effect of vitamin D and inhaled corticosteroid treatment on lung function in children. *Am J Respir Crit Care Med*. 2012;186:508–513. doi:10.1164/rccm.201202-0351OC
24. Mansour MM, Alhadidi KM. Vitamin D deficiency in children living in Jeddah, Saudi Arabia. *Indian J Endocrinol Metab*. 2012;16:263–269. doi:10.4103/2230-8210.93746
25. Esfandiar N, Alaei F, Fallah S, Babaie D, Sedghi N. Vitamin D deficiency and its impact on asthma severity in asthmatic children. *Ital J Pediatr*. 2016;42:108. doi:10.1186/s13052-016-0300-5
26. Brehm JM, Celedón JC, Soto-Quiros ME, et al. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. *Am J Respir Crit Care Med*. 2009;179:765–771. doi:10.1164/rccm.200808-1361OC
27. Omole KO, Kuti BP, Oyelami OA, Adegbola AJ, Omole JO. Serum vitamin D profile of Nigerian children with asthma: association with asthma severity and control. *Pediatr Pulmonol*. 2018;53:544–551. doi:10.1002/ppul.23969
28. Turkeli A, Ayaz O, Uncu A et al. Effects of vitamin D levels on asthma control and severity in pre-school children. *Eur Rev Med Pharmacol Sci*. 2016;20(1):26–36.
29. Havan M, Razi CH, Bulus AD, Köksal AO, Andıran N. Effects of 25 hydroxy vitamin D levels on the severity and asthma control in school age asthma patients. *Arch Argent Pediatr*. 2017;115:336–342. doi:10.5546/aap.2017.eng.336
30. Migliaccio S, Di Nisio A, Mele C, Scappaticcio L, Savastano S, Colao A; Obesity Programs of nutrition, Education, Research and Assessment (OPERA) Group. Obesity and hypovitaminosis D: causality or casualty? *Int J Obes Suppl*. 2019;9:20–31. doi:10.1038/s41367-019-0010-8
31. Sadat-Ali M, Al Elq A, Al-Farhan M, Sadat NA. Fortification with vitamin D: comparative study in the Saudi Arabian and US markets. *J Family Community Med*. 2013;20:49–52. doi:10.4103/2230-8229.108186