ORIGINAL RESEARCH ARTICLE

Association of Serum Level of Vitamin D3 and Pulmonary Function in Bronchial Asthma Patients in A Tertiary Care Hospital of South Gujarat, India

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ABSTRACT

Introduction: Asthma is a chronic lung disease characterised by reversible airway obstruction, cellular infiltration, and airway inflammation. The reaction is characterised by the interaction of genetic and environmental variables, as well as the activation of cells in the innate and adaptive immune systems.

Method: The study was conducted in the Department of General medicine, in Tertiary Care Center, to study association of serum level of Vitamin D3 and pulmonary function in bronchial asthma patients. As per inclusion and exclusion criteria ,137 patients of bronchial asthma were included in the study.

Result: In cases having serum vitamin D3 level <20 ng/ml mean value of FVC, FEV1, FEV1/FVC ratio, was 108.10±14.89, 68.56±13.40, and 62.35±5.17. In cases having serum vitamin D3 20-29 ng/ml, mean value of FVC, FEV1, and FEV1/FVC ratio was 109.72±12.22, 72.34±13.48, and 64.39±6.97. In cases having serum vitamin D3 >30 ng/ml mean value of FVC, FEV1, and FEV1/FVC ratio, was 115.0±4.27, 81.0±7.09, and 70.52±5.00**.**

Conclusion: Vitamin D3 deficiency was highly prevalent in asthmatic patients, there was a strong correlation between asthma severity and vitamin D3 concentrations and there was a direct and a positive significant correlation between vitamin D3 levels and pulmonary function test in asthmatic patients.

Keywords: Vitamin D3, Bronchial asthma, Pulmonary function tests, Tertiary Care Centre

INTRODUCTION

Asthma is a chronic lung disease characterised by reversible airway obstruction, cellular infiltration, and airway inflammation. The reaction is characterised by the interaction of genetic and environmental variables, as well as the activation of cells in the innate and adaptive immune systems.[1]

As assessed by disability-adjusted life years, asthma is rated 16th among the primary causes of years lived with disability and 28th among the leading causes of disease burden. Asthma affects around 300 million people globally, with an additional 100 million expected to be impacted by 2025.[2]

Despite significant improvements in the area, there is no cure for asthma at the moment. Corticosteroids (often used to manage asthma symptoms) with or without 2-adrenergic receptor agonists are among the treatment choices for treating illness symptoms (short-acting receptor agonists that relieve bronchoconstriction and long-acting receptor agonists that offers extended control of contractions).[1,3] Despite their anti-inflammatory characteristics, these medica-tions do not prevent long-term deterioration in lung function. Given the global growth of asthma, improved therapeutic options are required to battle the illness.

Over the last two decades, vitamin D has been demonstrated to exert immunomodulatory effects on a variety of immune cells, including dendritic cells, via activating the vitamin D receptor (VDR) (DCs),[4] macrophages, B and T lymphocytes[5,6] as well as structural cells in the airways[1]

A lack of vitamin D has been related to an increase in the occurrence of respiratory disorders such as asthma, with supplementation found to relieve these effects in certain cases.[5,7] The results of animal models and human cells investigations on the therapeutic benefit of vitamin D supplementation have contradicted those of several clinical trials. Researchers critically analysed the most current results on the function of vitamin D in the development, prophylaxis, and therapy of bronchial asthma in this review.

Several research groups have focused on the function of vitamin D in asthma etiology throughout the last two decades. These investigations found a relationship between vitamin D insufficiency and a worse overall result of lung function and symptoms in asthma patients.[7,8]

Spirometry was used to assess lung function, which includes forced expiratory volume in one second (FEV1) % predicted, forced vital capacity (FVC)% predicted, and FEV1/FVC ratio. To manage asthma patients, physicians in India rely mostly on international standards such as the GINA - Global Initiative for Asthma guidelines. Although the worldwide criteria are evidence-based, it is critical to recognize that they may not apply to local demographic. GINA-Global Imitative for Asthma guidelines are used to classify the severity of asthma based on clinical symptoms,

therapeutic options, and lung function measurements using spirometry.[9]

The study was conducted in the Department of General medicine, in Tertiary Care SMIMER hospital to study association of serum level of Vitamin D3 and pulmonary function in bronchial asthma patients.

