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Relationship Between Clinical Symptoms Control, Oxidative Stress Status and Serum Vitamin D among Adults with Bronchial Asthma

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ABSTRACT

Background: The most common chronic lung disease in the world is bronchial asthma. Nonetheless, oxidative stress indicators have been linked to the onset of asthma in a number of recent investigations. However, vitamin D has a role in the pathogenesis of asthma.

Objective: The aim of this study was to determine the relationship between serum vitamin D levels, oxidative stress state, and clinical symptom control in individuals with bronchial asthma.

Material and Methods: The average age and Body Mass Index (BMI) of two hundred Saudi patients with bronchial asthma, both male and female, were 42.36 ± 6.24 years and 26.88 ± 2.95 kg/m2. Participants were chosen from Abassia Chest Hospital, Cairo, Egypt. The study excluded participants who were pregnant, smokers, had hepatitis, pulmonary failure, renal failure, or heart failure. Participants were divided into three groups according to their vitamin D levels.

Results: Malondialdehyde (MDA) mean values were significantly higher in the vitamin D deficiency group (A) than in the vitamin D insufficiency group (B) and the normal vitamin D group (C). Furthermore, compared to groups (B) and (C), group (A) had considerably lower serum levels of glutathione (GSH), glutathione peroxidase (GPx), superoxide dismutase (SOD), and the Asthma Control Test (ACT). Furthermore, in all three groups, vitamin D was highly inversely connected with MDA levels ($P<0.05$) and directly correlated with levels of forced vital capacity (FVC), forced expiratory volume in one second (FEV1), Asthma Control Test (ACT), GPX, GSH, and SOD.

Conclusion: Vitamin D deficiency is associated with abnormal levels of oxidative stress biomarkers and the treatment of clinical symptoms in bronchial asthma patients.

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Introduction

Variable airway obstruction, respiratory symptoms, bronchial hyperresponsiveness, and airway inflammation were the hallmarks of bronchial asthma [1]. It is the most common chronic respiratory illness, affecting around 300 million people globally [2]. and its prevalence is continuously increasing, especially in developing countries [3]. Due to its prevalence, asthma is predicted to cost the US healthcare system $56 billion year [4].

Respiratory infections have been linked to vitamin D deficiency and are often the cause of asthma attacks [5,6]. Previous research has shown that low serum vitamin D levels are associated with poor asthma control, more exacerbations, more hospitalizations in the previous year, decreased lung function, decreased responses to inhaled corticosteroids (ICS), and ultimately increased use of ICS in patients with mild to moderate asthma [7-11]. Vitamin D insufficiency was also associated with lower forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1). Further analysis of data from the National Health and Nutrition Examination Survey showed that when vitamin D insufficiency decreased, so did the prevalence of asthma [12]. Additionally, there is a negative correlation between blood vitamin D and increased airway responsiveness, airway remodeling, and sensitivity to glucocorticosteroids [13,14].

Numerous studies have clearly shown that oxidative stress is a major consequence of the inflammatory response in asthma [15,16] and that it is associated with a shift in lung and blood antioxidant activity [17]. This is due to the fact that variations in protein and lipid oxidation can produce pathological modifications in respiratory epithelial cells, an increase in vascular permeability, an excess of mucus, smooth muscle contraction, or hyperresponsiveness of the airways [18,19]. Additionally, asthma patients' exhaled air has been found to include elevated amounts of a number of oxidative stress markers [20].

The purpose of this study was to investigate potential relationships between oxidative stress state, blood vitamin D levels, and clinical symptom control in individuals with bronchial asthma.

Subjects and Methods

Subjects

The average age and Body Mass Index (BMI) of two hundred Saudi patients with bronchial asthma, both male and female, were 42.36 ± 6.24 years and 26.88 ± 2.95 kg/m2. Participants were chosen from selected randomly from Abassia Chest Hospital, Cairo, Egypt. Spirometry tests were used to diagnose asthma. Asthma was diagnosed using the following standards, under the Global Strategy for Asthma Management and Prevention (GINA 2016): A family history of asthma; a normal or >80% from predicted FEV1; a post-bronchodilator increase in FEV1 > 12% or 200 mL from base level; respiratory symptoms (chronic paroxysmal cough, wheezing, and dyspnea); and an average daily PEF variation of 3-4% for controlled asthma and 6-7% for partially controlled asthma [21].

Patients with liver, heart, or kidney disorders were excluded. Every participant completed a consent form and was able to leave the study whenever they wanted. Following pre-training testing, participants were split into three groups according to their vitamin D levels: vitamin D deficiency group (A): 25-OHD <20 ng/ml, vitamin D insufficiency group (B): 25-OHD = 20–30 ng/ml, and normal vitamin D group (C): 25-OHD >30 ng/ml. Vitamin D pills were not given to any of the subjects. This study was approved by the Scientific Research Ethical Committee at Faculty of Physical Therapy, Badr University in Cairo, Egypt, The institutional review board registration Number with IRB00014233-38.

