International Journal of Contemporary Pediatrics
Wani KR et al. Int J Contemp Pediatr. 2020 Nov;7(11):2163-2167
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20204537

Original Research Article

Vitamin D levels in children with bronchial asthma

Kaisar R. Wani[1], Reyaz A. Malik[2], Asif Ahmed[2]*

[1]Department of Pediatrics, SKIMS Soura, Srinagar, Jammu and Kashmir, India
[2]Department of Pediatrics, SKIMS MCH, Srinagar, Jammu and Kashmir, India

Received: 23 September 2020
Accepted: 08 October 2020

***Correspondence:**
Dr. Asif Ahmed,
E-mail: drasifskims@gmail.com

ABSTRACT

Background: Bronchial asthma is a common chronic inflammatory disorder of the airways in childhood. Vitamin D, initially described as a vitamin that regulated calcium homeostasis, has also been shown to exert important antimicrobial effects and is also a potent immune system regulator having a potential role in various allergic diseases. The main objective of this study was to look the levels of vitamin D in children with bronchial asthma and to study the co relationship between vitamin D levels and severity of asthma.
Methods: This study included 80 (40 asthmatic children and 40 healthy controls) children aged between 4 and 15 year. Serum vitamin D levels where determined and compared between the two groups. The association between vitamin D levels and severity of asthma was studied in the asthmatic children.
Results: Among 40 asthmatic children the mean serum vitamin D level was 16.6±11.56 ng/ml, while as the mean vitamin D levels in healthy control subjects was 24.225±2.764 ng/ml and the difference between the two groups was statistically significant (p=0.001). Vitamin D deficiency was highly prevalent in asthmatic patients and there was a direct and a significant relationship between serum vitamin D levels and severity of asthma.
Conclusion: In this study, vitamin D levels were considerably lower in children with asthma than in healthy children. Also, in this study vitamin D deficient asthma patients have more severe asthma than the patients who have sufficient vitamin D levels.

Keywords: Vitamin D deficiency, Bronchial asthma, Chronic inflammatory disorder

INTRODUCTION

Bronchial asthma is a common chronic inflammatory disorder of the airways in childhood.[1] It is related with increased airway inflammation, airway hyper responsiveness and airflow obstruction in response to specific triggers leading to repeated episodes of wheezing, dyspnea, feeling of tightness in the chest and cough particularly at the night or in the early morning. These episodes are associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment. However, a substantial proportion of patients do not achieve optimal asthma control despite even high dose treatment[1]. In particular inadequately controlled patients with severe persistent asthma are at high risk of severe exacerbations and asthma related mortality. These patients represent the greatest unmet medical need among the asthmatic population today. The exact cause for asthma is not well understood. Varied etiological factors and changing environmental factors such as atmospheric pollution, dietary changes, allergens and lifestyle changes may be responsible for the rising prevalence of asthma.[1,2] Impaired immunogenic tolerance and interplay between cells and inflammatory mediators may promote airway obstruction, associated with the disorder.[3]

In recent years the physiological role of vitamin D has considerably expanded. Initially described as a vitamin that regulated calcium homeostasis, it has been shown

that it also exerts important antimicrobial effects and is fundamental in regulating the immune response. It is now considered a hormone rather than a vitamin because of its multiple and systemic effects. Clinical trials and many epidemiological studies are underway to evaluate the correlations between vitamin D levels in blood and many diseases, such as multiple sclerosis, rheumatoid arthritis, several types of cancers, asthma and COPD. Considerable evidence exists for an association between low vitamin levels and an increase in asthma severity parameters.[4-7]

The storage form of vitamin D (25-hydroxyvitamin D, 25-D3, calcidiol) is a hormone precursor that serves as substrate to the formation of the active form of vitamin D, (1,25-dihydroxyvitamin D,1,25-D3, calcitriol). A single enzyme, 25 (OH)D-1-alpha-hydroxylase (encoded by gene CYP27B1) is responsible for the conversion of 25-D3 to1,25-D3;[8,9] 1,25-D3 serves as a high affinity ligand for the vitamin D receptor (VDR).[10] The enzyme 1-alpha hydroxylase has been described in various immune cells including macrophages, dendritic cells and T and B lymphocytes.[11] The major drivers for CYP27B1 expression and activity in these cells are cytokines, not parathyroid hormone (PTH), and cytokines are not regulated by calcium and phosphate. Hence, activated T lymphocyte cell in asthma should express CYP27B1 in response to various cytokines present at heightened level in this disorder.

