

Vitamin D and modulation of Allergic Rhinitis

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Abstract: ***Background:** Allergic rhinitis is a common health problem caused by an immune-mediated inflammatory reaction after allergen exposure. It is not a life-threatening condition but in most cases it interferes with the patient's personal life and imposes a substantial burden on public health in economic terms. Vitamin D deficiency has been blamed as a cause of increased incidence of asthma and allergy symptoms. The significant impairment of quality of life and morbidity caused by allergic rhinitis, and the easily-treated vitamin D deficiency with which it may be associated, motivated the design of this study. **Aims & Objectives:** To evaluate nasal symptom scores in patients of AR, pre- and post-treatment with and without supplementation of vitamin D. **Materials and Methods:** Vitamin D levels were assessed in 27 patients with AR diagnosed clinically and evaluated prospectively during the period of 3 months. The study included patients with allergic rhinitis, who were referred to the Hospital (for routine visits) during a three month period between January 2016 and March 2016. Allergic rhinitis patients were diagnosed clinically using Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 criteria during a medical visit. They received oral vitamin D (chole-calciferol; 1000 IU) for a given period. The results were compared with the patients having AR - treated conventionally without supplementation of vitamin D. **Results:** Clinical improvement in terms of reduction in the total nasal symptom score was significant in the post-treatment patients. **Conclusion:** Supplementation of vitamin D in such patients alters natural course of AR toward significant clinical improvement.*

Keywords: Allergic rhinitis, vitamin D supplementation, immune-modulation

1. Introduction

Allergic rhinitis is a common health problem caused by an immune-mediated inflammatory reaction after allergen exposure. It is not a life-threatening condition but in most cases it interferes with the patient's personal life and imposes a substantial burden on public health in economic terms. The prevalence varies among countries, probably because of geographic and aeroallergen differences.^[1] In India, AR is considered to be a trivial disease, despite the fact that symptoms of rhinitis were present in 75% of children and 80% of asthmatic adults.

Severe AR has been associated with significant impairments in quality of life, sleep and work performance. There are good treatments available for AR, including antihistamines and topical corticosteroids. Yet, there is a need for new treatment options, particularly aiming at new targets and associated with reduced side effects.^[2]

Vitamin D deficiency has been blamed as a cause of increased incidence of asthma and allergy symptoms. In a study conducted by Hollams et al. in Australia, 689 subjects were seen longitudinally at both ages of 6 and 14 years. This study showed that vitamin D levels at ages 6 and 14 years were predictive of allergy/asthma outcomes at both ages, but more importantly, vitamin D levels at age 6 years were predictive of subsequent atopy and asthma-associated phenotypes at age 14 years.

Following patients with chronic rhinosinusitis (CRS), current clinical studies have shown that CRS patients had serum vitamin D levels 40–50% lower than the serum levels in the control group. In a study performed in Iran, vitamin D levels were assessed in 50 patients with allergic rhinitis and the study results were compared with vitamin D status in

normal population. The prevalence of severe vitamin D deficiency was higher in patients with allergic rhinitis than in normal population, 30% and 5.1%, respectively.^[3]

The significant impairment of quality of life and morbidity caused by allergic rhinitis, and the easily-treated vitamin D deficiency with which it may be associated, motivated the design of this study.

2. Materials and Methods

Study design and population

The study included patients with allergic rhinitis, who were referred to the Kirodimal Government Hospital, Raigarh-CG (for routine visits) during a three month period between January 2016 and March 2016. Allergic rhinitis patients were diagnosed clinically using Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 criteria during a medical visit. Twenty-nine patients were enrolled to complete a questionnaire that was designed by comparing 15 standard allergy questionnaires and modified to reflect regional characteristics. The questionnaire concerned demographic data, probable risk factors associated with allergic rhinitis, co-morbid diseases, multiple signs and symptoms of disease and the history of patient's medications.

Exclusion criteria concerned patients who had co-morbid disease in addition to allergic rhinitis that could affect vitamin D serum levels. Such diseases included rheumatoid arthritis, cystic fibrosis, multiple sclerosis, ulcerative colitis, Crohn's disease, celiac disease, rickets, osteomalacia, sarcoidosis and thyroid dysfunctions, and individuals who had received medications including corticosteroids, barbiturates, bisphosphonates, sulfasalazine, omega-3 and vitamin D components such as calcium-D were excluded.

According to the severity of the allergic rhinitis, patients were classified into mild, moderate and severe groups. Classification was based on the duration of symptoms, interference with daily activities and sleep disturbance; using ARIA 2008 criteria, interpolated in the questionnaires.

They (n=14) received tablet levocetirizine 5mg (in patients having score ≤ 10) for a short period (1week) to relieve acute phase without vitamin D3 which was followed by supplementation of oral vitamin D3 (chole-calciferol; 1000 IU) for 21 days.

