

Original Research Article

Serum vitamin D and immunoglobulin E levels in children of allergic rhinitis: a case-control study from Central India

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ABSTRACT

Background: Allergic rhinitis (AR) is the commonest type of non-infective rhinitis. Genetic and environmental factors play an important role in the development of the disease. Researchers are having interest in knowing the role of vitamin D in the pathogenesis of allergy. Immunoglobulin E (IgE) is integral to the pathogenesis of allergic disorders. However, the relationship between serum IgE levels and AR is still a matter of debate. Thus, this study aimed to know serum IgE and serum 25 (OH) vitamin D levels in patients with clinically diagnosed AR and control group.

Methods: A case-control study was performed from May 2019 to October 2019 in LNMC and JK hospital. All 54 children with physician diagnosed AR aged 12 to 18 years of both genders who have come in the OPD (total enumeration sampling) during the above mentioned period were enrolled into the study and their 54 healthy counterparts are taken as controls. Other parameters such as age, gender, occupation and region of residence were also compared between the groups.

Results: This study found highly significant difference in the mean serum IgE levels while there is a significant difference in the mean serum vitamin D levels between two groups.

Conclusions: The study group with AR had significantly higher mean level of serum IgE and lower mean serum vitamin D levels as compared to control groups. However, upon stratification of vitamin D levels, the differences were insignificant. Further studies should be conducted to know the value of IgE as a prognostic factor of AR severity and to throw more light on association of vitamin D with AR.

Keywords: Disease severity, Children, Serum IgE level, Allergen

INTRODUCTION

AR is one of the most common chronic diseases in children characterized by the symptoms of nasal congestion, rhinorrhea, sneezing and nasal itching. It is an immune-mediated phenomenon and is initiated when the allergen is exposed to the nasal mucosa, which potentiates an IgE-mediated inflammatory cascade.¹ 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 Also recently, new research was developed over the years to deal with the function of the immunomodulatory role of calcitriol (the active form of vitamin D) that correlated with AR.³ Vitamin D plays an important role in decreasing sensitivity to allergens. Previous studies have revealed that sensitivity to allergens is higher among children with vitamin D deficiency.⁴ Allergen specific IgE is integral to the pathogenesis of allergic disorders.⁵ However, the relationship between serum IgE levels and

AR is still a matter of debate. Vitamin D deficiency is also associated with increased serum IgE levels.⁶

AR negatively affects quality of life of the patient. It can impact school attendance, social life and routine day to day activities.⁷ Etiology of allergy is still an area of research and trials are ongoing to identify exact etiology of various types of allergy. The prevalence varies among countries, probably because of geographic and aeroallergen differences.⁸⁻¹¹ 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.¹² The prevalence of AR was 11.9% among Indian children aged 6-7 years and 24.4% in children aged 13-14 years, with an average of 17.13%.¹³ Nevertheless, previous findings of the relationship between serum vitamin D levels and AR were still controversial.

Some studies have revealed a correlation between vitamin D deficiency and allergic diseases, while some others have found no association between these two variables.^{14,15} In other words, the relationship between serum vitamin D levels with AR is still unclear, hence, further study is needed to obtain more accurate results. Main objective of this study was to assess serum IgE and serum 25 (OH) vitamin D levels in patients with clinically diagnosed AR and compare the same parameters in the control group where normal subjects were included.

METHODS

A case-control study was performed from May 2019 to October 2019 in paediatric OPD of LNMC and JK hospital. All 54 children with physician diagnosed persistent, moderate to severe AR patients as per ARIA-WHO guidelines aged 12 to 18 years of both genders who have come in the OPD (total enumeration sampling) during the above-mentioned period were enrolled in to the study as cases and their 54 healthy counterparts were included as the controls group after seeking informed consent. Controls were selected from the attendants of these patients to maintain socio-demographic equity.

Ethical approval

Ethical clearance was sort from institute's ethical committee and the study was approved by the Institutional Research Board of LNMC and JK hospital Bhopal (registration number: ECR/1190/INST/MP/2019).

Inclusion criteria

Patients having history of AR were included in the study.

Exclusion criteria

Patients aged less than 12 years and more than 18 years, patients taking/taken any form of vitamin D supplements

in past one year and patients with acute respiratory tract infections, acute and chronic paranasal sinusitis, severe septal deviation, obstructive nasal disease, upper respiratory infection, asthma under treatment and hypercalcemia were excluded.