Vitamin D deficiency has been associated with increased airway hyper responsiveness, lower pulmonary function, worse asthma control and steroid resistance.[12] High affinity receptors to 1,25(OH)D3 is present on monocytes and lymphocytes. Vitamin D inhibits cytokine synthesis and release in bronchial smooth muscle cells causing decrease in lung inflammation, inhibition of bronchial smooth cell proliferation and remodeling by inhibition of matrix metalloproteinase 9, matrix metalloproteinase 33 and platelet derived growth factor. It causes inhibition of differentiation, maturation and homing of mast cells to allergic airways and down regulation of CD40 and CD80/86 on dendritic cells and regulatory cells along with enhancement of interleukin-10 and transforming Growth factor beta synthesis. Thus, it is hypothesized that vitamin D supplementation may lead to improved asthma control by inhibiting influx of inflammatory cytokines in lung and increased secretion of IL-10 by T regulatory cells and dendritic cells.

With this background, this study was undertaken to see the relation of serum vitamin D levels and bronchial asthma in children.

METHODS

We performed a prospective case control study in the department of paediatrics of tertiary care teaching hospital in north India. This study was done over a period of two years from June 2017 through May 2019. Bronchial asthma patients of 4-15 years of age coming to paediatric outpatient department or emergency were classified according to global initiative for asthma (GINA) guidelines and were taken as cases. Children of age group 4-15 years attending paediatric outpatient department for minor illness with no features of asthma were taken as controls. The control subjects were selected in a way matching the age, gender, ethnicity of children, to give a good representative sample. A written informed consent was obtained from the parents for enrolling their children in study. 80 subjects (40 cases and 40 controls) were included in the study.

Inclusion criteria

All patients between 4 to 15 years of age diagnosed with asthma were taken as cases were included.

Exclusion criteria

Children having clinical diagnosis of rickets, PEM, taking drugs interfering with vitamin D metabolism like antiepileptic medications would be excluded from the study, children having chronic liver disease or chronic kidney disease or any other chronic illness would be excluded and history of intake of vitamin D or calcium supplements in the past one month.

Measurement of serum vitamin D

The specimen used for measuring vitamin D was serum. Blood was collected using standard venipuncture technique. The blood was collected in plain red top venipuncture tube without adding additives or anti-coagulants. Blood was then allowed to clot and samples were centrifuged at approximately 1000× gm for 10 minutes to separate serum from the cells. Serum samples were collected and frozen at -80°C. The stored samples were brought down to room temperature before using it for analysis of various parameters. 25-OH vitamin D levels were measured in serum using the chemiluminescence method.

Statistical methods

The recorded data was compiled and entered in a spreadsheet (Microsoft excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages. Student's independent t-test was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 80 children (40 cases and 40 controls) were included in this study. The mean age of the cases was 7.40±2.917 years and that of controls was 8.30±2.764

years. There were 55% males and 45% females in the cases group and 52.5% males 47.5% females in control group.

Serum vitamin D levels

Studied vitamin D levels of 40 cases and 40 control subjects in our study. The mean value of serum vitamin D levels of study group was 16.6±11.56 ng/ml while as mean value of vitamin D level in control group was 24.225±7.921 ng/ml (Table 1). The difference between the mean values of the two groups was statistically significant (p=0.001).

Table 1: Serum vitamin D level (ng/ml) in subjects.

Variables	Mean	SD	SE	P value
Cases	16.600	11.560	1.82	0.001*
Controls	24.225	7.921	1.252	

*statistically significant.

Serum vitamin D levels in case group

In this study, among the cases, there were 14 patients with sufficient vitamin D levels and 26 patients with deficient levels. The mean value of serum vitamin D levels in sufficient group was 30.85±6.237 ng/ml while in other group mean level was 8.92±3.62 ng/ml (Table 2). The difference between the mean values of the two groups was statistically significant (p<0.001).

Table 2: Serum vitamin D levels in study group.

Variables	N (%)	Mean vitamin D level (SD)	P value
Sufficient vitamin D	14 (35)	30.85 (6.237)	0.001*
Deficient vitamin D	26 (65)	8.92 (3.62)	

*statistically significant.

Severity of asthma

In this study there were 9 patients with intermittent asthma, 10 patients with mild asthma, 8 patients with moderate asthma and 13 patients with severe asthma.

