INTRODUCTION

Vitamin D is an essential vitamin with significant immuno-modulatory effect. While a large number of recent epidemiological studies have investigated the relationships between vitamin D levels and asthma, the results of these studies have been controversial. Several previous case-control and cross-sectional cohort studies have found no associations between vitamin D levels and asthma. Epidemiological studies have revealed that low vitamin D levels have resulted in increased asthma prevalence and severity; and are associated with more frequent asthma attacks, decreased pulmonary function and more frequent use of inhalant medications. However, methodological differences, such as the method of vitamin D measurement, the normal reference values used, and the season when the study was conducted, have affected the conclusions of these studies. Vitamin D deficiency is an important and very common public health issue in the general population. Serum 25-OH vitamin D levels are the most reliable indicator of an individual's vitamin D level.

In this study, the aim was to determine the association between serum vitamin D levels and pulmonary function test outcomes, IgE levels and inhalant panels in children with asthma between 7 and 17 years of age who have been followed-up in our outpatient pulmonology clinics.

METHODOLOGY

A total of 71 patients between 7 and 17 years of age, who had an asthma diagnosis and were followed-up at our pediatric pulmonology outpatient clinics between December 2012 and March 2013 were enrolled in this cross-sectional study; and 77 healthy individuals in the same age range, who were seen at pediatric outpatient clinics for sports physicals were enrolled as controls. Written consent and assent were obtained from the study participants and their families. The study was approved by the Ethics Committee of Sisli Hamidiye Etfal Research and Training Hospital, Istanbul-Turkey. Diagnosis of asthma was established by a pediatric pulmonary physician, based on the 2007 National Asthma Education and Prevention Program (NAEPP) asthma diagnosis and treatment guidelines. Patients with chronic diseases other than asthma (renal, hepatic, endocrine, metabolic, or neurological disorders) or who were taking vitamin D supplements, anti-epileptic agents or systemic steroids that could affect vitamin D levels, were excluded from the study. Demographic information

ORIGINAL ARTICLE

Vitamin D Status, Lung Function and Atopy in Children with Asthma

Sebnem Ozdogan¹, Gizem Sari¹, Ibrahim Hakki Aktan¹, Belma Aydin¹, Canan Irmak¹ and Sabanur Cavdar²

ABSTRACT

Objective: To determine the associations between serum 25-hydroxy vitamin D3 levels and pulmonary function test outcomes and atopy in children with asthma.

Study Design: Cross-sectional study.

Place and Duration of Study: Pediatric pulmonology outpatient clinic and pediatric outpatient clinic, from December 2012 to March 2013.

Methodology: A total of 71 asthmatic children and 77 healthy controls aged 7-17 years were recruited. Vitamin D status was assessed by measuring the serum 25-hydroxy vitamin D3 levels and compared between two groups. The relationship between serum vitamin D levels and pulmonary function test outcomes and serum IgE levels and inhalant panels were also examined in asthmatic patients.

Results: The serum levels of 25-hydroxy vitamin D3 were low in both the asthmatic and control participants (median = 11.8 and 9.8 ng/ml, respectively). Vitamin D levels were significantly low in the patients who had high IgE levels and high levels of specific IgE antibodies against inhalant allergens in asthmatic patients. No correlation was found between vitamin D levels and pulmonary function test outcomes in asthmatic patients (p>0.05).

Conclusion: Vitamin D levels are not associated with pulmonary function test outcomes. However, low vitamin D levels are associated with atopy.


INTRODUCTION

Vitamin D is an essential vitamin with significant immuno-modulatory effect. While a large number of recent epidemiological studies have investigated the relationships between vitamin D levels and asthma, the results of these studies have been controversial. Several previous case-control and cross-sectional cohort studies have found no associations between vitamin D levels and asthma. Epidemiological studies have revealed that low vitamin D levels have resulted in increased asthma prevalence and severity; and are associated with more frequent asthma attacks, decreased pulmonary function and more frequent use of inhalant medications. However, methodological differences, such as the method of vitamin D measurement, the normal reference values used, and the season when the study was conducted, have affected the conclusions of these studies. Vitamin D deficiency is an important and very common public health issue in the general population. Serum 25-OH vitamin D levels are the most reliable indicator of an individual's vitamin D level.

