

Study of vitamin D level in Paediatric Asthma at a Tertiary Care Center

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Abstract

Introduction: There are few studies that suggest low Vitamin D levels are associated with asthma. Present study was conducted to evaluate the association between vitamin D levels with asthma and its severity in children.

Methods: This cross-sectional study included 70 children (35 asthmatic and 35 controls) aged between three to 12 yrs. CBC, AEC, IgE, spirometry, chest X-ray, and serum vitamin D levels were measured. Vitamin D levels were categorized according to guidelines of the American Academy of Paediatrics (2008) and compared between the two groups. The association between vitamin-D levels with asthma and its severity was studied.

Result: The mean age of study group cases was 9.23 ± 2.62 yr. The male:female ratio in the study group was 2.5: 1. Cough and wheezing was the commonest manifestation (100%). Most of the patients had mild asthma (45.71%). Asthma was more common in the urban population (68.57%) and children belonging to lower socioeconomic status (51.43%). The markers of allergic disorders {Eosinophils, AEC and IgE} were elevated (all p-values ≤ 0.0001) in study group. Mean serum vitamin D levels in the study group and control group patients were 45.21 ± 28.52 nmol/L and 57.03 ± 40.01 nmol / L respectively. The mean levels of vitamin D in the study group were insufficient as per AAP criteria. Vitamin D levels were more deficient in severe asthma (26.19 ± 14.46 nmol/L).

Conclusions: In the present study Vitamin D insufficiency was seen in patients with asthma.

Introduction

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation affecting one to 18% of the population in different countries.¹ It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation. Symptoms are often triggered by factors such as exercise, allergen or irritant exposure, change in weather, or viral respiratory infections. Recently, many studies have shown that the prevalence of asthma and allergic conditions have increased in various regions of the world.² According to WHO, in 2005 around 300 million people suffered from asthma and 2,55,000 died of asthma.³ It is expected to increase to 400 million by 2025.⁴ Numerous studies conducted in different countries have reported an increase in asthma prevalence of approximately 50% per decade.⁵

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Asthma may have significant relation with serum Vitamin D level. There has been extensive studies regarding this matter. However, Indian studies are relatively lacking and inconclusive on this matter. For eg, Somashekar et al in their study conducted in Bangalore found that serum vitamin-D level was significantly lower in asthmatic children.⁶ On the other hand Dogru M et al found that no significant difference was found between mean serum vitamin D levels in asthmatic children and control.⁷

Keeping this background in mind, the present study was conducted to evaluate the vitamin D levels in asthmatic children and their association with the severity of asthma in North India.

Methods

This cross-sectional study was conducted at a tertiary care center in Agra, India between March 2015 and August 2016. Children between three to 12 years of age attending paediatric OPD and IPD, having clinical features suggestive of asthma, were enrolled as study subjects after taking informed consent from the parents or guardian. Patients with bronchial asthma were diagnosed using GINA guidelines (2015). Only newly diagnosed cases of asthma were taken as study subjects. Healthy children aged between three to 12 years, without a history or family history of asthma, coming to the paediatric outpatient department or ward, were enrolled as controls. Children with other systemic illnesses or receiving Vitamin D therapy or drugs that might affect vitamin D levels for the past one year were excluded from the study. Data were collected on demographic variables (age, sex, height, weight, place of residence, socioeconomic status, and family history) and compared between the study and control group. The patients included in the study group underwent a detailed history, thorough clinical examination, and relevant investigations.

Complete blood count, absolute eosinophil count, serum IgE levels, and vitamin D levels were done for both the study and the control groups. The serum IgE levels were measured by Chemiluminescence Immunoassay (CLIA) by using a CLIA kit. Vitamin D levels were determined by measuring 25-hydroxyvitamin D levels. Estimation of serum vitamin D was done by electrochemiluminescence binding assay. An X-ray chest (Plain radiograph) was done. Spirometry was done in children above six years of age. For the bronchodilator reversibility test, salbutamol was given by MDI / nebulization. An increase in FEV1 of > 12% predicted was considered positive for a diagnosis of asthma.

