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Asthma control not associated with vitamin D deficiency: A single-center retrospective study in Saudi Arabia.

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Abstract

Background: Asthma is one of the most common pulmonary diseases in Saudi Arabia with estimated prevalence of 24%. It has been found that almost half of Saudi asthmatics suffer from vitamin D deficiency, which is another common health problem in Saudi Arabia. The association between asthma control and vitamin D level, however, is controversial. Our objectives are to estimate the prevalence of vitamin D deficiency among asthmatic patients in Saudi Arabia and to evaluate the association between vitamin D level and asthma control.

Methods: We conducted a retrospective cohort study including all asthmatic patients presenting to the outpatient clinic in the period from 2014 to 2015 at a tertiary care center in the Western region of Saudi Arabia. Asthma control score was assessed using Global Initiative for Asthma guidelines (GINA) and vitamin D measurements were recorded.

Results: 194 asthmatics were included in the study. 41 (21.7%) of the subjects had uncontrolled asthma while 148 (78.3%) had controlled asthma. Vitamin D was deficient in 101 (52.1%) of the population. The mean vitamin D level for controlled and uncontrolled asthmatics was 53.4 and 51.5, respectively, which is not significantly different (p value 0.657). Surprisingly, 71.6% of our asthmatic populations were males. On the other hand, vitamin D deficiency was more common in females (P= 0.019).

Conclusion: Vitamin D deficiency is common among pediatric asthmatic patients in Saudi Arabia. Our study suggests that there is no significant association between asthma control and vitamin D level.

Keywords: Asthma, Vitamin D, Asthma control, Saudi Arabia.

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Introduction

Asthma is the most common chronic disease among children worldwide, and the WHO estimates that 235 million people have asthma [1]. Asthma is not only a public health problem for high-income countries. Indeed, more than 80% of asthma-related deaths occur in low- and lower-middle-income countries [1]. The data on asthma prevalence in pediatric age group is still lacking in Saudi Arabia. However, there is a study done in 1985 on 2,123 school-age children, which showed a prevalence of 8%. Another one included 1,008 children and showed increased in prevalence up to 23% in 1995 [2].

Asthma exacerbations are defined as acute or sub-acute worsening in control of symptoms that necessitates a visit to a healthcare provider or requires systemic corticosteroids treatment as it may cause severe distress or risk to health of patient. Asthma control is determined by the symptoms of asthma. Asthma control is classified according to Global Initiative for Asthma (GINA) guidelines to: well controlled, partially controlled, and uncontrolled asthma [3]. GINA developed a symptom score that consists of the presence or absence of four symptoms during the last four weeks [3].

Vitamin D deficiency is another major health problem. Many studies have shown some association of vitamin D deficiency with cancer, cardiovascular disease and type 1 DM [4,5]. In Saudi Arabia, a study performed in 2 large commercial centers in the capital city where participants

were selected randomly out of the general population showed that 29% of the 488 studied individuals were vitamin D deficient, 22.7% were in the relative insufficiency group and 47.5% had normal levels of 25-hydroxyvitamin D [6]. Another study performed in 2012 in 4 primary healthcare centers in Riyadh City included 331 individuals and tested their serum vitamin D levels. All of the participants were vitamin D deficient (serum levels <30 nmol/l) and 11.4% of them had severe deficiency (levels <12.5 nmol/l) [7].

Over the past few years, several studies have suggested the existence of an association between asthma and vitamin D levels. Bener et al. studied this association in Qatari children. The study included 483 asthmatic children and 483 controls. It concluded that asthmatic children were more likely to have reduced vitamin D levels compared to control group [8]. By contrast, other research studies have not shown a relationship between asthma and vitamin D levels in children. One of these studies, by Yao et al., examined Taiwanese children aged 5–18 years (N=1315) and did not find an association between vitamin D status and either allergic diseases or atopy [9]. Also, Wawro et al. studied 2815 children aged 10 years and showed no significant association between vitamin D levels and asthma or hay fever [10]. The relationship between vitamin D deficiency and asthma severity has also been studied. In Puerto Rico, a cross-sectional study of 560 children showed that children with vitamin D insufficiency (serum <74.88 nmol/l) had higher risk for having more severe asthma exacerbations [11].