In this study, the aim was to determine the association between serum vitamin D levels and pulmonary function test outcomes, IgE levels and inhalant panels in children with asthma between 7 and 17 years of age who have been followed-up in our outpatient pulmonology clinics.
was recorded for all of the participants. Blood samples were obtained from the participants to measure their serum total IgE levels and allergen-specific IgE levels (using an inhalant phadiotop panel). The serum total IgE levels were measured using an electrochemiluminescence method. The serum total IgE levels were determined to be normal or high, based on the participants’ age.

Vitamin D levels were measured with liquid chromatography-tandem mass spectrometry (LC-MS/MS) using a Quatro Premier XE device. The 25-OH-D2 and 25-OH-D3 levels were separately quantified and reported as the total 25-OH vitamin D level. High-performance liquid chromatography (HPLC) and liquid chromatography-mass spectrometry (LC-MS) have been variably reported to be the gold standard for vitamin D assays.

Vitamin D levels were measured once for each patient and healthy subject, and the levels were compared between the two groups.

The pulmonary function test measurements were made in accordance with the American Thoracic Society (ATS) standards using a MIR spirometer (MiniSpir®; Medical International Research Srl, Rome, Italy).

The best standards using a MIR spirometer (MiniSpir®; Medical International Research Srl, Rome, Italy). The best forced expiratory volume at 1 second (FEV1), forced vital capacity (FVC) and FEV1/FVC values were selected for analysis.

Statistical analyses were conducted using SPSS version 21 software, Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 statistical software (Utah, USA). Total 25-OH vitamin D was categorized into quartiles based on the distribution of 25-OH vitamin D. One-way Anova (Welch Test) and Oneway Anova tests were used to compare mean age, and pulmonary function test outcomes in 4 quartile groups based on vitamin D levels. Student's t-test was used to compare the mean age in asthma and non-asthma groups. Mann-Whitney U-test was used to compare the median vitamin D level among the participants. Vitamin D levels were measured once for each patient and healthy subject, and the levels were compared between the two groups.

Age, sex, participants' age.

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![Table I: Characteristics of patients with asthma and non-asthma.](image)

<table>
<thead>
<tr>
<th>Vitamin D Levels ng/mL</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st quartile (4-7.89)</td>
<td></td>
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<tr>
<td>Age (year); Mean ±SD</td>
<td></td>
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<tr>
<td>12.18 ±2.19</td>
<td></td>
</tr>
<tr>
<td>Sex (Female/Male); n (%)</td>
<td></td>
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<tr>
<td>15/2 (88.2/11.8)</td>
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<tr>
<td>FEV1; Mean ±SD</td>
<td></td>
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<tr>
<td>2.64 ±0.63</td>
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<tr>
<td>FEV1 %; Mean ±SD</td>
<td></td>
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<tr>
<td>106.53 ±10.95</td>
<td></td>
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<tr>
<td>FVC; Mean ±SD</td>
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<tr>
<td>3.15 ±0.58</td>
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<tr>
<td>FVC %; Mean ±SD</td>
<td></td>
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<tr>
<td>112.82 ±10.39</td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC; Mean ±SD</td>
<td></td>
</tr>
<tr>
<td>79.49 ±8.98</td>
<td></td>
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<tr>
<td>IgE levels (Normal/High); n (%)</td>
<td></td>
</tr>
<tr>
<td>1/16 (5.994)</td>
<td></td>
</tr>
<tr>
<td>Inhaled Panel (Positive/Negative); n (%)</td>
<td></td>
</tr>
<tr>
<td>16/1 (94.1/5.9)</td>
<td></td>
</tr>
</tbody>
</table>

Table II: Characteristics of patients with asthma.

**RESULTS**

A total of 148 subjects were investigated in this study, including 71 asthmatic children (36 males and 35 females) and 77 healthy control subjects. Table I shows the demographic information for the asthmatic and non-asthmatic subjects and the difference between the two groups. The median vitamin D level was 11.8 ng/mL in the asthmatic patients and 9.8 ng/mL in the non-asthmatic subjects. A comparison of the two groups with respect to age, gender, and the median vitamin D level revealed that the vitamin D levels of the asthmatic patients were significantly higher than those of the control subjects ($p=0.04$).

