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ORIGINAL ARTICLE

Effect of Vitamin D Deficiency in Childhood Asthma Severity

Hisham Samy Abd Elhameed, Osama Abdelaziz Gaber, Eman Mostafa Mohammed Khater*, Eman Mohammed Abdel Hady
Pediatrics Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt.

*Corresponding Author:
Eman Mostafa Mohammed Khater
Email:
dremankhater578@gmail.com

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ABSTRACT

Background: Asthma is a prevalent chronic respiratory disorder in children and is associated with significant morbidity and mortality. New evidence suggests that, Vit. D may play an immunomodulatory role in asthma pathophysiology by influencing airway inflammation, immune regulation and corticosteroid responsiveness. **Objective:** This study aimed at comparing serum Vit. D level in asthmatic group versus healthy controls and to assess the relationship between Vit. D status and asthma severity in children.

Methods: A case-control study included 74 children had been carried out at Pediatric Department, Zagazig University. The studied children were divided into two groups: 37 asthmatic patients and 37 age and sex-matched healthy controls. These children underwent a throughout Clinical evaluation and laboratory investigations including serum 25(OH) Vit D. The severity of asthma was determined according to GINA guidelines.

Results: Serum Vit. D levels were significantly lower in asthmatic cases compared to controls. Mean Vit. D levels decreased progressively with asthma severity in the asthmatic group, with critical differences between mild, moderate and severe asthma. A strong negative correlation was found between vitamin D levels and asthma severity. **Conclusion:** According to the study findings, serum Vit D level was significantly lower among the asthmatic group and related strongly to disease severity. These findings highlighted the potential role of Vit. D as a modifiable factor in asthma management.

Keywords: Asthma, Children, Vitamin D deficiency, Severity, Immunomodulation.

INTRODUCTION

Asthma is a chronic respiratory disorder in children, and its pathophysiology is characterized by hyperresponsiveness and inflammation of the airways. It affects hundreds of millions of people worldwide. Due to its high rates of annual exacerbations, chronic morbidity and asthma-related deaths are estimated as 346,000 worldwide. The disease burden has a critical effect on quality of life, healthcare utilization, socioeconomic costs for families and healthcare systems in addition to mortality statistics [1].

In Egypt, pediatric asthma is of critical concern, with prevalence reported across different age groups, ranging from infants to preschool and school-aged children. Studies had documented prevalence rates of 4.8% in Egyptian infants, children aged less than 4 years across five governorates, while school-aged cases show higher rates, with 9.4% prevalence rate was reported among 11 to 15year-old students in Cairo, in another study prevalence was 8.2% in age group from 3 to 15 years old. The disease commonly presents with symptoms such as wheezing, dyspnea, cough, chest tightness. These symptoms vary in intensity and

frequency and often become more profound in severe cases, leading to progressive impairment of lung function, accompanied by expiratory airflow limitation, and decline in pulmonary function [2].

The pathogenesis of asthma is a complex, multifactorial, involving genetic predisposition and environmental influence. The exact mechanism of asthma development is not fully understood, but it may be due to interactions between environmental factors and genetic susceptibility. This interaction gives rise to considerable heterogeneity in clinical presentation, inflammatory patterns and airway remodeling. The immunological basis of the disease had emphasized by the fact that allergy had associated with approximately 60% of both childhood and adult asthma cases [3].

Asthma phenotypes are identified based on clinical features, while endotypes are defined by distinct molecular mechanisms, both of which are crucial for understanding disease severity and guiding treatment. The pathogenesis and clinical manifestations demonstrate remarkable complexity and heterogeneity, displaying various phenotypes and endotypes. However, it is important to recognize that the same phenotype may encompass different pathophysiological mechanisms. Objective tools such as spirometry remain central in diagnosis and monitoring, while the use of serum biomarkers increase knowledge of underlying mechanisms and provides valuable insights into asthma pathophysiology [4].

