

Original Research Article

Impact of serum vitamin D level on severity of asthma in children

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ABSTRACT

Background: Asthma is the most common chronic respiratory disease among children characterized by reversible airway obstruction. Vitamin D plays an important role in many immune and allergic diseases and it may have a role in asthmatic patients, however this association yet remains uncertain. The present study was designed to assess the level of serum Vitamin D in patients with bronchial asthma and its correlation with disease severity.

Methods: A prospective observational study was performed from April 2019 to February 2020 in the Paediatric OPD of LNMC and JK Hospital Bhopal. All 90 children with physician diagnosed bronchial asthma (mild, moderate and severe) aged 10 to 18 years of both genders who have come in the OPD (total enumeration sampling) during the above mentioned period were enrolled in to the study. The patients were grouped on the basis of Vitamin D sufficiency and Vitamin D levels were correlated with disease severity.

Results: The study comprised 54 boys (60%) and 36 girls (40%) with mean age of 15.1 ± 3.96 . Out of 90 children enrolled, 46 had good control over asthma and 37 had uncontrolled asthma. As regards asthma control, 25-OH Vitamin D was lowest among patients with uncontrolled asthma.

Conclusions: Vitamin D deficiency was highly prevalent in asthmatic patients and there was a direct and a significant relationship between serum Vitamin D levels, severity of asthma, control of asthma, serum IgE levels and blood eosinophils count. Thus, measuring serum levels of Vitamin D followed by supplementation could be considered in the routine assessment of patients with bronchial asthma.

Keywords: Allergy, Children, Disease severity, Serum IgE level

INTRODUCTION

Paediatric asthma represents a huge burden on the child, family and society.¹ Children with asthma appear to be at increased risk of Vitamin D insufficiency. Vitamin D plays an important role in pulmonary health by inhibiting inflammation, maintaining regulatory T cells and influence the function of cells intrinsic to innate and adaptive immunity. Vitamin D modulates the adaptive immune system by direct effect on T-cell activation and on the phenotype and function of Antigen Presenting Cells (APCs) that might be relevant in the protection

against or reduction of asthma morbidity.^{2,3} Vitamin D has been shown to have a role in both innate and adaptive immunity by promoting phagocytosis and modulating the effects of Th1, Th2 and regulatory T cells.^{4,5} Vitamin D deficiency has been associated with increased airway hyper responsiveness (AWH), lower pulmonary function, worst asthma control and steroid resistance.⁶

Serum levels of 25-hydroxy (25-OH) vitamin D are considered the best circulating biomarker of vitamin D metabolic status and reflect contributions from all sources of vitamin D (i.e., diet and sun exposure).⁷ Studies on

vitamin D and asthma in children have variable results.⁸⁻¹¹ The objective of this study was to investigate the relationship between vitamin D status and severity and control of bronchial asthma in a group of asthmatic children and determine the critical level of vitamin D that is associated with poor asthma status. This is aimed to guide further studies using vitamin D supplementation as an adjuvant line in asthma management.

METHODS

A total of 90 asthmatic patients (54 males and 36 females) were enrolled in the study. A prospective observational study was performed from April 2019 to February 2020 in the paediatric OPD of LNMC and JK Hospital Bhopal. All 90 children aged 10 to 18 years of both genders with physician diagnosed bronchial asthma (mild, moderate and severe) on controller therapy who had come in the OPD (total enumeration sampling) during the above mentioned period were enrolled in to the study. Written informed consent was obtained from patient's parents prior to inclusion in the study.

Ethical approval

Ethical clearance was sort from institute's ethical committee and the study was approved by the Institutional Research Board of LNMC and JK Hospital Bhopal (Reg. No. ECR/1190/INST/MP/2019 dtd. 04.04.2019)

Exclusion criteria

Children whose parents did not give consent and those with systemic illness and history of intake of Vitamin D or calcium in last 1 month were excluded.

