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Original article

The frequency of vitamin D deficiency among asthmatic Egyptian children

Background: *Vitamin D plays a role in the pathogenesis of asthma as it has a potent immunomodulatory effect acting on the cells of the innate immunity. It also reduces the risk of respiratory viral infections which are important initiators of asthma exacerbations. Besides, it potentiates the anti-inflammatory action of corticosteroids which are considered the most effective controllers of asthma.* ***Objective:*** *To detect the frequency of vitamin D insufficiency and deficiency among Egyptian asthmatic children and to correlate vitamin D levels to the severity of asthma.* ***Methods:*** *This case control study was conducted on 60 asthmatic children and 40 healthy controls. All were subjected to clinical history taking including history of sun exposure and asthma medications and full clinical examination. Laboratory investigations included measurement of serum calcium, serum alkaline phosphatase and serum 25-OH-D levels and lung functions (spirometery).* ***Results:*** *There was a significant correlation between vitamin D deficiency and severity of asthma, yet there was no significant relation between sun exposure and 25-OH-D level. Moreover, there was a significant relation between decreased serum 25-OH-D levels and the intensity of corticosteroid use. Vitamin D was also significantly lower in asthmatic patients with coexistent allergic rhinitis.* ***Conclusion:*** *Vitamin D deficiency is prevalent in Egyptian children with asthma .Lower levels of serum vitamin D are associated with high asthma severity, reduced asthma control and increased corticosteroid use.*

Keywords: Vitamin D, Bronchial asthma, Egyptian, Children

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INTRODUCTION

Asthma is defined as a common chronic inflammatory disease of the airways characterized by variable and recurrent symptoms, reversible airflow obstruction, and bronchospasm. Children have smaller airways than adults, which makes asthma especially serious for them[1]. Asthma affects nearly 300 million people worldwide; it is the most common chronic disease among children where almost 90% of children are diagnosed by age of 6 years. Vitamin D is both a nutrient and a hormone. Bioactive vitamin D or calcitriol has long been known for its important role in regulating body levels of calcium and phosphorus, and in mineralization of bone. Vitamin D axis has tissue specific autocrine and perhaps paracrine roles distinct from the classical endocrine functions. Vitamin D deficiency has been documented in many populations worldwide[2], even in areas of the world with abundant sun exposure. Because of its potential role in decreasing the risk for a multitude of chronic diseases associated with westernization, vitamin D deficiency is an important public health problem. The role of vitamin D in inhibiting T_H1 immune responses has been well studied, but its effects on T_H2 responses are more complex and not fully elucidated. Vitamin D receptors (VDRs) and vitamin D metabolic enzymes have been identified in many other tissues aside from bone and intestine, suggesting involvement in the metabolism and function of many cell types. Specifically, VDR is expressed in cells of the immune system, such as T cells, activated B cells, and dendritic cells[3]. The 1-α-hydroxylase is also expressed in dendritic cells, suggesting that 25(OH) D can be converted to the metabolically active form locally and thus plays a role in immune signaling. In addition to effects on adaptive immunity, there is also a newly recognized role of vitamin D in innate immune responses to microbial agents. It is becoming apparent that vitamin D participates in Toll-like receptor signaling in response to infections by up regulating the production of cathelicidin and other antimicrobial peptides[4]. This effect of vitamin D is

the likely explanation for the observations that sunlight can treat tuberculosis and other infections [5]. These effects of vitamin D on the immune system make it a plausible critical regulator of immune system function, whose deficiency can predispose to asthma and allergies in the presence of other environmental stimuli[6].

Hence, this study was designed to detect the incidence of vitamin D insufficiency and deficiency among Egyptian asthmatic children and to correlate between vitamin D levels and severity of asthma.

METHODS

Study Population and Design

During the period from March, 2011 to September, 2011, this case–control cross-sectional study was carried out at the Pediatric Chest Clinic, Children's Hospital, Ain Shams University; Cairo, Egypt. It included 60 asthmatic children (Group I) and 40 age- and sex-matched healthy children as a control group (Group II). Patients were selected according to the global initiative for asthma ''GINA guidelines''[7]. A written informed consent was obtained from both patients and controls. The Pediatric Department Board ethically approved the study.

Group I (Asthmatic children): included 60 children; 38 (63.3%) males and 22 (36.7%) females. Their ages ranged from 2 to 18 years with a mean value of 8± 4.2 years.

Group II (controls): included 40 healthy children; 30 (75%) males and 10(25%) females. Their ages ranged from 2-18 years with a mean value 8.3± 3.4 years.

All children enrolled in the current study were subjected to clinical history taking including history of sun exposure and asthma medications, full clinical examination, laboratory investigations namely serum calcium, serum alkaline phosphatase and serum vitamin D (25-OH-D) levels and lung function tests (spirometery).

Analytical methods

Total serum calcium and alkaline phosphatase levels were assayed photo metrically using Hitachi 917 autoanalyser and Roche reagents. Reference range of serum calcium: 8.6-10.3mg/dl and serum alkaline phosphatase: 8.6-10.3mg/dl.

