

## Original Research Article

DOI: <http://dx.doi.org/10.18203/2349-3291.ijcp20201141>

# Influence of serum vitamin D levels on control and severity of asthma in children

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Received: 13 January 2020

Revised: 30 January 2020

Accepted: 05 February 2020

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## ABSTRACT

**Background:** To determine the association between the serum vitamin D levels with the control and severity of asthma.

**Methods:** A total of 113 asthmatic children were enrolled in the study who were on regular follow-up and treatment for the past 6 or more months. The demographic details, presenting complaints, aggravating factors, allergic rhinitis, atopic dermatitis, hospital and ICU stay, duration of sunlight exposure, drug compliance and detailed clinical examination findings were noted in the predesigned proforma. Control of asthma was assessed based on GINA guidelines 2018 as well controlled, partly controlled and poorly controlled. The partly controlled and the poorly controlled group were further combined and labelled as not well controlled group. Severity of asthma was categorized into intermittent, mild persistent, moderate persistent and severe persistent. Serum 25 hydroxy vitamin D was assessed by solid phase ELISA. The well controlled and partly controlled group were compared for all studied parameters.

**Results:** Asthma status of the subjects was categorized as well controlled (59%) as partly controlled (40%) and as poorly controlled (1%). Children with partly and poorly controlled asthma had significantly more vitamin D deficiency (10.9%) and insufficiency (32.6%) compared to well controlled group (4.5% and 4.5% respectively), with  $p$  value= 0.000. Low serum vitamin D levels are significantly associated with moderate and severe persistent asthma ( $p$  value= 0.009). Exercise significantly induced symptoms in 47.8% of not well controlled group and about 25.4% in well controlled group ( $p$  value= 0.014). Examination findings such as wheeze on auscultation was significantly more in not well controlled group.

**Conclusions:** Low serum vitamin D levels are associated with poor control of asthma in children and the severity of asthma is inversely proportional to the serum vitamin D levels.

**Keywords:** Asthma, Allergic rhinitis, Enzyme-linked immunosorbent assay, GINA, Pulmonary function test, Vitamin D

## INTRODUCTION

Asthma is a heterogeneous disease usually characterized by chronic airway inflammation. 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.<sup>1</sup> WHO estimates that currently there are 300 million people suffering from asthma worldwide, 10% of it i.e, 30 million are Indians. The prevalence of asthma in children range from 3% to 38%.<sup>2</sup>

The goal of preventive therapy in asthma is to control symptoms.<sup>3</sup> Serum vitamin D is widely studied as one of the modifiable factor for asthma control. Vitamin D has immunomodulatory functions, affecting both innate and adaptive components of immune system. It suppresses proallergic immune responses, maintains the integrity of epithelial barrier and reduces susceptibility to infections.

Studies have shown that the serum vitamin D concentration is inversely associated with asthma control and its deficiency is associated with poor asthma control.<sup>3-7</sup> However there are also studies which say that there is no role of vitamin D deficiency in asthma.<sup>8,9</sup> In view of these conflicting reports this study was chosen.

Aims and objectives are to determine the association between the serum vitamin D levels with the control and severity of asthma.

## METHODS

This cross-sectional study was undertaken in Pediatric asthma clinic of a tertiary care teaching Hospital, between January 2019 to June 2019.

### Inclusion criteria

- Children between the age group of 6 years to 18 years diagnosed as asthma according to GINA guidelines 2018 were enrolled in the study.

### Exclusion criteria

- Chronic respiratory complaints suggestive of diagnosis other than asthma.
- Children on long term medications like beta blockers.
- Children on vitamin D supplementation.
- Diseases affecting vitamin D absorption like chronic liver disease and kidney disease.

The study protocol was approved by the institutional ethical committee. 113 children were enrolled in the study calculated based on the prevalence of 8% of asthma amongst children attending asthma clinic at 0.05 significance level using the formula, sample size=Z<sup>2</sup>pq/d<sup>2</sup>, where Z=1.96, p is the prevalence of disease, d=95% confidence interval, q=1-p. Written informed consent was obtained from parents. The demographic details, presenting complaints, aggravating factors, allergic rhinitis, atopic dermatitis, previous hospital and ICU stay, duration of sunlight exposure, drug compliance and detailed clinical examination findings were noted in the predesigned proforma.

