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RESEAECH ARTICLE **CLINICAL BIOCHEMISTRY**

Association of Vitamin D Levels with Asthma Control among Pediatric Patients in Wadi Al-Shatti, Libya

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ABSTRACT

Background: Asthma is the most common chronic inflammatory respiratory diseas in children. It has significant impact on morbidity and reduced quality of life worldwide. While recent research has highlighted the potential of vitamin D as an immunomodulator in asthma pathophysiology and control, the evidence remains controversial. Furthermore, data regarding this relationship in North African populations, particularly in Libya, are notably limited. **Objective:** This study aimed to investigate the relationship between vitamin D status and asthma control among asthmatic children and adolescents in Wadi Al-Shatti region, southern Libya. It further sought to assess serum 25-hydroxyvitamin D (25(OH)D) levels and their associated factors, as well as exploring the correlation of the targeted cases with immunological responses and key biochemical indicators. **Methods:** A total of 50 children aged 1–15 years were enrolled in this observational study. Participants were identified and recruited from Brack General Hospital and Qaqam General Hospital. Data collection was performed in two intervals: January–March 2023 and December 2023–March 2024. Asthma control was assessed according to the GINA guidelines and the Childhood Asthma Control Test (C-ACT). Laboratory investigations included serum 25-hydroxyvitamin D, total immunoglobulin E, calcium, phosphorus, alkaline phosphatase, and complete blood count. Statistical significance was defined as $p < 0.05$ using SPSS version 26. **Results:** Among the 50 participating children, the majority of participants were males (64%), compared to female (36%), of whom 80% presented with uncontrolled asthma. Vitamin D deficiency was highly prevalent, with the majority of targeted individuals exhibiting serum levels below 20 ng/ml. A significant correlation was found between vitamin D levels and asthma control, with lower levels more frequently identified in children with uncontrolled disease. Furthermore, significant associations were identified between vitamin D levels and serum IgE concentrations, as well as serum phosphorus levels. Additionally, red blood cell counts showed a significant association with vitamin D status, whereas calcium and alkaline phosphatase levels remained non-significant. **Conclusion:** Children with poor asthma control have a high incidence of vitamin D deficiency. These findings suggest that vitamin D status may represent an important modifiable factor influencing asthma outcomes in paediatric populations.

علاقة التغير في مستويات فيتامين د بمستوى السيطرة على الربو لدى الأطفال المصابين بالربو في منطقة وادي الشاطئ

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الكلمات المفتاحية
السيطرة على الربو
فيتامين د
الأطفال
وادي الشاطئ
ليبيا

الملخص

الخلفية: يعد الربو من أكثر حالات أمراض الجهاز التنفسي التي تصيب الأطفال. إذ ينجم عنه أضرار وخيمة تهدد جودة الحياة في كافة أنحاء العالم. بينما يوجد هناك عدد من الدراسات التي سلطت الضوء على الدور المحتمل لفيتامين د كمنظم ومتحكم مناعي لبعض الوظائف الجهازية لمرضى الربو، وجود دليل قاطع لهذه العلاقة لازال محل جدل. إضافة الى ذلك، هناك ندرة ومحدودية في البيانات حول العلاقة بين التغير في مستوى فيتامين د والإصابة بالربو في شمال أفريقيا، خاصةً في ليبيا. **الهدف:** هدفت هذه الدراسة الى معرفة العلاقة بين حالة فيتامين د والإصابة الربو بين أطفال الربو بمنطقة وادي الشاطئ، جنوب ليبيا. تطلبت الدراسة قياس مستويات 25 هيدروكسي فيتامين د والعوامل المرتبطة بها، كما استهدفت الدراسة الكشف عن علاقة هذه المستويات بالاستجابة المناعية للمرضى وبعض المؤشرات الكيميائية الحيوية المهمة. **الطرق:** استهدفت الدراسة الحالية 50 طفل من أطفال الربو المترددين على كل من مستشفى براك العام ومستشفى قمم العام خلال فترتين زمنيتين (يناير-مارس 2023، ديسمبر 2023- مارس 2024). تراوحت أعمارهم 1-15 سنة. تم تقييم مستويات التحكم في مرض الربو في هذه الدراسة وذلك بالاعتماد على القياسات الموضوعة من قبل منظمة (جينا) بناءً على مقياس درجة التحكم في مرض الربو. تم في هذه الدراسة إجراء القياسات الكيميائية الحيوية في المصل (25 هيدروكسيفيتامين د، الجلوبيلون المناعي E، الكالسيوم، الفوسفور، الفوسفاتيز القاعدي، و الصورة الدموية الكاملة