Serum 25(OH) D was measured by Enzyme-linked immunosorbant assay (ELISA).

Principle of the test: This test kit is a competitive protein binding assay for the measurement of 25(OH) D. It is based on the competition of 25(OH) D present in the sample with 25 (OH) vitamin tracers, for the binding pocket of vitamin D binding protein (VDBP, Gc-globulin).

Ranges for 25 hydroxy vitamin D:

- Normal range for 25 hydroxy vitamin d 30-60 ng/ml.
- Deficiency was diagnosed at vitamin d level < 30 ng/ml or <75nmol/l
- Insufficiency was diagnosed at vitamin d level <20 ng/ml or <50nmol/l.

Lung Function Tests

Short-acting bronchodilators were stopped at least 8 hr before the test. Dynamic spirometry (Jaeger, Germany) was performed before sputum induction, with measurement of FEV1% of predicted, according to the standards of the European Respirator Society and the American Thoracic Academy. The highest value of FEV1 of three forced expiratory maneuvers was used.

Statistical Methods

Data were analyzed using standard computer program SPSS Windows version. (SPSS Corporation, USA). Continuous data were expressed in the form of mean ± SD. Categorical data were expressed as numbers and percentage. For comparison of continuous data we used student t test, while categorical data were compared using chi-square test. Anova test was used for comparing more than two groups of quantitative data. Linear regression analysis was used to determine the value of certain variables as predictors of the study outcome. Correlation between variables was done using correlation coefficient "r". P value of < 0.05 indicates significant results.

RESULTS

The demographic data of patients and control groups are shown in table (1). Of the asthmatic patients 6 (10%) had intermittent, 26 (43.3%) had mild persistent, 23 (38.3%) had moderate persistent and 5 (8.3%) had severe persistent asthma according to GINA guidelines[7].

The mean value of vitamin D was significantly lower and the mean value of alkaline phosphatase was significantly higher in patients than controls (Table 2).

There was no significant difference as regard serum calcium levels between asthmatic patients (9.6±0.44 mg/dl) and control children (9.7±0.42 mg/dl). Of the asthmatic children, 30% had allergic rhinitis and the mean value of vitamin D was statistically significant lower in asthma patients

with allergic rhinitis (39±12 nmol/l) compared to those with asthma only (53.6±11.8 nmol/l).

As shown in table (3) and figure (1) there was a negative correlation between serum vitamin D levels and the grades of asthma severity, yet there was no significant difference between lack of exposure to sun light and deficiency of vitamin D (Table 4).

As shown in table (5) there was a negative correlation between serum vitamin D levels in patients and corticosteroid use that reflects asthma grades.

Table 1. Demographic data of patients and control groups.

Variable		**Patients (n=60)**	**Controls (n=40)**
Sex	Male	38 (63.3%)	30(75%)
	Intermittent	6 (10%)	
	Mild	19 (31.66%)	
	Moderate	11 (18.33%)	
	Severe	2 (3.33%)	
	Female	22 (36.7%)	10 (25%)
	Intermittent	0 (0%)	
	Mild	7 (11.66%)	
	Moderate	12 (20%)	
	Severe	3 (5%)	
Age (years)		8 ±4.2	8.3±3.4
Allergic rhinitis		18 (30%)	0 (0%)

Table 2. Serum levels of 25(OH) D and alkaline phosphatase in patients and controls.

Variable		**Patient**	**Control**	**X^2**	**P value**
25(OH)D (nmol/l)	Deficient	27 (45%)	0%	57	<0.001 HS
	Insufficient	33 (55.8%)	15 (37.5%)		
	Normal	0%	25 (62.5%)		
Alkaline phosphatase (mg/dl)	High	60 (100%)	15 (37.5%)	50	<0.001 HS
	Normal	0%	25 (62.5%)		

HS= highly significant

Table 3. Serum levels of 25(OH) D in the different grades of asthma severity.

	Serum 25(OH)D(nmol/l)			**F value**	**P value**
	Range	**Mean**	**±SD**		
Intermittent	40-70	61.8	11.2	7.8	<0.001 HS
Mild	30-66	52.9	10.8		
Moderate	25-73	45.7	12.9		
Severe	20-40	31.1	9.5		

HS= highly significant

Table 4. Effect of sun light exposure on vitamin D status.

		Number	**Serum 25(OH)D level (nmol/l)**			**t-test**	**P value**
			Range	Mean	± SD		
exposure to sun light	Yes	40	30-73	50	12.5	-1.07	0.28 NS
	No	20	20-65	46	15.3		

NS=non-significant

Table 5. Use of steroid and serum level of 25(OH) D.

