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Research Article

ASSOCIATION BETWEEN SERUM VITAMIN D LEVELS AND ALLERGIC MARKERS WITH CHILDHOOD ASTHMA

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A B S T R A C T

Background: Vitamin D has been implicated in the pathogenesis of asthma by virtue of its role in keeping the bronchial epithelium and musculature healthy. Deficiency of Vitamin D has been linked with the increased incidence and severity of childhood asthma.
Objectives: This pilot case control study was done with an aim to find out the association between serum Vitamin D levels and allergic markers (IgE and Absolute eosinophil count) among asthmatic children in comparison with controls. Another objective was to find out the association between Vitamin D deficiency with severity of childhood asthma.
Methods: A case control study was done in which children between 4-12 years suffering from different grades of asthma were enrolled as cases with equal number of controls. Serum Vitamin D, IgE and absolute eosinophil count were measured among both the groups and descriptive analysis of the data was done.
Results: Median Vitamin D levels were significantly lower among asthmatic children (p value - 0.004) than control population while allergic markers were significantly high among asthmatics. However Vitamin D levels didn't fluctuate much among asthmatic children when analyzed according to the severity of asthma (p value 0.783).
Conclusions: Vitamin D deficiency may have association with increased incidence of childhood asthma but its role in the severity of the disease still remains obscure.

INTRODUCTION

Recent studies have emphasized a role of Vitamin D in pathogenesis of asthma as it is required for maintaining a healthy respiratory epithelium and bronchial musculature. [1] Vitamin D deficiency has been linked with increased incidence.[2, 3] and severity of childhood asthma. [4] The aim of this pilot study was to find out the association between serum Vitamin D levels and allergic markers (IgE and Absolute eosinophil count) among asthmatic children in comparison with control population and to correlate Vitamin D deficiency with severity of childhood asthma.

MATERIALS AND METHODS

This was a case control study conducted in the department of Pediatrics in a 699 bedded zonal hospital in East India between Oct 2017 to Jan 2018. The study population was a semi-urban, middle class community. All children with asthma between 4 - 12 years attending Pediatric OPD were classified as per Global initiative for Asthma (GINA) guidelines 2013 and were enrolled as cases.

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Children of the same age group who were attending Pediatric OPD for minor illnesses with no features of asthma or any other allergic illness were taken as controls. The exclusion criteria were children less than 4 years (because of inadequate sunlight exposure), children > 12 years, rickets, hepatic or renal dysfunction, malnutrition, on anti epileptic drugs and those who have taken vitamin D supplements in last 03 months.

A written informed consent was taken from the parents and the study protocol was approved by the hospital ethical committee. Blood samples were sent for 25-hydroxy vitamin D, IgE and absolute eosinophil count for both cases and controls. Serum concentration of 25 (OH) D was analyzed by an enzyme immunoassay competition method with a final fluorescent detection (ELFA technique) with an inter assay coefficient of variation of 20 %. 25 (OH) D levels of less than 20 ng/ml was considered as Vit D deficiency, levels between 20 and 29 ng/ml was labeled as insufficiency and levels > 29 ng/ml was considered as Vitamin D sufficient. Serum concentration of IgE was analyzed by similar ELFA technique within-run reproducibility CV% 3.7 - 4.5 and between run reproducibility 3.7- 5 and levels < 150 KIU/l were taken as normal.

Data was collected on a data sheet separately for the cases and controls. Statistical analysis was done utilizing Microsoft office "Excel" with Windows 8 operating system. Using SPSS (Statistical package software for the social sciences) version

24.0, descriptive analysis was done. Independent "T" test was used to find the difference of mean between cases and controls for the parametric data and Mann- Whitney U test was used to analyze the non parametric data. Mean Vitamin D, IgE and absolute eosinophil count (AEC) levels were compared among cases according to the severity of asthma using Kruskal - Wallis test. Fischer exact test was used to find the association between vitamin D status and the severity of asthma among cases. A p value of < 0.05 was considered to be statistically significant.

