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SERUM CHOLECALCIFEROL IN BRONCHIAL ASTHMA AND ITS ASSOCIATION WITH ASTHMA SEVERITY

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ABSTRACT

Objective: Determining the serum cholecalciferol in bronchial asthma and its association with asthma severity in adult patients. **Study Design:** Cross sectional study design. **Place and Duration:** Department of Medicine, Liaquat University Hospital, Hyderabad from March 2017 to May 2018. **Subjects and Methods:** 100 adults diagnosed of bronchial asthma and similar number of age and gender matched controls were analyzed for the serum cholecalciferol. Asthma severities were categorized as intermittent, mild, and moderate and sever persistent asthma. Serum cholecalciferol sufficiency, insufficiency and deficiency were defined as > 30 ng/mL), 20-30 ng/mL and < 20 ng/mL respectively. Serum cholecalciferol and serum IgE were detected from venous blood samples. Statistical software (SPSS v 22.0, IBM, Incorporation, USA) was used for data analysis at 95% confidence interval ($P \leq 0.05$). **Results:** Serum cholecalciferol in controls was 38.19±15.67 ng/dl compared to 24.87±13.54 ng/dl in cases (P=0.0001). Severe cholecalciferol deficiency was noted in mild persistent asthma cases (17.90±6.51 ng/dl). Serum IgE, Eosinophils and Serum Cholecalciferol shows statistically significant differences between controls and cases (P<0.05). Serum cholecalciferol insufficiency and deficiency in controls was found in 51% compared to 85% in cases (P=0.0001) (table IV). Pearson`s correlation shows negative association of Serum Ig E (r= - 0.523**, p=0.0001) and blood eosinophils (r= - 0.629**, p=0.0001) with serum cholecalciferol. **Conclusion:** The present study found low serum cholecalciferol in bronchial asthma that shows negative correlation with asthma severity, serum IgE and blood eosinophils.

KEYWORDS: Bronchial asthma, Serum cholecalciferol Serum IgE.

INTRODUCTION

Bronchial asthma is defined as a chronic inflammatory airway pulmonary disease of myriad origin. Bronchial airway tightening is a hallmark of asthma severity that varies over time. Bronchial asthma is a long term chronic inflammatory pulmonary affection that is characterized by airway bronchospasm and reversible airflow obstruction. Clinically, the patients present with complaints of shortness of breath, wheezing and cough.[1,2] In severe cases, the respiratory muscles may get exhausted resulting in respiratory failure and disturbed alveolar capillary gas exchange. Bronchospasm varies in intensity from time to time. Spirometry shows limited expiratory flow rate.[1,2] Bronchial asthma is a chronic lung disease with varying prevalence. Estimated prevalence approximates to 10-25% but it is increasing.[2,3] Bronchial asthma is one of leading pulmonary disease presenting at the emergency rooms, and often necessitate hospitalization. Bronchial asthma has a negative impact on the socio-economic conditions of families and countries. Patients suffering from bronchial asthma have disturbed sleep because of nocturnal exacerbation of Bronchospasm symptoms. This leads to poor daytime performance is in particular the work performance.[4,6] Recently, serum cholecalciferol (vitamin D) has been a topic of research and report in bronchial asthma pathogenesis. Primarily, the cholecalciferol is a prohormone that is vital for the bone health, but nowadays, its extra osseous effects have been of interest. Cholecalciferol exerts immune enhancing activity. Cholecalciferol sufficiency reduces the risk of autoimmune disorder, chronic infections, cardiovascular disease and malignancy.[5,6] Low serum cholecalciferol has been reported in bronchial asthma.[3,5] Its role has been highlighted in the childhood asthma too.[6,7] Vitamin D – cholecalciferol deficiency and

bronchial asthma are prevalent in Pakistan similar to other developing countries.[8] Bronchial asthma and cholecalciferol deficiency are common in the country.[9] The present cross sectional study was conducted at a tertiary care hospital of Sindh to analyze the serum cholecalciferol in bronchial asthma and its association with asthma severity, serum Ig E and blood eosinophils.