No previous studies have been conducted in Saudi Arabia on the relationship between vitamin D levels and having asthma or its severity. The high prevalence of both asthma and vitamin D deficiency in Saudi Arabia [1,2,7,8] prompted us to assess the relationship between vitamin D deficiency and asthma severity in the population of Saudi children with asthma.

Methods

This study was conducted at King Khaled hospital in King Abdulaziz Medical City, which is a tertiary care center in the Western region of Saudi Arabia. The study protocol was approved by Institutional Review Board (IRB). The study was a retrospective cohort study in which the medical records of all asthmatic children who attended respiratory pediatric outpatient clinics at this hospital from January 2014 to December 2015 were reviewed. Assessment of asthma control was done by the same time vitamin D measurements were obtained.

Each patient was classified as having controlled or uncontrolled asthma according to their level of asthma control by symptoms, using the Global Initiative for Asthma (GINA) guidelines [3]. The study sample size was calculated to detect a 30% difference between the two groups with a margin of error of 0.05 and 80% power. This revealed that we should include a total of 162 patients.

The inclusion criteria were age 2-14 years, available vitamin D measurements and a diagnosis of bronchial asthma made by pediatric pulmonologists according to the GINA guidelines. Patients with inherited bone disease, kidney disease, hypoparathyroidism or hyperparathyroidism were excluded from the study. Patients of both sexes were included in the study population.

The data collected in this study consisted of demographic data, an asthma severity assessment based on the symptom score by GINA guidelines, data about the additional factors that may affect asthma control, and recent vitamin D levels [12]. Patients with vitamin D levels of less than 50 nmol/L were considered to be vitamin D deficient. Vitamin D levels were measured by using immunochemiluminescent; Architect i2000SR, Abbott Laboratories, Abbott Park, Illinois, U.S.A.

We also considered other factors that may affect asthma control. These factors included assessment of environmental control at home per GINA guidelines, specifically exposure to smoking at home [12]. We also included factors that reflect good asthma control, for example, if the patients had history of having one or more exacerbation(s) in the last year, and if they have ever been intubated because of asthma. Lastly, we included history of other atopic disease in the patient or in his parents.

Simple descriptive statistics were determined and are reported as the means and Standard Deviations (SDs) for quantitative values or as the medians and interquartile ranges for qualitative values. For comparisons between categories, we used the independent variable t-test and the chi-square test. All analyses were performed using SPSS v22.

Results

In total, 355 patient files were reviewed. Of these, 161 did not meet the inclusion criteria and were excluded from the study (Figure 1). Overall, 194 patients were ultimately included in the study, 148 (78%) with good asthma control and 41 (22%) with poorly controlled asthma.

Table 1 lists the demographic characteristics of the patients, and other reported factors that may affect asthma control. The demographic characteristics of the two groups were similar, except that patients in the uncontrolled group reported experiencing more asthma exacerbations in the previous year compared with patients in the controlled group. Additionally, good environmental control was more commonly encountered among the controlled group than among the uncontrolled group. Asthmatic children were also classified depending on their disease severity into mild intermittent, mild persistent, moderate persistent, and severe persistent asthma. Only 3% of patients with good asthma control had severe persistent disease, while 20% of poorly controlled asthma children had severe persistent disease (Table 1).