Steroid intake	Serum 25(OH)D(nmol/l)		X^2	P value
No	2 (7.47%)	15 (45.5%)	15	0.001 S
Inhalation only	13 (48.1%)	15 (45.5%)		
Nasal & inhalation	12 (44.4%)	3 (9.1%)		

S=significant

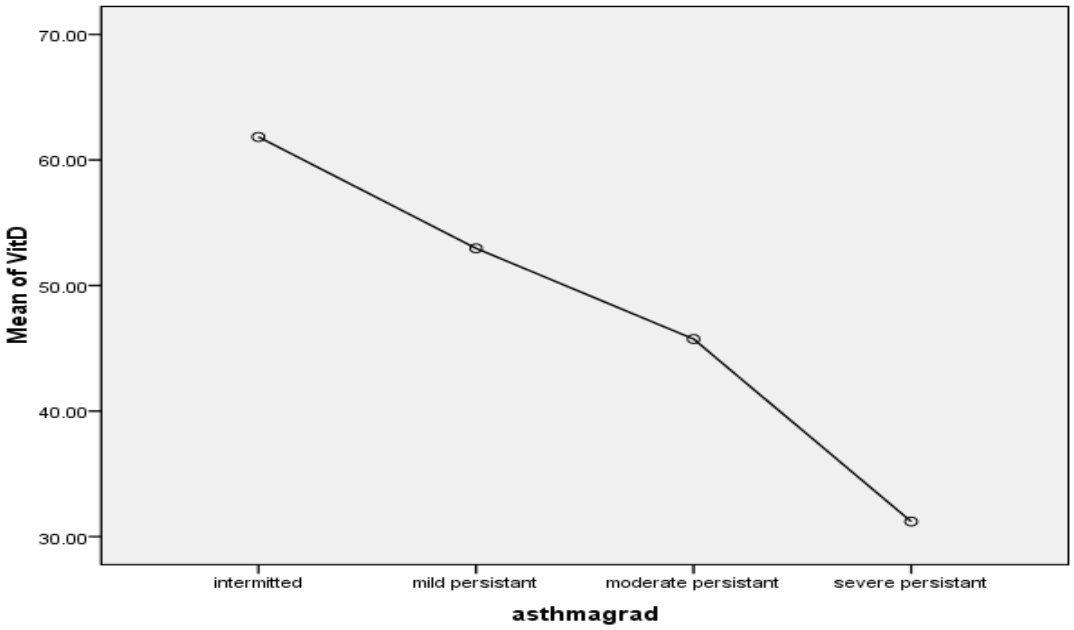

Figure 1. Comparison between serum level of 25(OH)D (nmol/l) and grades of asthma.

DISCUSSION

This study sought to detect the incidence of vitamin D insufficiency in terms of serum 25(OH)D <75nmol/l and deficiency <50nmol[8] among 60 Egyptian asthmatic children in comparison to 40 controls and to correlate the relation between vitamin D levels and severity of asthma. The study showed that 45% of the patients had vitamin D deficiency and 55.8% had insufficiency, while the controls had 37% insufficiency and 62.5% were sufficient. The mean value of 25(OH)D in asthmatic children was significantly lower than controls. Multiple studies have been done among Egyptian children about the status of vitamin D. Baroncelli et al.[9] reported that 37% of Egyptian children had vitamin D deficiency. Prentice et al.[10] showed that the average level of serum 25(OH)D was 25.3±10.3 which is deficient in Egyptian children. Fuleihan[11] studied vitamin D status in North and South Africa. She stated that inappropriate level of vitamin D was due to limited sun exposure due to cultural practices, prolonged breast feeding without vitamin D supplementation, limited outdoor activity, lack of government regulation for vitamin D fortification of food, decreased maternal intake during pregnancy and increased burden of infectious disease whereby utilization and turnover of vitamin D is increased.

In the current study patients had elevated serum levels of alkaline phosphatase than controls. This could be explained by vitamin D deficiency which causes secondary hyperparathyroidism leading to increase turnover of osteoid tissue and elevated serum levels of alkaline phoshatase[12]. The current study demonstrated a highly significant relation between the deficiency of vitamin D and the severity of asthma. This was demonstrated in the levels of serum 25(OH) D in asthmatic patients, intermittent: 61.8±11.2 nmol/l, mild persistent: 52.9±10.8 nmol/l, moderate persistent: 45.7±12.9 nmol/l and severe persistent: 31.2±9.5 nmol/l. This came in agreement with Brehm et al.[2] and Manbir and Thomas[13], who reported that asthmatic children with low serum level of vitamin D, may have a greater risk of suffering severe asthma attacks than those with higher levels of the vitamin. In the current study there was significant association between decreased serum vitamin D levels in asthmatic children with increased corticosteroid use. This came in agreement with Searing et al.[14]

the study aimed to investigate variables associated with vitamin D insufficiency in patients with childhood asthma. Of the asthmatic children, 30% had allergic rhinitis and the mean value of vitamin D was significantly lower in asthma with allergic rhinitis compared with asthma only. This enforced by the work of Brehm et al.[2], in their analysis of data, where they identified a higher prevalence of allergic rhinitis with vitamin D deficiency.

It is concluded that vitamin D deficiency is prevalent in children with asthma living in Egypt. Additionally lower levels of vitamin D were associated with higher asthma severity, reduced asthma control and increased corticosteroid use in asthmatic children was associated with lower levels of vitamin D. Therefore, vitamin D supplementation during childhood and adolescence, in adequate doses could be among the national nutritional priorities.

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