Assessment of serum vitamin d levels in different severities of asthmatic patients

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Background There is conflicting evidence about the association between low vitamin D levels and asthma.

Aim The aim of this work was to assess the relation between the serum level of vitamin D and the asthma severity.

Patients and method A total of 90 asthmatic patients were diagnosed of bronchial asthma clinically and functionally according to GINA guidelines classification 2012. The serum 25-hydroxy vitamin D level was measured in all the cases. The relation between the serum level of vitamin D and forced expiratory volume at 1 s (FEV_1) was analyzed. Then, it was correlated to age, sex, and BMI variables.

Results Patients were divided into three groups according to FEV_1 prebronchodilators. The mean value of vitamin D was 30.43 in mild cases, whereas it was 20.27 in moderate cases, and 11.97 in severe cases. These data stated that the lower the FEV_1, the greater the vitamin D deficiency levels, and this relation was statistically highly significant ($P<0.001$). When the three groups (of severity of airway obstruction: mild, moderate, and severe) were compared with each other, the *P*-value was less than 0.001 for all. When the three variables were added as a third cofactor (age, sex, or BMI) separately, we did not find any statistically significant effect on the results.

Conclusion In asthmatic patients, the serum level of vitamin D was found to be directly proportional to the severity of asthma with no relation to the age, the sex, or the BMI. Further studies are recommended to assess the effect of the correction of serum vitamin D levels on the severity of asthma and asthma control.

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Introduction

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation [1]. The coexistence of airway inflammation and remodeling has led to the hypothesis that the disease is inflammatory in nature [2].

Vitamin D is both a nutrient and a hormone. Bioactive vitamin D or calcitriol has long been known for its important role in regulating body levels of calcium and phosphorus, and in the mineralization of bone. The vitamin D axis plays tissue-specific autocrine and perhaps paracrine roles distinct from the classical endocrine functions. Vitamin D also plays an important role in immune regulation through interactions between 1,25-dihydroxy vitamin D and vitamin D receptors [3].

A connection between the vitamin D status and asthma has been considered since many years. Vitamin D deficiency has been blamed as one of the causes of increased asthma prevalence in the last decades [4]. Vitamin D receptors are expressed on a variety of airway immune cells, where they function as classic nuclear steroid hormone receptors and ultimately regulate the transcription of numerous genes associated with inflammation and immunomodulation [5]. It was also found that vitamin D exerts direct effects on target cells independent of gene transcription [6] and may therefore be of relevance to airway inflammatory disorders [7]; while vitamin D can suppress interleukin 17 (IL-17) and IL-4-mediated expression of IL-13, it can also shift the T-helper 1 Th1/Th2 balance toward Th2 dominance [8]. These contradictory actions may be due to the direct actions of vitamin D on $CD4^+$ T cells to promote an IL-10-secreting T-regulatory population [9].

Aim

This study was designed to assess the incidence of vitamin D deficiency in asthmatic adults and to correlate between vitamin D levels and the severity of asthma. Also, we added a third cofactor (age, sex, and BMI) to detect their effect on the relation between serum vitamin D and asthma.

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Patients and methods

Study design

The study protocol was approved by local ethical committee and informed consent was taken. This was a cross-sectional study, conducted from January 2014 to January 2015. A written informed consent was obtained from all patients.

Patients

All participants were diagnosed according to the Global Initiative for Asthma (GINA) guidelines [1]. All patients enrolled in the current study were subjected to clinical history taking, full clinical examination, and laboratory investigations namely serum 25-hydroxy vitamin D [25(OH)D] levels and lung function tests.

The analytical method

Serum 25(OH)D level was measured by an enzyme-linked immunosorbent assay.

The principle of the test: This test kit is a competitive protein-binding assay for the measurement of 25(OH)D. It is based on the competition of 25(OH)D present in the sample with 25-hydroxy vitamin tracers, for the binding pocket of the vitamin D-binding protein (Gc-globulin).

