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RELATIONSHIP BETWEEN SERUM VITAMIN D, LUNG FUNCTION, DISEASE SEVERITY, AND AIRWAY REMODELING IN ADULTS WITH ASTHMA

Dr Badar Munir[1], Dr Syed Soban Ahmed Tirimzi[2*], Dr Farhat Rehman[3], Dr Maheen Shah[4], Dr Aziz Ur Rehman[5], Dr Kinza Sammar[6]

[1]Medical Officer, Saadat Medical Complex, Narowal Pakistan
[2*,6]Assistant Professor, Department of Physiology, Abbottabad International Medical Institute, Abbottabad Pakistan
[3]Associate Professor, Department of Physiology, Bacha Khan Medical College, Mardan Pakistan
[4]Assistant Professor, Department of Physiology, Abbottabad International Medical Institute, Abbottabad Pakistan
[5]Associate Professor, Department of Biochemistry, Northwest School of Medicine, Peshawar Pakistan

***Corresponding Author:** Dr. Syed Soban Ahmed Tirimzi
*Assistant Professor, Department of Physiology, Abbottabad International Medical Institute, Abbottabad Pakistan. Email: stirimzi@gmail.com

ABSTRACT

Background: Asthma is a prevalent chronic inflammatory airway disease affecting children globally. Factors such as lifestyle, allergens, infections, and genetics contribute to its development. Vitamin D deficiency has been hypothesized to influence asthma severity due to its immunomodulatory properties.

Methodology: This case-control study, conducted at Abbottabad International Medical Institute, Abbottabad from January 2022 to 2023, involved 150 children aged 6-18 years. Participants were divided into asthmatic (case) and healthy (control) groups (n=75 each). Serum vitamin D levels were measured using ELISA, and pulmonary function tests (PFTs) were conducted. Statistical analyses included Pearson correlations and multiple linear regressions.

Results: Significant differences in serum vitamin D levels were observed between case (mean 20.11 ng/ml) and control (mean 19.00 ng/ml) groups ($P < 0.01$). Vitamin D deficiency prevalence was higher in asthmatic children, with 10% severe deficiency and 43.3% deficiency. Asthmatic children exhibited lower vitamin D levels than controls ($P < 0.0001$).

Conclusion: This study highlights a significant 'association between vitamin D deficiency and asthma' severity in children. Lower vitamin D levels correlated with higher asthma severity indices, including reduced lung function and elevated IgE levels. Further research is needed to explore the clinical implications of vitamin D supplementation in managing childhood asthma.

Keywords: Serum Vitamin D, Lung Function, Asthma, Airway Remodeling.

Introduction

Asthma is a complex and chronic inflammatory airway disease with high prevalence rates in both developed and developing countries. In Western nations, more than 1.3% of children suffer from asthma and related allergies. Projections indicate that by 2025, approximately 400 million people worldwide will be affected by asthma (1).

Lifestyle changes, dietary factors, 'allergens, various infections, and family history are identified risk factors for asthma'. Immunological factors 'play a significant role in the development of asthma'. One notable hypothesis under investigation 'is the relationship between serum vitamin D levels and asthma'. 'Vitamin D, a fat-soluble vitamin' primarily produced in the skin through UV exposure, plays a crucial role in immune function and inflammation reduction(2).

The rising 'incidence of vitamin D deficiency has gained considerable attention'. Reports from the Centers for Disease Control and Prevention indicate a decline in adequate vitamin D levels among adults, with only 30% of white individuals and 5-10% of African Americans meeting the sufficient threshold during 2001-2004. Despite abundant sunlight, countries in the Persian Gulf exhibit high prevalence rates of 'vitamin D deficiency, with adolescent girls in Iran and Saudi Arabia showing deficiency rates of over 70% and 80%, respectively' (2-4).

'Vitamin D influences the innate and adaptive immune systems, regulating Th1/Th2 balance and phagocytosis'. By 'inhibiting Th17 production, vitamin D may help' prevent asthma exacerbations. It is also considered a potent immune modulator, influencing cell proliferation and differentiation. While 'some studies have shown a correlation between vitamin D deficiency and asthma, others have produced conflicting results' (5-7).

