

Effect of Vitamin D deficiency on asthma among children in Saudi Arabia

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KEYWORDS

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ABSTRACT

Asthma is a prevalent condition, impacting over 300 million individuals and their families. Genetic predisposition, early allergen exposure, infections, food, tobacco smoke exposure, pollution, and vitamin D levels are all suggested to affect the onset and severity of asthma. This study aims to ascertain the effect of vitamin D deficiency on asthma among Saudi children.

A cross-sectional study was performed in the several government hospitals in Asir region, such as Asir Central Hospital, Khamis Mushayt Civil Hospital, Ayha Women, Maternity and Children Hospital, and Khamis Women, Maternity and Children Hospital. The serum 25-hydroxyvitamin D concentration was measured in children aged 1 to 14 years diagnosed with bronchial asthma (ages 6 to 14) or recurrent wheezing episodes (under 6 years). The severity of asthma was assessed using the Global Initiative for Asthma evaluation, the Asthma Control Test, and the Childhood Asthma Control Test. Demographic and clinical data were examined between patients with low and normal 25-OH vitamin D levels, and the relationship between asthma severity and 25-OH vitamin D levels was evaluated.

Among the 400 children studied, 25-OH vitamin D levels were deficient in 240 (60%) and insufficient in 120 (30%) children. Only 40 children (10%) exhibited adequate levels of 25-OH vitamin D. A notable link exists between the severity of asthma symptoms and 25-OH vitamin D insufficiency.

Introduction

Asthma is a chronic, genetically diverse condition. Airway hyperresponsiveness (AHR) and persistent airway inflammation are the primary pathophysiological features of asthma. Both variables contribute to the manifestations of recurrent wheeze, dyspnea, chest tightness, and cough (Wang et al., 2022). Asthma affects all age groups, particularly during childhood, which is a critical period with the highest prevalence of the condition (Erick Forno et al., 2020). Recent estimates from the World Health Organization (WHO) indicate that there are over 334 million individuals with asthma globally. The global morbidity and mortality associated with asthma are projected to rise, with an anticipated increase of 100 million asthma sufferers by 2025 (Ripon et al., 2024).

In Saudi Arabia, a distinctive nation that has transitioned from a predominantly rural to a prosperous urban economy over the last fifty years, characterized by varied topographic features and climatic conditions, the prevalence of allergic disorders, including asthma, is anticipated to be elevated due to industrialization, westernization, and shifts in population lifestyle, similar to trends observed in developed countries (Alomary et al., 2022). The highest asthma prevalence rates among Saudi children are observed in Hofuf (33.7%), Najran (27.5%), and Madinah (23.6%),

whereas the lowest rates are recorded in Abha (9%), a rural southern mountainous area, Qassim (3.2%), a northern rural oasis renowned for agriculture, and Dammam (3.6%) (Mohamed Hussain et al., 2018). The elevated prevalence of asthma is associated with various risk factors, including socioeconomic level, urbanization, dietary practices, lifestyle modifications, heightened exposure to tobacco smoke, sandstorms, dust, and vehicular or industrial pollution (Al-Moamary et al., 2021; Alahmadi et al., 2023; Gohal et al., 2024).

Research undertaken over the last three decades among Saudi youngsters indicates that the general prevalence of asthma has varied between 8% and 25% (Alahmadi et al., 2023). An analysis indicates that the frequency of childhood asthma varies across different regions of Saudi Arabia. The male gender, pet ownership, dietary practices, and environmental exposure are correlated with an increased prevalence of asthma (Mohamed Hussain et al., 2018).

Vitamin D is derived from two sources: cutaneous exposure to ultraviolet B radiation and nutritional consumption. Dietary sources comprise fish oil, fish, liver, egg yolk, and dietary supplements (Demay et al., 2024). Due to the scarcity of foods containing vitamin D, exposure to sunlight is the principal factor influencing vitamin D levels in people. In individuals with fair skin, an estimated 20 to 30 minutes of midday sunshine exposure on the face and forearms can produce approximately 2000 IU of vitamin D. Two or three exposures to sunshine per week are adequate to attain optimal vitamin D levels during the summer in the UK. In the absence of sufficient sun exposure, a daily intake of at least 800–1000 IU (20–25 mg) of vitamin D may be required to attain this level (Benedik, 2022).

