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CHILDHOOD BRONCHIAL ASTHMA;

SERUM CHOLECALCIFEROL IN CHILDHOOD BRONCHIAL ASTHMA AND ITS ASSOCIATION WITH ASTHMA SEVERITY

Nathumal Maheshwari[1], Omperkash Khemani[2], Sirichand[3], Bilawal Hingorjo[4], Mehmood Shaikh[5], Anjum Rehman[6]

1. MBBS, MCPS, FCPS
Assistant Professor Paediatrics
Shaheed Muhtrama Benazir Bhutto Medical College Layari General Hospital Karachi, Sindh, Pakistan.
2. MBBS, MCPS, FCPS
Assistant Professor Paediatrics
Shaheed Muhtrama Benazir Bhutto Medical College Layari General Hospital Karachi, Sindh, Pakistan.
3. MBBS, MCPS, FCPS
Assistant Professor Paediatrics
Hamdard Medical College Karachi.
4. MBBS, FCPS
Assistant Professor Pediatrics
Dow University of Health Sciences/ Civil Hospital Karachi Sindh, Pakistan.
5. MBBS, MCPS, FCPS (Paediatrics), FCPS (Neonatology)
Assistant Professor Paediatrics
Shaheed Muhtrama Benazir Bhutto Medical College Layari General Hospital Karachi, Sindh, Pakistan.
6. MBBS, MCPS, FCPS
Principal
Head of Department
Gynecology and Obstetrics
Shaheed Muhtrama Benazir Bhutto Medical College Layari General Hospital Karachi, Sindh, Pakistan.

Correspondence Address:
Dr. Nathumal Maheshwari
Department of Paediatrics
Shaheed Muhtrama Benazir Bhutto Medical College Layari General Hospital Karachi, Sindh, Pakistan.
drnathumal@gmail.com

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ABSTRACT… Objectives: Determine serum cholecalciferol in childhood bronchial asthma and its association with asthma severity. **Study Design:** Cross sectional study. **Place and Duration:** Department of Paediatrics, Layari General Hospital, Shaheed Muhtrama Benazir Bhutto Medical College Karachi from January 2015 – November 2016. **Subjects and Methods:** 100 diagnosed cases of childhood bronchial asthma and 100 controls were included. 5 ml venous blood was used for the full blood counts and sera were used for the serum cholecalciferol and IgE. Data was analysed on statistical software (SPSS v 22.0, IBM, Incorporation, USA) at 95% confidence interval ($P \leq 0.05$). **Results:** Mean ± SD age of controls and cases was noted 8.23±1.84 and 9.40 ±0.54 years. Low serum cholecalciferol was noted in the cases compared to the controls (25.7±14.5 vs. 38.3±15.5 ng/dl) (p=0.0001) with a rise in blood eosinophil, absolute eosinophil counts and serum Ig E. Serum cholecalciferol shows negative correlation with serum IgE, blood eosinophil and absolute eosinophil counts. **Conclusion:** The present study reports low serum cholecalciferol in childhood bronchial asthma. Cholecalciferol shows negative association with severity of asthma.

Key words: Cholecalciferol, Childhood Asthma, Serum Ig E, Eosinophils.

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INTRODUCTION

Asthma is a long term inflammatory lung affection characterized by recurring symptoms of reversible airflow obstruction and bronchospasm. Bronchial asthma is a chronic inflammatory lung airway disease of heterogeneous origin. Clinical symptoms include cough, wheezing and shortness of breath (SOB).[1,2] In its severe form, asthma may prove life threatening due to the exhaustion of respiratory muscles, impaired capillary gas exchange, and respiratory failure. Airway obstruction is a hallmark of asthma severity that varies over time. In severe cases airway obstruction varies in intensity with limited expiratory flow rate on spirometry.[1,2] Childhood asthma is a common chronic lung disease with varying prevalence through the World over. Childhood asthma is increasing, with estimated prevalence of 10-25%.[2,3] Childhood asthma is one of leading lung disease reporting at the emergency rooms often necessitating hospitalization. Childhood asthma has a great negative impact on the social and economic perspectives of families. Children with asthma suffer from loss of sleep due to nocturnal exacerbation of symptoms, and daytime performance is decreased, in particular the school performance.[4] Recently, much interest has grown on the serum cholecalciferol (vitamin D) and bronchial asthma. Vitamin D (cholecalciferol) is a prohormone. Primarily involved in bone mineralization, but extra osseous effects have been noted. It has an immune enhancing activity.