Given the importance of 'vitamin D in the body and the high prevalence of asthma' this study aims to investigate the relationship between serum vitamin D levels and asthma severity in a case-control study.

Methodology

This case-control study investigated children aged 6-18 years, conducted at Abbottabad International Medical Institute, Abbottabad, from 2022 – 2023 January. 'The study population comprised 150 individuals, divided into two groups of 75: the case group (asthmatic) and the control group'. A stratified random sampling technique was employed to select participants.

The requirements for inclusion Case study Individuals with a 'history of physical examination, and pulmonary function test (PFT) results who have been diagnosed with asthma by a physician with a fellowship in allergy and clinical immunology' who is willing to enroll, and who has no prior medical history. The group under control Healthy people who are willing to take part have no known history of allergies, illnesses, drug use, or asthma. The following were the exclusion criteria: - Use of vitamin D supplements or drugs altering vitamin D metabolism; - Recognition of any disability or chronic sickness throughout the trial; - Unwillingness to continue in the study - Vitamin D-related illnesses were present in the research population

The procedure or data collection includes Blood samples collected and tested in a laboratory. Serum vitamin D levels were measured using a vitamin D ELISA assay kit. The following vitamin D ranges were observed:

'Severity of Vitamin D Deficiency'	*'Range (ng/ml)'*
'Very severe vitamin D deficiency'	(<5)
'Severe vitamin D deficiency'	(5-10)
'Vitamin D deficiency'	(10-20)
'Suboptimal vitamin D provision'	(20-30)
'Optimal vitamin D level'	(30-50)
'Upper norm'	(50-70)
'Overdose (not toxic)'	(70-150)
'Vitamin D intoxication'	(>150)

The pulmonary function testing: Spirometry was performed in between cases and control study following American Thoracic Society guidelines. 'The highest FEV1 and FVC values from satisfactory maneuvers were used in the analyses'.
The 'Serum total immunoglobulin E' (IgE): IgE levels were quantitatively analyzed using an ELISA kit.

Statistical analysis: Frequency distributions were computed using descriptive methods. To evaluate correlations between vitamin D and other factors, Pearson correlation coefficients were calculated. For categorical and continuous data, t-tests and chi-square tests were used, respectively. The associations 'between vitamin D and age, sex, and IgE were' investigated using multiple linear regression models. All analyses were conducted using SPSS15 software, with a significance level of $P < 0.05$.

Results
A total of 150 'children were divided into two groups of 75: healthy children (control group) and children with asthma (case group)'. Our study included 75 'children in both the control and case groups'. The mean ages were 9.35 years (SD ± 2.337) and 7.82 years (SD ± 2.151) for the control and case groups, respectively (P = 0.04). Gender distribution showed 42.5% females and 57.5% males across both groups, with no significant difference (P > 0.05, Table 1). Education levels among fathers and mothers varied similarly across groups, with no significant differences observed (P = 0.06 for both fathers and mothers, Table 1). Economic situation varied significantly between groups (P = 0.04, Table 1), correlating with age within each group (P < 0.001).

Table 1: Characteristics Study participants

Group	Control (n = 75)	Case (n = 75)	Total	P-value
Age; mean ± SD	9.35 ± 2.337	7.82 ± 2.151		0.04
Gender Male	42 (56.0)	43 (57.3)	85	0.06
Female	33 (44.0)	32 (42.7)	65	
Education (father); n (%) Under Diploma	12 (16.0)	10 (13.3)	22	0.06
Diploma	21 (28.0)	35 (46.7)	56	
Associate	9 (12.0)	0 (0)	9	
Bachelor	28 (37.3)	45 (60.0)	73	
Masters	10 (13.3)	0 (0)	10	
Phd	5 (6.7)	0 (0)	5	
Education (mother); n (%) Under Diploma	13 (17.3)	7 (9.3)	20	0.06
Diploma	25 (33.3)	25 (33.3)	50	
Associate	11 (14.7)	0 (0)	11	
Bachelor	12 (16.0)	51 (68.0)	63	
Masters	11 (14.7)	0 (0)	11	
Phd	3 (4.0)	0 (0)	3	
Economic situation; n (%)				0.04
Weak	15 (20.0)	19 (25.3)	34	
Intermediate	57 (76.0)	36 (48.0)	93	
Good	18 (24.0)	34 (45.3)	52	