Vitamin D modulates calcium and phosphorus equilibrium and osseous metabolism. Furthermore, recent studies indicate that it possesses significant immunomodulatory effects, which suppress airway inflammation, enhance airway hyperresponsiveness, diminish glandular secretion, curtail the proliferation of bronchial smooth muscle cells, ameliorate airway remodeling, and augment the body's hormonal response (Bouillon et al., 2022). Recent epidemiological studies indicate that vitamin D deficiency may contribute to the development of many lung disorders, as researchers investigate the pathophysiology of asthma. Research indicates that vitamin D facilitates lung growth and enhances lung function. Maternal consumption of adequate vitamin D during gestation diminishes the likelihood of early asthma development in the infant (Ismailova & White, 2022).

The impact of vitamin D as a hormone has garnered heightened interest. In addition to its established functions (calcium absorption, bone mineralization, and neuromuscular function regulation) and non-classical actions (cellular differentiation, insulin secretion, and blood pressure regulation), vitamin D is also considered a significant regulator of the immune system, potentially influencing various allergic diseases (Ao et al., 2021). Vitamin D appears to exert regulatory effects on all components of the immune system, while vitamin D deficiency has been associated with several immunologically-based illnesses, including asthma. Regrettably, vitamin D insufficiency is prevalent in most Middle Eastern nations, despite ample sunlight, owing to the avoidance of sun exposure and the adoption of disguised clothing styles. Nonetheless, insufficient vitamin D levels have been documented despite sufficient sun exposure (LeBoff et al., 2022).

The purpose of this study is to investigate whether or not a lack of vitamin D is associated with asthma in Saudi children.

Patients and methods

Study population, design and setting

The Asir Central Hospital, Khamis Mushayt Civil Hospital, Ayha Women, Maternity and Children Hospital, and Khamis Women, Maternity and Children Hospital were the location where this cross-sectional study was carried out between 2022 and 2023. The participants in this study were

consecutive paediatric patients between the age range of 1 to 14 years old who were experiencing symptoms of asthma or wheezing.

Inclusion criteria

According to the criteria established by the Global Initiative for Asthma (GINA), patients were required to have a prior diagnosis of asthma and/or recurrent wheezing episodes (early asthma) in order to be eligible for participation in the study. (1) a physician's diagnosis of asthma; (2) symptoms of recurring (i.e., more than two) bouts of wheezing, cough, shortness of breath, or a combination of these; (3) confirmed reversibility with bronchodilators; and/or (4) usage of medicine for asthma in the last 6 months (Bateman et al., 2008).

Exclusion criteria

The study did not include any participants who were taking vitamin D supplements at the time of treatment. Additionally, a comprehensive physical examination was carried out on each individual patient, and full personal medical histories were documented for each of them. In addition, participants in the study were administered a screening to determine whether or not they had any other allergy illnesses besides asthma. These conditions included allergic rhinitis, atopic dermatitis/eczema, allergic conjunctivitis, and food allergies. In addition, a history of nursing over the course of the first six months of life was investigated.

The severity of asthma and the ability to control symptoms were evaluated using the following criteria: the GINA classification (Bateman et al., 2008), a validated Asthma Control Test (ACT) questionnaire in children aged 12 years or older, or the Childhood Asthma Control Test (C-ACT) in children aged between 4 and 11 years; (Lababidi et al., 2008) the utilization of systemic steroids; and admission to the hospital due to asthma within the past year. Within the framework of the GINA classification, patients were classified into one of four categories: intermittent asthma, mild persistent asthma, moderate persistent asthma, or severe persistent asthma. In the context of the ACT/C-ACT, a score of 19 or less was regarded to indicate weak control, whereas a score of 19 or more was considered to indicate good control.