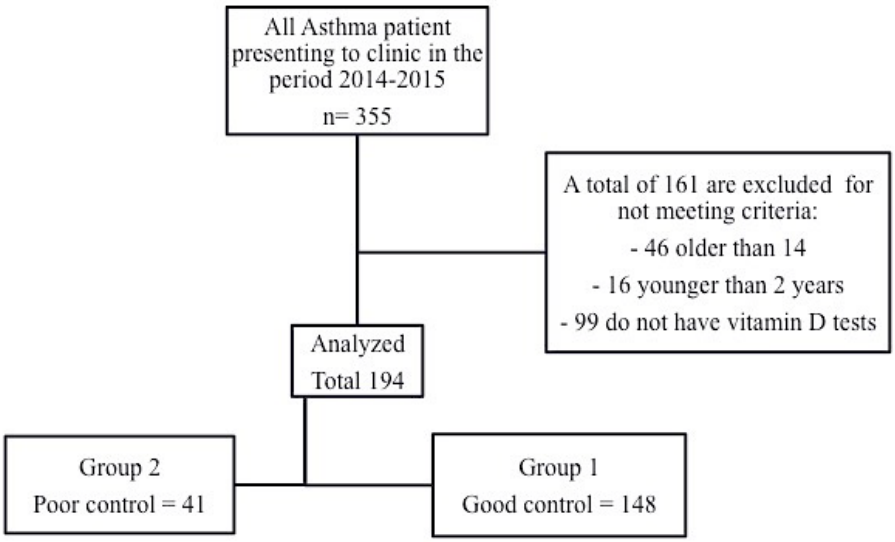

Figure 1. *Participants' selection of included patients*

Table 1. *Demographic and other characteristics*

Characteristic	Good asthma control group (n=148)	Poor asthma control group (n=41)	P value
Age (mean ± SD)	7.23 ± 3.43	7.53 ± 3.88	0.63*
Sex (% male)	70.9	73.2	0.78‡
Years since diagnosis (mean ± SD)	4.50 ± 2.94	4.48 ± 3.24	0.97*
BMI (mean ± SD)	16.43 ± 3.33	16.78 ± 3.76	0.58*
Asthma classification (%)			
Intermittent	4.7	0	<0.001‡
Mild persistent	66.4	43.6	
Moderate persistent	25.3	35.9	
Severe persistent	3.4	20.5	
Exposure to smoking (%)	24.4	24.1	0.98‡
Good environmental control (%)	72	46.9	0.007‡
Reported one or more asthma exacerbation(s) in the previous year (%)	27	54.1	0.002‡
Reported ever being intubated because of asthma (%)	2.3	2.9	0.82‡
History of other atopic diseases (%)	37	25	0.16‡
History of atopy in one of the parents (%)	62.1	54.5	0.43‡
* Indicates p value for student t-test ‡ Indicates p value for the chi-square			

	Good asthma control group (n=148)	Poor asthma control group (n=41)	P value
Vitamin D levels (mean ± SD)	53.4 ± 24.2	51.5 ± 25.3	0.657*
Vitamin D deficiency (<50 nmol/l) (%)	52.0	53.7	0.853‡
Males (%) with vitamin D deficiency	48.6	43.3	0.612‡
Females (%) with vitamin D deficiency	60.5	81.8	0.186‡
* Indicates p value for student t-test ‡ Indicates p value for the chi-square			

Table 2. *Vitamin D levels and status*

Figure 2 shows the comparison between vitamin D levels in patients with controlled and uncontrolled asthma. The mean vitamin D levels for the controlled and uncontrolled groups did not significantly differ, at 53.4 ± 24.2 and 51.5 ± 25.3, respectively (Table 2). The median vitamin D level for the controlled group was 49 and for the uncontrolled group were 49.2. Among males, 48.6% of good asthma control group had vitamin D deficiency and 43.3% of poor asthma control group had vitamin D deficiency. However, in females, the rate of vitamin D deficient children in the controlled and uncontrolled asthma groups was 60.5% and 81.8%, respectively (Table 2). It was noted that 70% of the children in each of the two groups were on treatment with vitamin D supplements. However, the rate of vitamin D deficiency in both controlled and uncontrolled asthma groups was high as shown in Table 2. In addition, we