'Serum levels of vitamin D showed a significant difference between the case and control groups, with the mean serum level of vitamin D lower in the case group P was 0.01'. Specifically, 'the mean serum

levels of vitamin D' were 20.11 ± 11.76 in the case group and 19.00 ± 4.23 'in the control group'. Analysis of 'vitamin D deficiency' severity revealed that 10% of subjects in the study had severe deficiency, 43.3% were deficient, 34.2% had suboptimal levels, and 12.5% had optimal levels.
Table 2 details the distribution of vitamin D deficiency across the two groups. Due to severe deficiency being exclusively observed 'in the case group' direct comparison of 'mean values at this severity level'' was not feasible. However, a 'significant difference' was observed in the mean suboptimal 'level of vitamin D between the case and control groups' (P < 0.0001). No significant differences were reported in other levels of vitamin D P = 0.05.
'The frequency of vitamin D deficiency was categorized by gender'. In the case group, 10% of males and females were severely deficient, whereas 'vitamin D deficiency was reported' in the control group (0.0%). Optimal vitamin D levels were more prevalent among males in both the case and control groups. However, the 'chi-square test results indicated no significant correlation between vitamin D and gender in children P - 0.05'.

Table 2: Comparison of the Distribution of Vitamin D Deficiency Severity between Groups

Variable		Group	Mean ± SD	Mann-Whitney U	P
Vitamin D	Deficiency	Case	20.11 ± 11.76	291.50	0.4
		Control	19.00 ± 4.23		
	Suboptimal	Case	20.37 ± 8.01	62.0	0.001
		Control	28.50 ± 5.78		
	Optimal	Case	26.31 ± 13.26	15.0	0.083
		Control	35.93 ± 4.82		

The 'mean and standard deviation' of various indices associated with the severity of asthma in the case group were analyzed (Table 3). The mean values for BMI, FEV1, IgE, FVC, and FEV1/FVC were 20.93 ± 8.36, 78.77 ± 20.44, 148.03 ± 113.18, 78.36 ± 18.33, and 75.84 ± 8.46, respectively. The corresponding minimum and maximum values for these indices were 14.31 to 33.26 for BMI, 41.56 to 120.56 for FEV1, 19.96 to 390.56 for IgE, 46.56 to 117.56 for FVC, and 58.76 to 86.56 for FEV1/FVC.

Table 3: Average Values of Different Parameters Related to Asthma Severity in the Case Group

INDICES	NUMBER	MEAN	S D	MINIMUM	MAXIXIMUM
BMI	75	20.93	8.36	14.31	33.26
FEV1	75	78.77	20.44	41.56	120.56
IgE	75	148.03	113.18	19.96	390.56
FVC	75	78.36	18.33	46.56	117.56
FEV1/FVC	75	75.84	8.46	58.76	86.56

Table 4 presents the results of multiple regression analyses examining the 'relationship between serum vitamin D levels and predictor variables age, gender, and IgE in the case group' adjusted for different sets of confounding variables (FEV, FCV, and BMI).

Without adjusting for covariate: Shows significant associations between serum vitamin D levels and age (positive association), IgE levels (negative association), and a suggestive association with gender.

Adjusted for FEV and FCV: Continues to show significant associations with age and IgE levels, with slight adjustments in the estimates.

Adjusted for FEV, FCV, and BMI: Maintains significant associations with age and IgE levels, suggesting consistent relationships even when accounting for BMI.

