

# Association between Vitamin D Deficiency and Bronchial Asthma in Pediatric Age Group

AFTAB ANWAR<sup>1</sup>, SAED AFTAB AHMAD<sup>2</sup>, AAMIR WAHEED<sup>3</sup>, MAHNOOR MOHYDIN<sup>4</sup>, SALEHA BASHIR<sup>5</sup>

<sup>1</sup>Assistant Professor of Pediatric Gastroenterology, Lahore General Hospital, Pakistan

<sup>2</sup>Professor Pediatrics, Hameed Latif Hospital, Lahore, Pakistan

<sup>3</sup>Assistant Professor of Pulmonology, Sialkot Medical College, Sialkot, Pakistan

<sup>4</sup>House Officer Services Hospital Lahore, Pakistan

<sup>5</sup>Student at Lahore Grammar School 55-Main, Lahore, Pakistan,

Correspondence to Dr. Aftab Anwar, Email :- dr.aftabanwar@gmail.com, Tel :- 0300-4474170

## ABSTRACT

**Aim:** To determine the association between Vitamin D deficiency and Bronchial asthma in paediatric age group

**Methodology:** This Case-Control study was conducted from April 2018 to February 2020 by the Department of Paediatrics in Sialkot Medical College, Sialkot, Pakistan. It included a sample size of 170 children of both genders between 6-12 years of age. 85 cases were diagnosed as per Global Initiative for Asthma Guidelines and the other 85 were controls from healthy school going children. Data was analysed by SPSS version 24.

**Results:** Mean vitamin D level in cases was 16.73±0.19 and in controls was 19.22±0.49 ng/ml (p<0.0001). Bronchial asthma was more prevalent in those with positive bronchial asthmatic family history and amongst the urban population. Serum IgE level was seen to be raised more in cases than in the controls.

**Conclusion:** Vitamin D is deficient in paediatric patients suffering from bronchial asthma. Thus, Vitamin D supplementation is important for control of disease.

**Keywords:** Vitamin D deficiency, Bronchial asthma, Paediatric age group

## INTRODUCTION

Bronchial asthma is a chronic, inflammatory disease of airways characterized by hypersensitivity, cough, recurrent wheezing and respiratory distress<sup>1</sup>. Various genetic and environmental factors as well as activation of innate and adaptive immune systems are involved<sup>2</sup>. The disease affects 300 million people worldwide making it a major public health problem globally. Moreover, its incidence is on the rise causing an economic burden of \$54 billion USD in the form of lost school and work days, medical costs and early deaths<sup>3</sup>. The global prevalence of childhood asthma is 8.6% while in Pakistan about 20% children have asthma<sup>4,5</sup>.

Management of bronchial asthma includes multiple modalities and a step-up approach in its pharmacotherapy have been suggested. Recent evidences demonstrate that vitamin D deficiency may play a role in pathogenesis of bronchial asthma<sup>6</sup>. Previously, vitamin D was associated with its classical skeletal action and regulation of bone homeostasis only. Nowadays, role of vitamin D in various other physiological processes is also well established<sup>7</sup>. It mediates human body's defense mechanism and functions against inflammation<sup>8</sup>. Airway epithelium cells express 1-alpha hydroxylase, which causes activation of inactive 25(OH) D to the active form, calcitriol. Activated vitamin D provides strong innate immunity to airways while decreases the infection and inflammation<sup>9</sup>. Vitamin D deficiency is associated with increasing incidence of bronchial asthma and its supplementation has shown to alleviate these effects in adult population<sup>10,11</sup>.

The question that whether or not vitamin D deficiency is risk factor for pediatric asthma needs statistical evidence. We conducted this study to find out the association between vitamin D deficiency and bronchial asthma, specifically in pediatric population.