RESULTS

Initially a total of 60 children with asthma were enrolled as cases. 06 out of these children didn't report back after blood tests and parents of 04 children refused to participate in the study, making a total number of cases equal to 50. An equal number of controls were enrolled for the study. The study population was semi urban, middle class community with normal distribution. Baseline demographic parameters of the study population has been depicted in Table 1.

Table 1 Demographics of the study population

Parameter	Cases , Mean ± SD	Controls ,Mean± SD
Male	35 (70 %)	31(62 %)
Female	15 (30 %)	19 (38 %)
Age (years)	6.92 ± 2.32	6.72 ± 2.07
Weight (Kg)	23.57 ± 7.64	23.58 ± 5.57

46 % of the children had moderate persistent and 18 % had severe persistent asthma among cases. The distribution of asthma according to severity among cases has been depicted in Figure 1 .

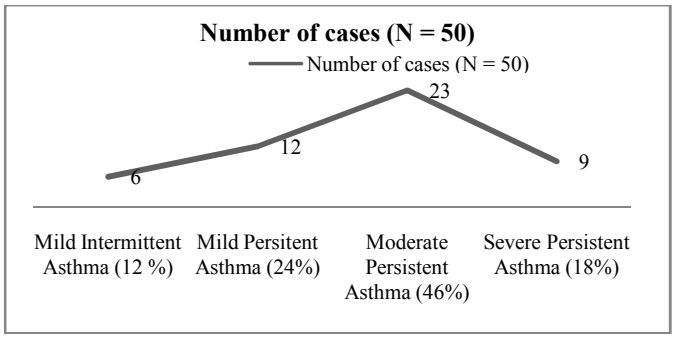

Figure 1 Distribution of Asthma according to severity among cases

Results of comparison of mean vitamin D3, IgE and AEC levels among cases and control population has been summarized in Table 2.

Table 2 Difference in the distribution of Vitamin D3, IgE and AEC values among cases and controls

Parameter	Mean ± SD		Median (Range)		P Value
	Cases (n=50)	Controls (n=50)	Cases (n=50)	Controls (n=50)	
Vit D (ng/ml)	16.84 ± 9.84	22.68 ± 12.00	15.25 (7.5- 55.89)	19 (7.6 - 56)	0.004
IgE (KIU/L)	664.22 ± 734.03	158.63 ± 251.20	344 (7 - 3000)	53.3(4.1- 1000)	0.000
AEC (cubic mm)	414.58 ± 254.36	325.98 ±249.18	350 (100 - 1550)	250(100- 1600)	0.003

*Independent "t"test for parametric data & Mann Whitney U test for non parametric data

Median Vitamin D levels were found to be lower among cases than in control group, with a p value of 0.004 which is statistically significant. Median IgE and AEC levels were found to be higher among cases than in control group with p value of 0.000 and 0.003 respectively which is statistically significant. Mean Vitamin D, IgE and absolute eosinophil count (AEC) levels were compared among cases according to the severity of asthma using Kruskal- Wallis test and has been depicted in Table 3.

Table 3 Distribution of Vitamin D3, IgE and AEC levels according to Severity of Asthma (Only for cases)

Parameter	Type of asthma	N (50)	Mean ± SD	Range	p Value
Vit D 3 (ng/ml)	Mild,	18	16.50 ± 6.82	8 - 30	0.783
	Moderate	23	16.74 ± 9.80	8- 43	
	Severe	9	17.89 ± 15.21	8- 56	
IgE (KIU/L)	Mild,	18	238.11 ± 320.32	7 - 1358	0.002
	Moderate	23	820.13 ± 711.23	42- 2218	
	Severe	9	1118.11 ± 990.34	130 - 3000	
AEC (Cmm)	Mild,	18	294.11 ± 95.79	200 - 900	0.017
	Moderate	23	451.96 ± 189.24	250 - 1550	
	Severe	9	560 ± 466.71	100 - 1550	

*Kruskal - Wallis test

On comparison it was found that mean serum Vitamin D3 levels were 16.50 ng/ml, 16.74 ng/ml and 17.89 ng/ml in children with mild, moderate and severe asthma respectively with a p value of 0.783 which is not statistically significant.