Table 3: Vitamin D status and severity of bronchial asthma.

Grades of asthma	Vitamin D status		Total
	Deficient (N)	Sufficient (N)	
Intermittent	3	6	9
Mild	4	6	10
Moderate	4	4	8
Severe	10	3	13

P value<0.001 (statistically significant).

Severity of asthma and vitamin D level

In this study there were total of 13 patients with severe asthma. Out of 13 patients with severe asthma, 10 patients had deficient vitamin D levels while as 3 patients had sufficient vitamin D levels (Table 3). The difference between the two groups was statistically significant (p<0.001).

DISCUSSION

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. A substantial proportion of patients do not achieve optimal asthma control despite even high dose treatment. A number of causative factors have been proposed, i.e. change in life style pattern, nutrient intake, exposure to microbial organism and air pollution. In a study by Datta et al it was observed that reduced vitamin D levels are highly prevalent in asthmatic patients and are associated with severity of the disease.[13]

This study was a case control study, in which 40 cases and 40 control subjects were included. Serum vitamin D levels were analysed in 40 asthmatic children and 40 non asthmatic control subjects. The mean serum 25 hydroxy cholecalciferol (vitamin D) in asthmatic children was 16.6±11.56 ng/ml while as the mean vitamin D levels in healthy control subjects was 24.225±2.764 ng/ml and the difference between the two groups was statistically significant (p=0.001). This means that asthma in children of 4 to 14 years of age is likely to be associated with low serum vitamin D levels. These findings are consistent with the study done by Kolokotroni et al in which serum vitamin D levels of 69 asthmatic and 67 non-asthmatic children were studied.[14] The mean vitamin D levels in asthmatic group remained significantly lower than non-asthmatic group. Another cross-sectional study done by Brehm et al on 616 asthmatic children between the ages of 4 and 14 years to examine the relation between 25 OH vitamin D level and markers of allergy and asthma severity showed similar results.[6] In multivariate linear regression models, vitamin D levels were significantly and inversely associated with total IgE and eosinophil count. In multivariate logistic regression a unit increase in vitamin D level was associated with reduced odds of hospitalization, any use of anti-inflammatory medication and increased airway responsiveness. Another case control study done by Somasheker et al on 88 subjects.[15] The mean vitamin D levels of asthmatic children were significantly lower than control subjects.

In this study within the asthma group (cases), there were 14 patients with sufficient vitamin D levels and 26 patients with deficient levels. The mean values of 25-OH vitamin D in the deficient group was lower as compared to the sufficient group. The difference between the mean values of the two groups was statistically significant (p<0.01). This is consistent with results from a study by Chinellato et al.[16] Vitamin D level values were used as a

continuous variable and were categorized in descriptive analyses as sufficient when level were >20 ng/ml and deficient when vitamin D levels were <15 ng/ml and insufficient when levels were between 15-20 ng/ml. Sutherland et al also concluded that those with increased airway hyperresponsiveness had lower vitamin D levels.[17]

We had 9 patients with intermittent asthma, 10 with mild asthma, 8 with moderate asthma and 13 patients with severe asthma. It was seen that severe asthma was associated with lower vitamin D levels. In present study 3 patients had severe asthma with sufficient vitamin D levels while as 10 patients with severe asthma had low vitamin D levels and this difference was statistically significant ($p<0.001$). In a study by Shebl et al 44% of asthmatic patients suffered from vitamin D insufficiency while in control group vitamin D insufficiency was present in 20% of them.[18] The more severe deficiency was associated with more severe asthma. Findings are in agreement with studies showing that insufficient vitamin D status is associated with an increase in the severity of asthma as shown in patients of CAMP cohort and an increased risk of asthma hospitalization in children with asthma as shown by Brehm et al.[7,19] Thus, it may be prudent to evaluate for vitamin D deficiency in all bronchial asthma patients, so that patients with vitamin D deficiency may be treated for the same and their asthma outcomes also improve with it.