Received on 16-08-2020

Accepted on 13-02-2021

## MATERIALS & METHODS

This case control study was conducted at the Sialkot Medical College's Department of Pediatrics from April 2018 to February 2020. Employing non-probability sampling technique, sample size of 170 (85 cases diagnosed as asthmatic and 85 controls from healthy school going children) was calculated with 95% confidence level, power of 80% and prevalence of asthma as 20% using Open Epi formula<sup>5</sup>. Subjects having age from 6-12 years of both male and female gender were included and diagnosed according to Global Initiative for Asthma Guideline<sup>12</sup>. Patients with history of other chronic pulmonary diseases, allergic diseases, and on any vitamin D supplements were excluded from cases. Patients who could not get their complete investigations or were not able to follow up, were also excluded. Subjects with no history of allergic diseases and negative atopic family history were enrolled as healthy controls. Approval of study was taken from institutional review board of the hospital. A written informed consent was obtained from the parents of the participants that were included.

Blood samples were collected from the subjects by venipuncture. The values for vitamin D lower than 20ng/ml were considered as deficient, while value above 21ng/ml were considered as optimum. Serum concentration of 25 (OH) vitamin D was assayed with an electrochemiluminescence method {Cobas E-4111 (Elecsys) Roche, Germany}. Biodata of patients and vitamin D level result were recorded on a predesigned proforma.

The data was subjected to statistical analysis using SPSS version 24. It was presented as mean ± standard deviation (SD). Student's t-test was used to measure the difference in mean baseline values of various measurements. The data was analyzed using Pearson chi-square test, odds ratio, a two tailed p value of <0.05 was considered as significant.

## RESULTS

Demographic data of included subjects having asthma and healthy controls is shown in Table 1. Comparison of all variables except age and gender distribution are significant ( $p < 0.05$ ). There was no difference in sex, age and BMI between asthmatic cases and healthy controls. Table 2 shows the comparison of mean values of vitamin D in asthmatic patients and healthy controls, which is also significant ( $p < 0.0001$ ).

Table 1: Demographic profile

Variable	Case	Control	p value
Age (Years)	8.6±1.8	8.8±1.8	0.4699
<b>Gender</b>			0.3569
Boys	44 (51.8%)	37(43.5%)	
Girls	41 (48.2%)	48(56.5%)	
Family history of asthma			<0.0001
Yes	61 (71.8%)	29(34.1%)	
No	24 (28.2%)	56(65.9%)	
Residence			0.0355
Urban	63	49	
Rural	22	36	
Total IgE	131.6±24.9	33.1±2.1	<0.0001

Table 2: Comparison of mean vitamin d levels of two groups

Variable	Case	Control	p value
Vitamin D level(ng/ml)	16.73±0.19	19.22±0.49	<0.0001
Vitamin D level	74 (87%)	59(69.4%)	0.0093
Insufficient	11 (13%)	26(30.6%)	
Sufficient			

## DISCUSSION

Bronchial asthma is a common chronic inflammatory condition of airways. The bronchi are hyperactive, become narrow in response to a wide range of stimuli and may progress to irreversible airflow obstruction in some cases<sup>13</sup>. Vitamin D promotes steroid sensitivity and can downregulate anti-inflammatory state via gene expression and cytokine production<sup>14</sup>. Activated vitamin D might have a role in tissue remodeling and probably lung function by inhibiting metalloproteinase, fibroblast proliferation and influencing collagen synthesis<sup>15</sup>. Along with these, inhibition of transforming growth factor beta, might result in airway remodeling, improved muscle movement, growth and contractility as an influence of vitamin D<sup>16</sup>.