The health of the respiratory system has recently been of interest, despite the fact that Vit. D had long been recognized for its crucial role in calcium homeostasis and bone metabolism. Vit. D receptors (VDR)were found in epithelial cells and immune cells of the airways which suggested its role in modulating airway and immune functions. Furthermore, airway epithelia contain high concentration of the enzyme responsible for converting inactive Vit. D to its active form, 25-dihydroxy-Vit. D3 [25(OH)D3]. Active Vit. D contributes to epithelial integrity, enhances antimicrobial activity, regulates immune responses by promoting regulatory T cells, suppressing inflammatory pathways and reducing airway hyperresponsiveness. Furthermore, Vit. D improves corticosteroid responsiveness, enhancing the efficacy of this medication, which is important in management of severe asthma [5].

Vitamin D deficiency is a common nutritional disorder in children which has been reported to be a significant risk factor for severe acute lower respiratory tract infections. Studies have reinforced that Vitamin D deficiency can increase our susceptibility to infections. This effect was noticed when the incidence of viral infections typically increased when sun exposure decreased during winter months as epidermal Vitamin D synthesis decreased and serum 25(OH) Vitamin D levels reached the lowest value [6].

Despite these potential mechanisms, the relationship between Vit. D status and asthma outcome remains a subject of ongoing investigations. While some epidemiological studies had suggested associations between low serum Vit. D level and increased asthma exacerbation, others failed to demonstrate such relationship [7]. The current study aimed at comparing between serum vit. D levels in asthmatic children and healthy controls and correlating the level of vitamin D with the degree of asthma severity.

METHODS

This study was designed as a case control study and was conducted at the Pediatric Department, Faculty of Medicine, Zagazig University. Based on previous studies, the prevalence of vitamin D deficiency was (73.6% in asthmatic children versus 39.1%

in controls), with a study power of 80% and a confidence level of 95%, the required sample size was calculated to be 74 participants. These were allocated equally into two groups (37 age and sex matched children in each group) using Open Epi software. The study included two groups of children: group 1 (asthmatic group): Children under 16 years of age diagnosed with asthma of varying severity according to the Global Initiative for Asthma (GINA) guidelines. group 2 (control group): Age and sex matched healthy children with no history of asthma or chronic illness. Children with chronic systemic diseases (such as chronic kidney disease, diabetes, hypertension, congenital or acquired heart disease, chronic liver disease, iron deficiency anemia, obesity, and thalassemia) were excluded. Additional exclusion criteria included severe acute infections (e.g., sepsis, meningitis, pneumonia, peritonitis), immunocompromised children, use of vitamin D supplementation, or refusal to participate. All participants were subjected to the following: detailed history taking as (Age, sex, socioeconomic status, parental consanguinity, onset and duration of asthma symptoms, asthma severity, associated allergic conditions, history of food allergy, family history of atopy, and exposure to cigarette smoke). Clinical examination included (general examination with assessment of body weight and body mass index (BMI),Vital signs including temperature, heart rate, respiratory rate, and blood pressure and complete chest examination comprising inspection, palpation, percussion, and auscultation).Laboratory investigations were done as (complete blood count (CBC) with differential white blood cells count, Erythrocyte sedimentation rate (ESR), CRP, measurement of total serum IgE concentration, arterial blood gas analysis and Serum 25-hydroxy vitamin D [25(OH)D] level was measured by enzyme-linked immunosorbent assay (ELISA) using commercially available kits (DIA Source Immunoassay's Co., Belgium). For this purpose, 3 mL of venous blood were collected from each participant).

Ethical approval

The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Zagazig University. Written informed consent was obtained from the legal guardians of all participating children prior to enrollment.

STATISTICAL ANALYSIS:

Data were analyzed using Statistics Package for Social Sciences (SPSS) version 22. Qualitative data were expressed as frequency and percentage. Continuous quantitative data were expressed as mean ± standard deviation (Mean ±SD). Independent sample T test (T), Chi-square test, Mann Whitney test, ANOFA test and Pearson's correlation coefficient (r) were used.

