RESEARCH PAPER

Association of Serum Vitamin D Levels with Level of Control of Childhood Asthma

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Objective: To study the association between serum vitamin D levels and levels of asthma control in children aged 5-15 years. ***Methods:*** Children with physician-diagnosed asthma who were under follow-up for at least 6 months were enrolled. Participants were categorized into three asthma control groups as per standard guidelines, and their serum 25-hydroxy vitamin D levels and pulmonary function tests were compared. ***Results:*** Out of 105 children with asthma enrolled in the study, 50 (47.6%) were controlled, 32 (30.5%) were partly controlled and 23 (21.9%) were uncontrolled. Median (IQR) serum vitamin D levels in these three groups were 9.0 (6.75, 15) ng/mL, 10 (6.25, 14.75) ng/mL and 8 (5, 10) ng/mL (P=0.24), respectively. ***Conclusion:*** We did not observe any association of serum 25-hydroxy vitamin D levels with the level of control of childhood asthma.

Key words: *Diet, Management, Symptom control, Vitamin D deficiency.*

Vitamin D may have a role in asthma due to its wide-ranging effects on airway epithelium, bronchial smooth muscle, and immune cells central to the pathogenesis of asthma [1]. Information on association between vitamin D and level of control of asthma in children is scarce. We, therefore, studied the association between vitamin D levels and level of control of asthma in children.

METHODS

A cross-sectional study was performed from January 2013 to September 2014 in the Pediatric Chest Clinic of the Department of Pediatrics at All India Institute of Medical Sciences (AIIMS), New Delhi, India. Children with physician-diagnosed asthma, aged 5-15 years, who had been in regular follow-up in the clinic for at least previous six months were enrolled into the study after ruling out chronic illness, clinical rickets or evidence of vitamin D supplementation in last six months, and after getting informed written consent. We planned to enroll a convenience sample of 100 children. The study protocol was approved by the Ethics Committee of the institute.

Detailed clinical history was obtained; this included dietary habits of the child and numbers of hours spent in outdoor during daytime to evaluate the sunlight exposure to the child. Respiratory system examination was performed. Nutritional status of the child was assessed based on WHO growth charts [2].

Spirometry was performed using Master Screen IOS (CareFusion, San Diego, California, USA). We categorized participants into different asthma control groups based on the Global (GINA) guidelines after assessing the symptoms status in the previous four weeks. Blood samples (2.5 mL) were collected in the study population in two plain vials. Serum was separated by centrifuging the sample at -4°C and was analyzed on the same day for levels of 25-hydroxy vitamin D [25(OH)D] and parathyroid hormone (PTH). Serum calcium, inorganic phosphate and alkaline phosphatase were analyzed on the same day using spectrophotometric analysis. Serum level of 25(OH)D was measured using chemiluminiscence by using LIAISON (DiaSorin, Italy). Serum 25(OH)D level of more than 20 ng/mL was considered sufficient, level between 12 and 20 ng/mL as insufficient, and value less than 12 ng/mL was considered as deficient [3,4].

Data were collected on structured performa and managed using MS Excel software. Statistical analysis was performed using Stata 11.0 (Stata Corp, College Station, TX). We used descriptive statistics for the characteristics of the subjects. Fisher's exact test/ chi-squared test were used for proportions. For continuous variables, ANOVA or Kruskal-Wallis test were used to assess statistical significance based on the distribution of variable (normal and non-normal, respectively). Vitamin D levels in children with different levels of control were compared by Kruskal-Wallis equality of population rank test.

RESULTS

A total of 108 children were enrolled into the study; 3 children were excluded from analysis because blood sample was not collected. The characteristics of the 105 enrolled children are shown in ***Table* I**.

Asthma status of 50 (47.6%) children were categorized as controlled, 32 (30.5%) as partly controlled, and 23 (21.9%) as uncontrolled. ***Table* II** compares the pulmonary function tests (PFT) values between these groups.

The median (IQR) serum 25(OH)D level in the study participants was 9 (6,14) ng/mL. The median serum 25(OH)D levels were comparable in the three groups based on control of asthma. The prevalence of vitamin D deficiency in uncontrolled asthma group was higher with 78.2% children being vitamin D deficient (*P*=0.52) (***Table* III**).

