

## Vitamin D Deficiency as a Factor Influencing Asthma Control in Children

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Received: June 01, 2016;  
Initial review: March 06, 2017;  
Accepted: July 24, 2018.

**Objective:** To study the association between asthma control and serum 25OH Vitamin D levels in children with moderate persistent asthma on preventer therapy. **Methods:** Children aged 6-18 years, with moderate persistent asthma, on preventer therapy for  $\geq 2$  months were included. Control was categorized as good, partial or poor as per GINA guidelines. Serum 25 (OH) Vitamin D levels were measured and their relationship with the level of control was studied. **Results:** Out of 50 children enrolled, 22 had well-controlled asthma, and 21 had partially controlled asthma. Vitamin D was deficient in 30 children and insufficient in 18 children. Children with vitamin D deficiency had significantly less well-controlled asthma as compared to those with insufficient or sufficient levels of 25 (OH) vitamin D (13.3% vs 88.9% vs 100%). **Conclusion:** Vitamin D deficiency is associated with suboptimal asthma control.

**Keywords:** Co-morbidity, Outcome, Treatment, Wheezing.

Pediatric asthma represents a huge burden on the child, family and society [1]. The goal of preventive treatment is to control symptoms. Though guidelines are available for preventer therapy, there is little data on the number of children who achieve good control with these regimes and the factors that influence the level of control. When these factors are identified and modified, better control is possible.

Studies have shown that Vitamin D inhibits sensitization in bronchial wall smooth muscle and that vitamin D deficiency can increase the occurrence and severity of asthma [2,3]. Given the pandemic proportions of this deficiency, this may be an important modifiable factor in the improvement of asthma control. We studied the association between serum 25 OH vitamin D levels and asthma control.

### METHODS

This prospective observational study was undertaken in the pediatric asthma clinic of a large teaching hospital between August 2013 and July 2014 after IEC approval. Children aged 6 to 18 years with moderate persistent asthma on preventer therapy for 2 months (+29 days) with good compliance and techniques were enrolled (period sample). Severity of asthma was categorized as per Global Initiative for Asthma guidelines [4]. Drug compliance was considered good if they had taken medication as prescribed for  $>5$  days/week in the previous two months. Children whose parents didn't give

consent and those with systemic illnesses were excluded.

In a predesigned proforma, demography details, history and physical examination findings and co-morbidities were noted. Rhinitis was defined as anterior or posterior rhinorrhoea, sneezing, nasal blockage and/or itching of the nose during two or more consecutive days for more than 1 hour on most days [5]. Sinusitis was defined as per the task force of Rhinology and Paranasal sinus Committee [6].

3 mL of blood was withdrawn for measuring serum 25 (OH) D and IgE levels. 25 (OH) D levels were assessed by chemiluminescence micro particle immunoassay (Abbott ARCHITECT i 2000 SR Immunoassay Analyzer) and serum IgE levels by chemiluminescence assay (Advia Centaur).

Serum 25 OH vitamin D level was described as sufficient ( $>30$  ng/mL), insufficient (21-29 ng/mL) or deficient ( $<20$  ng/mL) as per Endocrine Society guideline [7]. IgE levels were described as normal or abnormal based on age appropriate standard lab references [8]. Children were categorized as well controlled, partially controlled and poorly controlled as per GINA guidelines. Nutritional status was classified as per WHO standards using BMI charts.

Statistical analysis was performed using SPSS, version 17. Results were expressed as number and percentage. Chi-square test was used for comparison between two attributes.  $P$  value  $<0.05$  was considered significant.

**WHAT THIS STUDY ADDS?**

- Vitamin D deficiency is associated with inadequate asthma control in children with moderate persistent asthma on inhaled corticosteroids.

**RESULTS**

Out of 253 children seen in the asthma clinic during the study period, 87 children were 6-18 years of age with moderate persistent asthma and on preventer therapy (Budesonide 400 µg/day) for two months (+ 29 days); of these, 37 were excluded because of other systemic illnesses/refusal of consent and 50 children were enrolled in the study. The mean (SD) age was 11.2 (3.6) years.

Asthma control was poor in 7 children, 22 children had well-controlled asthma, and 21 had partial control. Age, gender, family history of asthma, type of device, serum IgE levels and presence of co-morbidities had no relationship to the level of control. Children who were underweight or obese had poorer control but the difference was not statistically significant. Children with well controlled asthma were significantly less likely to have been born low birth weight.

The serum 25 (OH) D levels ranged between 6.5 ng/mL and 32.5 ng/mL. The mean (SD) level was 19.6 (6.2) ng/mL, and median (IQR) was 18.6 (9.5, 14.9) ng/mL.

**Table I** depicts the association between the various factors studied and asthma control. Children with partially/poorly-controlled asthma were significantly more likely to have vitamin D deficiency.

**DISCUSSION**

In our study, overall only 44% with persistent asthma on regular preventer therapy had good control, which is similar to that reported in literature [1].

Associations between vitamin D deficiency and asthma has also been observed in other studies [9,10], but not consistently [11]. Vitamin D deficiency has been shown to increase the incidence and severity of asthma as well as the efficacy of preventive therapy with inhaled corticosteroids [12]. Vitamin D not only influences the immune system through its effects on helper T cell type 1 and 2 and regulatory T cells [13,14] but also modulates chemokines secreted by airway smooth muscle cells [15].

A limitation of this study was that the effect of vitamin D supplementation on the control of asthma by follow-up of these children was not done. Also, in order to have a homogenous study population, only children with moderate persistent asthma were included in this study.

The findings of this study may have implications in clinical practice. Currently, poor control is being managed by escalation of preventer therapy. Adding more drugs or increasing the doses may, over time, increase the toxicity of therapy. Evaluating serum 25 (OH) D levels and correcting identified deficiencies may prevent the need for escalation of preventer therapy.

*Contributors:* ATK: data collection, statistical analysis, manuscript drafting and final approval of manuscript; PVR, VK: designing the study, data analysis, critical appraisal of manuscript and final approval of manuscript; TSA: data analysis, manuscript drafting, critical appraisal of manuscript and final approval of manuscript.

**TABLE I** ASTHMA CONTROL AND ASSOCIATED FACTORS

<i>Variable</i>	<i>Well controlled (n=22)</i>	<i>Not well-controlled* (n=28)</i>
<i>Age</i>		
6-9 y	10 (45)	12 (43)
10-13 y	4 (18)	9 (32)
>13 y	8 (36)	7 (25)
<i>Male</i>	16 (73)	17 (61)
<i>Low birthweight</i>	13 (59)	6 (21)
<i>Nutritional Status</i>		
Normal	16 (73)	13 (46)
Underweight	3 (14)	10 (36)
Overweight/Obese	3 (14)	5 (18)
<i>Co-morbidities</i>		
Allergic rhinitis	9 (41)	19 (68)
Sinusitis	2 (9)	1 (3.5)
Allergic rhino-sinusitis	6 (27)	5 (18)
<i>Type of device</i>		
MDI	10 (45)	12 (43)
DPI	12 (55)	16 (57)
Elevated IgE levels	13 (59)	20 (71)
<i>Vitamin D levels#</i>		
Sufficient	2 (0.1)	0 (0)
Insufficient	16 (72)	2 (7)
Deficient	4 (18)	26 (93)

*All values in no. (%); \*Partially controlled (n=21) and Poorly controlled (n=7); MDI: Meter dose inhaler; DPI: Dry powder inhaler; #Sufficient ≥30 ng/mL; Insufficient: 21-29 ng/mL; Deficient ≤20 ng/mL.*

*Funding:* None; *Competing interest:* None stated.

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