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للدم. تم تحديد العلاقات الإحصائية بالإعتماد على قيمة الإحتمالية p باستخدام التطبيق الاحصائي SSP (الإصدار 26).
النتائج: من إجمالي العينات المستهدفة في الدراسة، 64% كانوا ذكور، 36% إناث. من إجمالي الحالات المستهدفة للدراسة، سجلت حالات الربو الغير مسيطر عليه 80% ، وغالبية هذه الحالات شهدت معدلات عالية للنقص فيتامين د (أقل من 20 نانوجرام/ مليمتر). أظهرت نتائج الدراسة وجود علاقة جوهرية بين مستويات فيتامين د ومستويات السيطرة على الربو، حيث كان هناك ارتباطاً جوهرياً بين المستويات المنخفضة لفيتامين د مع حالات الربو الغير مسيطر عليه. إضافة الى ذلك، تبين من خلال النتائج علاقة إحصائية قوية بين النقص في مستويات فيتامين د والجلوبيولين المناعي E في المصل، وكذلك مستوى الفوسفور المصلي. كما أن تعداد الخلايا الدم الحمراء شهد انخفاضاً ذو دلالة إحصائية في الحالات التي تعاني من نقص فيتامين د، في حين مستويات الكالسيوم والفوسفاتيز القاعدي لم تظهر تأثراً. **الاستنتاجات:** الأطفال الذين يعانون من الربو بمستويات غير متحكم فيها لديهم مستويات منخفضه من فيتامين د. نتائج هذه الدراسة تسلط الضوء على أن التغير في فيتامين د لدى حالات الربو المستهدفة يعد مؤشراً جوهرياً للدور المحتمل للتغير في مستويات فيتامين د كأحد العوامل الجوهرية المسببة للربو لدى الأطفال.

Introduction

Asthma is a common chronic inflammatory disease of the airways affecting more than 330 million individuals worldwide and represents the most common non-communicable disease in children. It substantially impairs the quality of life of children with Asthma [1]. It is characterized by persistent airway inflammation, airway hyper-responsivity (AHR) which leads to recurrent episodes of wheezing, shortness of breath, coughing, airflow limitation, and bronchospasm [2, 3]

Although asthma most commonly develops during childhood, it can occur at any stage of life. The incidence and prevalence of asthma vary by sex; rates are often higher in boys before puberty, then reverse during adolescence, with females tending to experience a more sustained disease burden in adulthood [4, 5].

The pathogenesis of asthma is a complex and multifactorial disorder that involves both genetic and environmental factors, including allergens, viral infections, and air pollution [6, 7]. Biologically, it is mediated by a type 2 helper T-cell (Th2) response, characterized by IgE production, eosinophilic airway inflammation, and chronic airway remodeling [8]. Clinically, asthma control is a description of the current state of symptom minimization through treatment, whereas asthma severity indicates the stable level of treatment required to manage the disease [9, 10]. Poor control and increased severity are often linked to genetic, environmental, and atopic factors [11].

Globally, asthma is among the top twenty chronic conditions responsible for pediatric disability. Its prevalence shows substantial geographic variation, influenced by seasonal patterns, with higher incidences typically reported during autumn and winter [12-15].

Parallel to the increasing prevalence of asthma, vitamin D deficiency has emerged as a major global public health issue, particularly among children. Beyond its classical role in calcium and bone metabolism, vitamin D plays a critical role in immune regulation [16]. Vitamin D receptors (VDRs) are widely expressed in immune cells, including macrophages, dendritic cells, and activated T and B lymphocytes, allowing vitamin D to modulate both innate and adaptive immune responses [17-19].

Vitamin D exerts anti-inflammatory effects by suppressing Th17 immune responses and interleukin-17 (IL-17) production, while enhancing regulatory T-cells and interleukin-10 (IL-10). Furthermore, it inhibits the maturation of dendritic cells, eosinophils, neutrophils, and airway smooth muscle, thereby attenuating airway hyper-responsiveness and airway remodeling [20, 21, 22]. Extensive literature confirms that low levels of vitamin D are associated with increased asthma prevalence, severity, and poor lung function [23, 24, 25, 26]. Various global studies have demonstrated the high prevalence of this deficiency among asthmatic children, suggesting its potential as a biomarker for predicting exacerbations [27, 28].