SUBJECTS AND METHODS

The present cross sectional study was conducted at the Department of Medicine, Liaquat University Hospital, Hyderabad from March 2017 to May 2018. A sample of; 100 adults diagnosed of bronchial asthma and similar number of age and gender matched controls were analyzed for the serum cholecalciferol, serum IgE and blood eosinophils. Asthma severities were categorized as intermittent, mild, and moderate and severe persistent asthma.[10] Bronchial asthma patients were selected through non-probability (purposive) sampling. Inclusion criteria were; diagnosed bronchial asthma cases of both gender, age 40 - 70 years presenting with acute exacerbation of bronchial asthma. Cases and controls with obesity, autoimmune lung disease, chronic liver and kidney disease, chronic steroid intake and those taking multivitamins were excluded from study protocol. Subjects were interviewed for the purpose of study and legal consent. Volunteers were explained about the purpose and benefits of study. They were informed that the study wants to analyze serum vitamin D levels in bronchial asthma cases and its association with asthma severity. The volunteers were informed that the study may help for the better management of bronchial asthma in the future by instituting vitamin D supplements. Clinical history, physical examination and blood samples were collected by a medical officer, a consultant physician and a senior staff nurse. Blood levels of serum cholecalciferol were defined as sufficient, insufficient and deficient (>30 ng/mL), 20-30 ng/mL and < 20 ng/mL respectively).[11,12] 5 ml venous blood was taken by researcher; 2 ml was taken in plain tube and 3 ml in EDTA glass tube. 2 ml venous blood samples were centrifuged, and sera were separated for analysis of serum cholecalciferol and serum IgE. Blood in Plain tubes was centrifuged at 3000 rpm (10- 15 minutes) for getting sera. Blood sera were put into sterilized Eppendorf tubes and stored at −20°C. Cholecalciferol and serum Ig E was detected by ARCHITECT I 1000 system and Elisa assay kit respectively. 3 ml venous blood was taken in EDTA tubes for the complete blood counts on Sysmex hematoanalyzer. Written consent was taken from the volunteers. Confidentiality of patients records were maintained strictly. All data were entered in a pre- structured proforma, and ethical permission was taken in prior. Statistical software (SPSS v 22.0, IBM, Incorporation, USA) was used for data analysis. Continuous and categorical were analyzed by student's t test and Chi (x^2) square test respectively. Pearson`s correlation was used for the association of serum cholecalciferol, serum Ig E and blood eosinophils. Scatter plots of correlation of serum cholecalciferol, serum IgE and blood eosinophils were produced by putting data in the Microsoft Excel sheet. Data was analyzed at α- level of significance of 95% ($P \leq 0.05$).

RESULTS

Age of controls and cases was 53.29±6.40 and 51.27±5.81 years respectively (p=0.05) (table I). Male and female in controls and cases were noted 73% and 27%, 71% and 29% respectively (P=0.98) (table II). Serum cholecalciferol in controls was 38.19±15.67 ng/dl compared to 24.87±13.54 ng/dl in cases (P=0.0001). Serum IgE, Eosinophils and Serum Cholecalciferol shows statistically significant differences between controls and cases (P<0.05). Table I shows the findings of controls and cases. Table III shows the serum cholecalciferol levels according to the severity of asthma. Severe cholecalciferol deficiency was noted in mild persistent asthma cases (17.90±6.51 ng/dl). Serum cholecalciferol Sufficiency (> 30 ng/mL), Insufficiency (20-30 ng/mL) and Deficiency (< 20 ng/mL) are shown in table IV (P=0.0001). Serum cholecalciferol insufficiency and deficiency in controls was found in 51% compared to 85% in cases (P=0.0001) (table IV). Scatter plots 1 and 2 show the negative correlation of serum cholecalciferol with serum IgE ($y = -13.565x + 959.33$, $R^2 = 0.2835$) and eosinophils ($y = -0.1345x + 8.7267$, $R^2 = 0.7071$). Pearson`s correlation shows negative association of Serum Ig E ($r = -0.523^{**}$, p=0.0001) and Blood eosinophils ($r = -0.629^{**}$, p=0.0001).

Table I: Characteristics of study subjects.

