

**Association of vitamin D status with pulmonary function in adult asthmatics****Reeta Rajagambeeram<sup>1</sup>, Abilash Muralidaran<sup>2</sup>, Pajanivel Ranganadin<sup>3</sup>, Ramesh Ramasamy<sup>4</sup>**<sup>1</sup>Associate Professor, Department of Biochemistry, <sup>2</sup>Compulsory Rotatory Residential Intern<sup>3</sup>Professor, Department of Pulmonary Medicine, Mahatma Gandhi Medical College and Research Institute, SBV, Puducherry, India<sup>4</sup>Professor, Department of Biochemistry, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, India*(Received: June 2019      Revised: August 2019      Accepted: September 2019)*Corresponding author: **Reeta R.** Email: reetapajanivel@gmail.com**ABSTRACT**

**Introduction and Aim:** The role of calcitriol in physiological and pathophysiological processes has been recognized in the last couple of years. It plays an important role in immune regulation through interactions with vitamin D receptors (VDRs) expressed on airway immune cells, regulating the transcription of genes of inflammation and immunomodulation. Higher calcitriol concentrations have been associated with better pulmonary function. This study was planned to find whether there is an association between the serum vitamin D levels and pulmonary function.

**Materials and Methods:** Sixty adults with asthma attending the outpatient department of pulmonary medicine and thirty healthy controls were included in the study. This case-control study was carried out in a tertiary health care hospital. The subjects were diagnosed according to GINA guidelines and grouped into three groups 1 constituted healthy controls, 2 and 3 included subjects with well controlled and uncontrolled asthma/acute exacerbation of asthma respectively. Serum 25(OH) Vitamin D, calcium, phosphate and pulmonary function test were measured and compared between the groups. One way ANOVA was used to compare the means of the parameters. Pearson's correlation analysis was used to find the correlation between vitamin D and pulmonary function test.

**Results:** This study documents high vitamin D levels in well controlled asthma when compared to uncontrolled group ( $p < 0.05$ ). We also observed significant positive correlation of vitamin D with FEV1 and FEV1/FVC ratio.

**Conclusion:** Vitamin D levels are significantly high in the well-controlled asthma patients when compared to uncontrolled group with a positive correlation between the vitamin D levels and pulmonary function test. This indicates that an increased vitamin D level is associated with a good pulmonary function.

**Keywords:** Asthma; pulmonary function test; vitamin D.

**INTRODUCTION**

Asthma is a disorder characterized by varying and recurring symptoms of airflow obstruction and bronchial hyper-responsiveness in the setting of inflammation (1). Though there are numerous advances in the field, at present there is no cure for asthma but control of symptoms is through steroids with or without a  $\beta_2$ -adrenergic receptor agonist. Despite of the anti-inflammatory effect of these drugs they seldom prevent the diminution of long term lung function. Most common chronic respiratory disease is bronchial asthma, worldwide case burden of approximately 358.2 million in 2015. One tenth of the world's asthmatics live in India (2, 3).

The role of calcitriol in calcium and bone homeostasis has been well documented. Its activity on other physiological and pathophysiological processes has been documented only in the last couple of years (4). Research shows that calcitriol plays a role in multiple chronic diseases such as cancer, autoimmune diseases, infections, and

cardiovascular disorders (5, 6). Calcitriol also has a role in several diseases involving the respiratory system. It plays an important role in immune regulation through interactions with vitamin D receptors (VDRs). VDRs are expressed on airway immune cells, where they function as nuclear steroid hormone receptors and regulate the transcription of numerous genes associated with inflammation and immunomodulation (7). Higher calcitriol concentrations have been associated with better pulmonary function as evaluated by forced expiratory volume in 1 s ( $FEV_1$ ) in a large cross-sectional study of the U.S. population in the NHANES III (8).

There are very few studies in south Indian population comparing pulmonary function with vitamin D status in asthmatic patients. This study was planned to find whether there is an association between the serum vitamin D levels and pulmonary function as measured by forced vital capacity (FVC), forced expiratory volume in 1 sec ( $FEV_1$ ), and  $FEV_1/FVC$  ratio.