Despite the growing global interest in the link between low levels of vitamin D and asthma pathophysiology, evidence from North Africa, particularly Libya, remains notably scarce. While the prevalence of adult asthma in Libya has been documented using the modified ISAAC questionnaire [29], there is a critical absence of research addressing pediatric and adolescent populations. Specifically, no prior studies have evaluated the prevalence of asthma, the level of disease control, or its association with vitamin D status among children in this region.

Given the increasing global burden of childhood asthma, the high prevalence rate of vitamin D deficiency, and the lack of pediatric data from southern Libya, this study aimed to determine the prevalence of vitamin D deficiency among children with asthma attending Brack General Hospital and Qaqam General Hospital. It also sought to establish the demographic, clinical, and laboratory characteristics of the study population, to examine the association between serum vitamin D levels and asthma severity and control, and to evaluate the relationship between asthma severity and selected demographic and laboratory variables.

Methodology

This study was conducted targeting two General Hospitals belonged to two municipalities in Wadi Al-Shatti, southwestern Libya. This region is predominantly rural and characterized by an arid desert climate. The local population primarily depends on agriculture and livestock farming.

Children with a confirmed asthma diagnosis attending Brack General Hospital and Qaqm General Hospital were enrolled in this observational study. During two time periods: January–March 2023 and December 2023–March 2024, Children aged 1–15 years with a physician-confirmed diagnosis of asthma were recruited for the study. A total of 50 children were included in the study, with verbal informed consent obtained from parents or guardians before participation.

Demographic, behavioral, and clinical data were collected using a structured questionnaire completed by their caregivers. Data included age, gender, socioeconomic status, and dietary habits, with particular emphasis on vitamin D, a clinical history of asthma, and a history of hospitalizations. Anthropometric measurements were also taken, and body mass index (BMI) was calculated and categorized using age- and gender-specific WHO growth charts.

Every individual participant was subjected to Asthma control

assessment according to the Global Initiative for Asthma (GINA) guidelines as follows: the Childhood Asthma Control Test (C-ACT) was used to assess symptom control over the past four weeks and to categorize asthma as controlled, partially controlled, or uncontrolled.

Sampling was aseptically performed for all the participants. Laboratory tests included a complete blood count and measurements of 25-hydroxyvitamin D, total immunoglobulin E, calcium, phosphorus, and alkaline phosphatase were utilised using standardized automated equipment.

Informed consent was taken from all the participants' parents or legal guardians. Ethical clearance for this study was approved by the Ethics Committee of the University of Wadi Al-Shatti and conducted according to the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analysis of the study was done using SPSS software version 26. Continuous variables were presented as mean ± SD, whereas categorical variables were presented as frequencies and percentages. A p-value <0.05 was considered statistically significant for the study.

Results

Out of overall samples targeted in this work (n = 50), males accounted for 64% over that those females (36%), as shown in Table 1.

The targeted cases classified into three age categories according to the World Health Organization (WHO) classifications, and 14% of the cases fell within the first age group (1 to <2 years), 24% fell within the second group (2 to <6 years), the third group (6 to <11 years) accounted for 38%, and the fourth group (>11 years) represented 24% (Figure 1). In this study, the severity of asthma was assessed using the Asthma Control Test [30]. Accordingly, 80% of the asthma cases in the current study classified as "uncontrolled" group, while the remaining (20%) were categorised as "controlled" asthma group. The results showed that the mean age was 6.96 ± 3.83 years for the participants suffered from uncontrolled asthma and 7.25 ± 3.49 years for those under control. Statistical analysis revealed no significant differences between the two groups (p<0.05). Similarly, the Body Mass Index (BMI) showed no significant differences between the uncontrolled and controlled groups, with mean BMI values of 15.88 ±2.701 kg/m² and 17.626 ±8.414 kg/m², respectively, as shown in Table 2. Based on BMI growth charts, study participants were divided into three weight categories: (1) Normal-weight children, accounted for 68% (34 participants), (2) underweight children at 26% (13 participants), and (3) the obesity individuals were the smallest cases at just 6% (3 participants) (Figure 1).