Parameter	Controls (n=100)	Cases (n=100)	P-value
Age (years)	53.29±6.40	51.27±5.81	0.059
Systolic BP (mmHg)	125.5±5.7	124.9±6.31	0.87
Diastolic BP (mmHg)	70.5±6.3	71.3±5.3	0.76
Serum IgE (IU/ml)	80.45±16.37	621.84 ±45.35	0.0001
Blood Eosinophils (%)	2.24±0.70	5.38±2.16	0.0001
Serum Ca++ (mg/dl)	9.06±1.16	8.91±1.21	0.431
Serum Albumin (mg/dl)	4.25±0.61	4.35±0.69	0.083
Cholecalciferol (ng/dl)	38.19±15.67	24.87±13.54	0.379
Creatinine (mg/dl)	0.96±0.17	0.90±0.18	0.78

Table II: Gender distribution of study subjects.

Gender	Controls (n=100)	Cases (n=100)	P-value
Male	73%	27%	0.98
Female	71%	29%	

Table III: Serum cholecalciferol distribution according to asthma severity in cases (n=100).

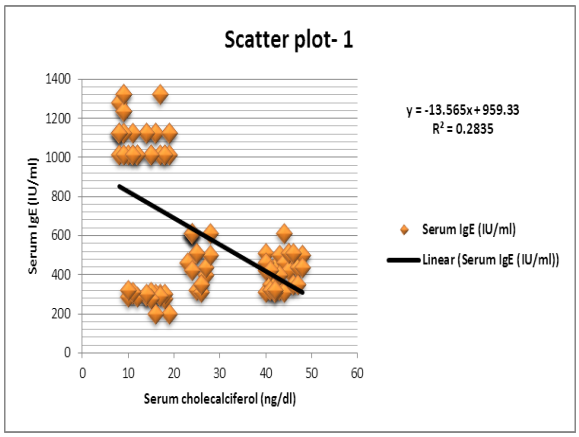
Asthma severity	Cholecalciferol		P-value
	Mean	SD	
Intermittent	27.48	7.79	0.0001
Mild Persistent	17.90	6.51	
Moderate Persistent	50.0	11.78	
Severe Persistent Asthma	49.15	9.37	

Table IV: Serum cholecalciferol categories of study subjects.

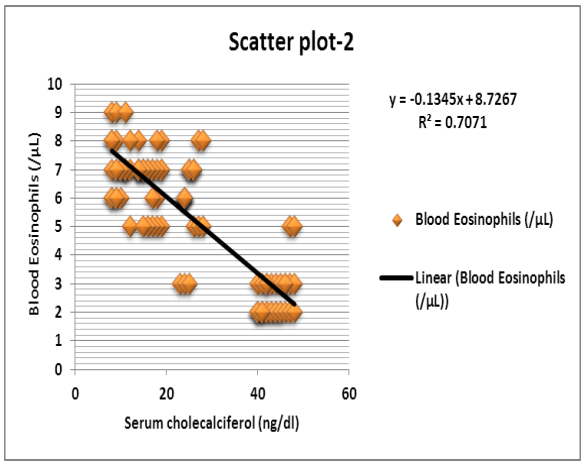
Cholecalciferol	Controls (n=100)	Cases (n=100)	P-value
Sufficiency (> 30 ng/mL)	49%	15%	0.0001
Insufficiency (20-30 ng/mL)	21%	14%	
Deficiency (< 20 ng/mL)	30%	71%	

Table V: Correlation co-efficient of Serum cholecalciferol.

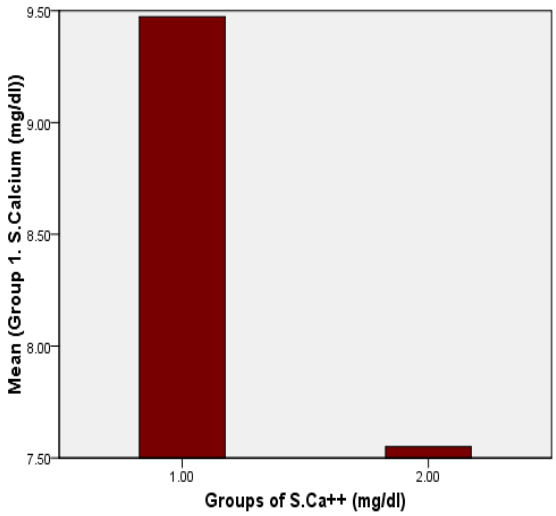
Cholecalciferol	r-value	P-value
Serum IgE	- 0.523**	0.0001
Blood Eosinophils	- 0.629**	0.0001



Graph 1: Negative linear correlation of Serum IgE and cholecalciferol.



