

## Association between Vitamin D Deficiency and Asthma Control in Children

**Rajnish Kumar<sup>1</sup>, Binoy Shankar<sup>2</sup>, Kumar Gaurav<sup>3</sup>, Nitish Kumar<sup>4</sup>, Avinash Kumar Sahay<sup>5</sup>**

<sup>1</sup>Assistant Professor, Department of Pediatrics, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India

<sup>2</sup>Assistant Professor, Department of Pediatrics, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India

<sup>3</sup>Assistant Professor, Department of Pediatrics, R.D.J.M Medical College and Hospital Muzaffarpur, Bihar, India

<sup>4</sup>Assistant Professor, Department of Pediatrics, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India

<sup>5</sup>Professor And Hod, Department of Pediatrics, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India

Received: 10-06-2023 Revised: 20-07-2023 / Accepted: 15-08-2023

Corresponding author: Dr Nitish Kumar

Conflict of interest: Nil

### Abstract

**Aim:** The aim of the present study was to assess the association between asthma control and serum 25-OH Vitamin D levels in children with moderate persistent asthma on preventer therapy.

**Material & Methods:** Children aged 6-18 years, with moderate persistent asthma, on preventer therapy for  $\geq 2$  months were included. Control was categorized as good, partial or poor as per GINA guidelines. Serum 25 (OH) Vitamin D levels were measured and their relationship with the level of control was studied

**Results:** Children with partially/poorly-controlled asthma were significantly more likely to have vitamin D deficiency. Asthma control was well controlled in 50 children and 50 had not well controlled. Age, gender, family history of asthma, type of device, serum IgE levels and presence of co-morbidities had no relationship to the level of control. Children who were underweight or obese had poorer control but the difference was not statistically significant. Children with well controlled asthma were significantly less likely to have been born low birth weight.

**Conclusion:** The findings of this study may have implications in clinical practice. Currently, poor control is being managed by escalation of preventer therapy. Adding more drugs or increasing the doses may over time increase the toxicity of therapy. Evaluating serum 25 (OH) D levels and correcting identified deficiencies may prevent the need for escalation of preventer therapy.

**Keywords:** Vitamin D, Asthma, Children, Allergy, Co-morbidity, Outcome, Treatment, Wheezing

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

### Introduction

Bronchial asthma remains the most common chronic disease of childhood [1-3] and is one of the leading causes of morbidity in children worldwide. [4] Currently, the burden of asthma in both the developed and the developing world is significant and increasing rapidly with more than 300 million people affected worldwide. Asthma is a chronic inflammatory airway disease that is characterized by bronchial hyper-responsiveness and tissue remodeling. [5] Asthma is usually triggered by a combination of genetic and environmental factors that end with inappropriate immune-mediated chronic inflammatory responses, which may

influence the severity of the disease and response to treatment. [5,6]

Recent studies are on their way to find the link between vitamin D deficiency and asthma in children.[7,8] Asthma is one of the most common chronic diseases among children [9], affecting approximately 300 million people in the last few decades, and has already prevailed worldwide. [10] A combination of genetic susceptibility, host factors, and environmental exposures has roles in asthma pathogenesis. [11] Narrowing of the airway causes asthma and its symptoms. [10] The roles of vitamin D in the regulation of metabolism and calcium-phosphorus absorption of bone are among

the known roles of this vitamin. However, the presence of vitamin D receptor (VDR) in other different organs and tissues shows that vitamin D physiology is not limited to mineral homeostasis and skeletal health maintenance. [12] Vitamin D could play effective roles in other systems, particularly, the immune system, and can help in the suppression of certain autoimmune diseases. [13] Our body receives vitamin D from a few number of foods, but the majority of vitamin D is produced through dermal synthesis. [14]

There are several lines of defense for the airways exposed to potential pathogens: the first one, mucus layer, that covers the ciliated epithelium and contains mucins; while the other one includes the antimicrobial peptides and antimicrobial proteins found in the surface fluid of the airways. It has been proven that low vitamin D levels may increase the risk of respiratory infections and asthma. [15] Unlike numerous in vitro and in vivo studies that indicate that vitamin D may alleviate symptoms of asthma, clinical trials show conflicting results. [16] As mentioned above, there is plenty of studies describing anti-inflammatory and potentially anti-asthmatic role of vitamin D. Considering that asthma may differently affect subjects belonging to a particular age groups, in order to picture potential role of vitamin D in asthma prevention and therapy, there is a vast need to understand its impact on varying life periods

The aim of the present study was to assess the association between asthma control and serum 25-OH Vitamin D levels in children with moderate persistent asthma on preventer therapy.