Ranges for 25(OH)D:

(1) The normal range of 25(OH)D is 30–60 ng/ml.
(2) Deficiency was diagnosed at vitamin D levels less than 30 ng/ml or less than 75 nmol/l.
(3) Insufficiency was diagnosed at vitamin D levels less than 20 ng/ml or less than 50 nmol/l [10].

Statistical methods

Descriptive statistics were performed using the count and the percentage for categorical variables. Means±SD were used for continuous variables. Comparison of means across different asthma severities was performed using analysis of variance; pairwise comparisons using the Bonferroni test were performed to check the significance between each pair of groups. Correlations were determined using the Pearson correlation for continuous variables and the Spearman correlation for ordinal variables. Adjusting for confounders in correlations was performed using partial correlation. All statistical analyses were performed using R (version 3.1.0; https://www.R-project.org/Licenses/).

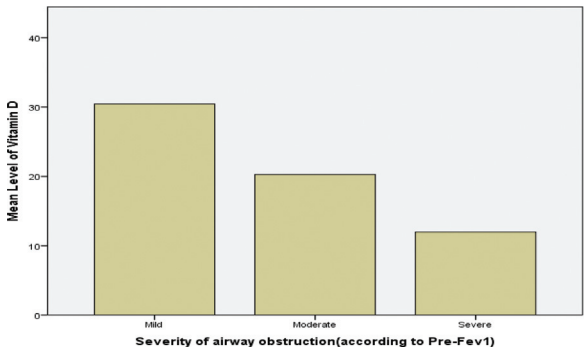
Results

Patients were divided into three groups according to forced expiratory volume at 1 s (FEV_1) prebronchodilators. The mean value of the serum level of vitamin D was found to be inversely proportional to the severity of airway obstruction. In mild airway obstruction (80%>FEV_1>60% of predicted), the mean value of vitamin D was 30.43; in moderate airway obstruction (60%>FEV_1>40% of predicted), it was 20.27; and in severe airway obstruction (FEV_1<40% of predicted), it was 11.97. This was proved to be statistically highly significant (P<0.001) (Fig. 1 and Tables 1–3).

There is no correlation between serum 25(OH)D and the change of FEV_1 before and after bronchodilator. P-value was nonsignificant (0.148) (Fig. 2).

Patients in the study were divided into four age groups: 23 patients were less than 40 years old, 46 patients were 40–59 years old, 19 patients were 60–79 years old, and the last group consisted of only two patients who were 80 years or older. The mean value of FEV_1 prebronchodilators was 79% in the youngest age group, 73% in the second group, 65% in the third group, and 56% in the oldest group. The mean value of serum vitamin D was 23 in the youngest age group, 22 in the second group, 18 in the older group, and 8 in the oldest group. The percent change of FEV_1

Figure 1



Relation between Severity of Asthma (According to Pre-FEV_1) and Vitamin D.

Table 1 Descriptive characteristics of the patients in the study

	Count (%)
Sex	
Female	17 (18.9)
Male	73 (81.1)
Severity of airway obstruction (according to pre-FEV_1)	
Mild	30 (33.3)
Moderate	30 (33.3)
Severe	30 (33.3)
Age (mean±SD)	50±14
BMI (mean±SD)	31±7

FEV_1, forced expiratory volume at 1 s.

Table 2 A summary of the asthma-related variables of the patients of the study

	Mean	SD
FEV_1 pre%	72	15
FEV_1 post%	85	17
FVC pre%	81	17
FVC post%	88	18
FEV_1/FVC pre%	75	9
FEV_1/FVC post%	80	9
FEV_1% of change	17	6
Level of vitamin D	21	9

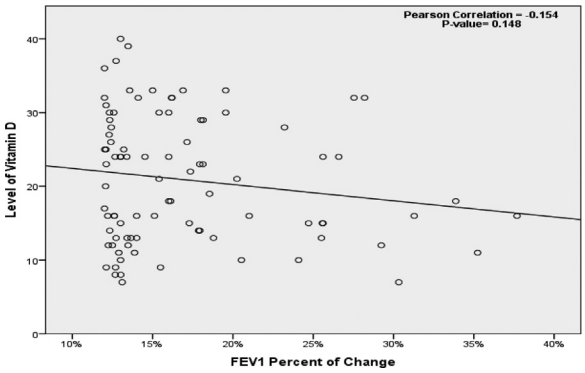
FEV_1, forced expiratory volume at 1 s; FVC, forced vital capacity.