Graph 2: Negative linear correlation of Blood eosinophils and cholecalciferol.



DISCUSSION

We are the first to report on the serum cholecalciferol in bronchial asthma and its association with asthma severity from a tertiary care hospital of Sindh. Adult bronchial asthma patients were analyzed for serum cholecalciferol. Age of controls and cases was 53.29±6.40 and 51.27±5.81 years respectively (p=0.05) (table I). Male and female in controls and cases were noted 73% and 27%, 71% and 29% respectively (P=0.98) (table II). These findings are in keeping with previous studies.[13,14] We found low serum cholecalciferol in asthmatic cases compared to healthy controls with raised serum immunoglobulin E and blood eosinophils (P<0.05). The findings are in consistent with previous studies. Severe serum cholecalciferol was found in intermittent cases of asthma in present study. The finding is supported by previous study.[15,16] Serum cholecalciferol in controls

was 38.19±15.67 ng/dl compared to 24.87±13.54 ng/dl in cases (P=0.0001). Serum cholecalciferol insufficiency and deficiency in controls was found in 51% compared to 85% in cases (P=0.0001) (table IV). These findings are consistent with previous studies.[13,15] A previous study[15] reported serum cholecalciferol deficiency, severe deficiency and insufficiency in 83.3%, 3.1% and 7.3% respectively. Serum cholecalciferol insufficiency and deficiency in controls was found in 51% compared to 85% in cases (P=0.0001). This finding is supported by a previous study[17] that reported cholecalciferol deficiency of in 60-90% of cases. Findings of cholecalciferol deficiency are supported by another previous study[18] that found cholecalciferol deficiency in 67% and 91% of intermittent and severe asthmatic patients respectively. Low serum cholecalciferol in bronchial asthma is in agreement with a previous study.[19] A previous study[20] reported that association of cholecalciferol deficiency and exaggerated inflammatory response in patients of bronchial asthma. A proposed molecular mechanism of exaggeration of bronchial asthma by cholecalciferol deficiency is through modulation of IL-10 cytokine that is considered an anti inflammatory cytokine.[21] A previous study[22] reported severe cholecalciferol deficiency in childhood bronchial asthma with positive correlation to asthma severity. This study[22] further added the cholecalciferol deficiency as risk for hypersensitivity conditions as bronchial asthma. The finding of low serum cholecalciferol in adult bronchial asthma of present study is consistent with previous studies.[20,21] It has been postulated that the cholecalciferol play role in anti inflammatory cellular signaling as these are involved in bronchial hyper-responsiveness to the pro-inflammatory cytokines.[20,21] In present study, raised serum IgE and blood eosinophils in cholecalciferol deficient asthmatics were found that is is in agreement with previous studies.[20-23] Scatter plots 1 and 2 show the negative correlation of serum cholecalciferol with serum IgE ($y = -13.565x + 959.33$, $R^2 = 0.2835$) and eosinophils ($y = -0.1345x + 8.7267$, $R^2 = 0.7071$). Pearson`s correlation shows negative association of Serum Ig E ($r = -0.523^{**}$, p=0.0001) and Blood eosinophils ($r = -0.629^{**}$, p=0.0001). Above findings are in agreement with previous studies.[21-25] A previous study[23] analyzed 2, 714 childhood asthma cases and found negative association of blood eosinophils with serum cholecalciferol. Above study also showed asthma severity was negatively associated with serum cholecalciferol similar to found in the present study. These findings are supported by previous studies.[24,25] Evidence based findings of low serum cholecalciferol in bronchial asthma, supported by published literature, suggests possible role of cholecalciferol deficiency and severity of bronchial asthma. Adult bronchial asthma patients should be screened for the serum cholecalciferol so that a modifiable aggravating factor should be removed for better asthma control. Cholecalciferol screening in cases of bronchial asthma and supplements may improve the health of this particular population.

CONCLUSION

We report low serum cholecalciferol in adult bronchial asthma patients that shows negative correlation with asthma severity. Patients of bronchial asthma should be screened for the serum cholecalciferol so that a modifiable aggravating factor may be corrected timely. Cholecalciferol screening in cases of bronchial asthma and supplements may improve the health of this particular population.

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