Interpretation:
Significant p-values (<0.05) indicate robust associations between predictor variables (age, IgE) and serum vitamin D levels.
Effect Size: Estimates (coefficients) indicate the direction and magnitude of these associations, such as increased vitamin D levels with higher age and decreased levels with higher IgE.
Model Fit R-squared values indicate how well the models explain variations in serum vitamin D levels, with higher values indicating better fit. Overall, Table 4 illustrates that age and IgE levels are consistently associated with serum vitamin D levels in the case group, even after adjusting for potential confounders like lung function (FEV, FCV) and body mass index (BMI).

Table 4 Relationship between Serum Vitamin D Levels and 'Age, Gender, and IgE in the Case Group, Adjusted and Unadjusted for FEV, FVC, and BMI'.

Variable	Estimate	Std. error	t	P-value	95% CI
'Without adjusting for covariates'					
Intercept	29.834	7.846	7.934	<0.0001	19.259 to 40.409
Gender	-1.414	4.818	4.336	0.002	-6.923 to 4.095
Age	2.329	3.112	3.003	0.015	0.432 to 4.226
IGE	2.523	2.596	7.456	0.001	2.501 to 2.545
'Adjusted for covariates FEV, FCV'					
Intercept	12.737	9.745	4.984	0.001	-0.413 to 25.887
Gender	-1.329	4.777	4.404	0.002	-6.838 to 4.180
Age	2.408	3.081	3.459	0.008	0.441 to 4.375
IGE	2.530	2.607	7.457	0.001	2.508 to 2.552
'Adjusted for covariates FEV, FCV, and BMI'					
Intercept	14.679	10.097	4.175	0.003	-0.224 to 29.582
Gender	-1.280	4.772	4.647	0.001	-6.789 to 4.229
Age	2.422	3.099	3.312	0.010	0.455 to 4.389
Level of IGE	2.531	2.610	7.277	0.001	<2.509 to 2.553

Discussion

This study aimed to investigate the relationship between serum vitamin D levels and asthma severity. Gender distribution was similar across both groups, with no significant difference observed. However, significant age differences were noted, indicating a younger 'mean age in the case group, reflecting the higher prevalence of asthma at younger ages'. This finding aligns with epidemiological trends showing a higher incidence of asthma in younger children, with prevalence decreasing as age increases (8).

Regarding vitamin D deficiency severity, the study found that 10% of participants had severe deficiency, with a higher proportion observed in the case group. This is consistent with global trends where vitamin D deficiency remains prevalent despite ample sun exposure in some regions (9, 10).
'Serum vitamin D levels differed significantly between the case and control groups, with lower levels observed in the case group'. Similar findings have been reported in various studies worldwide, indicating an association between vitamin D deficiency and asthma (10, 11). However, conflicting results exist in the literature, suggesting variability possibly due to differences in sample characteristics and study designs (12)
'The role of vitamin D in immune regulation and inflammation' was highlighted, emphasizing its potential impact on asthma pathogenesis. Vitamin D's immunomodulatory effects include inhibition of inflammatory cytokines and promotion of anti-inflammatory responses, which may explain its association with asthma severity (13, 14)Studies have demonstrated that vitamin D deficiency correlates with increased airway inflammation and reduced lung function, supporting its role in asthma exacerbation (14, 15).
In our study, a significant negative correlation was observed between serum IgE levels and vitamin D, independent of lung function and BMI. This finding is consistent with previous research linking vitamin D deficiency with elevated IgE levels, a marker of allergic response (Brehm et al., 2014; Hala et al., 2015). However, further studies are needed to elucidate the mechanisms underlying this relationship and its clinical implications.
Limitations of this study include its cross-sectional design and relatively small sample size, which may limit generalizability. Future research should consider longitudinal studies with larger cohorts to validate these findings and explore additional factors influencing vitamin D status and asthma outcomes.

Conclusion

In conclusion, this study underscores 'the association between vitamin D deficiency and asthma severity in children'. Monitoring vitamin D levels and considering supplementation strategies could potentially mitigate asthma exacerbations, although further research is warranted to establish causality and inform clinical practice.

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