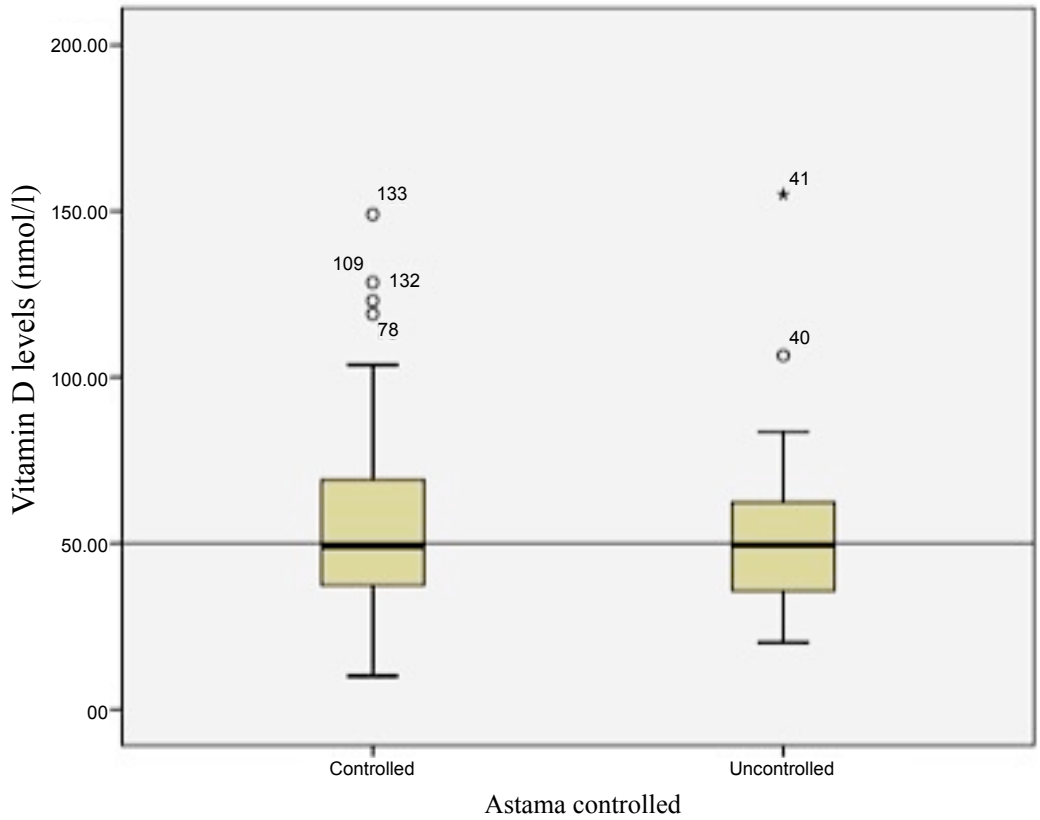

Figure 2. *Comparison of vitamin D levels between controlled and uncontrolled asthma patients. Horizontal line indicates vitamin D value cut-off on 50 nmol/l*

did find that vitamin D deficiency was more common in female patients (65.5%) than in male patients (46.8%), with a p value of 0.019. This was an observed finding for the cohort of patients as a whole.

Discussion

Our findings did not show evidence of a relationship between asthma severity and vitamin D levels in the studied population. These results are similar to those reported by Yao et al. in Taiwan [9]. We found two differences between the patient groups analyzed, asthma exacerbations and good environmental control, which were more common in the uncontrolled group and the controlled group, respectively. Of note, Yao at al. did not find an association between vitamin D deficiency and increased frequency of asthma exacerbations [9]. On the other hand, our findings do not support the study done by Kalmarazi et al. [13]. The mentioned study concluded that patients with asthma are more likely to have lower levels of vitamin D (17.98 in asthma group compared to 22.23 in controls).

The frequency of vitamin D deficiency in our population of patients with asthma was similar to that reported in previous studies performed in individuals from the general population in Saudi Arabia [6,7,14]. In addition, we found that vitamin D deficiency was more common in female individuals, which has also been reported by other studies conducted in the general population in Saudi Arabia and the Middle East [7,14-16]. This may be explained by the lifestyle of women in these countries and covering clothing.

This study had several notable limitations. First, most of the patients in this study had controlled asthma. Number of patients in uncontrolled asthma group was smaller than one specified for sample statistics which, in fact, may decrease the likelihood of finding statistically significant differences between the controlled and uncontrolled patient groups. Also, we did not take into consideration the seasonal effect on asthma. Asthma control can vary depending on the season, and there was no specification for inclusion or exclusion of patients depending on the season. Vitamin D can also be affected by the season. In the winter, people tend to get less exposure from the sun. However, in Western region of Saudi Arabia, the weather does not reach these extreme cold temperatures.

Conclusion

Our results do not support the use of vitamin D levels as a predictor of asthma severity, at least in populations similar to our study population. This study also shows high rate of vitamin D deficiency in Saudi population and that is more pronounced in females.

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