Detailed medical history was recorded including duration of asthma disease, frequency of asthma exacerbations, daytime and night time symptoms, Vitamin D supplementation, average dose of inhaled steroids and/or systemic steroids in the month before enrolment and compliance on treatment. The dose of inhaled steroids was considered low, moderate or high according to Global Initiative for Asthma (GINA).¹² Clinical examination was performed including detailed chest examination for the presence of respiratory distress, wheezes, chest infections and/or deformities, in addition to complete systematic examination.

3 mL of blood was withdrawn for measuring serum 25(OH) D, IgE levels and blood eosinophil count. 25(OH) D levels were assessed by chemiluminescence micro particle immunoassay (Abbott ARCHITECT i 2000 SR Immunoassay Analyzer), serum IgE levels by chemiluminescence assay (Advia Centaur) and blood eosinophil count by scatterimpedance on a Beckman Coulter Analyzer. Serum 25OH 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.¹³ IgE levels were described as normal or deficient based on age appropriate standard lab references.¹⁴ Children were categorized as well controlled, partially controlled and poorly controlled as per GINA guidelines.

Statistical analysis

Statistical analysis was performed using SPSS software version 20.0. The data was presented as mean \pm standard deviation (SD). The difference in the mean baseline values of various measurements within the group and between the groups was made using student's t-test. The data was analysed using chi square test. P value of <0.05 was considered significant.

RESULTS

A total of 90 asthmatic children were included in the study of age 10 to 18 years with a mean of 15.1 \pm 3.96. The gender distribution of the study subjects revealed that there were 54 males (60%) and 36 females (40%). The patients were further classified as mild, moderate and severe asthmatics depending on the severity of asthma. Asthma control was uncontrolled in 34 children, 42 children had well controlled asthma and 14 had partial control. Inhaled steroid dose parameter was moderate in 53 children and high in 8 children (Table 1). Serum level of vitamin D were analyzed in 90 asthmatic patients who were divided into vitamin D sufficient and vitamin D insufficient group. The asthma patients, who were having a sufficient level of Vitamin D were taken as controls in the study. Vitamin D deficiency was highly prevalent in asthmatic patients, and there was a direct and a significant relationship between serum vitamin D levels and serum IgE levels, serum eosinophil count (Table 2).

Table 1: Epidemiological and clinical data of enrolled patients.

Parameter	Classification	Number	Percentage
Gender	Boys	54	60
	Girls	36	40
Allergic manifestation	Asthma	90	100
Asthma severity	Mild	39	43
	Moderate	20	22
	Severe	31	35
Asthma control	Well controlled	42	46.6
	Partially controlled	14	15.6
	Uncontrolled	34	37.8
Inhaled steroid dose parameter	Low	29	32.2
	Moderate	53	59
	High	8	8.8

Table 2: Relationship of vitamin D levels on the status of absolute eosinophil count and serum IgE levels.

Parameters	Serum Vitamin D status	Number of patients	Mean	Standard deviation	P value
Absolute serum eosinophil count	Deficient	48	548.16	46.42	≤0.0001
	Sufficient	42	231.82	16.17	
Serum IgE (I.U./ml)	Deficient	48	774.562	72.1	≤0.0001
	Sufficient	42	228.261	31.68	

Serum 25-OH Vitamin D levels are compared among different grades of severity and revealed that asthma severity was mild in 15 children with insufficient Vitamin D and severe in 23 children with insufficient Vitamin D (Table 3).

Table 3: Asthma severity and it's association with Vitamin D level in asthmatic children.