All of our included subjects had suboptimal serum levels of vitamin D, reflecting its deficiency in all ages and genders<sup>17</sup>. Significantly lower mean vitamin D levels were found in our cohort of asthmatic patients, a finding similar to Jat KR et al and Liu J<sup>18,19</sup>. A higher prevalence of vitamin D deficiency was observed in our cohort of asthmatic patients also. This might be due to the fact, that asthmatic children are less exposed to sunshine, as they spend less time outdoors. Interestingly, our study showed that the prevalence of asthma is more in cities as compared to rural areas. This is in accordance with the most of the data favoring increased incidence of pediatric asthma in urban communities. Newer studies are challenging this long-standing belief<sup>20</sup>. Family history of asthma was recorded in 71.8% cases of our asthma cohort, a finding similar to Saya K et al<sup>21</sup>. We also found that mean serum IgE levels were increased in asthmatic patients with vitamin D deficiency as compared to healthier controls. In line with our

findings, Hatami G et al recorded raised serum levels of total IgE<sup>22</sup>.

Our study and evidences from the data above suggest a correlation between pediatric asthma and vitamin D deficiency. Supplementing vitamin D on regular basis during treatment of vitamin D may have a beneficial effect on control of disease. However, some studies have contradictory results as they suggest that vitamin D may induce imbalance between Th1 and Th2 type cytokines resulting in Th2 dominance<sup>23</sup>. Matheu et al, have shown dual effects of vitamin D in both enhancing and suppressing Th2 responses in pulmonary eosinophilic inflammation in murine models<sup>24</sup>. In line with these findings, Forno E and fellows did not support use of vitamin D in patients with asthma.

A small sample size and single center study are limitations of this study. A study involving multiple pediatric centers with a large sample size is required in future to determine regular supplementation of vitamin D in treatment of pediatric bronchial asthma.

## CONCLUSION

Vitamin D deficiency is common in our healthy and asthmatic population. Frequency of vitamin D deficiency is higher in pediatric patients with bronchial asthma. Supplementing vitamin D in asthmatic children might result in increased control of disease.

**Disclaimer:** None to declare.

**Conflict of interests:** None to declare

**Funding Disclosure:** All investigations were done from the Pathology laboratory of the hospital. No funds were taken from any pharmaceutical company.

## REFERENCES

- Horak F, Doberer D, Eber E, Horak E, Pohl W et al. Diagnosis and management of asthma - Statement on the 2015 GINA Guidelines. *Wien Klin Wochenschr* 2016;128(15-16):541-54.
- Hall SC, Fischer KD, Agrawal DK. The impact of vitamin D on asthmatic human airway smooth muscle. *Expert Rev Respir Med*. 2016; 10(2):127-135.
- Loftus PA, Wise SK. Epidemiology and economic burden of asthma. *Int Forum Allergy Rhinol*. 2015;5 Suppl 1:S7-S10. doi:10.1002/alr.21547
- Ferrante G, La Grutta S. The Burden of Pediatric Asthma. *Front Pediatr*. 2018;6:186. Published 2018 Jun 22. doi:10.3389/fped.2018.00186
- Sabar MF, Akram M, Awan FI, Ghani MU, Shahid M, Iqbal Z, et al. Awareness of Asthma Genetics in Pakistan: A review with some recommendations. *Adv Life Sci*. 2018;Nov 25;6(1):1-0.
- Guru H, Shah S, Rasool R, Qadri Q, Guru FR, Bashir S et al. Correlation between Asthma Severity and Serum Vitamin D Levels: Experience from a Tertiary Care Centre in North India. *J Biomedical Sci*. 2018;7(3):12
- Szymczak I, Pawliczak R. The Active Metabolite of Vitamin D3 as a Potential Immunomodulator. *Scand J Immunol*. 2016;83(2): 83-91, doi: 10.1111/sji.12403
- Barragan M, Good M, Kolls JK. Regulation of dendritic cell function by vitamin D. *Nutrients*. 2015 Sep;7(9):8127-51.
- Hansdotir S, Monick MM, Lovan N, Powers L, Gerke A, Hunninghake GW. Vitamin D decreases respiratory syncytial virus induction of NF- $\kappa$ B-linked chemokines and cytokines in airway epithelium while maintaining the antiviral state. *J Immunol*. 2010 Jan 15;184(2):965-74.