Table 1: Demographic Characteristics of Study cases

Variable	Category	No. of cases (%)
Gender	Male	32 (64%)
	Female	18 (36%)
Age Groups (WHO)	Group 1 (1 – <2 years)	7 (14%)
	Group 2 (2 – <6 years)	12 (24%)
	Group 3 (6 – <11 years)	19 (38%)
	Group 4 (>11 years)	12 (24%)
Asthma Control Status	Uncontrolled	40 (80%)
	Controlled	10 (20%)

Finding of present study allowed analysing the relationship between gender and Vitamin D, and no significant association was found between male and female neither among those with normal Vitamin D concentrations nor and the abnormal (deficient) levels (p>0.05).

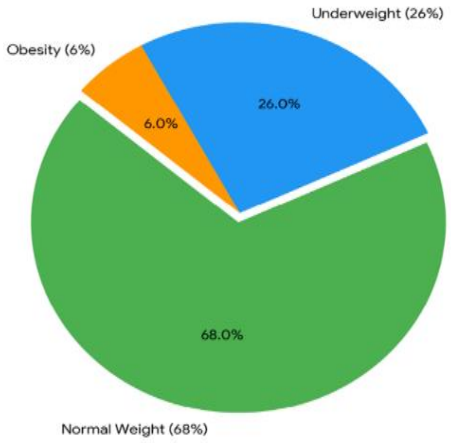

Figure 1: Distribution of Asthmatic Patients by BMI

Table 2: comparing the controlled and uncontrolled asthma cases with regard to mean age and BMI

Variables	Category	Mean ± SD
Mean Age (Years)	Uncontrolled Group	6.96 ± 3.83
	Controlled Group	7.25± 3.49
Mean BMI (kg/m²)	Uncontrolled Group	15.88 ±2.701
	Controlled Group	17.626 ± 8.414

The findings highlighted that the vast majority of pediatric asthma patients suffered from Vitamin D deficiency, and this was statistically significant (p<0.05). While gender did not significantly influence the specific concentration levels within each group (p > 0.05), the overall comparison between the frequencies of deficiency versus normal levels across the entire sample was found to be statistically significant (p > 0.05). The paediatric participants were categorized based on their asthma control status into two primary classes: "Uncontrolled" and "Controlled." Cases under each control category were further subdivided into three classes based on their serum Vitamin D levels: Sufficient (30–100 ng/mL), Insufficient (20–29 ng/mL), and Deficient (<20 ng/mL). The results indicated that the majority of patients fell within the deficient category (<20 ng/mL). Statistical analysis revealed a significant correlation between Vitamin D concentration levels and the degree of asthma control (p < 0.05), as shown in Table 2.

The relationship between Immunoglobulin E (IgE), asthma control, and Vitamin D status revealed significant variations. While 64% of children maintained normal IgE levels, 36% exhibited elevated concentrations. Statistical analysis showed that for those with normal IgE, Vitamin D levels varied significantly across groups (p=0.023). Furthermore, the study investigated the frequency of hospitalizations over the past year. Interestingly, a significant correlation was found between Vitamin D concentrations and the number of hospital visits only within the Controlled Asthma group (p=0.029), whereas no such significance was found in the uncontrolled group, as shown in Table 4.

The study evaluated key biochemical markers (Calcium, Phosphate, and Alkaline Phosphatase) across vitamin D status and asthma control groups. The Phosphorus levels decrease significantly from "Normal" (5.24) to "Insufficient" (5.00) to "Deficient" (4.645), with a p-value of 0.017. This indicates a confirmed correlation between Vitamin D status

Table 3: Impact of Vitamin D Concentration on Asthma Control Status

Asthma Control category	No. of Cases (%)	Sufficient (30–100 ng/mL) n (Mean±SD)	Insufficient (20–29 ng/mL) n (Mean±SD)	Deficient (< 20 ng/mL) n (Mean±SD)	p-value
Uncontrolled	40 (80%)	4 (37.8±23.40)	14 (23.93±3.07)	22 (16.99±2.33)	0.00*
Controlled	10 (20%)	1 (38.30)	2 (24.00±0.98)	7 (13.47±3.37)	0.00*