Cholecalciferol decreases the risk of chronic infections; cardiovascular disease, autoimmune disorders and malignancy.[5] Previous studies[3-5] have reported low serum cholecalciferol in asthma and negative association of it with bronchial asthma. Previous studies[6,7] have shown cholecalciferol deficiency in childhood bronchial asthma, and its correlation with severity of asthma symptoms. Cholecalciferol deficiency is very common in developing countries like Pakistan, where a large number of childhood population is simultaneously suffering from bronchial asthma.[8] Bronchial asthma and cholecalciferol deficiency are very common in Pakistan.[9] The present prospective study was conducted at our tertiary care hospital to determine the frequency of serum cholecalciferol deficiency in childhood asthma, serum immunoglobulin E, eosinophil counts in childhood asthma. Association of serum cholecalciferol with asthma severity was also determined.

SUBJECTS AND METHODS

The present case control study was conducted at the Department of Paediatrics, Layari General Hospital, Shaheed Muhtrama Benazir Bhutto Medical College Karachi, Sindh, Pakistan from January 2015 – November 2016. A sample of 100 diagnosed cases of bronchial asthma and 100 control subjects. Research study sample was selected by non-probability (purposive) sampling. Cases were selected according to pre- defined inclusion and exclusion criteria. Diagnosed asthma male children presenting with acute exacerbation of bronchial asthma of age 3 – 10 years was inclusion criteria. Children with obesity, chronic liver, kidney and lung disease, and taking cholecalciferol supplements and chronic steroid therapy, and multi-vitamin multi-mineral pills were excluded. Female asthmatic children were also excluded. Legal heirs were taken into confidence for the purpose and consent of study. They were interviewed that the inclusion in research is voluntarily. Clinical history was noted, and clinical examination was conducted by a medical officer followed by a consultant pediatrician. Asthma severity was classified as intermittent, mild, moderate, and severe persistent asthma.[10] Serum cholecalciferol levels of sufficiency, insufficiency and deficiency were defined as >30 ng/mL, 20 - 30 ng/mL and < 20 ng/mL respectively.[11] Nursing facilitators were recruited to communicate with volunteers if they are feeling worrisome, anxious, and problematic. Asthmatic children of voluntarily willing participants were asked blood sampling. 5 ml venous blood was taken by researcher; 3 ml was put into the EDTA glass tube and 2 ml into plain tube. Sysmex hematoanalyzer was used for full blood counts. Absolute eosinophil counts (AEC) was calculated by formula; AEC (μL) = % of Eosinophil from DLC x TLC / 100.[12] Plain tubes were centrifuged at 3000 rpm (10- 15 minutes) for sera to separate and were transferred to sterilized Eppendorf tubes and were stored at −20°C. Serum cholecalciferol was estimated by the ARCHITECT I 1000 system. Elisa assay kit detected the serum IgE. Consent form was signed in writing by volunteers heirs. Confidentiality of patient data was ensured. Data was collected on a pre- structured pre- designed proforma. Prior ethical permission was taken from the institutional ethical committee. Data was analysed on statistical software (SPSS v 22.0, IBM, Incorporation, USA). Continuous (e.g. age, cholecalciferol) and categorical (e.g. cholecalciferol categories) were analyzed by student's t test and Chi (x^2) square test respectively. Scatter plots of serum cholecalciferol with serum IgE and eosinophils were generated on Microsoft Excel sheet. All statistical analysis procedures were performed at α- level of significance of 95% ($P \leq 0.05$).

RESULTS

Mean ± SD age of controls and cases was noted 8.23±1.84 and 9.40 ±0.54 years (p=0.051) respectively. Serum cholecalciferol was noted 38.3±15.5 and 25.7±14.5 ng/dl (p=0.0001) showing deficiency in the cases. Serum IgE, Eosinophils (%) and AEC were noted as 80.7±15.9 and 631.9±15 (IU/ml) (p=0.0001), 2.25±0.69 and 5.31±2.39 (%) (p=0.0001), & 124.30±41.04 and 270.64±70.23 (/μL) (p=0.0001) in controls and cases respectively (Table-I). Cholecalciferol sufficiency, insufficiency and deficiency are shown in Table-II. Controls showed sufficient cholecalciferol in 71% compared to 37% in cases (p=0.0001). Table-III shows the serum cholecalciferol according to the asthma severity.