METHODOLOGY

The prospective study was conducted among OPD/ Indoor patients admitted to a tertiary care hospital. The study was started after taking institutional ethical committee. All cases were included based on inclusion criteria in which all cases were more than 18 years and Known cases of asthma and recently diagnosed cases of bronchial asthma based on PFT including FEV1, FVC and FEV1/FVC ratio. Here we excluded all cases who had a history of Age more than 70 years. Patients of any known case of skin, liver, or renal disease, known case of osteoporosis. Patients taking bisphosphonates History of lung disease, decompensated heart diseases, recent surgery of thorax, abdomen with chest wall deformities or neuromuscular diseases. History of intake of Vitamin D or calcium in past one month. Patients were on various drugs – Rifampicin, Isoniazid, Phenobarbital, Carbamazepine and Phenytoin, Taxol and related compound Patients with history of smoking. Pregnancy Patients of status asthmatics. The study was carried out on patients with bronchial asthma in wards/opd of tertiary care hospital. All the patients were enrolled after informed written consent. Detailed history was taken. Thorough general and systemic examination was carried out. All findings were recorded in the patient's proforma. Investigations including serum Vitamin D3 and pulmonary function test, as mentioned in the patient's proforma, will be carried out. If any abnormality was detected than the patient was given appropriate treatment under the guidance of the consultant of the treating unit.

Sample size was calculated by using formula $n = z^2pq / L^2$ where p =proportion of vitamin D deficiency among bronchial asthma patients 78.66%; q= 1-p; L = allowable error= 7%; Level of significance = 95%. The calculated sample size was 137.

Statistical Methods

Data was entered in MS Excel Spread sheet and analysed using Open-epi version 3.01 update 2013/04/06 & SPSS software version 20. The statistical analysis was done by appropriate Statistical method. Descriptive statistics was explained by frequency and percentage. Descriptive Analysis applied to represent data. Qualitative data represented by percentage whereas quantitative data represented by mean and Standard deviation (SD). Chi square test applied to compare the variables at 95%level of confidence. ANOVA applied to compare the mean of more than two independent groups at 95% level of confidence.

Ethical Consideration

The study was initiated after approval from Institutional Ethics Committee for study protocol. The study was conducted in compliance with the principles which have their origin in the Declaration of Helsinki, Indian GCP and ICMR guidelines. Informed written consent for allowing the clinical data of the patients to be used for study purpose was obtained from all the patients. No harm to any subject was done there and methods of blood collection and advantages and disadvantages of the study were explained to relatives. According to SMIMER hospital policy, user charges are levied on all routine investigations and the patients have to bear this additional expenditure. If any patient found with altered Serum potassium and serum amylase or any other abnormality after detailed evaluation, he is given appropriate treatment immediately under guidance of the consultant of treating unit.

RESULT

In our study, the Age groups ranged from 18 years to 70 years. Majority of the patients were in the age group of 31-40 years which comprised 40.88% of the study patients. while, 40.15% of the patients were males and 59.85% of the patients were females, 50(36.49%) patients had BMI of 25-27, 34(24.81%) patients had BMI of 27- 29, 28(20.43%) patients had BMI of <25 and 25(18.24%) patients had BMI of >30, Majority of the patients -71 (51.82%) had symptoms with less than 5 years followed by 55 (40.15%%) patients -(5-10years), 11 (8.03%) patients->10 years. Most common symptom was chest tightness and expiratory wheeze in 137 (100%) patients followed by cough 112(81.75%) patients, dyspnoea 70(51.09%) patients, nighttime awakening, and limitation of normal activity 15(10.95%), 55.47% of patients were on inhalation corticosteroids (INH.CS), and 13.87% of patients were on oral corticosteroid (ORAL CS) treatment**.**

Table 1: Basic profile of study participants

Variables	Cases (n=137) (%)
Age	
21-30	35 (25.55)
31-40	56 (40.88)
41-50	26 (18.98)
51-60	14 (10.22)
61-70	6 (4.38)
MEAN±SD	38.22± 10.7
Gender	
Male	55 (40.15)
Female	82 (59.85)
BMI (kg/m2)	
<25	28 (20.43)
25-27	50 (36.49)
27-29	34 (24.81)
>30	25 (18.24)
MEAN±SD	27.54±3.70
Duration of treatment (Years) of treatment	
<5	71 (51.82)
5-10	55 (40.15)
>10	11 (8.03)
MEAN±S	4.93±3.24
Presenting symptoms	
Cough	112 (81.75)
Expiratory wheeze	137 (100)
Chest tightness	137 (100)
Dyspnea	70 (51.09)
Night time awakening	15 (10.95)
Limitation of normal activity	15 (10.95)
Modality of treatment	
Inhalation corticosteroid	76 (55.47)
Oral corticosteroid	19 (13.87)