### Material & Methods

This prospective observational study was undertaken in the Department Of Pediatrics, Netaji Subhas Medical College And Hospital, Bihta, Patna, Bihar, India for one year during Feb 2019 to JAN 2020. Children aged 6 to 18 years with moderate persistent asthma on preventer therapy for 2 months (+29 days) (3Month) with good compliance and techniques were enrolled (period sample). Severity of asthma was categorized as per Global Initiative for Asthma guidelines. [17] Drug

compliance was considered good if they had taken medication as prescribed for >5 days/week in the previous two months.

### Exclusion Criteria

Participants who had a history of consumption of any drugs that modulate serum vitamin D levels, such as systemic glucocorticoids and anticonvulsants, and those who had chronic diseases and systemic illness were excluded. Children whose parents didn't give consent and those with systemic illnesses were excluded.

In a predesigned proforma, demography details, history and physical examination findings and comorbidities were noted. Rhinitis was defined as anterior or posterior rhinorrhoea, sneezing, nasal blockage and/or itching of the nose during two or more consecutive days for more than 1 hour on most days. [18] Sinusitis was defined as per the task force of Rhinology and Paranasal sinus Committee. [19]

3 mL of blood was withdrawn for measuring serum 25 (OH) D and IgE levels. 25 (OH) D levels were assessed by chemiluminescence micro particle immunoassay (Abbott ARCHITECT i 2000 SR Immunoassay Analyzer) and serum IgE levels by chemiluminescence assay (Advia Centaur). Serum 25 OH vitamin D level was described as sufficient (>30 ng/mL), insufficient (21-29 ng/mL) or deficient (<20 ng/mL) as per Endocrine Society guideline.<sup>27</sup> IgE levels were described as normal or abnormal based on age appropriate standard lab references. [20] Children were categorized as well controlled, partially controlled and poorly controlled as per GINA guidelines. Nutritional status was classified as per WHO standards using BMI charts.

### Statistical Analysis

Statistical analysis was performed using SPSS, version 17. Results were expressed as number and percentage. Chi-square test was used for comparison between two attributes. P value <0.05 was considered significant.

### Results

**Table 1: Asthma control and associated factors**

Variables	Well controlled (n=50)	Not well controlled (n=50)
<b>Age</b>		
6-9 years	23 (46)	22 (44)
10-13 years	10 (20)	15 (30)
>13 years	7 (14)	13 (26)
Male	36 (72)	30 (60)
Female	14(%)	20(%)
Low birthweight	30 (60)	10 (20)
<b>Nutritional status</b>		
Normal	36 (72)	22 (44)
Underweight	6 (12)	17 (34)
	48 total 50	48 total 50

Overweight/Obese	6 (12)	9 (18)
<b>Co-morbidities</b>		
Allergic rhinitis	20 (40)	31 (62)
Sinusitis	4 (8)	2 (4)
Allergic rhino-sinusitis	14 (28)	8 (16)
<b>Type of device</b>		
MDI	22 (44)	23 (46)
DPI	28 (56)	27 (54)
Elevated IgE levels	30 (60)	36 (72)
<b>Vitamin D levels</b>		
Sufficient	2 (1)	0
Insufficient	37 (74)	4 (8)
Deficient	11 (22)	46 (92)

Children with partially/poorly-controlled asthma were significantly more likely to have vitamin D deficiency. Asthma control was well controlled in 50 children and 50 had not well controlled. Age, gender, family history of asthma, type of device, serum IgE levels and presence of co-morbidities had no relationship to the level of control. Children who were underweight or obese had poorer control but the difference was not statistically significant. Children with well controlled asthma were significantly less likely to have been born low birth weight.

### Discussion

Compare with other study.

Pediatric asthma represents a huge burden on the child, family and society. [21] The goal of preventive treatment is to control symptoms. Though guidelines are available for preventer therapy, there is little data on the number of children who achieve good control with these regimes and the factors that influence the level of control. When these factors are identified and modified, better control is possible. Studies have shown that Vitamin D inhibits sensitization in bronchial wall smooth muscle and that vitamin D deficiency can increase the occurrence and severity of asthma. [22,23] Asthma is a chronic inflammatory airway disease that is characterized by bronchial hyper-responsiveness and tissue remodeling. Asthma is usually triggered by a combination of genetic and environmental factors that end with inappropriate immune-mediated chronic inflammatory responses, which may influence the severity of the disease and response to treatment. [24,25] Therefore, patients with asthma may experience recurrent episodes of wheezing, coughing, shortness of breath, and chest tightness that interfere with physical activity, sleeping habits, and ultimately, quality of life. [26] There is a possible association between asthma and certain psychological conditions including stress, anxiety, and depression. [27] This connection could be explained by an interaction between behavioral, neural, endocrine, and immune processes, which