Allergic rhinitis was classified into mild intermittent, moderate to severe intermittent, mild persistent and moderate to severe persistent based on ARIA classification.<sup>10</sup> On an average 30 minutes of sunlight exposure per day was considered adequate.<sup>11</sup> Drug

compliance was assessed on regular follow up by history and checking the dose in dose counter of meter dose inhalers. Control of asthma was assessed based on GINA guidelines 2018 as well controlled, partly controlled and poorly controlled.<sup>1</sup> Severity of asthma was categorized into intermittent, mild persistent, moderate persistent and severe persistent.<sup>10</sup>

Under aseptic precautions 3 ml of blood was drawn by venepuncture and collected in plain tube. Sample was centrifuged and stored at -20 degree Celsius. Serum estimation of 25(OH) Vitamin D was done by solid phase ELISA (CAL BIOTECH vitamin D ELISA kit) that works on the principle of competitive binding. Urea, creatinine and liver function tests were done to exclude renal and liver pathology respectively. Serum 25(OH)D levels were interpreted as per IAP guidelines as >20 ng/ml- sufficient, 12-20 ng/ml- insufficient, <12 ng/ml- deficient.<sup>12</sup>

Spirometry was performed by MIR Spirolab spirometer. Statistical analysis was performed using SPSS statistical package version 20 for windows. We used descriptive statistics such as mean, standard deviation, frequency and percent for the characteristics of the subjects. Inferential statistics Cramer's V and independent T test were used for group characteristics. The p value of <0.05 was considered significant.

## RESULTS

A total of 113 asthmatic children were enrolled in the study who were on regular follow-up and treatment for the past 6 or more months. Asthma status of the subjects was categorized as well controlled (59%) as partly controlled (40%) and as poorly controlled (1%). Partly controlled and poorly controlled were combined into one group as not well controlled group.

Table 1 compares the association between the various factors studied between the two asthma control groups. Exercise significantly induced symptoms in 47.8% of not well controlled group and about 25.4% in well controlled group. Examination findings such as conjunctival congestion and wheeze on auscultation was significantly more in not well controlled group. The incidence of wheeze, cough, shortness of breath, chest tightness and allergic rhinitis were comparable in both groups. The results of atopic dermatitis, hospital stay, and ICU stay, sunlight exposure, height, BMI were not statistically significant. The spirometric parameters in the not well controlled group had higher percentage of low FEV1 and lower FEV1/FVC. But it was not statistically significant.

Table 2 depicts that the children with partly and poorly controlled asthma were significantly more likely to have vitamin D deficiency and insufficiency. In Table 3 the association between asthma severity and vitamin D deficiency is depicted. Low serum vitamin D levels are significantly associated with increased severity of the disease.

**Table 1: Comparison of baseline characteristics between two control group.**

| Variable            | Well controlled (n=67)                   | Not well controlled (n=46) | p value |
|---------------------|--|----------------------------|---------|
| Age                 | 5-12 years 48 (71.6%)                    | 32 (69.6%)                 | 0.811   |
|                     | 13-18 years 19 (28.4%)                   | 14 (30.4%)                 |         |
| Gender              | Male 49 (73.1%)                          | 23 (50%)                   | 0.012   |
|                     | Female 18 (26.9%)                        | 23 (50%)                   |         |
| Presenting symptoms | Cough 54 (80.6%)                         | 37 (80.4%)                 | 0.983   |
|                     | Wheeze 55 (82.1%)                        | 38 (82.6%)                 | 0.943   |
|                     | Shortness of breath 26 (38.8%)           | 15 (32.6%)                 | 0.501   |
|                     | Chest tightness 3 (4.5%)                 | 3 (6.5%)                   | 0.634   |
|                     | Exercise 17 (25.4%)                      | 22 (47.8%)                 | 0.014   |
|                     | Atopic dermatitis 3 (4.5%)               | 1 (2.2%)                   | 0.515   |
|                     | Food allergy 7 (10.4%)                   | 5 (10.9%)                  | 0.943   |
|                     | Family history of asthma 19 (28.4%)      | 19 (41.3%)                 | 0.152   |
|                     | Hospitalization past 1 year 11 (21.7%)   | 10 (16.4%)                 | 0.475   |
|                     | ICU stay 3 (4.5%)                        | 3 (6.5%)                   | 0.634   |
|                     | Sunlight exposure <30 min 26 (40.6%)     | 12 (26.7%)                 | 0.132   |
|                     | Short stature 26 (59.7%)                 | 13 (71.7%)                 | 0.337   |
|                     | BMI                                      |                            |         |
|                     | Overweight 0 (0%)                        | 2 (4.3%)                   | 0.160   |
| Height              | Eye changes 7 (88.1%)                    | 14 (69.6%)                 | 0.021   |
|                     | Wheeze on auscultation 3 (4.5%)          | 8 (17.4%)                  | 0.023   |
| Aria                | Mild persistent 5 (27.8%)                | 7 (41.2%)                  | 0.676   |
|                     | Mild intermittent 10 (55.6%)             | 8 (47.1%)                  |         |
|                     | Moderate to severe persistent 2 (11.1%)  | 2 (11.8%)                  |         |
|                     | Moderate to severe intermittent 1 (5.6%) | 0 (0%)                     |         |
| PFT                 | FEV1 (<80%) 13 (25%)                     | 10 (27.8%)                 | 0.771   |
|                     | FEV1/FVC (<90%) 15 (28.8%)               | 11 (30.6%)                 | 0.863   |

