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Assessment of Association between Vitamin D Levels and Lung Function in Adult Patients with Bronchial Asthma

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Abstract

Background: Recently the effects of vitamin D as a hormone have gained attention. Vitamin D appears to have regulatory effects on every part of the immune system, vitamin D deficiency being linked to an array of immunologically based diseases focusing on asthma. Vitamin D deficiency has become more prevalent and is mainly attributed to diet, lifestyle, and behavioural changes. Recent reports have shown how decreased vitamin D levels may adversely influence asthma out comes. Vitamin D plays a key role in regulating the innate immune system, and is a major player in the production of antimicrobial peptides that kill microorganisms. Vitamin D deficiency has been linked to a predisposition to respiratory infections, which are major triggers for asthma attacks. Previous studies have shown that children with mild to moderate asthma who also had low serum vitamin D levels had poor asthma control, more exacerbations, more hospitalizations in the previous year, decreased lung function, reduced responses to inhaled corticosteroids. Furthermore, it has been reported that serum vitamin D levels are positively related with FEV1% predicted and the ratio of FEV1 to FVC. **Aims:** To Study the effect of vitamin d levels on lung function in adult bronchial asthma patients. **Material and Methods:** Demographic details of every patients will be collected. Detailed history and physical examination will be done in all patients. Information will be collected regarding symptoms and duration of symptoms of bronchial asthma. Asthma control will be assessed using the asthma control test (ACT). Blood samples for vitamin D measurements will be collected in EDTA tubes, then centrifuged, aliquoted, and stored at —80 °C. Plasma 25-hydroxyvitamin D will be measured using the Tandem test. Difference between two groups was determined using t test as well as chi square test. **Results:** Out of 270 subjects, low vitamin d level was found among 61.48% of the subjects. Mean BMI (kg/m2) among the subjects with low and normal vitamin d was 26.01±4.78 and 26.94±7.83 years respectively. Smoking was found to be present and absent in 89.16% and 10.84% of the subjects with low vitamin d level respectively with statistically significant difference. Mean FEVI/FVC ratio among the subjects with low and normal vitamin d was 56.24±6.13 and 48.59±7.02 respectively. Significant positive correlation ($r=0.87$, $p<0.01$) was found between ACT and vitamin d level. **Conclusion:** Vitamin D deficiency is highly prevalent in patients with exacerbations of bronchial asthma. Supplementation of Vitamin D has a significant positive effect in decreasing the severity and number of exacerbations of bronchial asthma. The association between ACT and vitamin D in the absence of any association with respiratory function could reflect the importance of low vitamin D as a marker for severity.

Keywords: Vitamin D, lung function, bronchial asthma.

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Introduction

Asthma is a chronic respiratory disorder of the airways characterized by bronchial hyper-responsiveness, respiratory symptoms, structural remodelling and reversibility, and variable airflow limitation. In developed and developing nations, it is the most common respiratory disorder with evidence suggesting that over the last two decades, its prevalence has increased worldwide.[1] Asthma is an important cause of morbidity and mortality in the world, especially in developing countries with an incidence of more than 300,000 every year, and the incidence has increased by nearly 10% over the last decade. Conventionally, asthma severity has been assessed with a combination of subjective (daytime and night time symptoms) and objective measures (Spirometry, peak flow recordings).[2] Nearly, 6% of Indian children and 2% of adults are presented with asthma symptoms per year in a population of 1.31 billion.[3]

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Asthma is a heterogeneous disease that is detected through its intermittent signs, including chest tightness, cough, and wheeze, which are resulting from reversible airflow obstruction.[4] Several phenotypes of asthma have been defined based on disease severity, the presentation of symptoms, the age of their onset, and the existence of other conditions, like eosinophilia and allergy with various long-term complications and response to corticosteroids (CS) therapy.[5]

Recently, use of rescue medications and assessment of risk factors for asthma exacerbations have been given its due importance in assessing asthma control. Due to the wide variation among different asthmatics, there is a need for other biomarkers to further classify these patients. For example, treatment-naïve asthmatics, with very low lung functions (forced expiratory volume in 1 s < 30%), may reach normal lung functions in 15 days and are highly treatment responsive. On the other hand, asthmatics with a lung function of 70% may continue to be symptomatic with hardly any change in their lung functions in spite of Step 4 or 5 treatments according to Global Initiative for Asthma guidelines. Therefore, clinicians need other biomarkers, which could help them manage their asthma patients better.[6]