Vitamin D measurement

Vitamin D levels were assessed by measuring serum 25-hydroxycholecalciferol (25-OH vitamin D), a vitamin D metabolite considered to be a reliable measure of serum vitamin D level. A venous blood sample (10 ml) was obtained; the blood was allowed to clot for 60 min, then serum was separated by centrifugation at 2000 rpm for 20 min at 4°C and stored at -70°C until analysis. Serum 25-OH vitamin D was measured using a Liaison® 25-OH Vitamin D Total assay kit with the Liaison® rapid automated assay system (DiaSorin, Stillwater, MN, USA), which utilizes a chemiluminescence immunoassay to detect both forms of 25-OH vitamin D (D2 and D3). Based on published guidelines and recommendations from previous studies, 25-OH vitamin D levels were categorized as deficient (<20 ng/ml), insufficient (20–29 ng/ml), or sufficient (>29 ng/ml) (Barake et al., 2012).

Statistical analyses

The study population sample size was calculated using OpenEpi software, version 3.0 (www.OpenEpi.com, updated 6 April 2013). The required sample size was calculated to be 400 patients (confidence level of 95%, $Z_{0.95} = 1.96$). Data are presented as mean $\pm$ SD for continuous variables and frequencies and percentages for categorical variables. 25-OH vitamin D deficiency in children with bronchial asthma is presented as frequency distributions.

Results

Significant insights into pediatric patients with wheeze or asthma can be derived from the demographic and clinical attributes of the research sample. The mean age is 6.8 years, with a

marginal predominance of males over females (55% males and 45% females). Patients frequently experience concomitant allergy diseases. Allergic rhinitis impacts around 45% of patients, followed by eczema/atopic dermatitis at 35%, conjunctivitis at 22.5%, and food allergy at 17.5%. A significant majority of patients (65%) utilize inhaled corticosteroids, indicative of the chronic nature of asthma affecting many individuals. Forty percent of the group exhibited exclusive breastfeeding during the initial six months. The distribution of asthma severity, based on the GINA categorization, was as follows: 22.5% with intermittent asthma, 32.5% with mild persistent asthma, 27.5% with moderate persistent asthma, and 17.5% with severe persistent asthma. The distribution of asthma severity reveals a broad spectrum, with a considerable proportion of individuals necessitating ongoing treatment.

Table 1 presents the demographic and clinical features of 400 pediatric patients who were diagnosed with wheeze (with ages ranging from 1 to 14 years) or asthma.

Characteristic	Study population (n = 400)
Age, years	Mean (SD): 6.8 (3.4)
Sex, male/female	220/180 (55%/45%)
Associated allergic conditions:	
Allergic rhinitis	180 (45%)
Conjunctivitis	90 (22.5%)
Food allergy	70 (17.5%)
Eczema/atopic dermatitis	60 (15%)
Use of inhaled corticosteroids	260 (65%)
Exclusive breastfeeding during first 6 months	160 (40%)
GINA classification, n = 400:	
Intermittent	90 (22.5%)
Mild persistent	130 (32.5%)
Moderate persistent	110 (27.5%)
Severe persistent	70 (17.5%)