Asthma severity N (%)	Asthma with insufficient Vitamin D (N=48)	Asthma with sufficient Vitamin D (N=42)	P value
Mild	15 (31%)	24 (57%)	<0.001
Moderate	10 (20.83%)	10 (23.8%)	
Severe	23 (47.91%)	8 (19%)	

DISCUSSION

Our study showed that 46% of asthmatics are well controlled and 37% are uncontrolled which is similar to that reported in literature.¹⁵ Associations between Vitamin D deficiency and asthma has also been observed in other studies but not consistently.¹⁶⁻¹⁸ Vitamin D deficiency has been shown to increase the incidence and severity of asthma with inhaled corticosteroids.¹⁹ Vitamin D not only influences the immune system through its effects on helper T cell type 1 and 2 and regulatory T cells but also modulates chemokines secreted by airway smooth muscle cells.²⁰⁻²² The present study showed that asthmatics with insufficient Vitamin D had a higher absolute eosinophil count as compared to the sufficient group ($p < 0.0001$). These results have also been observed by Brehm and colleagues, who showed that higher Vitamin D levels were inversely associated with IgE and peripheral blood eosinophil counts.

Serum IgE levels are associated with bronchial hyperresponsiveness and asthma independently of atopy status and specific allergic sensitizations.²³ In the present study, serum IgE levels in the Vitamin D sufficient group was significantly lower as compared to the deficient group ($p < 0.0001$). Satwani et al found serum total IgE to be a good predictor of allergy and significantly associated with severity of asthma.²⁴ Borish et al also demonstrated that severe asthma patients had higher IgE levels compared to mild asthma.²⁵ Our findings are in accordance with these studies.

In our study, 25-OH Vitamin D levels were comparable among different grades of asthma severity. However, as regards asthma control, 25-OH vitamin D was the lowest among patients with uncontrolled asthma. This supports the possible role of Vitamin D in asthma control in children and might reflect the importance of 25-OH Vitamin D monitoring and hence considering supplementation in deficient asthmatics regardless the degree of severity.

The degree of severity of asthma was inversely associated with lower Vitamin D levels ($p < 0.001$) which is similar to that observed in a cross sectional study of 616 Costa Rican children.²⁶ Other studies failed to find a significant relation between Vitamin D levels and asthma severity and control in children.²⁷ The variation in the result amongst different studies may be due to various genetic and environmental factor.

A limitation of this study was that the effect of Vitamin D by supplementation on the control of asthma was not done on these children.

CONCLUSION

Our study demonstrated that Vitamin D deficiency was highly prevalent in asthmatic patients, and there was a direct and a significant relationship between Vitamin D levels and severity of asthma, therefore measuring serum levels of Vitamin D followed by supplementation could be considered in the routine assessment of patients with bronchial asthma.

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REFERENCES

- Mutius VE. The burden of childhood asthma. Arch Dis Child. 2000;82(2):2-5.
- Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW, Strunk RC, et al. Serum vitamin D levels and

