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Vitamin D Level in Asthmatic Patients, Tabriz City, Iran

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ABSTRACT: Vitamin D deficiency and insufficiency are common worldwide and associated with pulmonary diseases. Epidemiological studies indicated low levels of serum Vitamin D is associated with impaired pulmonary function. The aim of present study was to evaluate the vitamin D levels and its correlation to adult asthmatic patients. 120 asthmatic patients older than 18 years of age submitted to Yas pulmonary clinic (Tabriz, Iran) from June 2014 to June 2015 were included in the study. The information of patients like sex, age (18-30 Years, 30-45 Years, 45-60 years and >60 years), duration of disease (>10 years, 5-10 years, 1-5 years and <1 year) and BMI (<20, 20-25, 25-30 and >30) were recorded. The severity of asthma and levels of asthma control were assessed according to the Global Initiative for Asthma guidelines at four levels (Intermittent, mild, moderate and severe) were recorded or investigated. Serum vitamin D levels were determined and defined at four levels (Sever, mild to moderate deficiency, insufficiency and normal). Duncan's new multiple range test was used to compare the means of vitamin D with other variables. Most of patients have been found to be severely deficient in vitamin D *(*44.3%). The normal range of serum vitamin D was observed in just 13/131 patients (9.9%). The patients aged more than 60 years old (22 ng/m) had the highest mean value of vitamin D that was significantly higher than the younger patients aged 30-45 years (12.44 ng/m) and 18-30 years (8.17 ng/m). There was not any significant correlation among vitamin D levels, severity and duration of asthma. The prevalence of vitamin D deficiency in thin people (12.09 ng/m) was significantly more than fat people (19.44 ng/m). The results of present study demonstrated the insignificant correlation between serum vitamin D levels and asthma in adults. Definitely, this relationship being affected by multiple factors other than vitamin D. further investigations should be conducted to find the interrelation between all effective factors.

Key words: Asthma, Severity, Patient, Vitamin D

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INTRODUCTION

The role of vitamin D in immunomodulation is considered to be of major importance (Berraies et al., 2014) moreover there is now a large body of evidence linking vitamin D deficiency to chronic conditions, including autoimmune, infectious, cardiovascular, and respiratory disease (Foong and Shaw, 2014). Vitamin D has been shown to have a role in both innate and adaptive immunity, by promoting phagocytosis and modulating the effects of Th1, Th2 and regulatory T cells (Matheu et al., 2003). Vitamin D deficiency has recently been proposed as one of the factors associated with asthma epidemics (Huang et al., 2013; Krobtrakulchai et al., 2013). Further evidence suggests that vitamin D alters human airway smooth muscle expression ofchemokines and inhibits the expression of a steroid resistant gene (Banerjee et al., 2008). Vitamin D insufficiency is increasingly recognized in the general population, and has been largely attributed to dietary, lifestyle and behavioral changes (Holick, 2007; Paul et al., 2012). Predictors of vitamin D deficiency included older age, female gender, African- or Mexican-American ethnicity, obesity, the use of electronic devices, and reduced dairy intake (Kumar et al., 2009).

The chronic multi factorial disorder characterized by inflammation, bronchial hyper responsiveness, narrowing of airway associated with variable symptoms of wheeze, breathlessness, cough and chest tightness is called asthma (GINA, 2012; Brown et al., 2012). The prevalence of asthma varies widely between countries and it is higher in developed countries than in developing countries (Beigelman and Bacharier, 2013; Huang et al., 2013). It is estimated that as many as 300 million people of all ages, and all ethnic backgrounds, suffer from asthma and according to some relatively standardized and comparable studies, prevalence rates of asthma varied between 1% and 18% for children and adults (Sonomjamts et al., 2014; Uğurlu et al., 2014).The specific mechanisms responsible for asthma are poorly understood, numerous aberrant immune responses are clearly associated with the disorder. For example, T-helper cell type-2 (T_H2) cytokines, such as interleukin **(**IL**)**-4, IL-5, and IL-13, are unregulated in the asthmatic airway and are associated with increased

eosinophilia, mast cell degranulation and increased levels of Immunoglobulin E (IgE)(Brown et al., 2012). The standard criteria for the diagnosis of asthma clinically remain the presence of the typical symptoms, plus evidence of airflow obstruction which is either variable, or reversible, or inducible. The standard technique for measuring variability in airflow obstruction is the portable peak flow meter. This simple tool for monitoring asthma control has also been useful in aiding diagnosis, particularly for occupational asthma. Pulmonary function testing for the demonstration of reversible or inducible airflow obstruction relies on the standard spirometric measurement of forced expiratory volume in 1 second (FEV1). An improvement in FEV1 of greater than 12% and 200 mL from baseline in response to bronchodilator administration defines significant reversibility of airflow obstruction which is diagnostic of asthma (Park et al., 2009; Thien, 2013) Risk factors of asthma can be outlined under personal and environmental factors. Heredity, atopy, gender and obesity are the main subtitles of personal factors.