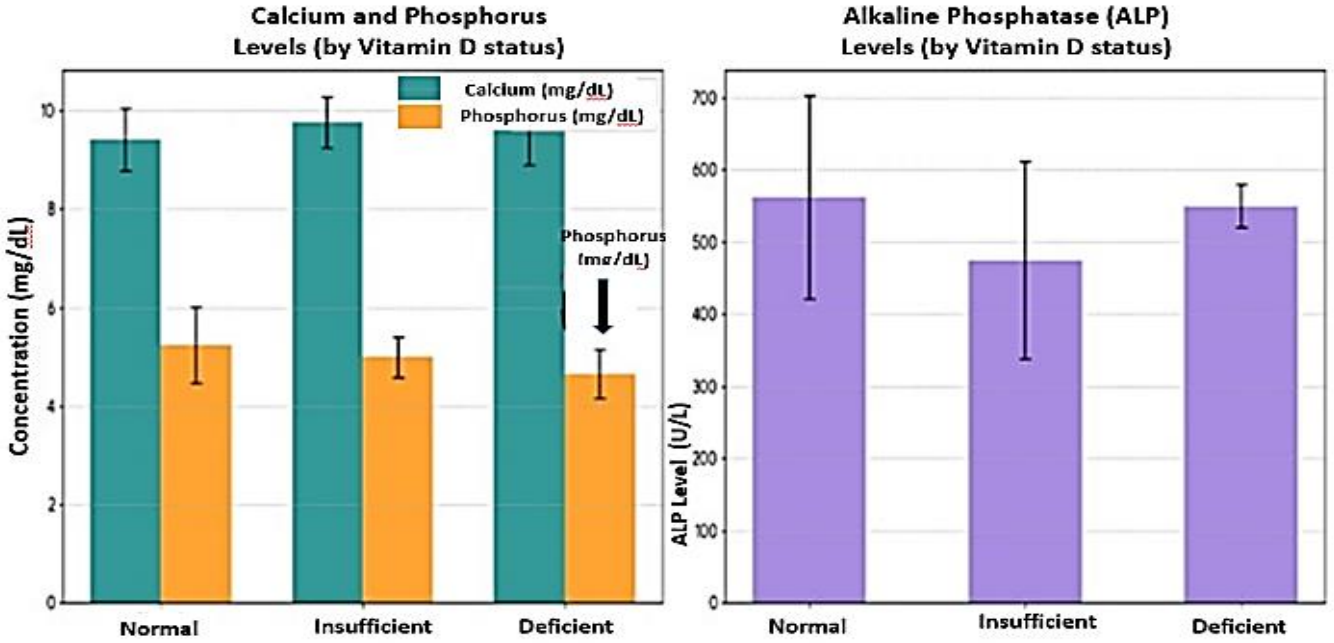

Figure 2: Biochemical Profiles According to Vitamin D Status and Asthma Control

Table 4: Correlation between Vitamin D Status, Serum IgE Levels, and Asthma-Related Hospitalization Frequency

Category	Sub-Category (vit D)	Mean IgE (± SD)	p-value
Normal IgE (< 295 IU/mL)	Sufficient (n=4)	65.5±45.3	0.023
	Insufficient (n=9)	108.8±66.6	
	Deficient (n=19)	157.6±65.1	
Elevated IgE (≥ 295 IU/mL)	Sufficient (n=1)	595.0±0.0	0.519
	Insufficient (n=7)	635.1±279.1	
	Deficient (n=10)	841.6±128.7	
Asthma Status	**Hospital Visits**	**Vit D (Mean ± SD)**	**p-value**
Uncontrolled	< 3 times	21.24±4.36	0.484
	3–6 times	22.60±8.55	
	> 6 times	19.66±7.39	
Controlled	< 3 times	22.05±12.06	0.029
	3–6 times	15.12±6.81	
	> 6 times	15.95±3.74	

and serum Phosphorus levels. In contrast, calcium and ALP levels showed no statistically significant variation according to vitamin D status or asthma control. Additionally, complete blood count (CBC) analysis revealed that red blood cell

To determine if these Vitamin D levels influenced hematological markers, we used a One-Way ANOVA analysis. Our results revealed a statistically significant difference between the three Vitamin D groups regarding Red Blood Cell (RBC) counts ($p < 0.05$). However, no other significant differences were observed across the remaining hematological variables studied ($p > 0.05$). When comparing hematological markers by gender, an independent t-test revealed no significant differences between males and females ($p > 0.05$ for all variables).