Measurements

An overnight fast All participants had blood samples taken in order to measure the following

Evaluation of Antioxidant Levels and Indicators of Oxidative Stress

According to Buege and Aust [22], Malondialdehyde (MDA), a lipid marker for peroxidation, was measured. In contrast, the Antioxidant Status and Glutathione (GSH) were evaluated using the method of Beutler and colleagues [23]. However, Nishikimi and associates' method looked at Superoxide Dismutase (SOD) and glutathione peroxidase (GPx) [24].

25-OH Vitamin D Levels in Serum

All patients and controls had their 25(OH) vitamin D levels measured using the commercial kit RIA (Elisa Kit; DiaSorin, Stillwater, MN, USA). A deficiency was defined as having less than 20 ng/ml of plasma 25(OH) vitamin D, and an insufficiency was defined as having less than 30 ng/ml [25].

Lung Function Testing

A CPFS/D Spirometer (MedGraphics, St. Paul, Minn., USA) was used to assess the forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), FEV1/FVC ratio, and forced expiratory flow during the middle half of the FVC maneuver (FEF25–75%).

Assessment of asthma control

The Italian version of the Asthma Control Test (ACT) is a reliable tool for assessing asthma control over time [26]. Each of the five questions that participants answer requires a five-point rating. The total score for the five questions is between 0 and 25. However, a total score of 19 or less denotes poorly managed asthma [27,28].

Statistical Analysis

The data was statistically analyzed by SPSS (Chicago, IL, USA) version 23. Descriptive statistics of quantitative variables were shown as mean ± SD, whereas qualitative aspects were presented as numbers and percentages. Analysis of variance (ANOVA) was used to compare the three groups, with a P-value of less than 0.05. Pearson's correlation coefficients (r) are used to assess the degree of relationship between vitamin D levels and MDA, GSH, SOD, GPx, ACT, FEV1, and FVC.

Results

The individual baseline characteristics for each of the three groups are listed in Table 1. Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), forced expiratory flow during the middle portion of the FVC maneuver, and forced expiratory volume in the first second (FEV1) all showed significant differences (FEF25–75%) between the groups classified as vitamin D deficiency (A), vitamin D insufficiency (B), and normal vitamin D (C). However, age, body mass index (BMI), hemoglobin, or the length of the condition showed no significant difference (Table 1).

Table 1: Participant's Initial Attributes

Variable	Group (A) 25-OHD deficiency	Group (B) 25-OHD insufficiency	Group (C) 25-OHD Normal	Significance
Age (year)	41.64 ± 4.14	44.39 ± 4.68	42.86 ± 5.71	0.074
BMI (kg/m^2)	26.53 ± 3.21	27.38 ± 2.97	25.35 ± 3.45	0.125
Disease duration(year)	12.51 ± 5.36	10.35 ± 5.28	10.15 ± 5.28	0.071
Hemoglobin (gm/dl)	12.65 ± 2.39	12.14 ± 2.47	11.72 ± 2.58	0.132
FVC (L)	2.69 ± 1.23*	3.41 ± 1.32	3.98 ± 1.51	0.004*
FEV1(L)	1.82 ± 0.84*	2.34 ± 1.13	2.72 ± 1.26	0.007*
FEV1/FVC (%)	61.31 ± 6.52*	69.52 ± 7.25	76.85 ± 6.91	0.003*
FEF25-75 %(L/s)	1.67 ± 0.54*	1.96 ± 0.71	2.43 ± 0.96	0.005*

BMI= Body mass index; FVC: forced vital capacity; FEV1: forced expiratory volume in the first second; FEV1/FVC: Ratio between forced expiratory volume in the first second and forced vital capacity; FEF25-75: forced expiratory flow during the middle half of the FVC maneuver; (*) indicates a significant difference between the two groups, $P < 0.05$.

Table (2) showed that vitamin D deficiency group (A) had a considerably higher mean MDA value than the vitamin D insufficiency group (B) and the normal vitamin D group (C). Moreover, group (A) had significantly lower serum levels of the Asthma Control Test (ACT), GPX, GSH, and SOD than groups (B) and (C).

Table 2: Comparison Between the Three Groups Concerning MDA, SOD, GPX, GSH and ACT

Variable	Group (A) 25-OHD deficiency	Group (B) 25-OHD insufficiency	Group (C) 25-OHD Normal	Significance
MDA (mmol/L)	27.72 ± 4.14*	21.25 ± 3.25	17.86 ± 2.53	0.011*
GPx (units/gHb)	19.89 ± 3.21*	24.47 ± 4.16	29.21 ± 5.28	0.014*
SOD (units/mL)	38.47 ± 6.74*	46.25± 8.11	55.31 ± 9.32	0.023*
GSH (mmol/gHb)	2099.21 ± 156.65*	2318.21 ± 172.32	2537.29 ± 198.27	0.015*
ACT (0–25)	17 (15–21)	20 (18–23)	22 (19–25)	0.016*

ACT: Asthma control test; MDA: Malondialdehyde; GPx: Glutathione peroxidase; SOD: Superoxide dismutase; GSH: Glutathione; * Significant level ($p<0.05$).