Scatter plots (Figures-1,2 and 3) show the negative correlation of serum cholecalciferol with serum IgE (y= -11.856x + 736.11, R^2 = 0.2659), blood eosinophil counts (y= -0.0945x + 6.8085, R^2 = 0.4366) and y=-1.7396x+253.2, R^2 = 0.0925 respectively.

DISCUSSION

The present study is the first study being reported forms our tertiary care hospital that shows the serum cholecalciferol was significantly low in the cases compared to controls, with raised serum IgE, eosinophils and absolute eosinophil counts (AEC) (P<0.05). These findings are in keeping with previous.[13,14] Serum cholecalciferol was found low with increasing asthma severity. Mean ± SD age of controls and cases was noted 8.23±1.84 and 9.40 ±0.54 years (p=0.051) respectively. These findings are in line with a recent study by Krishnan et al[15] who reported majority of study children belonged to 5- 10 years of age. However, Chhabra et al[16] reported 9-13 years as common age group of childhood asthma, this in disagreement with present and previous studies.[13-15]

Parameter	Controls (n=100)	Cases (n=100)	P-Value
Age (years)	8.23±1.84	9.40 ±0.54	0.051
Cholecalciferol (ng/dl)	38.3±15.5	25.7±14.5	0.0001
Serum IgE (IU/ml)	80.7±15.9	631.9±157	0.0001
Blood Eosinophils (%)	2.25±0.69	5.31±2.39	0.0001
AEC (/μL)	124.30±41.0	270.64±70.2	0.0001
Creatinine (mg/dl)	0.97±0.21	0.98±0.23	0.89

Table-I. Characteristics of study subjects

Cholecalciferol	Controls (n=100)	Cases (n=100)	P-Value
Sufficiency (> 30 ng/mL)	71%	37%	0.0001
Insufficiency (20-30 ng/mL)	15%	11%	
Deficiency (< 20 ng/mL)	14%	52%	

Table-II. Serum cholecalciferol categories of study subjects

Asthma Severity	Cholecalciferol		P-Value
	Mean	SD	
Intermittent	44.01	2.61	0.0001
Mild Persistent	25.72	1.67	
Moderate Persistent	14.72	2.95	
Severe Persistent Asthma	11.20	3.81	

