

ORIGINAL ARTICLE

THE EFFECT OF VITAMIN D SUPPLEMENTATION ON CHILDREN WITH ALLERGIC RHINITIS

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**Abstract**

**Background:** Allergic rhinitis (AR) is a common pediatric disorder. Vitamin D is known to have effect on helper T-cells, regulatory T-cells, activated B-cells and dendritic cells linking vitamin D to various immune-related conditions and allergies. Vitamin D can significantly affect the outcome of allergic responses in AR.

**Objective:** To study the effect of vitamin D supplementation in the treatment of children with AR.

**Materials and methods:** Forty-two children with AR and low 25 hydroxy (OH) D3 levels were included in the study. Total Nasal Symptom Score (TNSS) and 25 (OH) D3 levels were measured before and after treatment. They were divided in two groups randomly. Both groups were given standard treatment for AR. One group received oral vitamin D (cholecalciferol: 400-800 IU as per age of the child) for 21 days. The results were compared with the other group being treated similarly but without supplementation of vitamin D.

**Results:** Clinical improvement in terms of reduction in the TNSS was significant in the post-Vitamin D supplemented group (TNSS score pre-treatment and post treatment were  $10.6 \pm 2.65$  and  $2.76 \pm 1.6$  respectively in Vitamin D supplemented group and  $11.04 \pm 1.93$  and  $4.66 \pm 1.99$  in the pre and post-treatment group in those who were not supplemented) ( $p=0.01$ ). Significant improvement of Vitamin D levels was found post-treatment in Vitamin D supplemented group ( $23.06 \pm 9.73$  ng/ml) as compared to pre-treatment ( $18.13 \pm 4.55$  ng/ml) ( $p<0.05$ ) while there was no significant difference in group not supplemented with Vitamin D (pre and post treatment  $18.01 \pm 3.95$  ng/ml and  $17.99 \pm 3.83$  ng/ml respectively).

**Conclusion:** Supplementation of vitamin D in patients with AR leads to significant clinical improvement.

**Keywords**

Allergic rhinitis, vitamin D supplementation, immune-modulation.

**Introduction**

Allergic rhinitis (AR) is one of the most common chronic diseases in children characterized by the symptoms of nasal congestion, rhinorrhea, sneezing, and nasal itching. (1) Although AR is not a life-threatening disease, it has a significant influence on the quality of life of the patients. Even though the cause of AR has not been clearly identified, genetic, and environmental factors are known to play an important role in the development of the disease. (2) FOXP33279 AA genotype is more common in AR patients with higher association between polymorphism in FOXP3 gene and susceptibility to AR. (3) In a more recent classification, AR is categorized as mild-intermittent, moderate-severe intermittent, mild-persistent, and moderate-severe persistent. (4) AR is a type-I immunologic reaction characterized by watery rhinorrhea, sneezing, nasal congestion, and itching. The prevalence of the disease has increased during the last decades. (5,6) Treatment options consist of drugs like anti-histamines, intranasal corticosteroids, decongestants, and more

recently immunotherapy. (5,7)

Vitamin D has an effect on both innate and adaptive immunity. It blocks the expression of the Toll-like receptor (TLR) on monocytes, inhibits pro-inflammatory cytokine production, induces antimicrobial peptide synthesis, and affects T-cell activation and function of antigen-presenting cells. It may reduce Th1 cytokine secretion and modulate the immune system through the induction of CD4+ CD25+ regulatory T cells (Tregs). (8-12) There have been conclusive evidences that the immunomodulatory effect of vitamin D may have a major impact on the outcome of allergic illnesses in both adults and children. (13)

In recent years, there has been worldwide increase in allergic diseases more so in developed countries and this has been associated with low vitamin D. (14) Schaubert et al stated that the association between low serum vitamin D levels and an increase in immune disorders is not coincidental. (15) Current lifestyle has led to people spending more times indoors, leading to less sun exposure and less cutaneous vitamin D production. (16) Several studies have investigated the role of vitamin D in the treatment of allergic diseases and asthma, however the results are still controversial. (15-18) Treating Vitamin D deficiency can prevent AR occurrence and thus reduce morbidity. (19) In the present study, the vitamin D status of patients with AR was compared pre- and post-treatment with oral cholecalciferol (dose as per age) and the course of AR was assessed in patients with and without Vitamin D supplementation to find whether Vitamin D supplementation causes significant clinical improvement in patients of AR.

**Methods & Materials**

The study included patients with AR, who visited the pediatric outpatient department during the 1 year period from December 2015 to December 2016. The diagnosis was made by symptoms suggestive of AR (perennial) with thorough ENT examination including Total Nasal Symptom Score (TNSS) to grade severity along with eosinophilia on blood/nasal smear. A total of 44 patients between 5 and 15 years age of both gender with clinical diagnosis of AR were included in the study. Two were excluded later as their Vitamin D levels were normal. Patients who had co morbid disease in addition to AR that could affect vitamin D serum levels such as patients with Juvenile Idiopathic Arthritis, rickets, cystic fibrosis, ulcerative colitis, Crohn's disease, celiac disease, thyroid dysfunctions, and individuals who had received medications including corticosteroids, barbiturates, omega3 and vitamin D were excluded from the study. TNSS were recorded pre and post-treatment. Before and after treatment, patients rated their nasal symptoms (i.e., rhinorrhea, nasal blockage, sneezing, nasal itching, anosmia) using four point scale as follows: 0 = No symptom evident, 1 = symptom present but not bothersome, 2 = definite symptom that is bothersome but tolerable, 3 = symptoms that is hard to tolerate. Each patient's TNSS were calculated by