Serum IgE levels in children with mild, moderate and severe asthma were 238.11 Kiu/l, 820.13 Kiu/l and 1118 Kiu/l respectively with a p value of 0.002 which was statistically significant. Mean serum AEC levels were 294/cmm, 452/cmm and 560 cmm in children with mild, moderate and severe asthma respectively with a statistically significant p value of 0.017. The association between vitamin D status with severity of asthma among cases has been depicted in Table 4.

Table 4 Association between Severity of asthma and Vitamin D status (Cases)

Severity of Asthma	Vit D Status			Total	P Value
	Sufficient (> 29 ng/ml)	Insufficient (20- 29 ng/ml)	Deficiency (< 20 ng/ml)		
Mild Intermittent	0	1	5	6	0.609
Mild Persistent	1	2	9	12	
Moderate Persistent	2	5	16	23	
Severe Persistent	1	1	7	9	

*Fischer Exact test

Although 74 % of the children with asthma were having deficient Vitamin D levels but the severity of asthma was not found to be associated with their vitamin D levels with a p value of 0.609 which was statistically insignificant.

DISCUSSION

Recent studies have shown Vitamin D deficiency among children of all age groups in India contrary to the belief that it is quite rare in tropical countries.[5,6] Because of its role in keeping the respiratory mucosa and bronchial smooth muscles healthy , Vitamin D deficiency has been found to be associated with increased incidence of asthma and allergic symptoms.[7] In our study we found that only 10 % of the children with asthma had sufficient Vitamin D levels and 18 % had insufficient and 74 % had vitamin D deficiency. Results of our study were almost comparable with studies done by Chinellato *et al* (2011) and Freishtat *et al* (2010) in Italian and American children.[8,9]

As median Vitamin D levels were found to be significantly lower among cases than in control population, associating further the role of Vitamin D deficiency with increase incidence of childhood asthma. Median IgE and absolute eosinophil count were significantly higher in cases than in

control population, further implicating the role of vitamin D deficiency in allergic disorders.

On comparing Vitamin D levels, IgE and AEC among asthmatic children, mean IgE and AEC levels were found to be higher among children with more severe asthma in comparison to mild and moderate variety. However, mean Vitamin D levels didn't vary much among asthmatic children with different severity. This contemplates the fact that Vitamin D deficiency may be associated with increase incidence of childhood asthma but its precise role in the severity of asthma is still obscure.

An another study by Kavitha *et al* (2017) done at AIIMS concluded that Vitamin D deficiency was not found to have any association with asthma control in Indian children.[10] Harinarayan *et al* (2009) and Marwaha *et al* (2008) emphasized the lack of adequate Vitamin D stores among Indian children in their studies.[5,6,11] In our study too 15% of the children had Vitamin D deficiency, 56 % had insufficiency and 29 % had sufficient Vitamin D levels among controls.

This is imminent from our study that Vitamin D deficiency may be associated with increase plausibility of childhood asthma but its role in the severity of asthma and acute exacerbations still needs to be explicited by larger studies. The limitation of our study was small sample size, lack of detailed information about dietary Vitamin D intake, sunlight exposure and lack of spirometry findings (FEV1).

In developing countries like India where childhood asthma poses a significant disease burden of about 30 million, there is need to evaluate the feasibility and adopt a more practical approach for prophylactic Vitamin D supplementation.[12,13] More cogitation is required in this field with all the epidemiological , socioeconomic and demographic factors to reach a consensus about routine Vitamin D supplementation in asthmatic children.

CONCLUSION

The study shows that Vitamin D deficiency may have been associated with the increased incidence of childhood asthma but its role in the severity of the disease still remains obscure.

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