None of the major spirometric parameters showed statistically significant correlation with serum vitamin D level except FEF_{25} (% predicted) (r= 0.22; *P*=0.02) and

TABLE I COMPARISON OF CHARACTERISTICS OF STUDY SUBJECTS CLASSIFIED BY THE ASTHMA CONTROL STATUS

		Asthma Control Status			
	Whole Group (n=105)	*Controlled (n=50)*	*Partly controlled n=32*	*Uncontrolled n=23*	*P value*
Age, in years; mean (SD)	10.6 (2.4)	10.8 (2.5)	10.0 (2.5)	11 (2.2)	0.92
Onset of symptoms in years; mean (SD)	3.2 (2.6)	3.0 (2.7)	3.1 (2.3)	3.6 (2.7)	0.59
Family History of asthma (%)	57 (54.3%)	29 (58%)	16 (50%)	12 (52.2%)	0.76
Allergic Rhinitis; *n* (%)	61 (58.1%)	24 (48%)	18 (56.3%)	19 (82.6%)	0.017
Cough; *n* (%)	27 (25.7%)	8 (16%)	8 (25%)	11 (47.8%)	0.018
Wheeze; *n* (%)	12 (11.4%)	1 (2%)	5 (15.6%)	6 (26.1%)	0.004
Breathlessness; *n* (%)	12 (11.4%)	1 (2%)	5 (15.6%)	6 (26.1%)	0.004
Nasal Symptoms; *n* (%)	9 (8.5%)	2 (4%)	3 (9.4%)	4 (17.4%)	0.14
Chest pain; *n* (%)	8 (7.6%)	0 (0%)	5 (15.6%)	3 (13.0%)	0.006
BMI, kg/m^2; mean (SD)	16.6 (3.2)	16.6 (3.1)	16.5 (3.9)	16.7 (2.6)	0.95
Severity of Asthma					
Mild; *n* (%)	26 (24.8%)	11 (22%)	8 (25%)	7 (30.4%)	0.76
Moderate; *n* (%)	62 (59.0%)	31 (62%)	20 (62.5%)	11 (47.8%)	
Severe; *n* (%)	17 (16.2%)	8 (16%)	4 (12.5%)	5 (21.7%)	
Number of Hospital Admissions in past 1 yr; *n*	10	4	1	5	0.14
Number of emergency visits in past 1 yr; *n*	19	8	2	9	0.52
Exacerbations in 1 yr; Median (IQR)	1 (0, 2)	1 (0, 2)	1 (0, 2)	2 (1, 4)	0.03
Steroid bursts in 1 yr; Median (IQR)	0 (0, 1)	0 (0, 1)	0 (0, 1)	0 (0, 1)	0.86
Steroid (Budesonide) Current Use (mcg/d); Median (IQR)	400 (100, 800)	400 (100, 800)	400 (100, 700)	400 (200, 800)	0.30
Duration of use of Inhaled steroids in months; Median (IQR)	28 (19, 36)	26 (18, 36)	26.5 (21, 36)	33 (24, 45)	0.127
Symptoms used to assess control					
Day time Symptoms >2/wk; *n* (%)	11 (10.4%)	0	0	11 (47.8%)	<0.0001
Nocturnal Symptoms (Any); *n* (%)	36 (34.3%)	0	14 (43.8%)	22 (95.7%)	<0.0001
Limitation of Activities (Any); *n* (%)	29 (27.6%)	0	11 (34.4%)	18 (78.3%)	<0.0001
Need for Rescue >2/wk; *n* (%)	20 (19.1%)	0	4 (12.5%)	16 (69.6%)	<0.0001
PFT Abnormality; *n* (%)	27 (25.7%)	0	12 (37.5%)	15 (65.2%)	<0.0001

Abbreviations: PFT: Pulmonary function test; SD: standard deviation; IQR: Interquartile range.