Study subjects were categorized based on their vitamin D levels as classified by the American Academy of Paediatrics (2008).⁸⁻¹⁰

Severely deficient: ≤ 12.5 nmol / L (≤ 5 ng / ml)

Deficient: ≤ 37.5 nmol/L (≤ 15 ng / ml)

Insufficient: > 37.5 nmol/L to < 50 nmol / L (> 15 ng / ml to < 20 ng / ml)

Sufficient: ≥ 50 nmol / L to 250 nmol / L (≥ 20 ng / ml to 100 ng / ml)

Study was approved by ethical committee of the institute. The results of this study were analyzed and presented as numbers, percentages, or mean \pm SD. Statistical analysis was performed by applying the Student "t" test, Fisher's exact test, and the Analysis of variance (ANOVA) technique. A p-value less than 0.05 was considered to be significant for the statistical hypothesis.

Results

Thirty-five children suffering from asthma and 35 healthy children were included in our study. The mean age of study and control group cases was 9.23 ± 2.62 yr and 7.94 ± 3.05 yr respectively. The male:female ratio was 2.5:1 and 1.7:1 in the study and control groups respectively. The socio-demographic profile of the study and control group is shown in table no. 1.

Table 1: Demographic and Laboratory profile of study and control group

Demographic profile	Study (N=35)	Control (N=35)	p-value
Age group			
3-6 yr	3 (8.57%)	6 (17.14%)	0.5018
6-9 yr	11 (31.43%)	12 (34.29%)	
9-12 yr	21 (60%)	17 (48.57%)	
Gender			
Male	25 (71.43%)	22 (62.86%)	0.460
Female	10 (28.75%)	13 (37.14%)	
Rural	11 (31.43%)	12 (34.29%)	1.000
Urban	24 (68.57%)	23 (65.71%)	
SES			
Lower	18 (51.43%)	17 (48.57%)	0.1192
Middle	15 (42.86%)	10 (28.57%)	
Upper	2 (5.71%)	8 (22.86%)	
Laboratory parameters			
Eosinophilscount (%)	6.97 ± 3.58	0.85 ± 2.40	< 0.0001
AEC(cells/mm ³)	690.23 ± 418.67	278.14 ± 96.07	< 0.0001
IgE (IU/ml)	1035.69 ± 937.64	174.29 ± 217.31	< 0.0001
Vit. D (nmol/L)	45.21 ± 28.52	57.03 ± 40.01	0.1597

Cough and wheezing was the commonest presentation [35 / 35 (100%)] in the study group. Dyspnea was present in 28 / 35 (80%) and night symptoms in 17 / 35 (48.57%)

of patients. Twenty-one (60%) of asthmatic children had co-existing allergic rhinitis and four (11.4%) had atopic dermatitis. Of the study group cases, 13 / 35 (37.14%) cases had a positive family history of allergy. Of the total 35 children suffering from bronchial asthma, 16 (45.71%) had mild asthma, 15 (42.86%) had moderate asthma; only four (11.4%) children were suffering from severe asthma.

Mean FEV₁ values in mild, moderate, and severe asthma cases were 85.13 ± 3.72 , 74.85 ± 7.50 , and 51.33 ± 6.43 of the percentage predicted respectively. The value of FEV₁ / FVC in mild asthma was 94.67 ± 6.66 , in moderate was 81.54 ± 4.91 and in severe asthma was 65.33 ± 6.43 of the percentage predicted value. Comparisons of mean serum Eosinophils count (%), AEC, IgE, and Vitamin D levels in the study and control group had been described in table 1. Mean eosinophils counts ($6.96 \pm 3.58\%$), AEC (690.23 ± 418.67 cells / mm³) and IgE (1035.69 ± 937.64 IU / ml) levels were higher in the study group than in the control group and the difference was statistically significant. Mean vitamin D levels in the study group was 45.21 ± 28.52 nmol / L which was insufficient as per AAP guidelines. Mean serum vitamin D levels in mild, moderate and severe asthma cases were 52.56 ± 26.28 , 42.44 ± 31.88 and 26.19 ± 14.46 nmol / L respectively. The level of vitamin D showed declining trend with increasing severity of asthma. Patients with severe asthma have very low levels of vitamin D as compared to patients suffering from mild asthma ($p = 0.0249$).

