Severity of Asthma and Serum Vitamin D Levels in Asthmatic Children

ABSTRACT

Introduction Vitamin D deficiency has been rediscovered as a public health problem worldwide. It has been postulated that vitamin D deficiency explains a portion of the asthma epidemic. The purpose of this study was to assess the serum vitamin D levels in children with asthma as compared with the non-asthmatic population and to investigate the association of serum vitamin D levels with the severity of asthma.

Methods & Materials We measured serum 25-hydroxyvitamin D (25-OH vitamin D) levels in 50 children with mild intermittent to moderate persistent asthma at the time of enrollment and 50 age- and sex-matched non-asthmatic children in a case-control study. The independent sample t-test, χ^2 test, and spearman correlation coefficient were used to analyze the data.

Results Vitamin D level was 13.6 ± 1.1 ng/ml and 19.2 ± 1.8 ng/ml in asthmatic and non-asthmatic individuals, respectively. The mean (±SD) levels of serum vitamin D were statistically significant between asthmatic and non-asthmatic individuals. Females had lower levels of vitamin D than males. Asthma severity was inversely associated with serum vitamin D level.

Conclusion Findings of the present study demonstrate the significance of vitamin D in asthma. Sufficient doses of vitamin D should be administered to pregnant mothers and the babies monitored for symptoms of wheezing or asthma during childhood. Clinical trials are needed to definitively answer questions about the role of vitamin D in asthma.

Keywords: Asthma, Vitamin D, Vitamin D deficiency, 25-OH vitamin D

1. INTRODUCTION

Asthma is the most prevalent chronic respiratory disease in all age groups, affecting 300 million people worldwide. In children asthma is the most common chronic disease. The prevalence of asthma gas been increased in recent years. According to ISAAC global asthma prevalence raised from 11.1 to 11.6% in children and 13.2 to 13.7% in adolescents [1].

In Iran, the prevalence of asthma among children under 18 years of age varies from 1.26% to 11.6% depending upon sex, ethnicity, geography, and other factors [2]. Many factors can influence the severity of asthma, such as viral respiratory infections, male gender, food allergy, atopy, and air pollution. The role of these factors has been clearly proven over the past years [3]. Some recent studies have been conducted to determine the role of some vitamins and microelements in asthma occurrence and prevention [4-6].

Among the vitamins, the roles of vitamins C and D in the occurrence of asthma have been studied more seriously. Low levels of vitamin C and α-carotene are believed to be risk factors for asthma occurrence [5]. According to Chambers and Hawrylowicz supplementary vitamin D had an anti-inflammatory effect on the lungs and also increased the level of IL10, an anti-inflammatory mediator [7]. Vitamin D has a regulatory role in other inflammatory processes and diseases [8]. Some studies showed that low levels of vitamin D increases mortality in patients with breast and lung cancers [9-10]. Low levels of vitamin D are also correlated with some autoimmune disorders, such as type I diabetes mellitus [11] multiple sclerosis [12], rheumatoid arthritis [13], and inflammatory bowel diseases [14].

Vitamin D has an important role in the suppression of the inflammatory response of Th2 cells in the lungs. In animal models, it can induce surfactant synthesis and stimulate lung maturation [15]. The role of vitamin D and the synthesis of surfactant in the human fetus is more complex [16]. The risk of wheezing can be lowered in infants whose mothers have taken high doses of vitamin D during pregnancy [17].

Some studies have shown that vitamin D can be effective in regulating immune responses and can affect fetal lung growth [18]. Low levels of maternal serum vitamin D during pregnancy can increase the risk of occurrence of asthma during childhood [19]. Vitamin D supplementation can reduce asthma attack that requiring systemic corticosteroids for treatment [20]. However, some studies have presented contradictory results regarding the relationship between serum vitamin D levels and allergic diseases. Taking supplementary vitamin D can increase allergic diseases in children and an increased risk of asthma and allergies with high level of vitamin D was reported [21]. This study was designed to determine and compare the levels of serum vitamin D in children with asthma as compared with those of a control group. Moreover, the relationship between the severity of asthma and the level of serum vitamin D was investigated.

2. MATERIAL AND METHODS

In this cross sectional case-control study, 50 asthmatic children, aged 2–18 years, were enrolled via simple random sampling. The patients were referred to the Asthma and Allergy Clinic of Afzalipour Medical Center of Kerman University of Medical Sciences. Asthma was diagnosed and classified according to the National Asthma Education and Prevention Program's Expert Panel Report 3 [22].

