Evaluation of serum vitamin D and IgE in patients with bronchial asthma

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Background Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation.

Aim This study was carried out to evaluate the level of vitamin D and immunoglobulin E (IgE) in asthmatic patients during exacerbation and after remission.

Patients and methods This study was carried out on 30 patients with bronchial asthma diagnosed and classified according to Global Initiative for Asthma 2015 and 20 healthy individuals. Serum vitamin D and IgE were measured using enzyme-linked immunosorbent assay for all participants.

Results Vitamin D level was highly significantly lower in the asthmatic group during exacerbation compared with the asthmatic group after remission and the control group, and the total IgE level was highly significantly higher in the asthmatic groups compared with the control group.

Conclusion Asthmatic patients might have an increased risk of having vitamin D deficiency during exacerbation and after remission, whereas the levels of serum total IgE level was high in asthmatic patients compared with normal individuals.
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Introduction

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation [1]. There is a link between high prevalence of asthma and vitamin D deficiency. In support of this hypothesis, two studies have shown that vitamin D supplementation might prevent the development of asthma and improve the clinical response to steroids [2]. Vitamin D deficiency has been associated with increased airway hyperresponsiveness, lower pulmonary function, worse asthma control, and steroid resistance [3]. Allergic diseases, including asthma, are characterized by an increase in serum immunoglobulin E (IgE) levels [4].

Patients and methods

Patients

This study was carried out on 30 patients with bronchial asthma, diagnosed and classified according to Global Initiative for Asthma (GINA) 2015, attending to the Chest Department, Benha University Hospitals, during the period from December 2014 to March 2015, and 20 healthy volunteers were included as a control group. The participants in this study were divided into three groups: group I included 30 patients with bronchial asthma during exacerbation (age range 20–65 years; mean age 38.27±11.3); group II comprised the same patients from group I after remission; and group III included 20 healthy individuals as the control group (age range 20–45 years; mean age 36.05±6.4).

Exclusion criteria

Patients younger than 18 years, patients with renal or liver diseases, patients with diabetes mellitus, patients on systemic corticosteroids, and pregnant women were excluded from the study.

Methods

In this study, all participants were subjected to the following: full history taking, full clinical examination (general and local), plain chest radiograph (posteroanterior view), complete blood count, sputum eosinophil count, liver and kidney function tests, pulmonary function tests, serum vitamin D evaluation using enzyme-linked immunosorbent assay, and total IgE determination using enzyme-linked immunosorbent assay.

Results

This study included 30 patients diagnosed as having bronchial asthma (10 male and 20 female). Their ages ranged from 20 to 65 years, with a mean age of 38.27±11.3. A total of 20 healthy volunteers served as the control group

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(11 male and nine female). Their ages ranged from 20 to 45 years, with a mean age of 36.05±6.4. The mean BMI in the control group was 27.03±3.33 and that in the asthmatic groups was 28.87±5.58 (Table 1).

Discussion

The majority of participants in the asthmatic group were female (20 female and 10 male). There were 11 male and nine female patients in the control group. The mean age in the control group was 36.05±6.4 and that in the asthmatic groups was 38.27±11.3. The mean BMI in the control group was 27.03±3.33 and that in the asthmatic groups was 28.87±5.58 (Table 1).

The results of the present study demonstrated a nonsignificant difference between the studied groups as regards age, sex, smoking status, and BMI (Table 1).

The results of the present study showed that serum vitamin D level was highly significantly lower in the asthma group (during exacerbation and after remission) compared with the control group (Table 2). This study is in agreement with that by Li *et al.* [5], who studied serum vitamin D level in 435 asthma patients older than 18 years (268 women and 167 men); they found that the concentration of 25(OH) vitamin D [25(OH) D] ranged from 9 to 85 nmol/l. Of the 435 participants, 89.0% (387 participants) had serum 25 (OH)D less than 50 nmol/l (referred to as a deficiency), whereas only 2.8% (12 participants) had a concentration greater than 75 nmol/l (referred to as a sufficiency). Only 1.5% of women had sufficient vitamin D status, relative to 4.8% of men (P=0.05). Shaaban and Hashem [6] investigated serum vitamin D level in 75 adults with asthma and 75 healthy controls older than 18 years (35 male and 40 female for both groups). They observed that vitamin D deficiency (<20 ng/ml) was observed in 59 (78.66%) asthmatic patients (17.28±2.4 ng/ml); an overall 12.31% of asthmatic adults had sufficient vitamin D levels (≥30 ng/ml), whereas 85% of healthy controls expressed sufficient levels. They attributed this to the fact that reduced serum vitamin D levels are associated with increased expression of tumor necrosis factor-α , suggesting that enhanced expression of this proinflammatory cytokine is one potential pathway through which decreased vitamin D levels could exert a proinflammatory effect in asthma [7]. Observational studies suggest that vitamin D deficiency increases the risk for respiratory infection, which may contribute to the incidence of wheezing illnesses in adults and children and cause asthma exacerbations. [8]. Korn *et al.* [9] studied serum vitamin D level in 280 adults with asthma (45.0 ±13.8 years, 40% male, forced expiratory volume in 1 s 74.9±23.4%, 55% severe, 51% uncontrolled) and 40 healthy controls and noted that 25(OH)D concentrations in adult asthmatics were low (25.6 ±11.8 ng/ml) and that vitamin D insufficiency or deficiency (vitamin D<30 ng/ml) was common (67%).