**MATERIALS AND METHODS**

This was a case control study undertaken in adults aged 18 to 50 years with asthma attending the outpatient department of pulmonary medicine in a tertiary care hospital. The study protocol was ethically approved by the institute human ethical committee and a written informed consent was obtained from all the study participants.

This study involved thirty healthy controls with normal pulmonary function test (Group I), Sixty diagnosed case of asthma patients [thirty well-controlled asthma patients (Group II) and thirty poorly controlled asthma patients (Group III) based on criteria for asthma symptom severity, according to the Global initiative for Asthma management (GINA) (9)]. Subjects with emphysema, bronchiectasis, infective bronchitis, known diabetes mellitus, hypertension, coronary heart diseases, renal failure, endocrine disorder, and patient on drugs other than anti-asthmatic agents and those on vitamin supplements were excluded from the study. Five ml of venous blood was collected from the subjects after obtaining proper written informed consent; the sample was subjected to centrifugation at 5000 rpm for 10 minutes. Separated serum was used for estimation of various biochemical parameters using discrete random access automated clinical chemistry analyser. The following biochemical parameters were estimated based on established spectrophotometric and automated procedures, approved by the International Federation of Clinical Chemistry and Laboratory medicine (IFCC).

Vitamin D status – serum 25(OH) Vitamin D were assayed by electrochemiluminescence method. Vitamin D deficiency was defined as serum 25(OH) vitamin D less than < 20 ng/ml, 20-30 ng/ml were defined as insufficient and desirable or sufficient was

> 30ng/ml, Serum calcium by ortho cresol phtalein complexone (OCPC) method, Serum phosphate- by molybdate UV method, Pulmonary function test- was performed in all the participants according to European respiratory society guidelines using a portable MIR winspiro spiobank II spirometer. The following parameters were documented: FEV1, FVC and FEV1/FVC ratio.

**RESULTS**

All the data were expressed as mean+/- SD; one way ANOVA followed by Bonferroni was used to compare the means of the parameters. Pearson’s correlation analysis was used to find the correlation of serum vitamin D levels with lung function. A p value less than 0.05 was considered as statistically significant for all statistical tests. SPSS version 17 was used for all statistical analysis.

All physiological and biochemical parameters results were compared by using an ANOVA test (table 1). In the present study serum Vitamin D, serum calcium, phosphorus, FEV1 and FEV1/FVC ratio were significantly different from each other (p<0.05). Among the controls, well controlled / stable asthma compared to poorly controlled / exacerbated asthma patients a significant difference was observed in Vitamin D, FEV1 and FEV1/FVC ratio (p<0.05). We did not observe any statistically significant differences for the other parameters.

Table 2 shows the association of the serum Vitamin D levels with FEV1 and FEV1/FVC ratio. There was significant positive correlation between Vitamin D and FEV1 and Vitamin D with FEV1/FVC ratio with a p value <0.05 and r value of 0.643 and p value <0.05 and r value of 0.714 respectively, which indicates that increased Vitamin D levels is associated with a good pulmonary function.

**Table1: Comparison of parameters between well controlled and poorly controlled asthma patients**

Parameters	Controls n=30	Well controlled asthma n=30	Poorly controlled asthma n= 30	'p' value
	Mean ±SD	Mean±SD	Mean±SD	
Calcium (mg/dL)	9.5±0.45	9.2± 0.5	9.3± 0.3	0.01*
Phosphorous(mg/dL)	3.7±0.35	3± 0.3	3.1± 0.5	0.00*
Vitamin D (ng/mL)	29.2±2.4	26.9± 2.9	19.6± 1.9	0.00*
FVC % predicted	95.6±9.1	90.9± 15.8	93.2± 16	0.45
FEV1 % predicted	92.7±8.3	85.4± 16	53.2± 15.6	0.00*
FEV1/FVC ratio	97.8±12.6	92± 7	65.9± 7.4	0.00*