Table (3) showed that vitamin D was directly correlated with the levels of forced vital capacity (FVC), forced expiratory volume in one second (FEV1), Asthma Control Test (ACT), GPX, GSH, and SOD in all three groups and strongly inversely correlated with MDA levels ($P<0.05$).

Table 3: Correlation Coefficient (r) of Vitamin D and MDA, SOD, GPX, GSH, FVC, FEV1& ACT in the Three Groups

	Group (A) 25-OHD deficiency	Group (B) 25-OHD insufficiency	Group (C) 25-OHD Normal
MDA (mmol/L)	-0.673**	-0.524*	-0.731**
GPx (units/gHb)	0.671**	0.724**	0.597*
SOD (units/mL)	0.536*	0.716**	0.526*
GSH (mmol/gHb)	0.698**	0.683**	0.568*
ACT (0–25)	0.612*	0.597**	0.545*
FVC (L)	0.736**	0.658**	0.515*
FEV1(L)	0.541*	0.589**	0.511*

Spearman's correlation was used *: $P < 0.05$ **: $P < 0.01$

Discussion

Asthma attacks are frequently triggered by respiratory infections, which have been associated with vitamin D deficiency [29,30]. Furthermore, elevated airway responsiveness, airway remodeling, and sensitivity to glucocorticosteroids are adversely correlated with serum vitamin D [31,32]. Nonetheless, several of the main pathophysiological characteristics of asthma, such as mucus hypersecretion and airway hyperresponsiveness, have been linked to oxidative stress [33,34]. This study was carried out to ascertain the connection between oxidative stress state, blood vitamin D levels, and clinical symptom control in bronchial asthma patients.

Our study's findings indicate that serum 25 (OH)D concentrations were positively correlated with ACT scores, FVC, FEV1, and FEV1/FVC. We provided an explanation by pointing out that vitamin D affects collagen synthesis and prevents the production of matrix metalloproteinase and fibroblast proliferation. Because of these effects, 1, 25(OH)2D may have an impact on lung function and tissue remodeling [35]. Shaaban and Hashem 2012 found a strong correlation between enhanced lung function and higher serum vitamin D levels [36]. Furthermore, a positive association between FEV1 and 25(OH)D levels was discovered by Stephanie Korn et al. 2013 [37]. Furthermore, this study confirms the results of Eman Shebl et al. 2013 who found a positive relationship between FEV1% and 25(OH) D levels [38].

The results of Black and Scragg 2005, who discovered a positive relationship between blood vitamin D and both glucocorticoid response and FEV1 [39], are also supported by our investigation. Furthermore, Searing et al. 2010 discovered that serum vitamin D positively correlated with lung function and enhanced glucocorticoid action in peripheral blood mononuclear cells [40]. In a similar vein, other investigations discovered a positive correlation between vitamin D levels and the asthma control test (ACT) [41-43].

Vitamin D deficiency has been shown to increase the risk of severe asthma flare-ups and hospitalization [44]. Additionally, children with low serum vitamin D levels are more likely to have severe asthma exacerbations, ED visits, and hospitalization, regardless of whether they use ICS [45-47]. The mechanisms underlying vitamin D's role in the genesis of asthma are unknown. Vitamin D has been connected to both innate and adaptive immunity as well as airway remodeling [48].

Serum 25 (OH)D levels showed a negative correlation with oxidative stress indicators and a favorable correlation with anti-oxidative stress. These findings are in line with recent studies that discovered vitamin D insufficiency is associated with increased oxidative stress in individuals with severe asthma, diabetes, obesity, the elderly, and a variety of other conditions [49-55].

On the other hand, Igde and colleagues (2018) discovered a relationship between the oxidative state and serum vitamin D levels of ninety children with asthma [56]. However, Zhang et al. (2014) discovered that vitamin D deficiency may increase the risk of diseases caused by increased oxidative stress and obesity among 1488 Chinese schoolchildren [57]. Additionally, low levels of 25(OH) D increased oxidative/nitrosative stress, inflammation, and endothelial activation in children with extreme obesity [58]. Additionally, because oxidative stress plays a significant role in the pathophysiology of severe asthma exacerbations, vitamin D deficiency increased oxidative stress and DNA damage, which worsened the oxidative milieu changes in severe asthma exacerbations [55].

Conclusion

Vitamin D deficiency is associated with abnormal levels of oxidative stress biomarkers and the treatment of clinical symptoms in bronchial asthma patients.

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