Similarly, Felicia *et al.* [10] studied serum vitamin D level in 121 adults with asthma and found that 91% of

Table 1 Comparison between the asthmatic and control groups as regards personal data

	Asthmatic groups	Control group	Student's *t*-test	*P* value
Age				
Mean±SD (range)	38.27±11.3 (20–65)	36.05±6.4 (20–45)	0.795	0.431
Sex [*n* (%)]				
Male	10 (33.3)	11 (55.0)	χ^2=2.31	0.128
Female	20 (66.7)	9 (45.0)		
Smoking [*n* (%)]				
Yes	4 (13.3)	3 (15.0)	Fischer's exact test=0.0	1.0
No	26 (86.7)	17 (85.0)		
BMI [mean±SD (range)]	28.87±5.58 (20.8–40.4)	27.03±3.33 (21.4–35.9)	1.32	0.193

There were no significant differences between the studied groups as regards age, sex, BMI, and smoking state.

Table 2 Comparison between vitamin D level between the control group, the asthmatic group during exacerbation, and the asthmatic group after remission

	Control group	Asthmatic group (during exacerbation)	Asthmatic group (after remission)	*F*-test	*P* value
Vitamin D level (ng/ml) (mean±SD)	38.81±3.96	20.42±3.7	28.93±2.56	177.6	0.001**

Vitamin D level was highly significantly lower in the asthmatic group (during exacerbation), compared with the asthmatic group (after remission) and the control group.
**Highly significant

asthmatic patients had vitamin D below 20 ng/ml and 74% of patients had serum vitamin D levels between 20 and 30 ng/ml and had severe asthma as compared with only 50% of those with sufficient vitamin D of 30 ng/ml or higher.

The results of the present study showed that serum vitamin D was highly significantly lower in severe exacerbated asthma compared with moderate and mild exacerbated asthma (Table 3).

Korn *et al.* [9] reported that serum levels of 25(OH)D were significantly related to asthma severity (intermittent: 31.1±13.0 ng/ml; mild: 27.3±11.9 ng/ml; moderate: 26.5 ±12.0 ng/ml; and severe: 24.0±11.8 ng/ml; P=0.046). About 75% of patients with severe or uncontrolled asthma were vitamin D insufficient as defined by a level of 30 ng/ml or less. Patients with severe and uncontrolled asthma had the lowest 25(OH)D levels (23.7±12.3 ng/ml) compared with patients with intermittent, mild, or moderate and controlled or partly controlled asthma (27.1±11.7 ng/ml, P=0.014). Patients with severe or uncontrolled asthma had a 20 or 30% higher risk to be vitamin D insufficient compared with patients with intermittent, mild, or moderate disease, or with controlled or partly controlled asthma, respectively. They attributed this to the strong correlation between asthma severity and 25(OH)D concentrations, which suggests an impact of hormonal effects on the asthmatic inflammation or vice versa. Airway epithelia contain high levels of the enzyme that converts circulating 25-OH-vitamin D_3 to its active form 1,25-OH-vitamin D_3. The active form of vitamin D has local effects in response to respiratory infections and might dampen the inflammation that is the consequence of these infections [11]. This study is in agreement with the study by Eman Shebl *et al.* [12] as well, who reported that there was a significant increase in the number of severe bronchial asthma patients with vitamin D insufficiency (41.4%) compared with those with sufficient vitamin D. Arias *et al.* [10] also demonstrated that there was a significant association between vitamin D levels and the risk for severe asthma, the risk for hospitalization, or visit to the Emergency Department due to asthma.