Environmental factors comprise of allergens, infections (especially viruses), occupational sensitizers, smoking (active and also passive), air pollution (inner and outer) and lifestyle (rural life, diet, consumption of antibiotics etc.)(Uğurlu et al., 2014).While there is evidence that the condition of asthma is multifactorial in etiology, changing environmental factors may underlie the rising prevalence of asthma, such as atmospheric pollution, dietary changes, allergens, improvements in health and hygiene, and lifestyle changes.

Vitamin D deficiency and asthma are common conditions that share risk factors in Iran (Hashemipour et al., 2004; Moussavi et al., 2005; Hovsepian et al., 2011) and Middle East (Fuleihan and Deeb, 1999; Saadi et al., 2006). A large proportion of adolescent girls, up to 70% in Iran (Moussavi et al., 2005) had 25(OH) D levels below 25nmol/L. In another study the mean value of 25-OH vitamin D was 15.5 ng/m and 75% (132/176) of normal and patient cases in Sabzevar city, Iran had deficiency (Bidgoli and Azarshab, 2014). The mean 25(OH) D level was near 25nmol/L in Lebanese, Saudi and United Arab Emirates (Fuleihan and Deeb, 1999; Saadi et al., 2006). The proportion of subjects with vitamin D levels below specific cut-offs varied. It was between 60-65% for a vitamin D level below 25nmol/L in a study of elderly subjects from geriatric hospitals in Lebanon, Jordan and Iran (Fuleihan and Deeb, 1999; Mishal, 2001; Hashemipour et al., 2004). Various studies have investigated the difference in vitamin D levels between asthmatic and non-asthmatic children and the effects of vitamin D deficiency in children on the severity and control of asthma (Uysalol et al., 2013). Some authors claim that vitamin D deficiency is associated with the risk of increasing respiratory infections, leading to exacerbation of asthma and subsequent frequent hospitalizations. It is reported that relatively less incidence of asthma exacerbation is observed in asthmatic children taking vitamin D supplements. Some review articles have suggested a strong link between vitamin D levels and asthma severity, although the causality has not been proven (Krobtrakulchai et al., 2013). The present study was conducted to investigate the prevalence of vitamin D deficiency among adolescents and adult patients. Therefore, the aim of this study was to prospectively investigate the prevalence of vitamin D insufficiency and deficiency in adult and adolescent asthmatic patients.

MATERIALS AND METHODS

Present study was a combined descriptive – analytic study with cross sectional approach. 131 asthmatic patients older than 18 years of age submitted to Yas pulmonary clinic (Tabriz, Iran) from June 2014 to June 2015 were included in the study. Tabriz is located in northwest of Iran.

At the beginning of study a questionnaire was filled for each patient about patient's ID such as sex, age (18-30 Years, 30-45 Years, 45-60 years and >60 years) duration of disease (>10 years, 5-10 years, 1-5 years and <1 year), weight (Kg) and height (Cm). The weight (Kg)/height (M^2) formula was used to calculate Body Mass Index (BMI) at four levels (<20, 20-25, 25-30 and >30).

Spirometry test was done for all participants and the results were listed in the questionnaire. Asthma severity classified and investigated according to the Global Initiative for Asthma (GINA, 2012) criteria at four levels (Intermittent, mild, moderate and severe). Exclusion criteria defined as patients with other pulmonary disorders such as COPD, TB, allergic rhinitis, chronic disorders of liver and kidney, diabetes, hypertension, IHD, pregnancy, endocrine, use of anti-convulsion drugs, anti-epileptic therapy and use of vitamin D and calcium supplementation. 10 ml of peripheral blood of each patient has been taken in the morning and serum concentration of 25-hydroxy vitamin D (25-OHD) measured using chemiluminescence method. Normal range for serum 25-hydroxy vitamin D (25-OHD) is defined 30 to 80 nmol/l. Test values will be used to classify vitamin D status: vitamin D sever deficiency for values of 10 ng/mL or less; vitamin D mild

to moderate deficiency for values between 10.1 and 19.9 ng/mL and vitamin D insufficiency for values between 20.1 and 29.9 ng/mL.