Table 3 The difference between the severity of asthma (according to pre-forced expiratory volume at 1 s) and vitamin D levels

Severity of asthma (according to pre-FEV_1)	*N*	Vitamin D	
		Mean	SD
Mild	30	30.43	4.470
Moderate	30	20.27	4.705
Severe	30	11.97	2.846
Total	90	20.89	8.604

FEV_1, forced expiratory volume at 1 s. One-way analysis of variance. $P<0.001$.

Figure 2



Correlation between Vitamin D and % change in FEV_1.

Table 4 The correlation between the vitamin D level and the severity of asthma for age

	Age			
	<40	40–<60	60–<80	≥80
Count	23	46	19	2
FEV_1 pre%				
Mean	79	73	65	54
SD	14	13	14	9
FEV_1 post%				
Mean	92	85	76	61
SD	16	16	17	13
FEV_1% change				
Mean	17	17	17	13
SD	5	7	7	5
Level of vitamin D				
Mean	23	22	18	8
SD	8	9	8	1

Spearman's partial correlation=–0.872. FEV_1, forced expiratory volume at 1 s. $P<0.001$.

Table 5 The correlation between the vitamin D level and the severity of asthma for the BMI

	BMI		
	18.5–24.9 (normal weight)	25.0–29.9 (overweight)	≥30.0 (obese)
Count	15	33	42
FEV_1 pre%			
Mean	75	72	72
SD	17	15	13
FEV_1 post%			
Mean	87	85	84
SD	21	17	15
FEV_1% of change			
Mean	15	17	18
SD	3	6	6
Level of vitamin D			
Mean	21	20	21
SD	9	8	9

Spearman's partial correlation=–0.888. FEV_1, forced expiratory volume at 1 s. $P<0.001$.

prebronchodilators and postbronchodilators was almost the same in the different age groups, except for the oldest age group, wherein it had the lowest value. The *P*-value was less than 0.001, which is highly significant. However, when the Spearman partial correlation was performed, it was found to be -0.872, whereas it was 0.885 without correlation to age (Table 4).

According to the BMI, patients were divided into three groups: normal (BMI: 18.5–24.9), overweight (BMI: 25–29.9), and obese (BMI: >30). The mean value of FEV_1 prebronchodilator was 75% in normal-weight cases and 72% in overweight and obese cases. The mean value of serum vitamin D in the three groups was also almost equal (range: 21–22). The *P*-value was less than 0.001, but when the Spearman partial correlation was performed, it was found to be 0.888, whereas its value was 0.885 without correlation to the BMI (Table 5).

In Table 6, the sex was the third cofactor. We had only 17 women in this study and 73 men. The mean value of FEV_1 prebronchodilator was 77% in women and 71% in men. The mean value of serum vitamin D was 23 in women and 20 in men. The Spearman partial correlation of 0.888 was equal to that of the relation of vitamin D to asthma without the sex variable.

Discussion

In this study, almost all asthmatic patients involved were found to have low levels of serum vitamin D.

Table 6 The correlation between the vitamin D level and the severity of asthma for the sex

	Sex	
	Female	Male
Count	17	73
FEV_1 pre%		
Mean	77	71
SD	17	14
FEV_1 post%		
Mean	90	83
SD	19	16
FEV_1% of change		
Mean	17	17
SD	5	6
Level of vitamin D		
Mean	23	20
SD	10	8

Spearman's partial correlation=–0.888. FEV_1, forced expiratory volume at 1 s. $P<0.001$.

Cases with a mild obstructive pattern had a mean level of serum vitamin D of 30.43 (low normal), cases with a moderate obstructive pattern had a mean value of serum vitamin D of 29.27 (deficient), and cases with a severe obstructive pattern had a serum level of vitamin D of 11.97 (insufficient).