**Table 1. Effect of Vitamin D supplementation on (TNSS Score)**

Treatment Modality	TNSS		Difference	Significance
	Mean Pre-Treatment	Mean Post-Treatment		
Anti-allergic treatment followed by Vit D supplementation	10.6 ± 2.65	2.76 ± 1.6	7.84	P<0.01
Anti-allergic treatment only	11.04 ± 1.93	4.66 ± 1.99	6.34	

**Table 2. Levels of Vitamin D pre and Post treatment**

Treatment Modality	TNSS		Difference	Significance
	Mean Pre-Treatment	Mean Post-Treatment		
Anti-allergic treatment followed by Vit D supplementation	10.6 ± 2.65	2.76 ± 1.6	7.84	P<0.01
Anti-allergic treatment only	11.04 ± 1.93	4.66 ± 1.99	6.34	

**Table3. Levels of Vitamin D in various TNSS groups**

TNSS (SCORE)	VITAMIN D MEAN LEVELS (ng/ml)		
	PRE-TREATMENT	POST-TREATMENT	
		With Vit D supplement	Without Vit D supplement
>11	16.60	21.22	16.51
7-10	18.63	22.10	18.01
3-6	18.38	23.06	18.30
0-2	18.91	25.86	18.87

summing patients’ nasal symptoms. (8) Serum vitamin D3 levels were measured pre and post-treatment using Enhanced Chemi-luminance method. 25(OH) D3 levels greater than 30 ng/ml was considered as normal, that between 20-30 ng/ml was considered insufficient and that less than 20ng/ml was considered deficient. All patients were treated with fexofenadine (in patients having TNSS score ≤ 10) and fluticasone nasal spray (in patients having TNSS score ≥ 11).Patients were randomly divided into 2 groups. One group did not receive vitamin D3 supplement. The other group was treated with cholecalciferol (400-800 IU according to age) for 21 days. Post-treatment TNSS was assessed and compared for both groups. Also 25(OH) D3 levels were done after 21 days.

**Statistical analysis:** Data were analysed using SPSSR software (version17.0; SPSS, USA). Descriptive statistical analysis and non-parametric statistical tests were used.

**Results**

Male: female ratio was 23:19. Mean age of presentation was 8.6 years. Of the 42 patients evaluated, 16 (38.09%) were experiencing severe signs and

symptoms of the AR (TNSS>11), 20 (47.61%) were considered to be moderate (TNSS: 7-10) and 2 (4.76%) were classified as mild (TNSS: 3-6) and 4 (9.42%) were with TNSS: 0-2 Post-treatment, no patient had TNSS >11, 2(4.76%) had TNSS 7-10, 16(38.09%)had TNSS 3-6 and 24 (57.14%) had score 0-2. The improvement in TNSS scores pre and post treatment in both groups is depicted in Table 1. Post-treatment improvement in the TNSS was indicated by shifting of patients to a lower TNSS. The mean vitamin D level pre and post treatment in both the groups is depicted in Table 2. The levels of vitamin D at different TNSS score is depicted in Table 3.

**Discussion**

Vitamin D plays an important role in modulating immune function by decreasing cytokine release and increasing T-cell proliferation. (20,21) It increases IL-10 and decreases IL-2 production, leading to hypo-responsiveness in T regulatory cells. This type of effect is also seen with anti-allergic therapies such as corticosteroids or allergen immunotherapy. It also affects B lymphocytes functions which modulates the humoral immune response including secretion

of IgE. (20-23) In AR, exposure to allergen like dust mite, cockroach residues, animal dander, moulds, and pollens) causes mast cells, CD4-positive T-cells, B-cells, macrophages, and eosinophils to infiltrate the nasal lining. During the early phase cytokines are released which trigger a further cellular inflammatory response over the next 4-8 hours (late phase inflammatory response) which results in recurrent symptoms (usually nasal congestion). (24,25) Lymphocytes such as T-cell with Th1 and Th2 polarization are major players in adaptive immunity and vitamin D modulates their functions. Furthermore, some immune cells express vitamin D-activating enzymes facilitating local conversion of inactive vitamin D into active calcitriol with subsequent paracrine and autocrine effects. (26,27)

This study showed that the patients of AR showed deficiency in vitamin D. This has been supported by recent studies suggesting the importance of assessing vitamin D levels in patients of AR. (28) In a study performed by Moradzadeh et al (29) the prevalence of severe vitamin D deficiency was significantly greater in patients with AR than the normal population (30% vs. 5.1%;  $P = 0.03$ ) demonstrating that there is an association between serum vitamin D levels and AR. There was improvement in nasal symptoms in patients with Vitamin D supplementation. This observation correlates severity of AR with vitamin D deficiency as studied previously in adult patients with AR. (30) In present study, supplementation of Vitamin D in patients of AR along with treatment of the disease significantly improved the outcome. Very few studies have been done on pediatric patients to assess the correlation between AR and vitamin D. This study is a step towards the same as it compares the symptoms of AR as well as Vitamin D levels before and after treatment.

### Conclusion

There is a correlation between serum vitamin D levels and AR. Supplementation of vitamin D in such patients causes significant clinical improvement in the form of reduced symptoms (TNSS). Studies with a larger number of patients need to be conducted to further consolidate this association and to recommend vitamin D supplementation therapy along with anti-allergic treatment for children with allergic rhinitis.

### Contributor Statement

PU conceptualised study, collected data, did initial drafting of manuscript and approved final manuscript before submission. RJ collected data, searched literature, revised manuscript and approved final manuscript before submission.

**Funding:** None

**Conflict of Interest :** None

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**DOI :** 10.7199/ped.oncall.2017.49

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