RESULTS

Regarding to (table 1), there was a statistically significant difference in mean vitamin D levels among mild, moderate, and severe patient groups. Patients with mild symptoms had the highest mean vitamin D levels (29.19 ± 11.83 ng/ml), followed by moderate (21.68 ± 8.61 ng/ml), and severe cases showing the lowest levels (11.63 ± 3.77 ng/ml). The differences between mild and severe (P2 ≤ 0.001) and between moderate and severe groups (P3 = 0.02) were statistically significant. The difference between mild and moderate groups (P1 = 0.09) was not statistically significant.

There was statistically significant negative correlation between severity of asthma and serum vitamin D levels as shown in(table2) and (figure 1S).

There was no statistically significant difference between the studied groups

according to age, and gender as shown in (table 3).

Regarding to Vit D level between asthmatic and control groups there was statistically significant difference between the studied groups as Vit D level was higher among control group than asthmatic group as shown in (table 4).

There was no statistically significant correlation between age and serum vitamin D levels (r = 0.158, P = 0.179) as shown in (table 5).

(Table 6) showed the comparison of vitamin D levels between male and female patients. The mean vitamin D levels were 24.72 ± 13.98 ng/ml in males and 23.49 ± 9.98 ng/ml in females, with median values of 21.4 ng/ml and 22.4 ng/ml, respectively. The difference in vitamin D levels between genders was not statistically significant (P = 0.663).

Regarding (Table7) this table showed the association between asthma severity (mild, moderate, and severe) and vitamin D levels (≤30 ng/ml and >30 ng/ml). Among patients with vitamin D levels ≤30 ng/ml, there was a statistically significant difference across severity groups (P = 0.04), indicating that lower vitamin D levels were associated with greater asthma severity.

Table (1): Comparison of vitamin D level with severity of asthma in the case group.

	No. of patients	%	Mean vitamin D (ng/ml)	Median (Range)	P-Value
Mild	**12**	**32.43%**	**29.19±11.83**	**27.15(16-53)**	**0.001***
Moderate	**15**	**40.54%**	**21.68±8.61**	**21 (8-46)**	
Severe	**10**	**27.03%**	**11.63±3.77**	**11.75 (6-18)**	
Total	**37**	**100%**	**21.40±11.04**	**19 (6-53)**	**-**
	P1: 0.09, P2: ≤0.001, P3: 0.02				

P- value (between groups) >0.05: Not significant, P- value <0.05 is statistically significant, p<0.001 is highly significant. P1: between mild and moderate groups. P2: between mild and severe groups. P3: between moderate and severe groups. tested by ANOFA test.

Table (2): Correlation between Severity of Asthma and serum vitamin D levels

	vitamin D levels	
	R	**P value**
Severity of Asthma	**-.940**	**≤0.001**

Table (3): Comparison of demographic data between the studied groups.

	Control group N=37	Case group N=37	Test	P-Value
Age Mean± SD Median (Min-Max)	**7.27± 3.39 7 (2.3- 15)**	**6.9± 3.79 6.5 (2.5-15)**	**t = 0.442**	**0.659**
Gender				
Female	**24 (64.9%)**	**15 (40.5%)**	**X^2= 4.391**	**0.062**
Male	**13 (35.1%)**	**22 (59.5%)**		

P value >0.05: Not significant, P value <0.05 is statistically significant, p<0.001 is highly significant. Tested by correlation test

Table (4): Comparison of Vitamin D Levels Between Control and Case Groups.

	Control group N=37	Case group N=37	P-Value
Vit D Mean± SD Median (Min-Max)	 27.68±9.15 28 (11-51)	 21.40±11.04 19 (6-53)	0.001*

P- value >0.05: Not significant, P- value <0.05 is statistically significant, p<0.001 is highly significant. Tested by Mann Whitney test.

Table (5): Correlation between serum level of vitamin D and age.

	vitamin D levels	
	R	P value
Age	0.158	0.179

Table (6): Relation between Gender and serum level of vitamin D.

	Male	Female	Test	P-value
Vitamin D Mean± SD Median (Min-Max)	24.72± 13.98 21.4 (6-53)	23.49± 9.98 22.4 (5.9-41)	t = 0.4389	0.663

This table WAS tested by t-test.