Table 2: Study variables of the study participants

Variables	Cases (n=137) (%)
Level of Vit D3(ng/ml) (M±SD)	21.7±9.73
<20	65 (47.45)
20-29	47 (34.31)
>30	25 (18.25)
FEV1 (M±SD)	72.2±13.3
<60	15 (10.95)
60-80	74 (54.01)
>81	48 (35.04)
FEV1/FVC Ratio (M±SD)	64.7±6.5
<57%	15 (8.91)
58-64%	55 (37.95)
65-70%	42 (32.37)
>70%	25 (20.76)

Maximum number of patients, that is 47.45% of patients had vitD3 of <20 ng/ml and 34.31% of patients had vitD3 of 20-29 ng/ml, 18.25% of patients had vitD3 of >30ng/ml. Majority of the patients - 74(54.01%) had FEV1 value between 60-80 followed by 48(35.04%) patients > 81, 15 (10.95%) patients <60. Majority of the patients -55 (37.95%) had FEV1/FVC Ratio of 58-64% followed by 42(32.37%) patients 65-70%, 25(20.76%) patients >70% and 15(8.91%) patients <57%.

There was no correlation between duration of asthma treatment and serum vitamin D3 level, grade of obstruction, FEV1 (%) predicted, and FEV1/FVC Ratio (%) were shows statistically significant corelation with vitamin D3 level.

Table 3: Association of study variables with vitamin D3 level

Variables	Vit D3			P Value
	<20 ng/ml (Deficiency)	20-29 ng/ml (Insufficient)	>30 ng/ml (Normal)	
n	**65**	**47**	**25**	
Duration of Treatment of asthma				
< 5	29 (44.62%)	25 (53.19%)	17(68%)	0.133*
5 to 10	29 (44.62%)	20 (42.55%)	6(24%)	
>10	7 (10.77%)	2 (4.26%)	2(8%)	
Symptoms				
Cough	65 (100%)	38(80.85%)	9(36%)	
Expiratory wheeze	65(100%)	47(100%)	25(100%)	
Chest tightness	65 (100%)	47(100%)	25(100%)	
Dyspnea	43 (66.15%)	23(48.49%)	4(16%)	
Night time awakening	10 (15.38%)	5(10.64%)	0(0%)	
Limitation of normal activity	10(15.38%)	5(10.64%)	0(0%)	
Grades of obstruction				
Intermittent	0(0.00%)	9 (19.15%)	16 (64%)	<0.001*
Mild	22 (33.85%)	15 (31.91%)	5 (20%)	
Moderate	33 (50.77%)	18 (38.30%)	4 (16%)	
Severe	10 (15.38%)	5 (10.63%)	0 (0%)	
FVC (%) predicted	108.10±14.89	109.72±12.22	115.0±4.27	0.071#
FEV1 (%) predicted	68.56±13.40	72.34±13.48	81.0±7.09	<0.001#
FEV1/FVC Ratio (%) predicted	62.35±5.17	64.39±6.97	70.52±5.00	<0.001#

*Chi-square test; #ANOVA test; FEV1 - Forced Expiratory Volume In 1 Second; FVC - Forced vital capacity

DISCUSSION

A meta-analysis study of Vitamin D3 and pulmonary function in bronchial asthma by Jian Liu et al[10],in 2019 conducted that insufficient Vitamin D3 level had lower FEV1.FEC1/FVC ratio than those with sufficient vitminD3 level. These data suggest that impaired pulmonary function in patient who were deficiency of serum Vitamin D3. Sutharland et al, [11] in 2010 conducted cross sectional study with serum Vitamin D3 level, lung function and steroid response in adult observed that low level of Vitamin D3 which associated with frequent exacerbation & severity of bronchial asthma.