The clinical characteristics of the asthmatic patients were stratified by vitamin D level quartiles (Table II). No statistically significant difference was observed in the mean age, FEV1, FEV1%, FEV1/FVC, FVC or FVC% among vitamin D level quartiles. Evaluating the correlations between the vitamin D level by quartile and gender, the group with the lowest vitamin D level included a statistically significantly greater number of females ($p=0.001$). The IgE levels were statistically significantly higher and the inhalant panel positivity was statistically significantly more common among the subjects in the 1st quartile ($p=0.02$ and $p=0.002$, respectively). The association between vitamin D levels and pulmonary function test outcomes were analyzed. There was no significant association between vitamin D levels and the pulmonary function test outcomes (Table III).
DISCUSSION

While many studies have investigated the association between asthma and vitamin D levels, none has clearly elucidated this association. Epidemiologic data in most of the reported studies suggest that low serum vitamin D in children with asthma is associated with more symptoms, exacerbations, reduced lung function, increased markers of allergy and severe disease.\(^{15}\) Pulmonary function test outcomes are the indicators of asthma severity and asthma attacks. The researchers here did not find any significant association between pulmonary function test outcomes, and serum vitamin D levels. Similarly, two separate studies conducted in adolescents between the ages of 12 and 20 years (NHANES 2001-2006 and ACE) were compared in a study by Gergen et al. Both studies reported low levels of vitamin D and showed no association between vitamin D levels and asthma, asthma morbidity, hospitalization, asthmatic exacerbations, inhaler steroid use, FEV1 % predicted, FEV1/FVC, positive IgE, and positive skin tests.\(^{16}\) In a study of Costa Rican children, Brehm et al. failed to show a relationship between FEV1 and vitamin D levels.\(^{15}\) On the other hand, in a study by Alyasin et al., a significant correlation was observed between vitamin D levels and the pulmonary function test parameters FEV1 and FEV1/FVC. Pulmonary function test outcomes were observed to be low in patients with low vitamin D levels.\(^{17}\)

There appears to be an association between vitamin D and atopy, allergic rhinitis and asthma; however, previous studies have failed to describe this association clearly.\(^{18-20}\) In a study of Costa Rican children, low vitamin D levels were associated with an increased bronchodilator response, eosinophilia and increased IgE levels among children with asthma.\(^{15}\) In this study, vitamin D levels were very low in patients who had high IgE levels and high levels of specific IgE antibodies against inhalant allergens. Based on these data, it was concluded that vitamin D deficiency was very common among both asthmatic and healthy children, but no association was detected between vitamin D levels and pulmonary function test outcomes. In line with literature, low vitamin D levels are associated with atopy.

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There is no consensus about the optimal vitamin D levels for non-musculoskeletal health. A single measurement may not be sufficient to determine representative vitamin D levels in a given individual. In this study, it was determined each participant's vitamin D level with a single measurement, and the level was measured using the tandem mass method, which is the gold standard for measuring vitamin D levels.

Regardless of the normal limit, vitamin D deficiency is becoming more common, and it affects the general population. Vitamin D deficiency is commonly observed even in countries such as Turkey, where sunlight is abundant.\(^{21}\) Vitamin D levels were observed to be very low both in the asthmatic patients and the healthy subjects. These low levels may be attributed to the fact that the study was conducted between December and March, when the sunlight level was low and when people are likely to spend more time indoors.

Vitamin D deficiency is more common among females than males. The reasons for this are their lower levels of exposure to the sun, the season, their dressing styles and poor vitamin D intake.\(^{22}\) In this study very low levels of vitamin D were detected in the girls.

There are several limitations to our study. The study was conducted in winter, and the vitamin D levels were determined via a single measurement. Moreover, non-asthmatic group may not represent the general population and none of the subjects had normal vitamin D levels.

CONCLUSION

The researchers found no association between vitamin D levels and pulmonary function tests outcomes. However, it can be suggested that low vitamin D levels are associated with atopy.

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