Epidemiologic and genetic studies as well as research using animal models suggest vitamin D plays a vital and complex role in immune system function and regulation.[7,8] Vitamin D modulates a variety of processes and regulatory systems including host defense, inflammation, immunity, and repair.[9] Furthermore, a significant relationship between higher percent-predicted forced expiratory volume in 1 second (FEV1), force vital capacity (FVC) values and the increased circulating concentrations of 25-hydroxyvitamin D [25(OH)D] has been demonstrated in a large study of approximately 14000 subjects in the United States.[10]

In children, low vitamin D levels have been found to be associated with increased frequency of asthma exacerbations,[11] increased markers of allergy and asthma severity.[12,13] All these findings suggest a possible role of vitamin D in respiratory health outcomes. Despite the significant role of sunlight in vitamin D synthesis, the studies carried out in the last two decades have shown a high prevalence of VDD in tropical countries, such as China, Turkey, India, Iran and Saudi Arabia. The prevalence of VDD reported varies between 30% and 93% in different studies.[14,15,16] Prevalence of 92% of VDD has been identified in healthy asymptomatic volunteers in a study from Agha Khan University hospital.[17] Prevalence of VDD of 92% and 81% in ambulatory patients has been reported from centres in Karachi and Lahore recently.[18] Prevalence of vitamin D deficiency and insufficiency was found out to be 80% in healthy adults living in urban Tehran, Iran.[19] Similarly, studies had done in India report the prevalence of low levels of vitamin D to be ranging between 80-85% in-group of postmenopausal women and local hospital staff.[20,21]

Also, in one study it has been found that maternal vitamin D deficiency is associated with an increased risk of asthma in offspring; however in another performed study no clear association has been shown between maternal vitamin D status and asthma in children. In another study the cord blood vitamin D levels and its relationship to immune system function has been examined and no correlation has been found. In some studies, lower levels of vitamin D have been found in asthmatic patients that lead to decline in airway functions. Vitamin D supplementation in asthmatic patients can reduce the severity of the disease and can enhance airway responsiveness to glucocorticoids. However, some other studies did not find an association between vitamin D and the airways function.[22-27]

With regard to the existing controversies we performed this study with the aim to examine the relationship of serum vitamin D levels with asthmatic state and severity of asthma.

Methodology

AIMS

To study the effect of vitamin d levels on lung function in adult bronchial asthma patients.

Inclusion criteria

The sample selected in the study by convenience sampling were diagnosed Stable asthma patients (defined as no history of exacerbation at the time of presentation or within last 2 week) with age more than 18 years and below 80 years. Clinical findings and spirometry interpretations were done. Both genders of patients were enrolled in the study.

Exclusion Criteria

- Age less than 18 years.
- Pregnancy or evidence in their medical records of comorbidities, including, coronary artery disease, cancer
- Chronic obstructive pulmonary disease (COPD), or reported use of vitamin D supplements, >10 pack years of cigarette smoke exposure that could overlap with COPD, or hospitalization for asthma in the previous month, and.
- Patients who have received medications including systemic steroids, bisphosphonates, omega 3 fatty acids, phenytoin and theophylline.

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Assessment Tools:
Demographic details of every patient were collected. Detailed history and physical examination were done in all patients. Information was collected regarding symptoms and duration of symptoms of bronchial asthma such as Wheezing, Dyspnea/Breathlessness, Cough, Chest tightness
General examination was done & pulse, BP, respiratory rate, pallor, cyanosis was observed. Systemic examination including CNS, CVS was performed. Then examination of respiratory system was done.

Asthma Control Test:
Asthma control was assessed using the asthma control test (ACT). The ACT is a standardized, validated questionnaire that assesses asthma control on a scale of 5 to 25. ACT assesses the frequency of shortness of breath and general asthma symptoms and the effect of asthma on daily functions.
Laboratory investigations done in the hospital included the following:
• Sputum eosinophil count
• Blood eosinophilic count
• Measurement of serum 25 hydroxy Vitamin D levels.
• Serum IgE level measurement
• Chest x-ray.
• Spirometry
Previous document of spirometric evidence of asthma.
Spirometric evidence of asthma at the time of presentation.
FEV; < 80% of predicted,
FVC < 80% of predicted,
FEVi/FVC < 70%, and improvement of FEVi by >200 ml and 12% after 400 yg of salbutamol inhalation through metered dose inhaler with spacer was considered spirometric evidence of asthma.