Table (7): Association between severity of asthma and vitamin D levels.

	vitamin D levels		P-Value	P-Value
	≤ 30	>30		
Mild	8 (25%)	4 (80%)	P=0.014	0.04*
Moderate	14 (43.7%)	1 (20%)	P=0.314	
Severe	10 (31.3%)	0 (0%)	P=0.143	
Total	32 (100%)	5 (100%)	-	
	P1:0.114, P2:0.3, P3:0.578	P1:0.057, P2:0.29, P3:0.07		

P value >0.05: Not significant, P value <0.05 is statistically significant, p<0.001 is highly significant. P1: between mild and moderate groups. P2: between moderate and severe groups. P3: between mild and severe groups.

DISCUSSION

Asthma is a complex, multifactorial disease influenced by both genetic predisposition and environmental factors, leading to inflammation and structural airway changes [7]. Allergic sensitization, which accounts for over 60% of cases, remains a key driver of disease pathogenesis [8].

It is important to distinguish between asthma endotypes, which reflect underlying pathophysiological mechanisms and phenotypes, which have been defined by clinical traits [9]. Such stratification had facilitated biomarker driven approaches for diagnosis and management of asthma with the spirometry is considered the gold standard for functional assessment [3].

Vit. D was previously known for its role in bone, calcium-phosphate metabolism, had now seen as a pleiotropic hormone with a wide range of immunomodulatory effects [10]. Vit. D receptors (V.D. Rs) are expressed in immune cells and respiratory epithelium [11]. Vit. D improves epithelial barrier integrity, antimicrobial defense mechanisms, immune responses and reduces

air way inflammation. In addition, it had been demonstrated that, Vit. D enhances corticosteroid responsiveness in steroid-resistant phenotypes, indicating its therapeutic value in severe cases of asthma [12]. According to our findings, the severity of asthma was inversely correlated with Vit. D levels. Cases with severe asthma exhibited markedly lower mean serum Vit. D level compared to those with mild, moderate disease. This was in a line with Asseri et al., [13], who discovered critical differences in Vit. D level based on severity, despite the fact that some subgroup analysis failed to reach statistical significance, most likely due to limitation in sample size. Our correlation analysis demonstrated a strong negative relationship between Vit. D, asthma severity ($r = –0.94$, $p \leq 0.001$), consistent with reports from both prospective cohort Malheiro et al., [14], systematic reviews Chanie et al., [15], the latter had detected the high prevalence of Vit. D deficiency among cases with asthma in resource-limited settings. These results were parallel to findings from Malheiro et al., [14], who reported critically lower Vit. D levels in cases with severe asthma compared to those with mild or moderate disease, as well as a correlation with reduced lung function. A recent meta-analysis by Ladeira et al., [16] similarly confirmed lower Vit. D level in children with severe asthma across multiple studies, reinforcing our finding.

In our study, there was no statistically significant difference between the asthmatic and control groups in gender. These findings aligned with observational research in pediatric asthma populations by Allegorico et al., [17] who reported no significant sex differences.

In addition, our subgroup analysis revealed that cases with Vit. D level below 30 ng/mL had a higher prevalence of moderate, severe asthma, whereas cases with level above this threshold tended to be mild. These were consistent with the Southwest Saudi Arabian cohort by **Asseri et al.,** [13] which uncovered significant vitamin D differences when stratifying by asthma severity but found that the associations did not reach statistical significance in some subgroup analysis.

While **Asseri et al.,** [13] reported lower Vit. D levels in Saudi asthmatic cases as they got older, our study found no significant correlation between Vit. D levels and age. This variation might be due to methodology, population characteristics, sun exposure or nutritional status. Despite the observations linked low Vit. D levels to asthma severity, interventional trials had produced mixed results, for example while a study by **Forno et al.,** [18] found that there was no benefit from Vit. D3 supplementation on time of asthma exacerbation in high-risk cases, meta-analysis by **Fedora et al., [**19] had concluded that Vit D supplementation might reduce exacerbation in certain subgroups, the overall evidence remains inconclusive.

