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Research Article

The relationship between serum vitamin D level and asthma severity in asthmatic children (aged 1-15 years) in Ardabil, 2012-13

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ABSTRACT

Background: Vitamin D plays an important role in many immune and allergic diseases, and its deficiency is more in areas with low solar radiation. Asthma is a common disease in children of Ardabil city. The present study was designed to evaluate vitamin D levels in asthmatic children in Ardabil.
Methods: A total of 100 asthmatic children (40% boys and 60% girls) with a mean age of 5.7 ± 3.46 years (1-15 years) and who visited the Bou-Ali pediatric hospital were included. Vitamin D levels, disease course, IgE levels, and eosinophil counts were evaluated. A group of healthy children was also included to compare vitamin D levels between asthmatic and non-asthmatic children. All data were analyzed by statistical methods in SPSS v.16.
Results: The vitamin D levels in asthmatic children were lower than those in the healthy group. Furthermore, the increase in the vitamin D level was significantly associated with lower history of hospitalization (P = 0.02), better response to bronchodilator treatment (P = 0.01), lower IgE level (P = 0.02), and decrease in the mean age of children (P = 0.04). However, no significant association between vitamin D levels and sex (P = 0.08), history of anti-inflammatory drug use (P = 0.78), and eosinophil count (P = 0.08) was observed in asthmatic children.
Conclusion: Results showed that vitamin D deficiency was more common in asthmatic than in non-asthmatic children and the level of vitamin D was directly associated with the response of the children to treatment.

Keywords: Asthma, Vitamin D level, Children, Allergic diseases

INTRODUCTION

Surveys around the world have shown that asthma prevalence is highest in industrialized nations.[1] Although there is a trend for increased prevalence of asthma in countries farthest from the equator, this disease is common in some tropical countries (e.g., Costa Rica).[1] Epidemiologic data has shown an association between vitamin D deficiency and asthma incidence.[2-5] In fact, sufficient prenatal vitamin D intake may reduce childhood asthma risk up to 40%.[6] Increased asthma severity in older children has been linked to low vitamin D levels.[6,7]

Higher maternal intake of vitamin D during pregnancy is associated with a lower risk of recurrent wheezing in young children.[8,11] Although it was believed earlier that vitamin D deficiency was eradicated with fortification of foods, this problem has re-appeared and is associated with many disorders.[9] Despite food fortification, multiple studies have shown that vitamin D deficiency is highly prevalent even in sunlight-replete areas of the world and that vitamin D supplementation and fortification of foods

in current doses are inadequate.[10] The associations between vitamin D level and asthma and allergy remain unclear. While some suggest that prenatal and postnatal exposure to vitamin D may be protective for allergy, others suggest that vitamin D supplementation may increase the risk of allergy. Previous studies have reported the correlations between serum vitamin D levels and asthma severity in children and lung function in adults.[12,13] The findings of in vitro studies[14] suggest that vitamin D may reverse steroid resistance in patients with asthma, which explains the role of vitamin D in the control of asthma. Ginde et al.[15] found an inverse association between serum vitamin D levels and recent upper respiratory tract infections, especially in chronic respiratory diseases such as asthma. The vitamin D levels are routinely tested by assessing the concentration of the major circulating form of vitamin D, 25(OH)D3, in the serum. The present study examined the relationship between serum 25(OH)D3 levels and severity of asthma in asthmatic children.

METHODS

This cross-sectional study was conducted on 100 asthmatic children (60 boys and 40 girls) aged 1-15 years (mean age = 5.7 years) who had been referred to the Bu-Ali pediatric hospital between 2012 and 2013.

The subjects were diagnosed based on the following criteria: 1) symptoms of recurrent (i.e., >2) episodes of wheezing, cough, shortness of breath, or a combination of these and 2) documented reversibility with bronchodilators. A total of 20 healthy controls without a history of any allergic disorders in them or their first-degree relatives were also included in the study. The two groups were matched for age and sex.