CONCLUSION

In this study, vitamin D levels were considerably lower in children with asthma than in healthy children. Also, in present study vitamin D deficient asthma patients have more severe asthma than the patients who have sufficient vitamin D levels. Thus, it may be prudent to evaluate for vitamin D deficiency in all bronchial asthma patients, so that patients with vitamin D deficiency may be treated for the same and their asthma outcomes also improve with it.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. From the Global strategy for asthma Management and prevention. Global initiative for Asthma (GINA) 2020. Available at: http://www.ginasthma.org/. Accessed on 20 August 2020.
2. Vander Werff SD, Diaz JR, Reyneveld R, Heymans MW, Campos PM, Bonet GM et al. Prediction of asthma by common risk factors: a follow up study in Cuban school children. J Investig Allergol Clin Immunol. 2013;23(6):415-20.
3. Holt PG, Strickland DH. Interactions between innate and adaptive immunity in asthma pathogenesis: new perspective from studies on acute exacerbations. J Allergy Clin Immunol. 2010;125:963-72.
4. Black PN, Sragg R. Relationship between serum 25-hydroxyvitamin D and pulmonary function in the third national health and nutrition examination survey. Chest. 2005;128(6):3729-8.
5. Camargo CA Jr, Rifas-Shiman SL, Litonjua AA, Rich-Edwards JW, Weiss ST, Gold DR et al. Maternal intake of vitamin D pregnancy and risk of recurrent wheeze in children at 4 years of age. Am J Clin Nutri. 2007;85(3):788-95.
6. Bhrem JM, Celedon JC, Scoto-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 Respiratory Crit Care Med. 2009;179(9):765-71.
7. 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(1):52-85.
8. Mawer EB, Hayes ME, Heys SE, Davies M, White A, Stewart MF. Constitutive synthesis of 1,25-dihydroxyvitamin D3 by a human small cell lung cancer cell line. J Clin Endocrinol Metabol. 1994;82(1):118-22.
9. Schwartz GG, Whitlatch LW, Chen TC, Lokeshwar BL, Hollick MF. Human prostate cells synthesize 1,25-dihydroxyvitamin D3 from 25-hydroxyvitamin D3. Cancer Epidemiol Biomarkers Prev. 1998;7(5):391-5.
10. Cross HS, Bareis P, Hofer H, Bischof MG, Bajna E, Kriwanek S et al. 25 Hydroxyvitamin D3,1 alpha hydroxylase and vitamin D receptor gene expression in human colonic mucosa is elevated during early cancerogenesis. Steroids. 2001;66(3-5):287-92.
11. Hewison M, Burke F, Evans KN, Lammas DA, Sansom DM, Liu P et al. Extrarenal 25 hydroxyvitamin D3-1alpha-hydroxylase in human health and disease. J Steroid Biochem Molecular Biol. 2007;103(3-5):316-21.
12. Sandhu MS, Casale TB. The role of vitamin D in asthma. Am J Allergy Asthma Immunol. 2010;105:191-9.
13. Datta S, Pal M, Malik SK. Blood Vitamin D concentration in adult asthmatic patients. J Drug Deliv Therap. 2014;4(2)36-8.
14. Kolokotroni O, Papadopoulou A, Middelton N, Kouta C, Nicolaidou VR et al. Vitamin D Levels and status amongst asthmatic and non asthmatic adolescents in Cyprus. BMC Public Health. 2015;15:48.
15. Omashker AR, Prithvi AB, Vanitha MN. Gowda et al. Vitamin D and its role in bronchial Asthma. J Clin Diagn Res. 2014;8(10):PC4-7.
16. Chinellato L, Piazza M, Sandri M, Peroni DG, Cardinale F, Piacentini GL et al. Serum vitamin D levels and exercise induced bronchoconstriction in children with asthma. Eur Respir J. 2011;37:1366-70.
17. Sutherland ER, Goleva E, Jackson LP, Stevens AD, Leung DYM. Vitamin D levels, lung function, and

steroid response in adult asthma. Am J Respir Crit Care Med. 2010;181:699-704.
18. Shebl RE, Shehata SM, Elgabry M, Ali SAI, Elsaid HH. Vitamin D and phenotypes of bronchial asthma. Egy J Chest Dis Tuberculosis. 2013;62(2):201-5.
19. Szefler S, Weiss S, Tonascia A, Adkinson NF, Bender BG, Cherniack R et al. The Childhood Asthma Management Program Research Group. Long-term effects of budesonide or nedocromil in children with asthma. N Eng J Med. 2000;343(15):1054-63.

Cite this article as: Wani KR, Malik RA, Ahmed A. Vitamin D levels in children with bronchial asthma. Int J Contemp Pediatr 2020;7:2163-7.