Patients who suffered from disorders interfering with vitamin D metabolism or kidney disease and those who were taking antiepileptic drugs, supplementary vitamin D or other vitamins were excluded from the study. Fifty participants referring to the out-patient pediatric clinic of Afzalipour Medical Center due to simple and uncomplicated disorders, e.g., common cold and otitis media were selected as the control group. For each case, one control subject was randomly selected and matched to the index case according to age and gender. For each person, a data collection sheet containing name, age, gender, asthma severity, and other demographic data was filled out. The study was approved by the Research Ethics Committee of the University, and written informed consent was obtained from all cases and controls. A 5-mL sample of peripheral venous blood was collected from each individual. After the separation of serum by centrifugation at 2000 rpm, the level of 25-OH vitamin D was measured using a commercial ELISA kit (DLD Diagnostica, Gmbh) according to the manufacturer's instructions. Serum levels of 25 (OH) vitamin D were divided into three groups, including deficient (<20 ng/ml), insufficient (20–30 ng/ml), and sufficient (≥30 ng/ml) [23-24]. SPSS v.15 (SPSS Inc., Chicago, IL.) was used for statistical analysis of data. The independent sample t-test and chi-square analysis were used for comparison of the two groups. The Spearman correlation coefficient was calculated to identify the correlation between serum 25-OH vitamin D level and severity of asthma. $P < 0.05$ was considered to indicate statistical significance.

3. RESULTS

Vitamin D level was 13.6 ± 1.1 ng/ml and 19.2 ± 1.8 ng/ml in asthmatic and non-asthmatic individuals, respectively. The mean (±SD) levels of serum vitamin D were statistically significant between asthmatic and non-asthmatic individuals ($P = 0.01$). Amongst all participants, 52% of cases (n = 26) and 62% (n = 31) of controls were male. The mean

(±SD) age was 6.8 ± 0.4 years for cases and 7.6 ± 0.5 years for the controls. The serum vitamin D levels were lower in patients with moderate persistent asthma than in other patients (Table 1), but this difference was not statistically significant. However, there was a significant negative correlation between serum vitamin D level and asthma severity (r = 0.242, *P* = 0.015).

Table 1. Serum vitamin D levels in asthmatic and non-asthmatic individuals according to age

Age	Vitamin D level (ng/mL) Asthmatics	Vitamin D level (ng/mL) Non-asthmatics	P value
Below 5 years	17.4 ± 1.3	25.7 ± 3.8	0.05*
5–10 years	11.5 ± 1.6	15.7 ± 2.1	0.1
Above 11 years	10.3 ± 3.7	16.1 ± 3.1	0.27

The serum vitamin D levels were 10.6 ± 1.4 ng/ml and 16.3 ± 1.4 ng/ml in female and male individuals, respectively. The difference between the genders was found to be statistically significant (*P* = 0.009). Serum vitamin D levels were compared in asthmatic and non-asthmatic individuals according to age (Table 2). The level of vitamin D was significantly lower in asthmatic patients under 5 years (P<0.05). However in older ages no significant difference was demonstrated between the two groups. In the case group, children >11 years had the lowest serum vitamin D levels (10.3 ± 3.7 ng/ml) and children <5 years had the highest levels (17.4 ± 1.3 ng/ml), a difference that was statistically significant (*P* = 0.02). This difference was also found to be significant in the control group (*P* = 0.04).

Table 2. Serum vitamin D levels and asthma severity according to National Asthma Education and Prevention Program's Expert Panel Report (4)

Asthma severity	Mild intermittent	Mild Persistent	Moderate persistent	P Value
Vitamin D level	15.1 ± 2	13.6 ± 1.4	10.2 ± 3.8	0.4

Serum vitamin D levels according to the type of dwelling and childcare situation are shown in Table 3. The serum vitamin D levels in home-cared children were significantly different in asthmatic (3.2 ± 1.3 ng/mL) and non-asthmatic subjects (20.9 ± 2.1 ng/mL, P=0.004).

Table 3. Serum vitamin D level according to childcare situation, type of dwelling, maternal age, mother's education and history of taking vitamin D during infancy.

	Case	Control	P value
Childcare situation			
Kindergarten	14.8 ± 1.8	13.2 ± 2.8	0.65
Home	13.2 ± 1.3	20.9 ± 2.1	0.004
P value	0.5	0.04*	
Type of dwelling			
Villa building	14.1 ± 1.2	19.7 ± 2	0.02
Apartment	10.9 ± 2.6	15.3 ± 1.7	0.23

P value	0.3	0.4	
Taking vitamin D during infancy			
Complete	13.6 ± 1.5	18.3 ± 2.8	0.16
Incomplete	12.9 ± 1.9	17.3 ± 3	0.21
Not taking	15.1 ± 3.1	24.1 ± 2.6	0.046*
P value	0.8	0.4	

There was statistically significant difference in serum vitamin D levels between asthmatic and non-asthmatic subjects in terms of the type of dwelling. Significantly lower vitamin D concentrations were detected in the asthmatic children living in villa buildings than the control group (P=0.02). However no significant difference was documented in those living in apartments.