TABLE II PULMONARY FUNCTION TESTS IN CHILDREN WITH DIFFERENT LEVELS OF CONTROL OF ASTHMA

		Asthma Control Status			
	Whole group (n=105)	*Controlled (n=50)*	*Partly controlled (n=32)*	*Uncontrolled (n=23)*	*P value*
PFT Abnormality; *n* (%)	27 (25.7%)	0 (0%)	12 (37.5%)	15 (65.2%)	<0.0001
Percentage Predicted FEV_1; Mean (SD)	87.7 (17.4)	94.1 (15.7)	83.3 (16.3)	80.1 (17.9)	0.0009
Percentage Predicted PEFR; Mean (SD)	84.7 (26.8)	93.8 (27.9)	74.5 (16.7)	78.9 (29.8)	0.0025
Percentage Predicted FEV_1/FVC; Mean (SD)	95.9 (11.8)	99.9 (8.3)	94.4 (11.6)	89.4 (15.2)	0.001
Percentage Predicted FVC; Mean (SD)	91.3 (16.4)	94.1 (14.6)	87.8 (20.1)	89.8 (13.5)	0.22
Percentage Predicted FEF 25; Mean (SD)	57.9 (25.7)	64.7 (21.6)	52.0 (24.2)	51.2 (32.7)	0.033
Percentage Predicted FEF 75; Mean (SD)	81.6 (25.5)	91.2 (21.3)	73.8 (22.0)	71.4 (31.1)	0.0007

FEV_1: Forced Expiratory Volume-1 second; FVC: Forced Vital Capacity; PEFR: Peak Expiratory Flow Rate; FEF_{75}: Forced Expiratory Flow 75; FEF_{25}: Forced Expiratory Flow 25.

TABLE III VITAMIN D IN DIFFERENT ASTHMA CONTROL GROUPS

Characteristic	*Asthma Control Status*			*P value*
	Controlled (n=50)	*Partly Controlled (n=32)*	*Uncontrolled (n=23)*	
Serum 25(OH)D (ng/mL); Median (IQR)	9.0 (6.75, 15)	10 (6.25, 14.75)	8 (5, 10)	0.24
Serum PTH (pg/mL); Median (IQR)	46.3 (33.0, 64.4)	39.7 (29.9, 55.2)	40.9 (28.9, 62.1)	0.65
Vitamin D status, n (%)				
Sufficient - (25(OH)D >20 ng/mL)	5 (10%)	1 (3.1%)	1 (4.3%)	
Insufficient - (25(OH)D 12-19 ng/mL)	13 (26%)	11 (34.8%)	4 (17.4%)	
Deficient - (25(OH)D <12 ng/mL)	32 (64%)	20 (62.5%)	18 (78.26%)	0.52

PEFR (r=0.19; *P*=0.049).

The asthma control subgroups did not show any significant seasonal differences with the time of sampling. Median (IQR) cumulative inhaled steroid use were 423 (214.5, 684) mg, 456 (241.5, 576) mg, and 363 (330, 600) mg in deficient, insufficient and sufficient vitamin D status groups (*P*=0.98). Daily sunlight exposure was comparable in vitamin D sufficient participants and others (*P*=0.97).

DISCUSSION

We did not observe any significant association between serum vitamin D levels and the level of asthma control in children. We also did not observe any correlation between the 25(OH)D levels and various spirometric parameters (percent predicted) except for a statistically significant positive correlation of vitamin D levels with FEF_{25} and PEFR values (% predicted).

Limitation of our study was a small sample size. We did not collect detailed information about dietary intakes, particularly vitamin D, and did not measure serum IgE levels. We did not have healthy children as controls as we compared the levels of vitamin D in children with various levels of control of asthma.

In a case-control study, Awasthi, *et al*. [5] reported significant association between asthma control and vitamin D deficiency. In another study, vitamin D levels were lower in children with severe treatment resistant asthma as compared to moderate asthma group and control subjects [6]. In a cross-sectional study among 100 children, Searing, *et al*. [7] reported positive correlation between vitamin D levels and FEV_1 (percent predicted) and FEV_1/FVC. On the other hand, a study done in Thailand by Krobtrakulchai, *et al*. [8] in 125 asthmatic children, vitamin D levels were similar between three asthma control groups, and there was no association between vitamin D levels and PFT values. Recent trials in children and adults with asthma have also failed to demonstrate the effect of vitamin D supplementation on symptom control [9,10].

We conclude that there is unlikely to be any association between vitamin D levels and the control of asthma in children.

Contributors: TKK: study design, data collection and writing of

WHAT THIS STUDY ADDS?

- Vitamin D deficiency was not found to have any association with asthma control in Indian children.

manuscript; RL, SKK: designed the study, analyzed the data and wrote the manuscript; NG: laboratory assays and writing of manuscript.

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