Participants who had a history of intake of any supplements of vitamin D or drugs that modulate serum vitamin D levels, such as systemic glucocorticoids and anticonvulsants, and those who had chronic diseases were excluded.

Blood samples from all the subjects were collected during examination, centrifuged, aliquoted, and frozen at −70°C until required. The serum concentrations of 25(OH)D3 were assayed using an RIA Kit (DRG, Marburg, Germany) after extraction with acetonitrile, and the levels in the two groups (asthmatic group and healthy control) were compared. In addition, the relationship between vitamin D levels and the following parameters was also examined: eosinophil count, use of anti-inflammatory drugs in the previous year, hospitalization within the past year, and duration and severity of asthma. Based on a descriptive analysis, the vitamin D levels were classified as deficient (<20 ng/mL), insufficient (≥20 and <40 ng/mL), sufficient (≥40 ng/mL).[9,16]

A peripheral smear was performed, and after wright staining, the eosinophils were counted.

Statistical analysis

The data were statistically analyzed using Student's *t*-test and chi-square (linear by linear correlation) tests, as applicable (with a preset probability of $p<0.05$). The results are presented as arithmetic mean ± SD. The statistical tests were conducted using the SPSS software package, version 16 (SPSS Inc., Chicago, IL, USA) on a personal computer. Furthermore, the simultaneous effects of confounding variables such as, age, sex, and vitamin D levels on the asthmatic state were determined.

RESULTS

A total of 100 asthmatic and 20 non-asthmatic children with a mean age of 5.7± 3.46 years were examined in this study. The mean 25(OH)D3 levels in the non-asthmatic and asthmatic groups were 38.17 and 18.98, respectively, and this difference was statistically significant (P = 0.02) (Table 1). Furthermore, the characteristics of the asthmatic participants were stratified according to vitamin D quartiles. As shown in Table 2, in the asthmatic subjects, there were statistically significant differences between the strata in terms of sex, age, and hospitalization in the previous year (P <0.05). Female gender was a significant predictor of lower 25(OH)D3 levels, and there were no other statistically significant differences among the quartiles (P >0.05). Categorization of the vitamin D levels revealed statistically significant association between the levels of vitamin D and asthmatic state.

Univariate analysis of the relationship between asthmatic state and age, sex, and vitamin D levels showed that younger age and lower vitamin D levels were associated with significantly increased odds of asthmatic state ($p<0.05$). Thus, increased vitamin D levels were correlated to a greater decrease in the probability of the asthmatic state. There were no statistically significant differences between the vitamin D levels and sex (P = 0.08), history of anti-inflammatory drug (P = 0.78), and eosinophil count (P = 0.08) of the asthmatic children. Linear association analysis to determine the correlation between the vitamin D levels and eosinophil counts and other outcomes (any hospitalization or unscheduled visits for asthma within the past year and duration of the disease) revealed significant association (P >0.05). Furthermore, there were statistically significant trends toward lower IgE with increasing vitamin D quartiles (0.02).

Table 1: Vitamin D levels according to asthmatic state.

Vitamin D (ng/dl)	Non-asthmatics N (%)	Asthmatics N (%)	P value
<20	2 (10%)	55 (55%)	0.02
20-30	4 (20%)	30 (30%)	0.02
30-40	6 (30%)	10 (10%)	0.02
> 40	8(40%)	5(5%)	0.02

Table 2: Characteristics of asthmatic patients.

Characteristics	Asthmatic patients	1st quartile (<20 ng/dl)	2nd quartile (20-30 ng/dl)	3rd quartile (30-40 ng/dl)	4th quartile (40 ng/dl <)	P value
No of patients	100	55	30	10	5	0.02
Age (year)	5/7 ± 3/46	9/7	8/9	6/7	5/6	0.04
Hospitalization in the previous year (yes/no)	25/75	11 (11%)	7 (7%)	5 (5%)	2 (2%)	0.02
Unscheduled visits	65/100	3 (3%)	12 (12%)	15 (15%)	25 (25%)	0.01
Use of anti-inflammatory drugs	76/100	3 (3%)	14 (14%)	18 (18%)	13 (13%)	0.78
Eosinophil count (cells/mm^3)	520	670	460	630	540	0.08
IgE serum	136	278	135	89	23	0.02