10. Yawn J, Lawrence LA, Carroll WW, Mulligan JK. Vitamin D for the treatment of respiratory diseases: Is it the end or just the beginning? *J Steroid Biochem Mol Biol*. 2015; 148:326–337.
11. Kerley CP, Elnazir B, Faul J, Cormican L. Vitamin D as an adjunctive therapy in asthma. part 2: A review of human studies. *PulmPharmacolTher*. 2015; 32:75–92.
12. Global Initiative for Asthma. 2019. GINA report, global strategy for asthma management and prevention. Available at: [ <http://www.ginasthma.org>]
13. Wayse V, Yousafzai A, Mogale K, Filteau S (2004) Association of subclinical vitamin D deficiency with severe acute lower respiratory infection in Indian children under 5 y. *Eur J Clin Nutr* 2004;58: 563.
14. Ginde AA, Mansbach JM, Camargo CA. Vitamin D, respiratory infections, and asthma. *CurrAllergy Asthma* 2009;Rep 9:81-87.
15. Damera G, Fogle HW, Lim P, Goncharova EA, Zhao H, et al. Vitamin D inhibits growth of human airway smooth muscle cells through growth factor-induced phosphorylation of retinoblastoma protein and checkpoint kinase 1. *Br J Pharmacol* 2009;158: 1429-1441.
16. Gupta A, Sjoukes A, Richards D, Banya W, Hawrylowicz C, et al. Relationship between serum vitamin D, disease severity, and airway remodeling in children with asthma. *Am J Respir Crit Care Med* 2011,184: 1342-1349
17. Masood Z, Mahmood Q, Ashraf KT. Vitamin D deficiency-an emerging public health problem in Pakistan. *JUMDC*. 2010;1(1):4-9.
18. Jat KR, Khairwa A. Vitamin D and asthma in children: A systematic review and meta-analysis of observational studies. *Lung India*. 2017 Jul;34(4):355-63.
19. Liu J, Dong YQ, Yin J, et al. Meta-analysis of vitamin D and lung function in patients with asthma. *Respir Res*. 2019;20(1):161. Published 2019 Oct 8. doi:10.1186/s12931-019-1072-4
20. Li X, Song P, Zhu Y, Lei H, Chan KY, Cambell H et al. The disease burden of childhood asthma in China: a systematic review and meta-analysis. *J Glob Health*. 2020;10(1):010801. doi:10.7189/jogh.10.01081
21. Kumar Saya, Ganesh & Roy, Gautam & Lakshminarayanan, Subitha & Sahu, Swaroop. Prevalence of bronchial asthma and its associated factors among school children in urban Puducherry, India. *Journal of natural science, biology, and medicine*. 2014;5: 59-62. 10.4103/0976-9668.127289.
22. Hatami G, Ghasemi K, Motamed N, Firoozbakht S, Movahed A, Farrokhi S. Relationship between Vitamin D and Childhood Asthma: A Case-Control Study. *Iran J Pediatr*. 2014;24(6):710-714.
23. Cantorna MT, Zhu Y, Froicu M, Wittke A. Vitamin D status, 1,25-dihydroxyvitamin D<sub>3</sub>, and the immune system. *Am J Clin Nutr* 2004;80: 1717-1720.
24. Matheu V, Back O, Mondoc E, Issazadeh-Navikas S. Dual effects of vitamin D-induced alteration of TH1/TH2 cytokine expression: enhancing IgE production and decreasing airway eosinophilia in murine allergic airway disease. *J Allergy Clin Immunol* 2003;112: 585-592
25. Forno E, Bacharier LB, Phipatanakul W, Guilbert TW, Cabana MD, Ross K et al. Effect of Vitamin D<sub>3</sub> Supplementation on Severe Asthma Exacerbations in Children With Asthma and Low Vitamin D Levels: The VDKA Randomized Clinical Trial. *JAMA*. 2020;324(8):752–760. doi:10.1001/jama.2020.12384.