A study of correlation between serum vitamin D levels with level of control of childhood asthma

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Abstract
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 Word: Diet, Management, Symptom control, Vitamin D deficiency

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INTRODUCTION

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. 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.

MATERIAL AND METHODS

A cross-sectional study was performed from January2016 to September 2017 in the Department of Pediatrics at Darbhanga Medical College & Hospital, Laheriasarai, Bihar. 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. 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 -4ºC 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. 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; 3children 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 serum25(OH)D levels were comparable in the three group sbased on control of asthma. The prevalence of vitamin D deficiency in uncontrolled asthma group was higher with78.2% children being vitamin D deficient (P=0.52) (*Table* **III**). None of the major spirometric parameters show edstatistically significant correlation with serum vitamin D level except FEF25 (% predicted) (r= 0.22; P=0.02) and 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 texposure was comparable in vitamin D sufficient participants and others (P=0.97).

Table 1: Comparison Of characteristics Of study subjects classified By The asthma control status

	Whole Group (n=105)	Controlled (n=50)	Partly controlled n=32		Uncontrolled n=23	P value
			Asthma Control Status			
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%)	(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%)	(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/m²; 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%)	(16%)	4	(12.5%)	5 (21.7%)	
Number of Hospital Admissions in past 1 yr; *n*	10		1		5	0.14
Number of emergency visits in past 1 yr; *n*	19		2		9	0.52
Exacerbations in 1 yr; Median (IQR)	1 (0, 2)	(0, 2)	1 (0, 2)		2 (1, 4)	0.03
Steroid bursts in 1 yr; Median (IQR)	0 (0, 1)	(0, 1)	0 (0, 1)		0 (0, 1)	0.86
Steroid (Budesonide) Current Use (mcg/d);	400 (100, 800)	400 (100, 800)	400 (100, 700)		400 (200, 800)	0.30

Median (IQR) 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		11 (47.8%)	<0.0001
Nocturnal Symptoms (Any); *n* (%)	36 (34.3%)		14 (43.8%)	22 (95.7%)	<0.0001
Limitation of Activities (Any); *n* (%)	29 (27.6%)		11 (34.4%)	18 (78.3%)	<0.0001
Need for Rescue >2/wk; *n* (%)	20 (19.1%)	4 (12.5%)		16 (69.6%)	<0.0001
PFT Abnormality; *n* (%)	27 (25.7%)		12 (37.5%)	15 (65.2%)	<0.0001

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

Table 2: Pulmonary functiontests In children with different levels Of control Of asthma

			Asthma Control Status		
	Whole group	Controlled	Partly controlled	Uncontrolled	P value
	(n=105)	(n=50)	(n=32)	(n=23)	
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: Forced Expiratory Volume-1 Second; FVC: Forced Vital Capacity; PEFR: Peak Expiratory Flow Rate; FEF: Forced Expiratory Flow 75; FEF_{25}[1]: Forced Expiratory Flow 25.'

Table 3: Vitamind 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

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 withFEF25 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 Ig Elevels. We did not have healthy children as controls as we levels of control of asthma. In a case-control study, Awasthi, *et al*. 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. In a cross-sectional study among 100 children, Searing, *et al.* reported positive correlation between vitamin D levels and FEV1 (percent predicted) and FEV1/FVC. On the other hand, a study done in Thailand by Krobtrakulchai, *et al.* in 125 asthmatic children, vitamin D levels were similar between three asthma control groups, and there was no association between vitamin D level s 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.

CONCLUSION

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

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