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Association of Pulmonary Function Tests and Serum Vitamin D Levels in Asthmatics With Vitamin D Deficiency

Mahnaz Amini[1], Zahra Mirfeizi[2*], Houshang Rafatpanah[3], Leila Ghofraniha[1], Shahrzad Mohammadzadeh Lari[1], Saeid Eslami[4,5], Habibollah Esmaily[6], Mostafa Abasalti[1]

Abstract

Objective: The effects of serum vitamin D levels on the evolution or severity of asthma have been widely researched; however, conflicting results have been achieved. This study was designed to evaluate the relationship between serum vitamin D levels and pulmonary function tests in asthmatic and non-asthmatic people with vitamin D deficiency.

Materials and Methods: This was a prospective cross-sectional study on healthy adults and asthmatic patients. Standard spirometry and serum 25-hydroxyvitamin D test were performed for all participants.

Results: Forty asthmatic patients and 40 healthy controls were tested. The mean age of participants was 42.86 ± 1.6. High prevalence of vitamin D deficiency was found in both the asthmatic and control groups. No significant correlation was found between serum vitamin D levels and spirometry parameters in either of the groups ($P=0.83$).

Conclusion: Serum levels of 25-hydroxyvitamin D were not correlated with the severity of asthma as evaluated by pulmonary function tests in asthmatics.

Keywords: Asthma, Vitamin D, Respiratory function test

Introduction

Asthma is the most common chronic respiratory disease that is characterized by the inflammation of the airways, leading to bronchial hyper-responsiveness and airflow obstruction (1).

Recent evidence has suggested that 25-di-hydroxy-vitamin D (25(OH)D) plays an important role in preventing inflammation (2). Recent research has shown the relationship between 25(OH)D and cancer, autoimmune diseases, cardiovascular diseases, and higher risks of infection (3). Some studies show vitamin 1,25(OH)D receptor (VDRs) variants are a risk factor for asthma (4). Moreover, the potential immunomodulatory properties of vitamin D in regulating airway smooth muscle function and airway inflammation in bronchial asthma have been studied (5).

Burns et al showed the relationship between the serum levels of 25(OH)D and lung function in adolescents (6). Studies that had been conducted in this regard did not share the same results; some confirmed the positive relationship between asthma and vitamin D deficiency (7,8), while others failed to show any association between the risk factors (9,10). This study was designed to evaluate the relationship between serum vitamin D levels and pulmonary function tests in asthmatic and non-asthmatic people with vitamin D deficiency.

Materials and Methods

Study Participants

This was a cross-sectional study with non-probability and an easy sampling method. The sample size was calculated based on a similar study (11) and with considering 36% correlation between vitamin D and severity of asthma, 99% confidence and 90% power with 33 samples. Sample size was increased to 40 participants in both groups, to remove any effects of confounding factors and increase confidence as much as possible. For the patient group, 40 asthmatic patients were recruited from pulmonary clinic of Imam Reza hospital during the winter, 2013.Asthmatic patients were diagnosed according to the American Thoracic Society criteria. They met the inclusion criteria and were recruited from pulmonary clinic by a pulmonologist.

Inclusion and Exclusion Criteria

The inclusion criteria comprised of: (1) FEV_1/FVC <0.7, more than 12% and 200 cc increases in FEV_1 after

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[1]Lung Disease Research Center, Faculty of Medicine, Mashhad University of Medicine Sciences, Mashhad, Iran. [2]Rheumatic Diseases Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [3]Inflammation and Inflammatory Diseases Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [4]Pharmaceutical Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran. [5]Department of Medical Informatics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [6]Department of Biostatistics, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran.

***Corresponding Author:** Zahra Mirfeizi, Tel: +985138012753, Fax: +985138401036, Email: mirfeiziz@mums.ac.ir

inhalation of 400 µg albuterol, (2) lack of clinical evidence of asthma exacerbation in the last 2 months, and (3) willingness to participate in the study. The exclusion criteria were as follows: (1) simultaneous existence of other pulmonary inflammatory diseases such as chronic obstructive pulmonary disease (COPD), bronchiectasis, tuberculosis, etc (2) history of known gastrointestinal malabsorption, inflammatory bowel disease, gastrectomy and chronic diarrhea, (4) history of hypoalbuminemia and hypocholesterolemia, (5) body mass index (BMI) of <18.5 kg/m^2, and (6) use of vitamin D supplements, systemic corticosteroids, and anticonvulsant agents in the last 6 months.

Patients' medical history was documented including the length of their disease and symptoms, pack-year of smoking, complete drug history including inhaled corticosteroids and long-acting beta-agonists. Clinical examination including measuring the height, weight, and chest size for all participants was made.

The subjects of control group were selected from healthy individuals who did not have any diseases and who were matched with the patient group with respect to their age, gender, and nutritional condition. The study aims and procedures were explained for participants and informed written consent was obtained.

Laboratory Methods

After completion of questionnaires, 5 mL of brachial vein blood was taken from the participants in both groups. The blood serum was separated immediately via centrifugation, (universal centrifuge: model PIT 320). Samples were kept in -70°C, and at the end of sampling all the samples were sent for measuring 25(OH)D level by chemo-immunoassay method using Cobas E411 ECL Analyzer. Serum levels of 25(OH)D were defined as follows: <10 nmol/L as severe deficient, 10-15 nmol/L as moderately deficient, 15-20 nmol/L as mildly deficient, 20-30 nmol/L as insufficient, >30 nmol/L as sufficient.