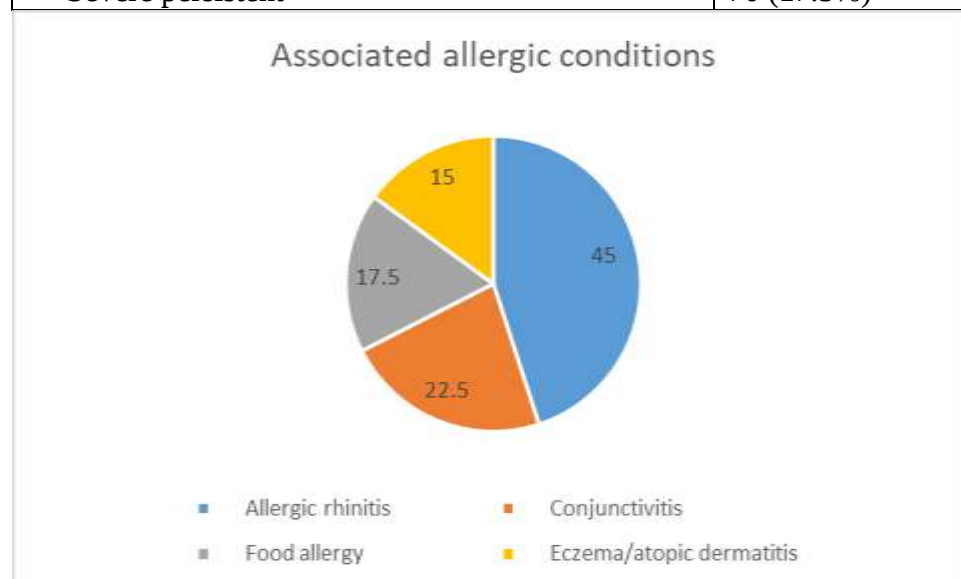


Figure 1. Associated allergic conditions among 400 children.

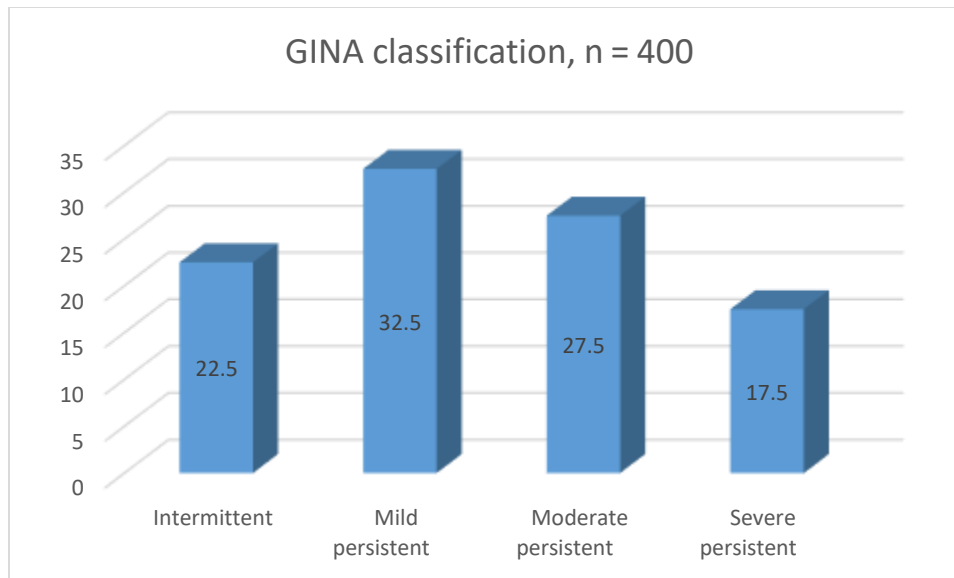


Figure 2. GINA classification among 400 children.

Four hundred pediatric patients were diagnosed with asthma or wheeze, and Table 2 illustrates the distribution of vitamin D status and age among these individuals. Sixty percent of the patients were classified as having vitamin D deficiency, defined as levels below 20 ng/ml. Thirty percent had inadequate levels, ranging from 20 to 29 ng/ml, while just ten percent demonstrated appropriate levels exceeding 29 ng/ml. The mean age among the groups displayed a notable variance, with the deficient group presenting a mean age of 7.5 years and a substantial standard deviation (± 12.7 years), signifying a wide age range. In the insufficient group, the mean age was 5.2 years, indicating a lower average. Conversely, the group deemed sufficient exhibited the greatest mean age of 8.5 years.

Table 2. Comparison of frequencies and age among 400 pediatric patients with asthma or wheeze, classified by serum 25-OH vitamin D levels.