The mean level of vitamin D (95%CI) was measured according to the parental history of providing supplementary doses of vitamin D to children (Table 3). Higher levels of vitamin D were shown in non-asthmatic children who were not taking supplementary vitamin D compared to the children with asthma (P=0.046).

4. DISCUSSION

This study shows that the serum 25-OH vitamin D level in asthmatic children was lower than those in the controls. The role of vitamin D in the pathogenesis of asthma is not fully understood. Vitamin D can influence immune responses by affecting Th1 and Th2 function [25]. Polymorphisms in vitamin D receptor-coding genes can correlate with different phenotypes of asthma [26]. There was a significant negative correlation between the serum 25-OH vitamin D level and severity of asthma in this study. Alyasin et al showed the serum 25-OH D3 levels and childhood asthma severity are inversely associated and suggested a direct relationship between pulmonary function test results and vitamin D deficiency in Iranian asthmatic children [27]. In Qatar, with a similar social and climate conditions to Iran, Bener et al found asthmatic children had significantly reduced levels of serum vitamin D compared to the non-asthmatic controls [28]. Brehm et al showed that the severity of asthma and increased markers of allergy are correlated with a low level of serum vitamin D [28].

Litonjua shows that the use of supplementary vitamin D in the diet can play a primary preventive role in the incidence of asthma, reduce the severity of asthma, and improve recovery from steroid-resistant asthma. In this study, there was no significant difference in the serum vitamin D levels in children with a history of taking sufficient amounts of vitamin D in supplemental form with those who did not take supplementary vitamin D (at least 400 IU per day) during infancy. Failing to remember vitamin D supplementation by mothers is a factor that should be taken into consideration. Studies showed that children who have taken supplementary vitamin D during the first year of life have a lower risk of asthma at 31 years of age, but there was no report of vitamin D levels during this period [29]. A meta-analysis of randomized trials show the rate of asthma exacerbation can reduce by vitamin D supplementation especially in patients with vitamin D insufficiency [30]. Litonjua (2019) suggested vitamin D supplementation can prevent asthma and wheeze in early life, and may help in treatment of asthma [31].

Gale shows that the prevalence of asthma at the end of the first decade of life has a negative correlation with the serum vitamin D levels of mothers in the third trimester of pregnancy [32]. A deficiency of vitamin D in the prenatal period can influence the development of the fetal lungs and immune system [18].

This study shows that serum vitamin D levels were lower in female than in male patients, this difference may be due to body coverage in female patients. In one study conducted in Turkey, the lowest serum vitamin D levels were found in women who cover their whole body from sunlight [33]. Gender is a significant factor in vitamin D insufficiency as indicating in our findings as well as in a study carried out in Tehran by Rabbani et al. They found the prevalence of vitamin D insufficiency in healthy subjects was 53.6% in girls and 11.3% in boys [24]. A study in Saudi Arabia showed the levels of vitamin D in asthmatic and non-asthmatic females was lower than males which is in accordance with the results of the present study [34]. Despite higher sunny days in the region throughout the year, these findings can be attributed to the body coverage of females due to the social, cultural and behavioral aspects of this issue.

Mirsaeid Ghazi et al showed that children under 10 years of age have higher serum vitamin D levels in contrast to older age groups and the level of serum vitamin D decreases with increasing age [35]. These data are in accordance with our findings. The difference in the serum vitamin D levels in the early years of life in contrast to later years can be due to more attention given by parents to vitamin D supplementation of children in the early years of life and more exposure to sunlight due to more time spent on outdoor activities by this age group.

It has been shown that low levels of serum vitamin D are correlated with more severe forms of asthma. Brehm demonstrated that vitamin D insufficiency can develop more severe forms of asthma exacerbation in Puerto Rican children [36]. Tabak et al reported that using some foods, such as fish, containing high amounts of vitamin D can protect children from asthma [37]. Vitamin D deficiency is common in different parts of Iran [38]. Twenty-six percent of primary school children in Isfahan had vitamin D deficiency [39]. In Shiraz 81.3% of healthy children were vitamin D efficient [40]. In Zahedan, southeast of Iran, vitamin D deficiency was reported in 94.7% of apparently health subjects [41]. High prevalence of vitamin D deficiency may be due to the low dietary intake of vitamin D, reduced sunlight exposure and low physical activity [40-41].

In conclusion findings of the present study demonstrate the significance of vitamin D in asthma. The level of serum vitamin D in asthmatic patients was significantly lower than those in controls. The severity of asthma had a significant negative correlation with serum vitamin D levels. Further studies are required to determine the role of vitamin D in the prevention of asthma and in decreasing its severity. To this end, sufficient doses of vitamin D should be administered to pregnant mothers and the babies monitored for symptoms of wheezing or asthma during childhood in future years.

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