- severe asthma exacerbations in the childhood asthma management program study. *J Allergy Clin Immunol.* 2010;126:52-8.
3. Goleva E, Searing DA, Jackson LP, Richers BN, Leung DY. Steroid requirements and immune associations with vitamin D are stronger in children than adults with asthma. *J Allergy Clin Immunol.* 2012;129:1243-51.
 4. Gombart AF, Borregaard N, Koeffler HP. Human cathelicidin antimicrobial peptide (CAMP) gene is a direct target of the vitamin D receptor and is strongly up-regulated in myeloid cells by 1,25-dihydroxyvitamin D₃. *FASEB.* 2005;19:1067-77.
 5. Matheu V, Bäck O, Mondoc E, Navikas S. Dual effects of vitamin D-induced alterations of TH1/TH2 cytokine expression: enhancing IgE production and decreasing airway eosinophilia in murine allergic airway disease. *J Allergy Clin Immunol.* 2003;112:585-92.
 6. Sandhu MS, Casale TB. The role of vitamin D in asthma. *Ann Allergy Asthma Immunol.* 2010;105:191-9.
 7. Hollis BW, Wagner CL. Normal serum vitamin D levels. *N Engl J Med.* 2005;352(5):515-6.
 8. Gale CR, Robinson SM, Harvey NC, Javaid MK, Jiang B, Martyn CN, et al. Princess anne hospital study group maternal vitamin D status during pregnancy and child outcomes. *Eur J Clin Nutr.* 2008;62:68-77.
 9. Oeffelen AA, Bekkers MB, Smit HA, Kerkhof M, Koppelman GH, Nies A, et al. Serum micronutrient concentrations and childhood asthma: The PIAMA birth cohort study. *Pediatr Allergy Immunol.* 2011;22:784-93.
 10. Nwaru BI, Hadkhale K, Hämäläinen N, Takkinen HM, Ahonen S, Ilonen J, et al. Vitamin D intake during the first 4 years and onset of asthma by age 5: a nested case-control study. *Pediatr Allergy Immunol.* 2017;28(7):641-8.
 11. Menem MT, Aziz MM, Guindy WM, Banna NA. The frequency of vitamin D deficiency among asthmatic Egyptian children. *Egypt J Pediatr Allergy Immunol.* 2013;11(2):69-73.
 12. Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2014. Available at <http://www.ginasthma.org/>. Accessed on 01 May 2017.
 13. Holick MF, Binkley NC, Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin d deficiency: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2011;96:1911-30.
 14. 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.
 15. Mutius VE. The burden of childhood asthma. *Arch Dis Child.* 2000;82(2):2-5.
 16. Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW, Strunk RC, Zeiger RS, et al. Serum vitamin D levels and severe asthma exacerbations in the childhood asthma management program study. *J Allergy Clin Immunol.* 2010;126:52-8.
 17. Chinellato I, Piazza M, Sandri M, Peroni D, Piacentini G, Boner AL. Vitamin D serum levels and markers of asthma control in Italian children. *J Pediatr.* 2011;158:437-41.
 18. Kavitha TK, Gupta N, Kabra SK, Lodha R. Association of serum vitamin D levels with level of control of childhood asthma. *Indian Pediatr.* 2017;54:29-32.
 19. 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. *J Allergy Clin Immunol.* 2010;125:995-1000.
 20. Cantorna MT, Zhu Y, Froicu M, Wittke A. Vitamin D status, 1,25-dihydroxyvitamin D₃, and the immune system. *Am J Clin Nutr.* 2004;80:1717-20.
 21. May E, Asadullah K, Zugel U. Immunoregulation through 1,25-dihydroxyvitamin D₃ and its analogs. *Curr Drug Targets Inflamm Allergy.* 2004;3:377-93.
 22. Banerjee A, Damera G, Bhandare R, Gu S, Lopez-Boado Y, Panettieri R, et al. Vitamin D and glucocorticoids differentially modulate chemokine and glucocorticoids differentially modulate chemokine expression in human airway smooth muscle cells. *Br J Pharmacol.* 2008;155:84-92.
 23. Beeh KM, Ksoll M, Buhl R. Elevation of total serum immunoglobulin E is associated with asthma in non allergic individuals. *Eur Respir J.* 2000;16:609-14.
 24. Satwani H, Rehman A, Ashraf S, Hassan A. Is serum total IgE levels a good predictor of allergies in children? *J Pak Med Assoc.* 2009;59:698-702.
 25. Borish L, Chipps B, Deniz Y, Gujrathi S, Zheng B. Total serum IgE levels in a large cohort of patients with severe or difficult to treat asthma. *Ann Allergy Asthma Immunol.* 2005;95:247-53.
 26. Brehm JM, Celedon JC, Quiros ME, Avila L, Hunninghake GM, Forno E, et al. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. *Am J Respir Crit Care Med.* 2009;179(9):765-71.
 27. Krobtrakulchai W, Praikanahok J, Visitsunthorn N, Vichyanond P, Manonukul K, Pratumvinit B, et al. The effect of vitamin D status on pediatric asthma at a university hospital, Thailand. *Allergy Asthma Immunol Res.* 2013;5(5):289-94.

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