Vitamin D Status	Frequency	Age, years
Deficient (<20 ng/ml)	240 (60%)	7.5 $\pm$ 12.7
Insufficient (20–29 ng/ml)	120 (30%)	5.2 $\pm$ 6.1
Sufficient (>29 ng/ml)	40 (10%)	8.5 $\pm$ 2.2

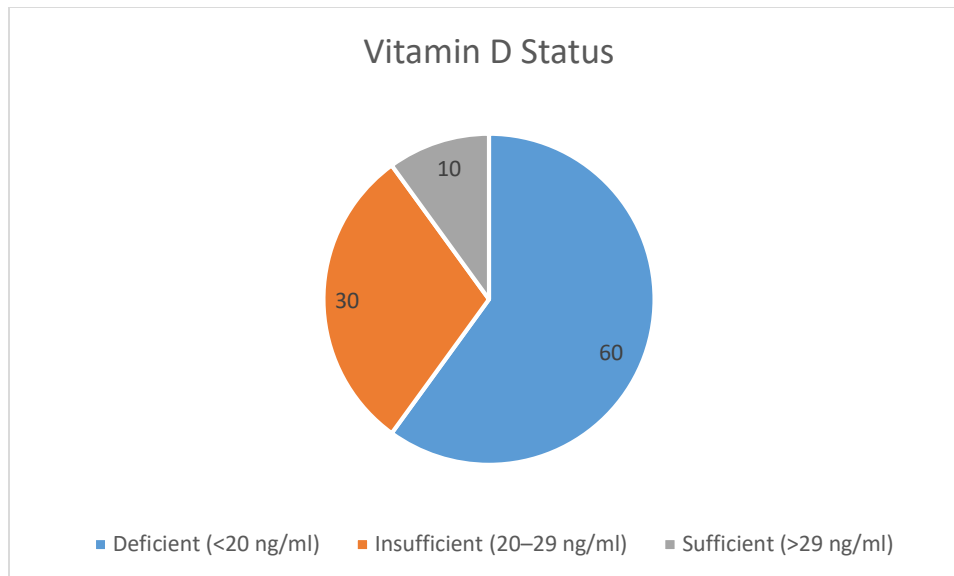


Figure 3. Vitamin D Status among 400 pediatric patients with asthma

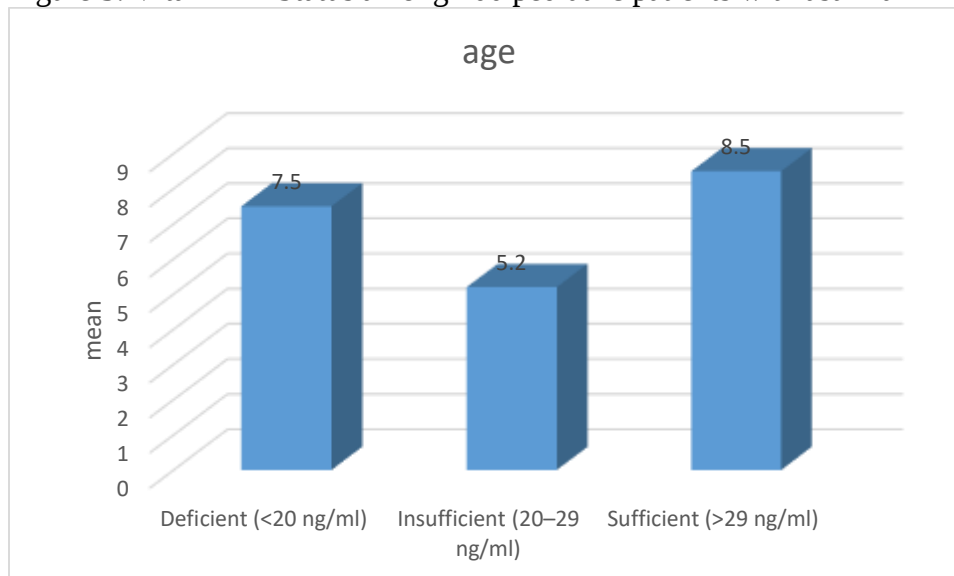


Figure 4. Mean age among 400 pediatric patients with asthma

Discussion

This cross-sectional study evaluated serum 25-OH vitamin D concentrations in children with bronchial asthma or wheezing episodes in Saudi Arabia. A significant prevalence of 25-OH vitamin D deficiency (<20 ng/ml) and insufficiency (20–29 ng/ml) was noted in children with asthma. Consequently, adequate levels of 25-OH vitamin D (≥ 30 ng/ml) were observed in just 10% of these patients. This study aligns with other research indicating that vitamin D insufficiency is widespread among children with asthma in several global regions, especially in the Middle East (Bassil et al., 2013).

A research in Qatar revealed that 52.9% of children with bronchial asthma exhibited inadequate levels of 25-OH vitamin D (Bener et al., 2012). A comparable study in Turkey indicated that 67% of children with asthma exhibited deficient levels of 25-OH vitamin D, while 20% were classified as insufficient in 25-OH vitamin D (Uysalol et al., 2013). Global reports have also corroborated

the significant incidence of 25-OH vitamin D insufficiency in children with asthma (Litonjua, 2012).

An aim of the present study was to determine whether a correlation could be established between 25-OH vitamin D levels and different demographic and clinical characteristics in the study population. Age was the sole significant relation of 25-OH vitamin D levels, with younger children exhibiting elevated serum 25-OH vitamin D concentrations. This aligns with studies from other nations, including the USA, the UK, and New Zealand, where the incidence of poor vitamin D status escalates with age, particularly affecting teens the most (Spiro & Buttriss, 2014).

In terms of the correlation between vitamin D deficiency and asthma severity, a study demonstrates a substantial association between the severity of asthma assessed by the GINA classification and 25-OH vitamin D deficiency status. Children with severe and moderate chronic asthma exhibited a higher likelihood of 25-OH vitamin D insufficiency compared to those with intermittent or mild asthma. This