The results of the present study showed that serum IgE level was highly significantly higher in the asthma group (during exacerbation and after remission) compared with the control group (Table 4). Our study is in agreement with the study by Thirunavukkarasu *et al.* [13], who investigated serum IgE level in 60 asthmatic patients between 18 and 60 years of age, classified according to the GINA classification (31 male and 29 female), and 13 healthy controls between 18 and 60 years of age. They

Table 3 Comparison of serum vitamin D level among mild, moderate, and severe exacerbated asthma

Severity	Mild	Moderate	Severe	*F*-test	*P* value
Vitamin D level during exacerbation (ng/ml) [mean±SD (range)]	26.07±0.73 (24.99–27.01)	22.28±0.91 (20.82–23.67)	17.31±1.84 (14.22–19.33)	80.28	0.001**

Serum vitamin D level was highly significantly lower in severe compared with moderate and mild exacerbated asthma group.
**Highly significant

Table 4 Comparison of IgE levels among the control group, the asthmatic group (during exacerbation), and the asthmatic group (after remission)

	Control group	Asthmatic group (during exacerbation)	Asthmatic group (after remission)	*F*-test	*P* value
IgE level (IU/ml) (mean±SD)	55.11±36.31	556.43±238.35	174.54±82.75	74.74	0.001**

IgE levels were highly significantly higher in the asthmatic group (during exacerbation) compared with the asthmatic group (after remission) and the control group.
IgE, immunoglobulin E.
**Highly significant

Table 5 Comparison of serum IgE levels among mild, moderate, and severe exacerbated asthma

Severity	Mild	Moderate	Severe	*F*-test	*P* value
IgE level during exacerbation (IU/ml) [mean±SD (range)]	289.02±75.68 (180.2–390.9)	460.7±195.2 (50.1–693.2)	709.41±185.4 (400–1004.1)	12.75	0.001**

IgE levels were highly significantly higher in severe exacerbated asthma, compared with moderate and mild exacerbated asthma.
IgE, immunoglobulin E.
**Highly significant.

found that the mean IgE level in the control group was 151 IU/ml and that in the asthmatic group ranged from 404 to 1045 IU/ml. They attributed this to the fact that there is a link between total IgE and asthma, which appears to be independent of allergen sensitization. One of the typical aspects of airway inflammation of asthma is the infiltration of the airway wall by T-helper type 2 cells. These cells are attracted to inflammatory sites by adhesion molecules and chemokines, among which CCR3 and CXCR4 receptors appear to be of importance. Differentiation of B-cells into IgE-secreting plasma cells is a complex cascade of events in which cytokines play a crucial role. Both interleukin (IL)-4 and IL-13 induce IgE synthesis, whereas interferon-γ and IL-12 block IgE synthesis. IgE production by B-cells not only requires the presence of IL-4 or IL-13 but also a physical interaction between T and B cells, involving a number of surface and adhesion molecules such as CD40-CD40L and CD28/CD80. Production of T-helper type 2-cytokines is not restricted to T-cells, as basophils and mast cells can produce them, indicating that these cells may be of importance in the synthesis of IgE [14].

The results of the present study showed that serum IgE level was highly significantly higher in severe exacerbated asthma, compared with moderate and mild exacerbated asthma (Table 5). This study is in agreement with the study by Davila *et al.* [15], who investigated 383 patients with allergic asthma (129 mild, 82 moderate, and 172 severe; mean age: 38 ±15, 46±16, and 45±15 years, respectively). They found that serum total IgE levels in adult patients with persistent allergic asthma were high (two-thirds with levels>150 IU/ml) and extremely variable. They did not find a significant association between serum total IgE levels and asthma severity or airflow limitation, except for a higher percentage of patients with IgE greater than 400 IU/ml in the severe subgroup. This is in agreement with the study by Sandeep *et al.* [13], who investigated serum IgE level in 60 asthma patients between 18 and 60 years of age (31 male and 29 female asthmatic patients), classified according to the GINA classification, and 13 healthy controls between 18 and 60 years of age. They found that the mean IgE level in the control group was 151 IU/ml, and that in the asthmatic group was as follows: a mean of 404 IU/ml for patients with mild asthma (n=19), a mean of 404 IU/ml for patients with moderate asthma (n=18), and a mean of 1045.32 IU/ml for patients with severe asthma (n=23). IgE levels were highly significant higher in severe exacerbated asthma, compared with moderate and mild exacerbated asthma (P>0.001). It may be attributed to various other factors involved in the causation of bronchial asthma, because other cells in affected bronchi can also produce the mediators; this is inclusive of vascular endothelium, airway epithelium, and inflammatory cells already present in asthmatic patients suffering a recurrent attack [16]. It may be proposed that the levels of IgE are quite high locally at the site of inflammation and the serum levels do not necessarily reflect the levels in lungs and bronchus. It is also known that IgE is bound to mast cells with rather high affinity [17] and hence the circulating IgE may not give a conclusive evidence of the severity of inflammation.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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