Discussion

The prevalence and severity of asthma and allergic diseases in children continue to increase worldwide. Based on the results of various studies conducted in India as well as in other countries, the association of vitamin D deficiency with asthma is still controversial and confusing. Several studies suggest a positive correlation between serum vitamin D levels and asthma but some studies are contradicting the same.^{6,7,11,12}

The mean age group and male-female ratio in our study and control group were comparable to several other studies.^{6,13} In the study as well as in the control group most of the cases belonged to urban areas. This is comparable with several other studies where the prevalence of asthma was higher in children belonging to urban areas.^{14,15} Increased number of cases from urban areas can be explained by the easy accessibility of health care facilities in urban areas. Most of the cases in our study belonged to lower SES followed by middle and upper SES. Asthma and allergic disorders are more related to tobacco smoking, air pollution (Wood or coal-burning smoke, dust, etc.), poor housing conditions, and indoor allergens (animal dander, dust mites, cockroaches, molds), and diet which were related to lower SES.⁵ It may also be explained by the fact that most of the

patients visiting Government hospitals belonged to lower SES because of relatively cheaper healthcare facilities. In the study group, 37.14% of cases had a positive family history of asthma. Other studies also showed similar trends of prevalence of family history.^{16,17} Several studies show the co-existence of allergic disorders with asthma which is similar to our study.^{18,19}

In our study subjects, most of the children were suffering from mild asthma followed by moderate and severe asthma which is consistent with a study done by Lal et al.¹⁵ The mean value of eosinophil count (%), serum AEC levels, and IgE levels were significantly elevated in the study group than in control group (all p -value = < 0.0001). Eosinophil count $\geq 4\%$ in peripheral blood is a risk factor for early childhood asthma.⁵ The presence of > 500 eosinophils / ml in peripheral blood is the most common hematologic abnormality of allergic patients.²⁰ Average total IgE levels are higher in the population of allergic patients than in comparable populations without allergic disease.²⁰ Ehlayel et al also observed the mean IgE levels were significantly higher (p -value = < 0.001) in asthmatic children.¹³

Mean serum vitamin D levels in the study group and control group patients were 45.21 ± 28.52 nmol / L and 57.03 ± 40.01 nmol / L respectively. Though the levels of vitamin D in the study group was insufficient as per AAP criteria, the difference in the levels of vitamin D between the two groups was not statistically significant (p -value = 0.1597).⁸⁻¹⁰ These findings were comparable with several studies done in various parts of the world.^{7,12,21} In the study subject vitamin D deficiency was present only in 48.57% of subjects which was consistent with a study done by Yao TC et al in which vitamin D deficiency was present in 51.0% of study subjects.¹²

In our study cases from rural areas had sufficient vitamin D levels while cases belonging to urban areas had deficient levels of vitamin D and the difference was statistically significant (p -value = 0.0462). There was also an increased prevalence of asthma in the urban population. This is the only point that suggests some association between vitamin D levels and asthma. A similar result was seen in a study done in central Ethiopia where vitamin D deficiency was significantly higher among students in an urban setting.²² The present study found that children from the upper and middle socioeconomic groups had insufficient vitamin D levels. While children belonging to low SES had sufficient vitamin D levels. Prevalence of asthma was more in patients who belonged to lower SES as compared to upper SES.

The maximum no. of patients in our study belonged to mild asthma followed by moderate and severe asthma. Vitamin D levels in patients suffering from mild and moderate asthma were sufficient and insufficient respectively. Only patients with severe asthma had vitamin D deficiency. Increased severity of asthma was associated with decreased levels of

vitamin D in several other studies.²³ As the sample size of the present study is relatively small, more studies are needed to look for any consistent correlation between vitamin D deficiency and asthma. The small sample size in our study can be considered one of the limitations in our study.

Conclusions

In the present study, Vitamin D levels were insufficient (as per AAP classification) in study group and deficiency was more pronounced in patients with severe asthma.

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