association was also notable in other indicators of asthma severity; children with diminished 25-OH vitamin D levels were more inclined to utilize systemic steroids for managing asthma exacerbations, and those exhibiting inadequate asthma control (assessed via ACT/C-ACT scores) demonstrated reduced vitamin D levels. Patients with insufficient vitamin D levels exhibited a greater rate of hospital admissions and systemic corticosteroid usage compared to those with appropriate levels; nevertheless, the difference lacked statistical significance. This may have resulted from the comparatively limited sample size in the current study population (Al-Zayadneh et al., 2020).

A substantial Childhood Asthma Management Program (CAMP) study examined the correlation between serum 25-OH vitamin D levels and subsequent severe asthma exacerbations or hospitalizations, revealing that 25-OH vitamin D deficiency correlates with an increased incidence of severe exacerbations in asthmatic children (Brehm et al., 2010).

In contrast to the current findings, certain studies have indicated inverse relationships or a lack of associations between asthma or recurrent wheeze and vitamin D levels, which may illustrate the variability of asthma, variations among populations, research methodology, or diagnostic instruments. Prior clinical trials of vitamin D supplementation demonstrated inconsistent results. Certain research indicate that prenatal vitamin D administration or supplementation during infancy leads to improved lung function and asthma management in childhood (E. Forno et al., 2020).

Conclusion

The current findings indicated that vitamin D deficiency was significantly widespread among pediatric asthma patients, and a correlation was established between vitamin D deficiency and asthma severity in children. These findings indicate the significant role of vitamin D in the etiology and severity of asthma and potentially other allergy disorders. Consequently, evaluating blood 25-OH vitamin D levels in individuals with bronchial asthma is crucial and may enhance assessment, monitoring, and treatment. This observational study indicates that additional research is necessary to elucidate the impact of low vitamin D levels on asthma among the Saudi community. Future studies should evaluate the impact of vitamin D supplementation on asthma severity and symptom management.

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