Our goal is to determine the relationship between blood Vitamin D3 levels and lung function in patients with bronchial asthma. Our goal is to assess blood Vitamin D3 levels in bronchial asthma patients and discover a link between serum Vitamin D3 levels and pulmonary function in the form of spirometry**.**

In our study mean age of patient was 38.22±10.7year, range was 18-70 year and medium age was 36-year 35 (25.55%) patient where belong to age group 21–30-year, 56 (40.88%) patient 31–40-year, 26 (18.98%) patient 41–50-year, 14 (10.22%) patient 51-60 year and 6(4.38%) patient >61 year of age group. A.N. Aggarawal et al [12], in 2005 conducted a study where out of 70 patients-46 (30-42%) patient were <30 year and 24 (20.95%) patient were >30 year of age group. According to Nimit V. Khara et al[13],in 2016 conducted a study where total patients were divided into four groups that was <40 year 8(15.1%), 41-80 year in 12 (22.6%), 51-60 in 13 (24.5%), 61-70 in 14 (26.4%). In study by SN Jindal et al [14], in 2012 where 2.05% Patient are of > 15 year and 3.49 % adult aged ≥35 year. In study by P R Gupta et al [15], 2016 prevalence of asthma 2% among women aged 15-49 year and 1.00 % among young women aged 15-19 year as well men aged 15-49 year. In study Manjit Kumar et al [16], in 2020 mean age was 25.9 ± 3.92 year. According to Mohamed Yoursy A. Shahin et al[17] in 2017 conducted a study where mean age was 35.5 ± 8 year. According to Mostata M. Shaaban et al[18], mean age group was 39±1.2 year.

In present study out of 137 cases majority of the patient were female-82(59.85%)and male were- 55(40.15%).According to Nowin U. Chowdhury et al[19],.in 2021 out of total cases- female 56.75% and male was 43.25%.As per study by Jai Pirkash et al[15], in 2012 among total cases female where 12.6% than male were 6.0%.According to Mohamed Yousy A Shahin et al [20] 2017 conducted a study were out of total 70% patient 39% where female and 31% were male. S Agrawl et al[21], in 2005 prevalence of asthma

cross sectional survey1.8% (95% CI 1.6.2.0) among men and 1.9% (15% CI 8.2.0) among women. Manjit Kumar et al[22], in2020 conducted a study where out of total patients 61% were female and 39% were male. According to Mostatam Shaban et al[18]among total patient 53% were female and 47% were male.

In our study, out of total 137 patients -71 (51-82%) had mean duration of treatment in asthma was less than 5 year, 55(40.15%) patient -5 to 10 year,11(8.03%) patients >10 years. Mean duration of treatment in asthma in this study was 4.93±3.29 years. Median duration of treatment was 4 years. In study by Chudhry K .et al[23], in 2006 among 50 cases patient who were Mild asthma duration of treatment <3 year and moderate persistent asthma had duration of treatment 3-5years and severe persistent asthma had duration of treatment 10-15 year.

In current study most common symptoms was chest tightness and expiratory wheeze in 137(100%) patients followed by cough in 112(81.75%) patients, dyspnea in 70(51.09%) patients, night-time awakening, and limitation of normal activity in 15(10.95%) patients. A study by Gary Globe et al[24], in 2015 most frequent reported symptom in adult where chest tightness 33(97.1%), wheezing 31(91.2%), coughing 30(88.2%) and dyspnoea 25(73.5%) patients. A study by AN Agarawal et al[25], in 2005- most frequent reported symptoms in adult where wheezing 56%, cough 52%, dyspnoea in 42% and night-time awakening and limitation of normal activity in 20% patient.

In our study, in patients with serum vitamin D3 levels <20 ng/ml, the mean values of FVC, FEV1, and the FEV1/FVC ratio were 108.10±14.89, 68.56±13.40, and 62.35±5.17 respectively. The mean values of FVC, FEV1, and the FEV1/FVC ratio in a patient with serum vitamin D3 levels of 20-29 ng/ml were 109.72±12.22, 72.34 ±13.48, and 64.39 ±6.97, respectively. In patients with serum vitamin D3 >30 ng/ml, the mean values of FVC, FEV1, and the FEV1/FVC ratio were 115.0±4.27, 81.0±7.09, and 70.52±5.00 respectively. An ANOVA was used to determine the mean significance difference between the serum vitamin D3 level and different PFT parameters such as the FVC (%), FEV1 (%), and FEV1/FVC (%) ratio. A significant correlation was noted between serum vitamin D3 and different parameters of the PFT.

A study by M.M. Shaaban et al. [18], in a cross-sectional study including 75 asthmatic adults of the age group 18 to 75 years. which were divided into two groups—35 percent males and 40 percent females—and assessed serum Vitamin D3 level and lung function.