Assessment of Vitamin D:
Blood samples for vitamin D measurements were collected in EDTA tubes, then centrifuged, aliquoted, and stored at -80•C. Plasma 25-hydroxyvitamin D was measured using the Tandem test (liquid chromatography/mass spectrometry).

Statistical Analysis:
Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using t test as well as chi square test and the level of significance was set at $p < 0.05$.

RESULTS
The present observational study was conducted in the Department of Respiratory Medicine, PIMS, Umarda, and Udaipur from March 2021 to August 2022 among 270 diagnosed stable asthma patients. The aim of the study was to find out association between Vitamin D levels and asthma control and lung function among adult bronchial asthma patients. Out of 270 subjects, low vitamin d level was found among 61.48% of the subjects. [Table 1]

Table 1: Vitamin D levels among study sample

Vitamin d	N	%
Normal (Sufficient+Insufficient)	104	38.52
Low	166	61.48
Total	270	100

Smoking was found to be present and absent in 89.16% and 10.84% of the subjects with low vitamin d level respectively with statistically significant difference. [Table 2]

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Table 2: Smoking distribution in study sample

Smoking	Vitamin d				Chi Square	p value
	Normal		Low			
	N	%	N	%		
Yes	71	68.27	148	89.16	6.78	0.029*
No	33	31.73	18	10.84		
Total	104	100.00	166	100.00		

*Statistically Significant

Mean FEVI/FVC ratio among the subjects with low and normal vitamin d was 56.24±6.13 and 48.59±7.02 respectively. Hence mean FEVI/FVC ratio was found to be lesser in subjects with low vitamin d level as compared to normal, with statistically significant difference. [Table 3, Figure 1]

Table 3: Mean FEV1/FVC ratio among study sample

Vitamin d	FEVI/FVC Ratio		t test	p value
	Mean	SD		
Normal	56.24	6.13	3.78	0.013*
Low	48.59	7.02		