These results raised the possibility that Vit. D deficiency served as a biomarker of disease severity more than a direct therapeutic target, or that the effects of supplementation had been dependent on baseline Vit. D status, genetic background, or asthma phenotype.

CONCLUSION

Our study detected a critical inverse relationship between serum Vit. D level and asthma severity in cases younger than 16 years. Vit. D level was critically lower in cases with severe asthma, without any correlation with age or gender. These findings support the evidence that Vit. D might have an important regulatory role in asthma pathogenesis and progression.

Limitation of the study

The small sample size, case control design limited results of the study.

Recommendation

Larger multicenter longitudinal studies and interventional trials are needed to clarify the role

of Vit. D supplementation in improvement clinical outcomes in pediatric asthma.

Conflict of Interest:

The authors declare that they have no competing interest.

Financial Disclosures:

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Availability of the data:

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors contribution:

All the listed authors contributed critically to the conception and design of study, acquisition and analysis of data, interpretation of results, and drafting of the manuscript, thereby justify authorship.

Supplementary files: Fig. S1

REFERENCES

1. Chen L, Hou W, Liu F, Zhu R, Lv A, Quan W, et al. Blockade of NLRP3/Caspase-1/IL-1β regulated Th17/Treg immune imbalance and attenuated the neutrophilic airway inflammation in an ovalbumin-induced murine model of asthma. J Immunol Res 2022;1–12.
2. Refaat MM, El Sayed E, Abd El-Fattah W, Elbanna AH, Sayed HME. Relationship between sputum periostin level and inflammatory asthma phenotypes in Egyptian patients. J Asthma 2021;58(10):1285–91.
3. Jackson DJ, Fitzgerald P, Taylor A, Topliss D, McNeil JJ. Biomarkers in asthma: Past, present, and future. J Allergy Clin Immunol 2023.
4. Al-Jawaldeh A, Abul-Fadl A. Regional disparities in prevalence of obesity among school-aged children in Egypt: A country case study from the Eastern Mediterranean region. Indian J Child Health 2021;8(7):262–8.
5. Pavón-Romero GF, Serrano-Pérez NH, García-Sánchez L, Ramírez-Jiménez F, Terán LM. Neuroimmune pathophysiology in asthma. Front Cell Dev Biol 2021;9:1–12.
6. Abdo AAH, Elshal AS, Sarhan DT, Jaber NA. Study of vitamin D level in children with lower respiratory tract infections in Zagazig University Hospitals. Zagazig Univ Med J 2022;28(3):401–10.
7. Ullmann N, Becker D, Williams R, Martin P, Thompson A. Advances in understanding asthma pathogenesis: From inflammation to remodeling. Front Pediatr 2022.
8. Licari A, Laganà P, La Grutta S, Cuppari C, Giannotta A. Allergy and asthma in children: Coexisting disorders or overlapping endotypes? Allergy Asthma Proc 2021.
9. Agache I, Akdis CA. Endotypes and phenotypes of chronic airway diseases. Immunol Rev 2022.
10. Aranow C, Kelsall D, McNeil L, Thomas A, Peterson T. Vitamin D and the immune system: Beyond bone health. Rheum Dis Clin 2020.
11. Jolliffe DA, Phipatanakul W, Barben J, Miller D, Flanagan A. Vitamin D in respiratory health and disease. Nat Rev Pulmonol 2022.
12. Gupta A, Miller S, Patel S, Singh N, Gupta R. Role of vitamin D in asthma pathogenesis and treatment. Ann Allergy Asthma Immunol 2021.
13. Asseri AA. Serum Vitamin D Profiles of Children with Asthma in Southwest Saudi: A Comparative Cross-Sectional Study. Int J Gen Med 2024;6323–33.
14. Malheiro APG, Gianfrancesco L, Nogueira RJN, Grotta MB, Morcillo AM, Ribeiro JD, et al. Association between serum Vitamin D levels and asthma severity and control in children and adolescents. Lung 2023;201(2):181–7.
15. Chanie ES, Zhang G, Le Souef P. The serum level of vitamin D and prevalence of vitamin D deficiency among children with asthma in Asia and Africa: A systematic review and meta-analysis. Arch Public Health 2024;82(1):103.
16. Ladeira JM, Zacas O, Ferreira AM, Stegun PCG, DE SOUZA TIA GO, Grotta M, et al. The Role of Vitamin D in the Severity and Control of Asthma in Children and Adolescents: A Systematic Review and Meta-analysis. Authorea Preprints 2023.
17. Allegorico A, Ruggiero L, Capristo C, Parisi G, Indolfi C, Umano GR, et al. Vitamin D and asthma in children: insights from total and free 25-hydroxyvitamin D and vitamin D binding protein measurements. Pediatr Respir J 2023;1(4):148-56.
18. Forno E, Bacharier LB, Phipatanakul W, Guilbert TW, Cabana MD, Ross K, et al. Effect of vitamin D3 supplementation on severe asthma exacerbations in children with asthma and low vitamin D levels: the VDKA randomized clinical trial. Jama 2020;324(8):752–60.
19. Fedora K, Setyoningrum RA, Aina Q, Rosyidah LN, Ni'mah NL, Titiharja FF. Vitamin D supplementation decrease asthma exacerbations in children: A systematic review and meta-analysis of randomized controlled trials. Ann Med 2024;56(1):2400313.