In our study (12.31%) patient had sufficient vitamin D level (>30ng/ ml) and 59 (78.66%) patients had vitamin D deficiency (<20ng /ml) observed. In asthma patient serum level of Vitamin D3 was positively correlated with FEV1(%) predicted and FEV1/FVC ratio. (p value-<0.05).

A study by E Rand Sutharland et al[26], 2010 total 54 patients of asthma, among them (FEV1, 82.9 ± 15.7% Predicted (mean SD), Serum vitamin D3 Level of 28.1. ±10.2 ng/ml)were enrolled .Higher vitamin D3 levels were associated with greater lung function, with 22.7±9.3 ml (mean SD) increase in FEV1 for each ng per millilitre increase in vitamin D (p value -0.02).Patient with vitamin D3 insufficiency (<30ng/ml) demonstrated 20% fall in FEV1 of 1.03±(0.2) mg/ml versus 1.92(±0.2) mg/ml in those with serum vitamin D of 30ng/ml or higher (p value -0.01)showed that vitamin D3 level associated with impaired lung function.

A study by F Montero et al[27] vitamin D levels in serum collected from 121 asthmatic adults to investigate the association between vitamin D levels (categorized as sufficient, ≥30 ng/mL, or insufficient, <30 ng/ml) asthma severity, baseline forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC). When the population was stratified by vitamin D status, 91% of asthmatic patients with vitamin D levels below 20 ng/mL (n=36) and 74% of patients with vitamin D levels between 20 and 30 ng/mL (n=73) had severe asthma versus 50% of those with vitamin D sufficiency (n=12; P=0.02). Vitamin D insufficiency was associated with a higher risk of severe asthma (odds ratio [OR], 5.04; 95% C], 1.23-20.72; P=0.02).

A study by Haider guru er al [28],in 2018.in our study, serum levels of vitamin D, pulmonary function tests, were analyzed in 120 asthmatic patients who were divided into vitamin D sufficient and vitamin D insufficient group. The age of the subjects in the study group ranged from 18 to 80 years with a mean of30.81 ± 8.97. The gender distribution of the study subjects revealed that there were 72 males (60%) and 48 females (40%). The patients were further classified as intermittent, mild, moderate, severe asthmatics depending on the severity of asthma. Vitamin D deficiency was highly prevalent in asthmatic patients, and there was a direct and a significant relationship between serum vitamin D levels, severity of asthma, control of asthma (P<0.001)

LIMITATION OF STUDY

The study population was small; it needs a bigger population and extensive data to define the significant difference in a more accurate way. This was a cross-sectional study with no follow up. There may be other confounding factors too which could have affected the result of this Study, since patients were selected only based on a simple history taking and clinical examination. Smoking and hypertension were the exclusion criteria, so it was difficult to collect male asthmatic who were non-smokers and without known case of skin, liver and renal disease and osteoporosis. Smoking was ruled out based on patients' history, and there is a question of reliability. Cardiac disease was ruled out on the basis of history electrocardiogram. Echocardiogram was not done for the asthmatic, so silent ischemia due to vitamin D deficiency contributes to cardiovascular disease through its association with other risk factors was not ruled out confidently. This study did not include diffusion capacity assessment, which can give more explanation towards the obstructive pattern in spirometry in the asthmatics. Pulmonary impairment leads to decreased physical working capacity in asthmatics. Since majority of the work force in our country is in 30s and 40s age group, the pulmonary dysfunction in the early years of asthma could affect productivity drastically at both individual and community levels. Hence, it is important to do periodic lung function as part of asthma check-up for early detection of abnormalities.

CONCLUSION

In our study Vitamin D3 deficiency was highly prevalent in asthmatic patients, there was a strong correlation between asthma severity and vitamin D3 concentrations and there

was a direct and a positive significant correlation between vitamin D3 levels and pulmonary function test in asthmatic patients. In asthma, reduced vitamin D3 levels are associated with impaired lung function of obstructive pattern, increased airway hyper responsiveness and reduced glucocorticoid response, so the measurement of serum vitamin D3 levels and pulmonary function test in patients with bronchial asthma is very useful. Early estimation of serum vitamin D3 and PFT should be routinely considered as it is a good prognostic marker with cost benefits and easy availability, so that supplementation of vitamin D3 levels in patients with asthma may improve multiple parameters of asthma severity and treatment response.

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