Another 13 patients between 15 and 50 years of age both gender having a history of AR were assessed in the similar way for pre- treatment score and treated using similar criteria i.e. levocetirizine 5mg (in patients having score ≤ 10) for a week but without supplementation of vitamin D and followed similarly after given period. Post- treatment score were assessed and compared.

Follow- up clinical assessment for nasal symptom score were obtained after 21 days.

3. Statistical Analysis

Data were analyzed using SPSSR software (version 17.0; SPSS, USA). Descriptive statistical analysis and non- parametric statistical tests were used.

Table 1: Nasal Symptoms Scoring System

Rhinorrhea	0-3
Obstruction	0-3
Sneezing	0-3
Itching	0-3
Anosmia	0-3
NSS	0-3
0-Absent, 1-Mild, 2- Moderate, 3-Severe, NSS nasal symptoms score	

4. Results

Initially there were 29 patients. 2 of them dropped. Of the 27 patients enrolled in the study, 14 (51.85%) were men and 13 (48.14%) were women [Table 2]. The mean age of the patients was 26.47 ± 9.25 years. Of the 27 patients evaluated, 9 (33.33 %) were experiencing severe signs and symptoms of the AR(NSS>11), 6(22.22%) were considered to be moderate (NSS: 7-10) and 7 (25.92%) were classified as mild (NSS: 3-6) and 5(18.51%) were with NSS: 0-2 [Table 3].

Table 2: Sex distribution of disease

Sex	No. of patients	Percentage
Male	14	51.85
Female	13	48.14
Total	27	99.99

Table 3: Distribution of patients according to severity pre and post treatment

NSS	No. of patients (%)	
	Pre-treatment	Post-treatment
>11	9 (33.33)	1 (3.7)
7-10	6 (22.22)	4 (14.81)
3-6	7 (25.92)	8 (29.62)
0-2	5 (18.51)	14 (51.85)
NSS-Nasal Symptom Score		

The clinical improvement in terms of reduction in the nasal symptom score was assessed using Wilcoxon signed rank test for pre and post- treatment in our study group where value of $P = 0.0001$. Which shows statistically significant differences between these two groups.

In the control group, this improvement in NSS was also significant when assessed by Wilcoxon signed rank test suggested by value of $P = 0.0001$

In one group of patients with supplementation of Vitamin D the mean pre-treatment NSS score was 9.4 ± 1.50 which got improved following treatment with vit.D & anti- allergic medication & mean post-treatment NSS score was 2.43 ± 0.95 . (Table 4)

In another control group of patients without supplementation of vitamin D, the mean pre-treatment NSS score was 10.5 ± 1.62 which get improved following anti-allergic treatment & mean post-treatment NSS score was 5.32 ± 0.52 . (Table 4)

5. Discussion

Several epidemiological studies have suggested that vitamin D deficiency is associated with an increased incidence of asthma and allergy symptoms, and a number of hypotheses have been advanced to explain the pathogenetic link between asthma and vitamin D deficiency. As mentioned earlier, vitamin D deficiency may weaken pulmonary defenses against respiratory infections and this would contribute to the triggering of asthma exacerbations caused by respiratory tract infections. This was suggested by Jartti et al., who found that serum 25OH vitamin D levels were inversely associated with RSV and rhinovirus infection in wheezing children necessitating hospitalization. There is an increasing body of evidence to support the hypothesis that infections carry a greater morbidity in asthmatic subjects than in the healthy population, indicating a weaker antiviral response in asthmatics. In a study on children in Costa Rica, lower vitamin D levels were associated with increased airway responsiveness and higher eosinophil counts and IgE levels, while higher vitamin D levels were associated with a lower likelihood of hospitalization for asthma exacerbations. [4]

The International Study of Asthma and Allergies in Childhood (ISAAC) demonstrated the highest prevalence of asthma symptoms in countries such as the United Kingdom, Australia, New Zealand, and the Republic of Ireland. This data helped form the foundation for the description that people living in more westernized, developed nations have

higher reported rates of asthma, atopic dermatitis, and hay fever.^[5]

The worldwide increase in allergic diseases such as asthma, allergic rhinitis and food allergy is associated with low serum vitamin D levels. The aim of this study was to measure serum vitamin D levels in patients with allergic rhinitis. Serum vitamin D (25-hydroxyvitamin D), calcium, phosphorus, alkaline phosphatase and parathyroid hormone levels were assessed in 200 patients with allergic rhinitis diagnosed clinically and the results of skin prick tests for aeroallergens. Subjects with serum containing less than 20 ng/ml vitamin D were deemed deficient. The mean vitamin D levels in the study group was found 14.7 ng/ml and 68% of patients had vitamin D deficiency. The present study showed that the majority of allergic rhinitis patients had vitamin D deficiency. Therefore measuring vitamin D serum levels could be helpful in the routine assessment of patients with allergic rhinitis.^[6]