SUPPLEMENTARY FILES

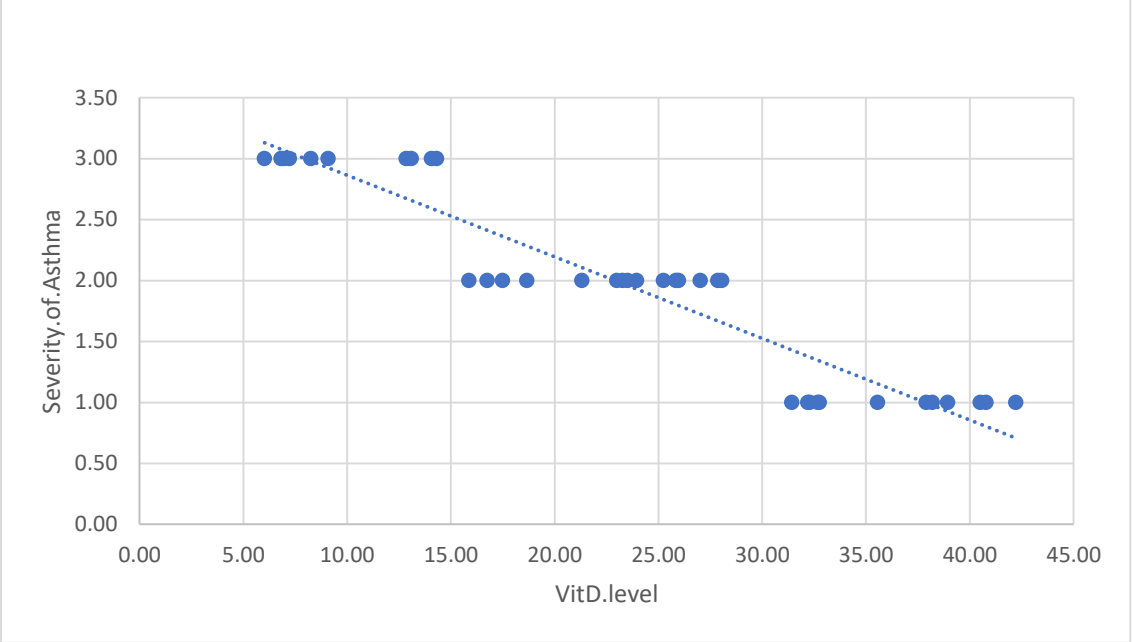

Fig. (S1): Correlation between Severity of Asthma and serum level of vitamin D.

Citation

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