may trigger bronchial inflammatory responses, hyper responsiveness and the development of asthma. In addition, studies have reported that patients with asthma have higher prevalence of anxiety disorders, suggesting that the relationship between asthma and anxiety could be bidirectional. [28,29] Regardless of the nature of association between asthma and the psychological symptoms, these mental health issues can interfere with the optimal management of asthma and inversely affect asthma control. [30]

Children with partially/poorly-controlled asthma were significantly more likely to have vitamin D deficiency. Asthma control was well controlled in 50 children and 50 had not well controlled. Age, gender, family history of asthma, type of device, serum IgE levels and presence of co-morbidities had no relationship to the level of control. Children who were underweight or obese had poorer control but the difference was not statistically significant. Children with well controlled asthma were significantly less likely to have been born low birth weight. Associations between vitamin D deficiency and asthma has also been observed in other studies [31,32], but not consistently. [33] Vitamin D deficiency has been shown to increase the incidence and severity of asthma as well as the efficacy of preventive therapy with inhaled corticosteroids. [34] Vitamin D not only influences the immune system through its effects on helper T cell type 1 and 2 and regulatory T cells [35,36] but also modulates chemokines secreted by airway smooth muscle cells. [37]

### Conclusion

The findings of this study may have implications in clinical practice. Currently, poor control is being managed by escalation of preventer therapy. Adding more drugs or increasing the doses may, over time, increase the toxicity of therapy. Evaluating serum 25 (OH) D levels and correcting identified deficiencies may prevent the need for escalation of preventer therapy.

### References

1. Janahi IA, Bener A, Bush A. Prevalence of asthma among Qatari schoolchildren: international study of asthma and allergies in childhood, Qatar. *Pediatric pulmonology*. 2006 Jan;41(1):80-6.
2. Masoli M, Fabian D, Holt S, Beasley R, Global Initiative for Asthma (GINA) Program. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy*. 2004 May;59(5):469-78.
3. Robertson CF, Roberts MF, Kappers JH. Asthma prevalence in Melbourne schoolchildren: have we reached the peak?. *Medical Journal of Australia*. 2004 Mar; 180(6):273-6.
4. Mannino DM, Homa DM, Akinbami LJ, Moorman JE, Gwynn C, Redd SC. Surveillance for asthma—United states, 1980–1999. *MMWR SurveillSumm*. 2002 Mar 29; 51(1):1-3.
5. Murdoch JR, Lloyd CM. Chronic inflammation and asthma. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*. 2010 Aug 7;690(1-2):24-39.
6. Mukherjee AB, Zhang Z. Allergic asthma: influence of genetic and environmental factors. *Journal of Biological Chemistry*. 2011 Sep 23;286(38):32883-9.
7. Berraies A, Hamzaoui K, Hamzaoui A. Link between vitamin D and airway remodeling. *Journal of asthma and allergy*. 2014 Apr 1:23-30.
8. Hall SC, Fischer KD, Agrawal DK. The impact of vitamin D on asthmatic human airway smooth muscle. *Expert review of respiratory medicine*. 2016 Feb 1;10(2):127-35.
9. Forno E, Celedón JC. Predicting asthma exacerbations in children. *Current opinion in pulmonary medicine*. 2012 Jan;18(1):63.
10. Ali NS, Nanji K. A review on the role of vitamin D in asthma. *Cureus*. 2017 May 29;9(5).
11. Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. *Frontiers in pediatrics*. 2019 Jun 18;7:246.
12. Alshahrani F, Aljohani N. Vitamin D: deficiency, sufficiency and toxicity. *Nutrients*. 2013 Sep;5(9):3605-16.
13. DeLuca HF. Overview of general physiologic features and functions of vitamin D. *The American journal of clinical nutrition*. 2004 Dec 1;80(6):1689S-96S.
14. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *The American journal of clinical nutrition*. 2008 Apr 1;87(4):1080S-6S.
15. Bartley J. Vitamin D: emerging roles in infection and immunity. *Expert Rev Anti Infect Ther*. 2010;8(12):1359–69.
16. Hall SC, Agrawal DK. Vitamin D and Bronchial Asthma: An overview of the last five years. *Clin Ther*. 2017;39(5):917–29.
17. Global Strategy for Asthma Management and Prevention. Updated 2012 [Internet]. Global Initiative for Asthma (GINA); 2012 [cited 2013 Jun 27].
18. International Consensus Report on the Diagnosis and Management of Rhinitis. International Rhinitis Management Working Group. *Allergy*. 1994;49:1-34
19. Report of the Rhinosinusitis Task Force Committee Meeting. Alexandria, Virginia, August 17, 1996. *Otolaryngol Head Neck Surg*. 1997;117:S1-68
20. Lindberg RE, Arroyave C. Levels of IgE in serum from normal children and allergic children as measured by an enzyme immunoassay. *J Allergy Clin Immunol*. 1986; 78:614-8.
21. von Mutius E. The burden of childhood asthma. *Archives of disease in childhood*. 2000 Jun 1;82(suppl 2):ii2-5.
22. Bossé Y, Maghni K, Hudson TJ. 1 $\alpha$ , 25-dihydroxy-vitamin D3 stimulation of bronchial smooth muscle cells induces autocrine, contractility, and remodeling processes. *Physiological genomics*. 2007 Apr;29(2):161-8.
23. Brehm JM, Celedón JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, Laskey D, Sylvia JS, Hollis BW, Weiss ST, Litonjua AA. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. *American journal of respiratory and critical care medicine*. 2009 May 1;179(9):765-71.
24. Murdoch JR, Lloyd CM. Chronic inflammation and asthma. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*. 2010 Aug 7;690(1-2):24-39.
25. Mukherjee AB, Zhang Z. Allergic asthma: influence of genetic and environmental factors. *Journal of Biological Chemistry*. 2011 Sep 23;286(38):32883-9.
26. Globe G, Martin M, Schatz M, Wiklund I, Lin J, von Maltzahn R, Mattera MS. Symptoms and markers of symptom severity in asthma—content validity of the asthma symptom diary. *Health and quality of life outcomes*. 2015 Dec; 13:1-9.
27. Di Marco F, Santus P, Centanni S. Anxiety and depression in asthma. *Current opinion in pulmonary medicine*. 2011 Jan 1;17(1):39-44.
28. Del Giacco SR, Cappai A, Gambula L, Cabras S, Perra S, Manconi PE, Carpinello B, Pinna