Vitamin D interferes with T-cell proliferation by suppressing Th1 cytokine secretion. The effect of vitamin D on Th2 cells

is still under debate. However, there is one study which demonstrates that vitamin D leads to an increase in interleukin (IL)-10 expression and a decrease in IL-2 expression followed by hypoergia in regulatory T cells, which is associated with a harmful immune response. Also, vitamin D decreases IL-12 production; thus it can reduce the differentiation of Th1 cells and increase the differentiation Th2 cells, which are responsible for allergic reactions. Vitamin D also modulates the secretion of IgE by interrupting the proliferation of B-lymphocytes.⁽⁷⁾

In our study we supplemented the patients of AR with oral vitamin D supplements & such patients were followed to evaluate their clinical status regarding AR. There was an improvement in the nasal symptom score as it is concluded from the presented study.

When the clinical improvement was compared in the control group in which vitamin D supplements were not given, they showed a difference of 5.18 in NSS score which is lower than our study group which showed a difference of 6.97 in NSS score.

Table 4: Effect of vitamin D supplementation

Treatment modality	NSS		Difference
	Mean Pre-treatment	Mean Post-treatment	
Anti-allergic treatment followed by vitamin D supplementation	9.4±1.05	2.43±0.95	6.97
Anti-allergic treatment only without vitamin D supplementation	10.5±1.62	5.32±0.52	5.18
NSS- Nasal Symptom Score			

In a study by Bener et al. the prevalence of vitamin D deficiency among patients with AR was 18.5% versus 10.5% in healthy people.^[8]

In one study patients of allergic rhinitis showed deficiency in vitamin D indicated by mean vitamin D level of 19.52±17.35 ng/ml. This result shows the importance of assessing vitamin D levels in patients of allergic rhinitis. There are other studies coming in support of this fact as stated by SabaArshi et al. The prevalence of severe vitamin deficiency was significantly higher in patients of allergic rhinitis than the normal population. In a study performed by Moradzadeh et al the prevalence of severe vitamin deficiency was significantly greater in patients with allergic rhinitis than the normal population (30% vs 5.1%;p=0.03) demonstrating that there is an association between serum vitamin D levels and allergic rhinitis status.^[9]

6. Conclusion

This study shows a overall improvement in NSS in patients receiving vitamin D along with anti allergic medication which suggest a role of vitamin-D in modulating the immune system in a variety of ways. Although the sample size in our study was less, more studies with a larger number of patients should be conducted to validate the role of vitamin-D supplementation along with initial anti-allergic treatment

7. Acknowledgment

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8. Conflict of Interest

None declared.

References

- [1] Saba A, Babak G, Seyyed-Kamran K, Mina A. Vitamin D serum levels in allergic rhinitis: any difference from normal population? Asia Pac Allergy. 2012 Jan; 2(1): 45–48.
- [2] Modh D, Katarkar A, Thakkar B, Jain A, Shah P, Joshi K. Role of vitamin D supplementation in allergic rhinitis. Indian J Allergy Asthma Immunol 2014, 28:35-9.
- [3] Mehmet H, Maria Z, Leonard D, Gentian V. Vitamin D and Its Role as a Protective Factor in Allergy. Int Sch Res Notices. 2014: 951946.
- [4] Bozzetto S, Carraro S, Giordano G, Boner A, Baraldi E. Asthma, allergy, and respiratory infections: the vitamin D hypothesis. Allergy 2012; 67: 10–17.
- [5] Daniel A Searing, Donald Y M Leung. Vitamin D in Atopic Dermatitis, Asthma and Allergic Diseases. Immunology and Allergy Clinics of North America, Volume 30, Issue 3, Pages 397-409.
- [6] Sukran K, Süheyla SS, Arzu Didem Y, Basak Gol S, Gulsun C. Vitamin D serum levels in allergic rhinitis. World Allergy Organ J. 2015; 8(Suppl 1): A67

- [7] Lee SJ, Kang BH, Choi BS. Vitamin D serum levels in children with allergic and vasomotor rhinitis. Korean Journal of Pediatrics. 2015; 58(9):325-329.
- [8] Vitamin D Deficiency and Allergic Rhinitis in Children: A Narrative Review. Ghaffari J, Alireza R, Annegret Quade. J Pediatr Rev. 2015 July; 3(2):e2623.
- [9] Moradzadeh K, Larijan B, Keshtkar AA, Hossein-Nezhad A, Rajabian R, Nabipour I, *et al.* Normative values of vitamin D among Iranian population: A population based study. Int J Osteoporos Metab Disord 2008; 1:8-15