The serum level of vitamin D is directly proportional to FEV_1. Patients with a severe obstructive pattern had lower values of vitamin D than patients with moderate and mild obstructive patterns. Values of serum vitamin D were increasing gradually with higher FEV_1 values. There was no relation between the percent of change in FEV_1 and the serum level of vitamin D.

Abd El Aaty *et al*. [11] investigated 50 cases: 40 patients were diagnosed with bronchial asthma and 10 were healthy volunteers. They found that the serum vitamin D level was highly significantly lower in the asthmatic patient group compared with the control group, and the lowest value of serum 25(OH)D in the severely exacerbated asthma group [11].

Shebl *et al*. [12] included 66 nonsmoking adult asthmatic patients and 30 healthy adult controls, and found that 40% the asthmatic patients suffered from vitamin D insufficiency, whereas in the control group, vitamin D insufficiency was present in 20% of them with a significant increase in the number of severe asthmatic patients with vitamin D insufficiency compared with those with sufficient vitamin D [12]. This study is also in agreement with the study conducted by Shaaban and Hashem [13], who investigated serum vitamin D levels in 75 adults with asthma and 75 adult healthy controls, and demonstrated that vitamin D deficiency was observed in 78.66% the asthmatic patients, whereas 85% of the healthy control individuals expressed sufficient levels.

Sutherland *et al*. [14] enrolled 54 adults with asthma in a study [FEV_1 (mean±SD): 82.9±15.7% predicted, serum vitamin D levels: 28.1±10.2 ng/ml). Higher vitamin D levels were associated with greater lung function: with a 22.7±9.3 ml (mean±SE) increase in FEV_1 for each nanogram per milliliter increase in vitamin D (P=0.02) [14].

Li *et al*. [15] found similar data in a cross-sectional study included 435 Chinese patients ages more than 18 years with newly diagnosed asthma. Vitamin D deficiency was prevalent in Chinese adults with asthma, with 88.9% of the participants having 25 (OH)D less than 50 nmol/l. The serum 25(OH)D concentration was positively correlated with FEV_1% predicted (P=0.02, r=0.12). After adjusting for the age, the sex, the BMI, smoking, the month of blood collection, and the symptom duration, they found significant positive associations between 25(OH)D concentrations and FEV_1 (in l), FEV_1% predicted, and FEV_1/forced vital capacity (FVC) (P for trend<0.05 for all). Adjusted odds ratios for the highest as against the lowest 25(OH)D quartile were 0.50 (0.26–0.96) for FEV_1 less than 75% predicted and 0.44 (0.20–0.95) for FEV_1/FVC% less than 0.75 [15].

Alyasin *et al*. [16] performed another cross-sectional study that was conducted on 50 asthmatic children and 50 healthy controls ages 6–18 years. A univariate analysis of the relationship between asthma and vitamin D showed that decreased vitamin D levels were associated with significantly increased odds of an asthmatic state (P=0.002). In asthmatic patients, 25 (OH)D levels had direct and significant correlations with both the predicted FEV_1 (R^2=0.318, P=0.024) and the FEV_1/FVC (R^2=0.315, P=0.026) [16].

Although age is a factor that affects FEV_1, in this study, we did not find it to be a cofactor that affects the relation between vitamin D and FEV_1. When we added the BMI to the equation between FEV_1 and the serum level of vitamin D, we found that it was not an effective cofactor, although the role of obesity and its effect on FEV_1 is proved by many studies. Sex difference was not found to be related to the changes in FEV_1 values in relation to serum vitamin D.

Although several studies were conducted to detect variations in the asthma severity in relation to the

age, the sex, and the BMI, no studies mentioned their correlation to the serum level of vitamin D.

Conclusion

The serum level of vitamin D was found to be low in almost all asthmatic patients. The percent predicted value of FEV_1 is directly proportionate to the serum level of vitamin D.

Recommendations

The serum level of vitamin D should be determined in asthmatic patients, especially those with difficult-to-control asthma.

Further studies are recommended to include apparently normal individuals as a control group to study the serum level of vitamin D among them. Also, do need to know the effect of vitamin D supplementation on symptoms, control, and pulmonary function tests of asthmatic patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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