(ARIA- allergic rhinitis impact on asthma, PFT- pulmonary function test)

**Table 2: Serum vitamin D in the two control groups.**

| Serum vitamin D level(ng/ml) | Well controlled | Not well controlled | p value |
|------------------------------|-----------------|---------------------|---------|
| <12                          | 3 (4.5%)        | 5 (10.9%)           | 0.000   |
| 13-20                        | 3 (4.5%)        | 15 (32.6%)          |         |
| >21                          | 61 (91%)        | 26 (56.5%)          |         |

**Table 3: Comparison between serum vitamin D and the severity of asthma.**

| Serum vitamin d(ng/ml) | Asthma severity     |                        |                            |                         | p value |
|------------------------|---------------------|------------------------|----------------------------|-------------------------|---------|
|                        | Intermittent (n=18) | Mild persistent (n=47) | Moderate persistent (n=44) | Severe persistent (n=4) |         |
| <12                    | 1(5.6%)             | 2(4.3%)                | 4(9.1%)                    | 1(25%)                  |         |
| 13-20                  | 2(11.1%)            | 2(4.3%)                | 12(27.3%)                  | 2(50%)                  |         |
| >21                    | 15(83.3%)           | 43(91.5%)              | 28(63.6%)                  | 1(25%)                  | 0.009   |

## DISCUSSION

It is important in our practice to differentiate between severe asthma and uncontrolled asthma. Severe asthma refers to intrinsically severe disease while uncontrolled asthma may be related to additional factors like appropriateness of therapy, adherence, techniques of

inhalation, management of comorbidities.<sup>13</sup> Uncontrolled asthma is what we often come across in clinical practice, hence correction of modifiable factors lead to good control.<sup>13</sup>

This study showed that the low serum vitamin D levels influence the control of asthma as well as severity of

asthma. More number of children (43.5%) in the partly controlled and uncontrolled group (which are together taken as not well controlled) had reduced serum vitamin D levels (<20 ng/ml) as compared to well controlled groups (9%).

The study by Kaaviyaa et al, reported that the vitamin D deficiency is associated with suboptimal asthma control.<sup>3</sup> Whereas in the study by Kavita et al, which involved 105 asthmatic children, did not observe any association between vitamin D levels and on control of asthma.<sup>8</sup> However this study did not include assessment of compliance which is major modifiable factor in control of asthma. Calcitriol is known to inhibit airway smooth muscle proliferation through growth factor induced phosphorylation of RB-protein and check point kinase.<sup>14</sup>

Vitamin D receptors (VDR) are present on cells of immune system such as dendritic cells, macrophages, monocytes, activated T and B lymphocytes.<sup>4</sup> Vitamin D as a immunomodulator regulate transcription of various genes taking part in immune mechanism. It suppresses proinflammatory cytokines (IL-17 and IL-13) and promote anti-inflammatory cytokine IL-10.<sup>4</sup>

This study also showed that insufficient vitamin D levels are significantly associated with moderately persistent and severely persistent asthma. The study by Searing, et al showed vitamin D deficiency increased the incidence and severity of asthma as well as the efficacy of preventive therapy with inhaled corticosteroids.<sup>15</sup> A study by N Esfandir et al, observed that though vitamin D deficiency effectively increases risk for childhood asthma, however the severity or control status may not be predicted by confirming Vitamin D deficiency.<sup>16</sup>

The limitation of our study is that the children were not followed up to see the effect of vitamin D supplementation on control and severity of asthma.

Authors conclude that low serum vitamin D levels are associated with poor control of asthma in children and the severity of asthma is inversely proportional to the serum vitamin D levels. Hence in clinical practice we recommend that, estimating serum vitamin D levels is very important in the management of a child with partly controlled/uncontrolled asthma and in severe asthma.

## ACKNOWLEDGEMENTS

Authors thank to Dr Sudha Rudrappa, Head of the Department, Department of Pediatrics, MMC and RI, Mysuru and Dr P K Vedanthan, International asthma services for their support for asthma clinic.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Savitha MR, Pawar GR. Influence of serum vitamin D levels on control and severity of asthma in children. *Int J Contemp Pediatr* 2020;7:843-7.