\*p value <0.05 which is considered statistically significant

FVC: Forced Vital Capacity

FEV1: Forced Expiratory Volume in 1 Second

**TABLE 2: Association of Serum Vitamin D values with FEV<sub>1</sub> and FEV1/FVC Ratio**

Variables	FVC %	FEV1/FVC ratio
Serum vitamin D(ng/dL)	p =0.000* r= 0.643	p =0.000* r= 0.714

\*p value <0.05 which was considered statistically significant. Association was evaluated by Pearson’s correlation method

## DISCUSSION

In the present study poorly controlled asthma patients had low levels of serum vitamin D. Low serum vitamin D concentrations were significantly associated with airway obstruction, as evaluated by FEV1 and FEV1/FVC ratio. Similar observations of positive association between vitamin D status and lung function in asthma patients have been shown by Scragg *et al.*, and Li *et al.*, (10, 11).

In the present study, well controlled asthma patients have significantly higher levels of vitamin D when compared to poorly controlled asthma patients. Higher calcitriol concentrations have been associated with better pulmonary function as measured by FEV1 in a large cross-sectional study of the U.S population in the NHANES III participants (8). Also studies by Rappaport *et al.*, and Richards *et al.*, have demonstrated that low serum Vitamin D is associated with poor lung function and asthma control (12, 13). This may be due to the fact that vitamin D inhibits smooth muscle proliferation by influencing the down regulation of glucocorticoid receptor by its ligand (14, 15).

The present study is consistent with the above mentioned studies, i.e. a higher level of vitamin D is associated with better pulmonary function with a value  $p < 0.05$ . Research by Boswell S *et al* have shown an association between low vitamin D status and poor clinical responsiveness to glucocorticoids in asthma patients (15). National health and nutrition survey by Keet *et al.*, have shown that exacerbation of asthma occurs if there is a decline in vitamin D concentration such that a 10ng/mL was associated with 8% increase in the odds of asthma symptoms. It has also been recorded that lower concentration of vitamin D decreased lung function and increased the utilization of health care facilities (16). These studies suggest that Vitamin D may have therapeutic potential in severe asthma patients as a steroid enhancing agent, thereby decreasing the requirement for inhaled corticosteroids and may protect from developing respiratory infections that could serve as a trigger for a deterioration of asthma (4). The prevalence of calcitriol deficiency has been increasing in the general population in recent decades; high levels are required for various other diseases as well. 7 dehydrocholesterol present in the skin is activated by sunlight to yield cholecalciferol which is bio transformed to the active form calcitriol. The large portion of circulating 25 hydroxy cholecalciferol is the pre cursor of calcitriol derived from sun exposure, with a limited dietary contribution. The increased prevalence of vitamin D deficiency is ascribed to evasion of sun exposure, indoor lifestyle, use of sunscreen, and decreased intake of vitamin D-containing foods (4). There are observational studies that are contradictory to the

protective effects of sufficient levels of vitamin D (17, 18).

Jensen *et al.*, in their trail have discovered that in children less than five years with asthma showed no difference in serum D3 levels between the two groups after administering vitamin D3 or placebo, daily for 6 months (19). However; a question arises whether Vitamin D is to be estimated in all asthma patients. It may not be a pragmatic approach practically. There is need for further studies in large scale and also proof of underlying mechanisms how vitamin D modulates the pathogenesis of asthma.

## CONCLUSION

In conclusion in this study we have important information regarding vitamin D levels in adult asthmatics in Puducherry population. We were able to show that vitamin D deficiency in asthma patients is common and more so in uncontrolled asthma and on acute exacerbation of asthma. We also found significant correlations between vitamin D and pulmonary function test. Deficiency of vitamin D is associated with severity of asthma and also decreased lung function. This study would suggest that intake of adequate vitamin D may decrease the severity of asthma, exacerbations could be decreased and there could be an improvement in pulmonary function as well.

## Limitations

1, 25 dihydroxy cholecalciferol could also have been estimated along with 25-hydroxycholecalciferol. Other immunological parameters like Ig E, Eosinophils might contribute to the study.

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