Discussion

The present study investigated the relationship between serum vitamin D levels and asthma control among children residing in Wadi Al-Shatti, southern Libya. A high prevalence of vitamin D deficiency was observed in this study and was significantly linked to poor asthma control. This result is consistent with existing research, further supporting the established connection between vitamin D status and disease severity. In the current study, males represented 64% of the asthmatic children. This pattern is consistent with prior observations reported by Alyasin et al. (2011) and Al-Zayadneh et al. (2021) [31, 32], which demonstrated a higher prevalence of asthma among boys during early childhood. Several biological explanations have been proposed for this difference, including anatomical differences in airway size relative to lung volume, a phenomenon described as dysanapsis. Such physiological characteristics may predispose males to increased resistance and heightened susceptibility to environmental triggers during early life.

A substantial proportion of the study population (80%) exhibited uncontrolled asthma according to clinical assessment. Statistical analysis demonstrated a significant association between reduced vitamin D levels and poor asthma control ($p < 0.05$). Similar findings have been reported in studies conducted in Saudi Arabia and Thailand, where [33, 34] identified vitamin D deficiency as an important factor associated with increased asthma severity and poor disease management. Vitamin D is recognized as an important immunomodulatory hormone that influences both innate and adaptive immune responses. Through activation of vitamin D receptors (VDR) expressed on various immune

cells, vitamin D contributes to the regulation of inflammat or pathways. In the present study, the majority of children within the uncontrolled asthma group demonstrated marked vitamin D deficiency (<20 ng/mL), suggesting that inadequate vitamin D status may contribute to persistent airway inflammation and increased bronchial hyperresponsiveness.

The study also demonstrated a significant reduction in serum phosphorus levels with increasing severity of vitamin D deficiency ($p = 0.017$). This observation is consistent with established physiological mechanisms linking vitamin D metabolism with mineral homeostasis, as described by [35]. Vitamin D plays a central role in maintaining calcium and phosphorus balance through its regulatory effects on intestinal absorption and hormonal control. Furthermore, a significant association was identified between red blood cell (RBC) counts and vitamin D status ($p < 0.05$). This finding supports previous reports suggesting that vitamin D may influence erythropoiesis and iron metabolism, potentially through modulation of the hepcidin-ferroportin pathway, as proposed by [36]. Although the exact mechanisms remain under investigation, these observations highlight the potential systemic effects of vitamin D beyond skeletal health.

Analysis of healthcare utilization indicated that higher vitamin D levels were associated with reduced hospitalization rates among children with controlled asthma ($p = 0.029$).

These findings are consistent with those reported by Brehm et al. (2009), [37] who suggested that adequate vitamin D levels may reduce the risk of severe asthma exacerbations requiring hospital care. Regarding allergic sensitization, elevated IgE levels were predominantly observed among children with uncontrolled asthma. This finding supports the established role of allergic inflammation and type-2 immune responses in the pathophysiology of asthma, as previously described [38]. This has also been noted to influence other inflammatory diseases like rheumatoid arthritis [39].

To the best of our knowledge, this is the first study to investigate the relationship between vitamin D status and asthma control among children in southern Libya. Despite the region's abundant sunlight exposure, the high prevalence of vitamin D deficiency observed in this study suggests that environmental and lifestyle factors, such as limited outdoor activity and cultural practices that reduce sun exposure, may significantly restrict endogenous vitamin D synthesis. These results are consistent with those reported by others [16], who also documented a high incidence of vitamin D deficiency in Brack Al-Shati population even with similar climatic conditions. The agreement between both studies supports the notion that living in a sun-rich environment does not necessarily ensure adequate vitamin D levels, and highlights the important role of behavioral and socio-cultural factors in determining vitamin D status.

It is important to note that our study has limitations; the small sample size ($n = 50$) may constrain the generalizability of our findings. Additionally, due to the cross-sectional nature of this observational study, we cannot establish a causal relationship between vitamin D deficiency and the severity of asthma.

Conclusion

The present findings indicate that vitamin D deficiency is highly prevalent among asthmatic children in Wadi Al-Shatti and is significantly associated with poor asthma control. These results highlight vitamin D status as a potentially modifiable factor that may influence asthma outcomes in pediatric populations. Routine screening for vitamin D deficiency and appropriate nutritional interventions may therefore represent valuable strategies for improving asthma management in this region. Further large-scale, well-designed studies are needed to better understand this relationship and to evaluate the potential clinical benefits of targeted vitamin D supplementation.

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