*Statistically Significant

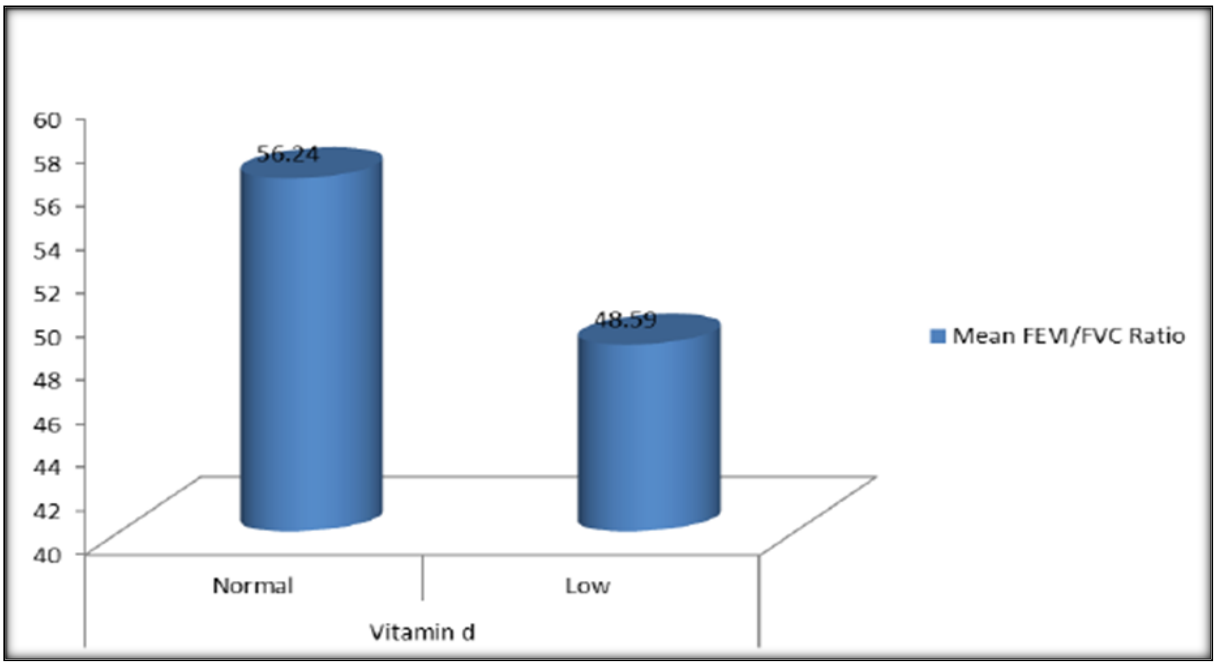

Figure 1: Mean FEV1/FVC ratio among study sample

Median ACT among the study subjects was 18 with IQR of 14. Significant positive correlation (r=0.87, p<0.01) was found between ACT and vitamin d level i.e. with increase in ACT score, vitamin d level also increases. [Table 4]

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Table 4: Correlation between Asthma Control Test and Vitamin D levels

Parameters	ACT and Vitamin d
r value	0.87
p value	<0.01**

***highly significant

DISCUSSION

VITAMIN D

Out of 270 subjects, low vitamin d level was found among 61.48% of the subjects in this study.

Moamena ME et al,[28] in their study reported that vitamin d level was found to deficient among 66% of the subjects.

According to Nadia A. Mustafa et al,[29] 47.7% of the patients had vitamin D deficiency (serum 25(OH)D <20ng/ml).

Khalid A. Abualnassr et al,[30] in their study reported that low vitamin D level was prevalent and represent a health problem among Saudi patients. The mean vitamin D level among the patients was 14.51±4.43 ng/mL with 85.7% of patients was vitamin D deficient and 14.3% of them were vitamin D insufficient.

FEVI/FVC RATIO

Mean FEVI/FVC ratio among the subjects with low and normal vitamin d was 56.24±6.13 and 48.59±7.02 respectively. Hence mean FEVI/FVC ratio was found to be lesser in subjects with low vitamin d level as compared to normal, with statistically significant difference in this study.

Similar findings were reported by Shaheen et al in 2011. Also Black and coworkers reported in a population based national survey a positive association between serum 25-hydroxyvitamin D and FEV1and FVC32.

Khalid A. Abualnassr et al,[28] in their study too revealed that vitamin d level decreases with decrease in FEVI/FVC ratio.

Epidemiological studies in healthy subjects have reported a strong relationship between 25-hydroxyvitamin D serum levels and pulmonary function, as assessed by FEV1 and FVC.

ACT

Median ACT among the study subjects was 18 with IQR of 14. Significant positive correlation ($r=0.87$, $p<0.01$) was found between ACT and vitamin d level i.e. with increase in ACT score, vitamin d level also increases.

Moamena ME et al,[28] in their study revealed similar positive correlation between ACT and vitamin d level.

The association between low vitamin D and asthma exacerbation and poor control may be explained by its influence on the innate immunity and increased incidence of respiratory viral infection. Vitamin D increases the production of antimicrobial and anti-inflammatory peptides including anti-viral factors. The active vitamin D is known to exert an inhibitory effect on airway hyperreactivity and increase glucocorticoid bioavailability.[28]

This study opens up newer vistas for possible intervention in bronchial asthma in our endemically Vitamin D-deficient population.

The strength of our study lies in the investigation of the relation between 25(OH) D with both the clinical and functional asthma parameters among adults. On the other hand, the limitations of the current study is that presence of other confounding factors were not addressed in the analysis including sun exposure, physical activity, dietary habits, dose, and the form of corticosteroid medications.

CONCLUSION

Vitamin D deficiency is highly prevalent in patients with exacerbations of bronchial asthma. It is associated with increased number and severity of exacerbations, poorer asthma control and lower lung functions. It has been also proven that supplementation of Vitamin D has a significant positive effect in decreasing the severity and number of exacerbations of bronchial asthma and this requires to be further confirmed by randomised studies in future.

The association between ACT and vitamin D in the absence of any association with respiratory function could reflect the importance of low vitamin D as a marker for severity. Therefore, we can recommend screening for low vitamin D in patients with uncontrolled asthma or poor response to therapy. Improve knowledge and awareness of asthmatic patients to sources of vitamin D and its relation to bronchial asthma.

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