Ethical issues

A written informed consent taken from each participant after the full explanations about the study according to the Tabriz University of Medical Sciences Ethics Committee's procedure.

Statistical analyses

Data analyses carried out using Statistical Package for Social Sciences (SPSS) Software, (Version 16, Chicago, USA). The data were analyzed by an analysis of variance (ANOVA) using the General Linear Model (GLM). Duncan's new multiple range test was used to compare the means of vitamin D with other variables at P<0.05 level (SAS Institute, 2001) and standard division was calculated. The relationship of the severity of asthma with other quality variables was computed by Crosstabs *and* Chi-squared test.

RESULTS AND DISCUSSION

The mean values of serum vitamin D presented in table 1. The present results indicated 73.3% of patients were vitamin D deficient *and* most of them have been found to be severely deficient in *vitamin D (*44.3%). Kashi et al. (2011) reported that prevalence of 25-OH vitamin D deficiency (among mean age 37 years) was 87.5% in winter and 78.6% in summer in north of Iran. Bidgoli and Azarshab (2014) reported that 25-OH vitamin D in 75% of eastern Iranian peoples of normal and breast cancer patients detected in suboptimal levels and also 50% of these people were very severe or severe vitamin D deficient which is near to our findings in northwest of Iran. Hatami et al. (2014) indicated 50% of asthmatic children in South of Iran were vitamin D deficient. Also in another study 50.8% of the adult population of Isfahan, a centrally located city in Iran were vitamin D deficient (Hovsepian et al., 2011).

The normal range of serum vitamin D was observed in just 13 patients (9.9%) which is according to findings of Kashi et al. (2011). There is a hypothesis about improving suboptimal vitamin D status might be effective in prevention and treatment of asthma (Korn et al., 2013; Hatami et al., 2014) but previous investigation denied this hypothesis (Martineau et al., 2015) and also our findings indicated that vitamin D level in more than 90% of the asthmatic patients was under 30 ng/m however there is not any significant relationship between vitamin D and severity of asthma in present study (Table 3).

Table 1. Serum vitamin D levels in asthmatic patients during 2015 year, Tabriz, Iran

Vitamin D	Number of patient	%	Mean value (ng/m)±SD
Severe deficiency	58	44.3	6.50±0.210
Mild to moderate deficiency	38	29.0	14.94±0.25
Insufficiency	22	16.8	23.78±0.28
Normal	13	9.9	42±1.22
Total	131	100	15.24±1.17

SD: Standard Deviation

The most of submitted patients in present study were female (61.1%) and the mean value of vitamin D in women (16.41) was more than men (13.4) (P>0.05). Although the 44.27% of the men and women had severely deficiency of vitamin D (58 of 131). 98% (50 of 51) of men had severe, mild or moderate deficiency and insufficiency although it was 85% (68 of 80) in women. According to data originally from the US Third National Health and Nutrition Examination Survey (NHANES III) 78.2% of American men >70 years and 76.7% of women across all ages had vitamin D concentrations <30 ng/ml (Calvo, 2004). Bates et al. (2014) indicated the mean year-round 25 (OH) D in adult (19-64 years) women (47.3 nmol/l) was more than adult men (43.5 nmol/l) and also the year-round mean value of vitamin D in men upper 65 years (47 nmol/l) was more than men aged 19-64 years (43.5 nmol/l). There are many other reports that determined vitamin D levels in adult women were more than adult men (Van der et al., 2012 and Austrian Nutrition Report, 2012). Regardless to present finding Robin et al. (2012) reported the prevalence of vitamin deficiency was more in women and old persons. In present study just the old people were not vitamin D deficient which reveal the poor nutrition and life style of young men and women in Iran. However, the relationship of sex and vitamin D level was not significant (P>0.05) (Table 2).

The most of patients were aged 30-45 years. The correlations of serum vitamin D levels and age of asthmatic patient showed highly significant results (P<0.01). The mean value of vitamin D in asthmatic patients aged 18-30 years (8.17) was extremely significant lower than the elder patients and specially who aged 45-60 years (17.56) and more than 60 years old (22) (P<0.01). The patients aged more than 60 years old had the highest mean value of vitamin D that was extremely significant higher than the

younger patients aged 30-45 years (12.44) and 18-30 years (P<0.01) (Table 2).