Standard spirometry was performed using Spirolab III (MIR, Italy) for all participants. All the participants were visited by 1 physician, and all measurements were performed with the same devices. The study was carried out during the winter, 2013.

Statistical Analysis

The collected data was analyzed using the SPSS software version 11.0. All variables were evaluated with descriptive statistical method which included frequency tables, frequency distribution charts, and measures of central tendency and dispersion statistics. Normality of data was first assessed via the Kolmogorov-Smirnov test to evaluate study assumptions, then chi-square and *t* test were used for 2 independent groups. The one-way analysis of variance (ANOVA) was used for normal observations, and equal tests like Mann-Whitney U and Kruskal–Wallis were employed for non-parametric variables. Any correlation between 25(OH)D and respiratory parameters was assessed by Spearman correlation test.

Results

Forty adult asthmatic subjects and 40 healthy adults participated in this study. Sex distribution, mean of age, and BMI were not different between 2 groups ($P=0.17$, $P=0.668$ and $P=0.57$, respectively). The demographic characteristics of asthmatic and control groups are shown in Table 1.

High prevalence of vitamin D deficiency was found in both asthmatic and control groups and this is shown in Table 2 (87.5% and 92.5%, respectively).

As expected, results of pulmonary function tests were significantly different between the groups of asthmatic and non-asthmatic adults with mean FEV1 of 2.16 L versus 2.8 L, mean FVC 0f 2.88 versus 3.39, and mean FEV1/FVC of 67% versus 86% ($P<0.001$, $P<0.001$, and $P=0.026$, respectively).

The correlation between 25(OH)D and pulmonary function parameters was evaluated with the use of Spearman correlation test (Figure 1). No significant correlation was found between serum vitamin D level and spirometry parameters (FEV1% predicted, FVC% predicted, MMEF% predicted, and FEV1/FVC) in both groups ($P=0.835$, 0.637, 0.792, and 0.871, respectively).

Discussion

The aim of the present study was to evaluate the association between serum 25(OH) D level and respiratory parameters in asthmatic and healthy individuals in a 25(OH)D deficient population. Most subjects in the case and control groups were deficient in their 25(OH)D serum levels. However, no correlation was discovered between serum 25(OH)D level and lung function tests in either groups.

Few studies have been reported for vitamin D deficient regions. Li et al conducted a large cohort study on vitamin D deficient population with 89.0% vitamin D deficiency. They used serum 25(OH)D concentrations in the form of log-transformed to assess correlation with FEV_1 % predicted. They showed significant correlation between log-transformed serum 25OHD (nmol/L) concentrations and FEV_1 % predicted ($P=0.02$, adjusted $r=0.12$) (12). The present study analyzed 25(OH)D levels in its actual form which is clinically more relevant.

Some studies have shown a reverse correlation between 25(OH)D level and asthma which is in stark contrast to

Table 1. Age and Anthropometric Chracterestic of Participants

Variable	Participants		*P* Value
	Case	Control	
Age (y), mean (±SD)	43.56 (±2.27)	42.18 (±2.28)	0.668
Male (%)	39%	50%	0.179
BMI, mean (±SD)	26.2 (±0.81)	25.41(±0.73)	0.578

Table 2. Frequency of Different Levels of 25(OH)D Between Asthmatics and Non-asthmatics

25(OH) D, (nmol/L)	Severe Deficiency	Mild Deficiency	Insufficiency	Sufficient	Overdose
Patient, No. (%)	4 (10)	7 (17.5)	24 (60)	4 (10)	1 (2.5)
Control, No. (%)	3 (7.5)	16 (40)	18 (45)	2 (5)	1 (2.5)
P value	0.26	0.551	0.320	0.071	0.501
Total, No. (%)	7 (8.8)	23 (28.8)	42 (52.5)	6 (7.5)	2 (2.5)

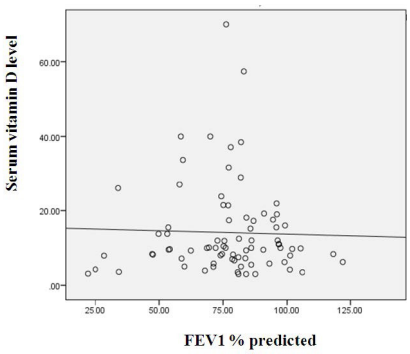

Figure 1. Scatter Plot of FEV1 % Predicted Plotted Against Serum Vitamin D Level.

our findings. Samrah et al studied 68 asthmatic women and 77 healthy women and found that although prevalence of 25(OH)D deficiencies was higher in asthmatic women, this difference was not statistically significant. The degree of 25(OH)D deficiency was associated with poor asthma control and the need for more medications (13). Although a clear association was demonstrated between infectious pulmonary disease and 25(OH)D, the link between 25(OH)D deficiency and asthma epidemic is still unclear and debatable (14).

Conclusion

This is one of the first studies on the association between serum 25(OH)D level and pulmonary function in adult asthmatic patients in a 25(OH)D deficient population which indicated no such association.

The main limitation of the study was the small sample size on which the study was carried out. Further comprehensive studies are required to fully define the nature of association between 25(OH)D and asthma pathogenesis. Studies from 25(OH) D deficient countries should be concluded in meta-analyses of effect of 25(OH) D on either the etiology or the severity of asthma.

Conflict of Interests

The authors declare that they have no conflict of interests.

Ethical Issues

The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences. Informed consents were obtained from both patient and control groups. This study was adherent to the Declaration of Helsinki and Good Clinical Practice (GCP).

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