- F. The asthma-anxiety connection. *Respiratory medicine*. 2016 Nov 1;120:44-53.
29. Lu Y, Mak KK, Van Bever HP, Ng TP, Mak A, Ho RC. Prevalence of anxiety and depressive symptoms in adolescents with asthma: A meta-analysis and meta-regression. *Pediatric allergy and immunology*. 2012 Dec; 23(8):707-15.
30. Baiardini I, Sicuro F, Balbi F, Canonica GW, Braido F. Psychological aspects in asthma: do psychological factors affect asthma management?. *Asthma research and practice*. 2015 Dec;1(1):1-6.
31. Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW, Strunk RC, Zeiger RS, Weiss ST, Litonjua AA, Childhood Asthma Management Program Research Group. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. *Journal of Allergy and Clinical Immunology*. 2010 Jul 1;126(1):52-8.
32. Chinellato I, Piazza M, Sandri M, Peroni D, Piacentini G, Boner AL. Vitamin D serum levels and markers of asthma control in Italian children. *The Journal of pediatrics*. 2011 Mar 1;158(3):437-41.
33. Kavitha TK, Gupta N, Kabra SK, Lodha R. Association of serum vitamin D levels with level of control of childhood asthma. *Indian pediatrics*. 2017 Jan;54:29-32.
34. Searing DA, Zhang Y, Murphy JR, Hauk PJ, Goleva E, Leung DY. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. *Journal of Allergy and Clinical Immunology*. 2010 May 1;125(5):995-1000.
35. Cantorna MT, Zhu Y, Froicu M, Wittke A. Vitamin D status, 1, 25-dihydroxyvitamin D<sub>3</sub>, and the immune system. *The American journal of clinical nutrition*. 2004 Dec 1;80(6):1717S-20S.
36. May E, Asadullah K, Zugel U. Immunoregulation through 1, 25-dihydroxyvitamin D<sub>3</sub> and its analogs. *Current Drug Targets-Inflammation & Allergy*. 2004 Dec 1;3(4):377-93.
37. Banerjee A, Damera G, Bhandare R, Gu S, Lopez-Boado YS, Panettieri Jr RA, Tliba O. Vitamin D and glucocorticoids differentially modulate chemokine expression in human airway smooth muscle cells. *British journal of pharmacology*. 2008 Sep;155(1):84-92.