There was not any significant correlation (P<0.05) among vitamin D levels, severity and duration of asthma (Table 3). The highest mean value of vitamin D indicated in people with severe asthma (16.68) and more than of 10 years duration asthma (16.57) compared to other groups but differences between groups were not significant (P>0.05). Table 3 show fat people (BMI upper 30) (19.44) had significantly higher (P<0.05) vitamin D level compared to other groups although most of studies reported that the obese persons had low vitamin D levels and were at asthma risk (Parikh et al., 2004; Beuther and Sutherland, 2007; Robin et al., 2012) and one of the most significant effects of obesity in asthma relates to its association with an impaired response to glucocorticosteroids (Haldar et al., 2008; Sutherland et al., 2009). Higher vitamin D levels in adults with asthma are not only correlated with improved pulmonary function and reduced bronchial hyperresponsiveness, but also with an improved in vitro response to glucocorticosteroids (Sutherland et al., 2010).

The present finding showed that most of patients were at mild to moderate deficiency levels but the obese persons had better mean value and maybe caused a better response to glucocorticosteroids.

Table 2. Correlations among serum vitamin D levels with sex and age of asthmatic patients during 2015 year, Tabriz, Iran

	Vitamin D						
	Severe deficiency	**Mild to moderate deficiency**	**Insufficiency**	**Normal**	**Total**	**Mean value (ng/m)±SD**	**P value**
Sex							0.09
Male	23	17	10	1	51 (38.9%)	13.4±0.73[a]	
Female	35	21	12	12	80 (61.1%)	16.41±1.37[a]	
Total	58	38	22	13	131	15.24±1.17	
Age (year)							0.001
18-30	17	2	1	-	20 (15.3%)	8.17±0.5[a]	
30-45	24	15	4	3	46 (35.1%)	12.44±0.86[ab]	
45-60	11	11	11	5	38 (29%)	17.56±1.1[bc]	
>60	6	10	6	5	27 (20.6%)	22±1.63[c]	
Total	58	38	22	13	131	15.24±1.17	

SD: Standard Deviation.*within a row with no common superscript differ significantly (P<0.05).

Table 3. Correlation among serum vitamin D levels with severity of disease, BMI and duration of disease in asthmatic patients during 2015 year, Tabriz, Iran

	Vitamin D						
	Severe deficiency	**Mild to moderate deficiency**	**Insufficiency**	**Normal**	**Total**	**Mean value (ng/m) ±SD**	**P value**
Severity							0.85
Mild	26	19	13	6	64	15.26±1[a]	
Moderate	19	9	4	3	35	13.87±1.21[a]	
Severe	13	10	5	4	32	16.68±1.26[a]	
Total	58	38	22	13	131	15.24±1.17	
Duration of asthma (year)							0.27
>10	13	15	11	4	43	16.57±1.09[a]	
5-10	16	12	3	4	35	14.88±1.24[a]	
1-5	17	9	5	4	35	15.21±1.22[a]	
<1	12	2	3	1	18	12.82±1.18[a]	
Total	58	38	22	13	131	15.24±1.17	
BMI							0.04
<25	19	10	3	2	37	12.09±1.13[a]	
25-30	28	15	9	3	55	14.42±1.11[a]	
>30	8	12	9	7	36	19.44±1.25[b]	
Total	58	37	21	12	128	15.16±1.17	

SD: Standard Deviation.*within a row with no common superscript differ significantly (P<0.05).

It seems that factors, such as style of clothing, air pollution, skin pigmentation, and insufficient vitamin D intake, lack of routine enrichment of foods with vitamin D in Iran, could be responsible for the findings of our study (Hashemipour et al., 2004; Moussavi et al., 2005; Hovsepian et al., 2011).

Table 4. Correlation between severity of asthma with sex and BMI in asthmatic patients during 2015 year, Tabriz, Iran

	Severity				
	Mild	**Moderate**	**Severe**	**Total**	**P Value**
BMI					P=0.14
20-25	19	12	6	37 (28.90%)	
25-30	30	13	12	55 (42.97%)	
>30	12	10	14	36 (28.12%)	
Total	61 (47.65%)	35 (27.34%)	32 (25%)	128 (100%)	
Sex					P<0.05
Male	24	19	8	51	
Female	40	16	24	80	
Total	64	35	32	131	

*within a row with no common superscript differ significantly (P<0.05).

CONCLUSION

This study has demonstrated the correlation between serum vitamin D levels and asthma in adults. Definitely, this relationship being affected by multiple factors other than vitamin D, further investigations should be conducted to find the interrelation between all effective factors.

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