DISCUSSION

The level of maternal vitamin D intake during pregnancy has been associated with asthma symptoms in children.[6,17] Vitamin D is well known for its role in calcium homeostasis and maintenance of bone metabolism.[18,19] However, recent evidence suggests that vitamin D plays important roles in both innate and adaptive immunity.[20] Vitamin D is involved in the maintenance of immune homeostasis, and has an important role in innate immunity, particularly through the direct induction of antimicrobial peptide (cathelicidin) gene expression.[21,22] In addition, some evidences have suggested the effects of vitamin D on lung growth and development in neonates[23] and lung function in adults.[13] Although a definitive role of vitamin D in the pathogenesis of asthma has not yet been determined, this vitamin may be related to asthma severity in several ways. First, vitamin D influences the immune system through its effects on helper T cell type 1, helper T cell type 2, and regulatory T cells.[24-26] Second, vitamin D inhibits the formation of matrix metalloproteinase as well as fibroblast proliferation and influences collagen synthesis. These actions signify that the level of 1,25(OH)2D3 may influence tissue remodeling and probably lung function;[27] however, we did not observe this effect in the present study. Based on the categorization of vitamin D levels, 55%, 30%, 10%, and 5% of the asthmatic subjects had serum vitamin D levels of <20 ng/mL (compared with 10% in the control group), 20-30 ng/mL (compared with 20% in the control group), 30-40 ng/mL (compared with 30% in the control group), and ≥40 ng/mL (compared with 40% in the control group; (P = 0.02), respectively, which were statistically significant. Brehm et al.[28] found that 25% and 3.4% of asthmatic patients had serum vitamin D levels of <30 and <20 ng/mL, respectively.

Comparison of the serum 25(OH)D3 levels in the asthmatic subjects with those in the healthy control group revealed higher prevalence of vitamin D insufficiency and deficiency in asthmatic children. This difference was statistically significant (P = 0.02) in the univariate analysis, and a strong inverse association was found between the serum vitamin D levels and asthmatic state. Thus, our data confirm the presence of lower vitamin D levels among asthmatic patients.

Brehm et al. found an inverse relationship between the circulating levels of vitamin D and several markers of allergy and asthma severity, such as eosinophil count, IgE levels, asthma exacerbation airway responsiveness, and skin-test reactivity.[12] Furthermore, Litonjua et al. noted that children with insufficient levels of 25(OH)D3 were more likely to have severe exacerbations; however, they did not find any association between the vitamin D levels and bronchodilator response or airway hyper responsiveness.[28] In the present study, the prevalence of vitamin D deficiency was detected in an equatorial population of children with asthma, and lower levels of vitamin D were associated with increased odds of hospitalization for asthma and increased IgE levels; however, there were no associations between the vitamin D levels and eosinophil counts and anti-inflammatory drug use. It has been reported that vitamin D deficiency is highly prevalent even in sunlight-replete areas of the world.[29] Some possible explanations for this occurrence include behavioral factors (e.g., sunscreen use, increased time spent indoors, and clothing coverage) and intrinsic factors (e.g., skin melanin content, ethnicity (dark-skinned person), and decreased cutaneous production of vitamin D3).[30,31]

CONCLUSION

In the present study, lower serum 25(OH)D3 levels were noted in asthmatic children when compared with those in the controls, and a direct relationship between serum 25(OH)D3 levels and IgE levels and asthma severity was found. Observational studies suggest that vitamin D deficiency increases the risk of respiratory infection, which may contribute to the incidence of wheezing illnesses in children as well as adults and cause asthma exacerbations.[15] Thus, vitamin D may be related to asthma and its severity. Results showed that vitamin D deficiency was more common in asthmatic than in non-

asthmatic children and the level of vitamin D was directly associated with the response of the children to treatment.

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