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

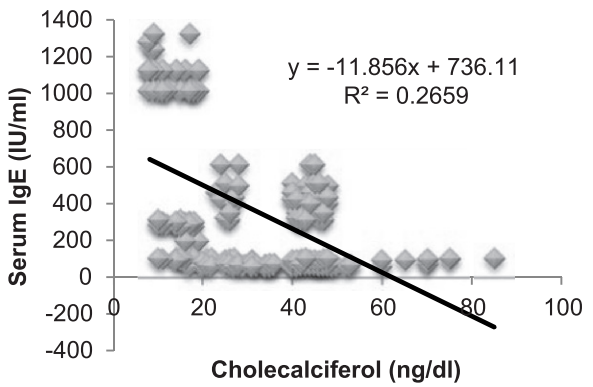

Figure-1. Scatter plot of serum cholecalciferol and IgE

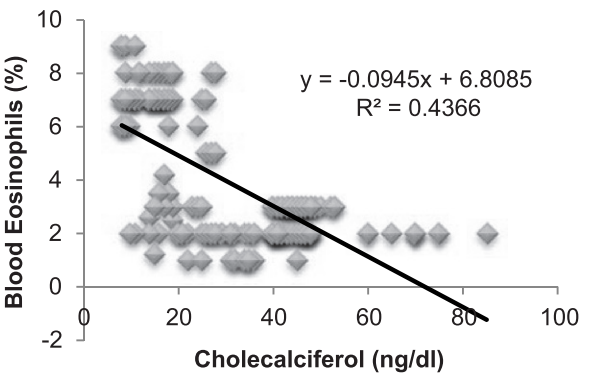

Figure-2. Scatter plot of cholecalciferol and eosinophils

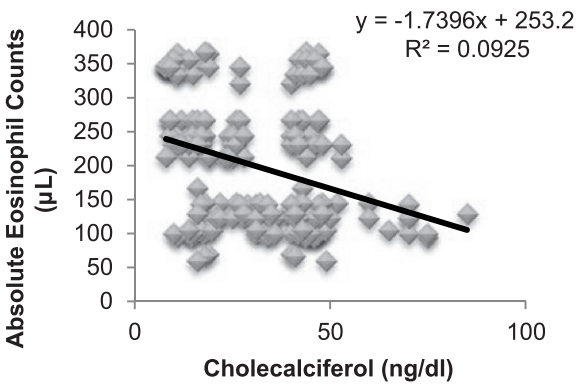

Figure-3. Scatter plot of absolute eosinophil counts and cholecalciferol

Cases showed severe deficiency of serum cholecalciferol 25.7±14.5 ng/dl compared to 38.3±15.5 ng/dl in controls (p=0.0001). Controls showed sufficient cholecalciferol in 71% compared to 37% in cases (p=0.0001). Sufficiency, insufficiency and deficiency of serum cholecalciferol were noted in 37%, 11% and 52% of cases respectively. These findings are consistent with previous study[15] that reported deficiency, severe deficiency and insufficiency of serum cholecalciferol in 83.3%, 3.1% and (7.3%) respectively. Our findings are also supported by a previous study[17] which reported vitamin D deficiency of in 60-90% of cases. Mora et al[18] reported cholecalciferol deficiency in 67% and 91% of severe asthmatic patients respectively. Ginde[19] also reported serum cholecalciferol was low in the bronchial asthma. It has been postulated that the cholecalciferol deficiency may augment the inflammatory cascade resulting in exaggeration of bronchial asthma.[20] Another proposed mechanism of exaggeration of bronchial asthma by cholecalciferol deficiency is through modulation of anti inflammatory IL-10 cytokine.[21] Vithalani et al[22] reported from Georgia severe cholecalciferol deficiency in childhood allergies and positive correlation was proved. This previous study[22] reported cholecalciferol deficiency is a risk for allergic conditions like bronchial asthma in children. Our finding of low serum cholecalciferol is in agreement with previous studies.[20,21] These previous studies[20,21] reported cholecalciferol plays pivotal role in cellular signals involved in the bronchial hyper-responsiveness to the inflammatory cytokines. The present study reports high eosinophils, AEC and serum IgE in cholecalciferol deficient asthmatics which is in agreement with previous studies. Scatter plots (Figures-1-3) show the correlation of serum cholecalciferol with serum IgE, blood eosinophils and AEC (p=0.0001). Our findings are consistent with previous studies.[15, 23-25] Berhm et al[23] studied 2, 714 children with asthma and found negative correlation of serum cholecalciferol and eosinophil. Berhm further reported inverse association of cholecalciferol and asthma severity, similar to found in the present study. Our findings are also in keeping with previous studies.[24,25] In the light of above discussion and literature review, the findings of present study are supported and point towards the health issue of cholecalciferol in asthmatic children which should be screened properly. Asthmatic children must be investigated for and supplemented with vitamin cholecalciferol. Strategies should be put into practice at national level for the childhood asthmatic population to manage a preventable problem of cholecalciferol deficiency. If the cholecalciferol deficiency is treated and removed at proper time, this will benefit the childhood asthmatics and will reduce asthma related mortality and morbidity.

CONCLUSION

The present study reports low serum cholecalciferol in childhood bronchial asthma. Cholecalciferol shows negative association with severity of asthma. Cholecalciferol also reveals negative associations with blood eosinophils, absolute eosinophil counts and serum immunoglobulin E. Cholecalciferol supplements may be prescribed to alleviate the symptoms of childhood bronchial asthma.

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Chop your own wood and it will warm you twice.

– Unknown –

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Nathumal Maheshwari	Concept, Literature review, Materials handling, compilation of results, statistical analysis, Manuscript write up, Proof reading, Correspondence.	
2	Omperkash Khemani	Concept, materails handling, Interpretation lab investigations, Manuscript write up, Proof Reading.	
3	Sirichand	Concept, Materials handling, COllection of materials, compilation of resutls, statistical analysis, manuscript write up.	
4	Bilawal Hingorjo	Literature review, Concept, Materials handling, Interpretation lab investigations, Manuscript write up, Proof Reading.	
5	Mehmood Shaikh	Concept, Materials handling Interpretataion lab investigations, Manuscript write up, Proof Reading.	
6	Anjum Rehman	Concept, Materials handling, Interpretation lab investigations, Manuscript write up, Proof reading. Concept, Materials handling, Collection of materials, compilation of results, statistical analysis, manuscript write.	