For all study participants, demographic characteristics included in the study were age, gender, residence (rural/urban) and occupation (indoor/outdoor) were recorded. Clinical characteristics including height and weight were recorded in meters and kilograms, respectively. Body mass index (BMI) was calculated as weight divided by height squared. BMI was classified as underweight (<18.5 kg/m²), ideal (18.5-24.9 kg/m²) and obese (>25 kg/m²) as evident by the WHO classification.¹⁶

3 ml of blood was withdrawn for measuring serum 25 (OH) D, IgE levels. 25 (OH) D levels were assessed by chemiluminescence micro particle immunoassay (Abbott ARCHITECT i2000 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.¹⁷ IgE levels were described as normal or deficient based on age appropriate standard lab references.¹⁸

For biostatistical analysis, SPSS version 21.0 (IBM Corp., Armonk, NY) was utilized. For continuous variables, mean and standard deviation (SD) were calculated and the independent t test was used for comparison. For stratified variables, frequencies and percentages were calculated and chi-square was used for comparison. A p value of ≤ 0.05 was considered statistically significant.

RESULTS

Our study comprised of 108 participants. 54 cases in group I and 54 controls in group II. Study population had slightly greater number of male subjects both in case and control groups. Most of the study samples belonged to rural area (n=70, 65%) and did outdoor jobs (n=65, 60%). When comparison was made regarding gender, residence and occupation between case and controls, statistically there was no significant difference (Table 1).

Cases of AR children had mean age of 15.6±3.4 years and of controls as healthy counter parts had mean age of 17.2±3.9 years. The difference was statistically non-significant (p=0.02). When serum IgE levels between both the study groups was studied it was seen that the patients of allergic rhinitis had mean serum IgE level of 546.5±50.9 IU/ml as compared to 214.2±29.2 IU/ml in controls. The difference was statistically highly significant; p<0.0001. Mean serum vitamin D levels in

patients of AR group was 16.4 ± 8.4 ng/ml as compared to 21.4 ± 7.1 ng/ml in controls. The difference was statistically significant ($p=0.002$). But when further stratification of vitamin D levels into adequate,

inadequate and deficient was made and each subgroup was compared between cases and controls, it was found to be statistically not significant ($p=0.09$) (Table 2).

Table 1: Comparison of the characteristics of AR patients and their healthy counter parts in the study.

Parameters	Group I cases (N=54) (%)	Group II controls (N=54) (%)	P value
Gender			
Male	39 (72)	43 (79)	0.20
Female	15 (28)	11 (21)	
Region of residence			
Urban	20 (37)	18 (33)	0.48
Rural	34 (63)	36 (67)	
Occupation			
Indoor jobs	15 (28)	28 (52)	0.005
Outdoor jobs	39 (72)	26 (48)	
BMI (kg/m²)			
Under weight (<18.5)	15 (28)	25 (46)	0.04
Ideal (18.5-24.9)	23 (43)	16 (30)	
Obese (>25)	16 (29)	13 (24)	
Serum IgE (IU/ml)			
Normal	15 (28)	46 (85)	<0.00001
Raised	39 (72)	8 (15)	
Serum 25 OH vitamin D (ng/ml)			
Adequate (>30)	6 (11)	14 (26)	0.09
Inadequate (20-30)	35 (65)	32 (59)	
Deficient (<20)	13 (24)	8 (15)	

Table 2 : Baseline parameters of AR patients and their healthy counter parts in the study.

Variables	Group I cases (N=54)	Group II controls (N=54)	P value
	Mean±SD	Mean±SD	
Age	15.6±3.4	17.2±3.9	0.02
Serum IgE (IU/ml)	546.5±50.9	214.2±29.2	<0.0001
Serum vitamin D3 (ng/ml)	16.4±8.4	21.4±7.1	0.002

DISCUSSION

In AR, numerous inflammatory cells, including CD4-positive T-cells, B-cells, macrophages and mast cells, infiltrate the nasal lining upon exposure to an inciting allergen (most commonly cockroach residues, molds, pollens and airborne dust mite residues).¹⁹ During the early phase of an immune response to an inciting allergen the mediators and 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).²⁰ Infiltration of inflammatory cells is evident in both seasonal and perennial form, though the magnitude of these cellular changes is somehow different in seasonal and perennial AR.²¹

In our study, the study group with AR had significantly higher mean level of serum IgE as compared to the control group. Similar results were found in the study conducted by Angelo et al.²² The study conducted by Rene et al contradicts the outcome of our study and shows that high IgE levels did not have correlation with the higher frequency of concurrent infections.²³ IgE is the basis of all allergic responses, it has been shown to have an inverse relationship with serum vitamin D levels. Patients with low levels of vitamin D have high levels of IgE.²⁴ Similar results were found in the study conducted by Milovanovic et al which stated that there was a significant negative correlation between serum vitamin D levels and IgE.²⁵ The study conducted by Yip et al found that vitamin D could suppress the activity of IgE mediated mast cells.²⁶

The T-cells infiltrating the nasal mucosa are predominantly T helper 2 (Th 2) in nature and release cytokines (IL-3, IL-4, IL-5 and IL-13) that promote IgE production by plasma cells. IgE production, in turn, triggers the release of mediators such as histamine and leukotriene which leads to arteriolar dilation, increased vascular permeability, itching, rhinorrhoea (runny nose), mucous secretion and smooth muscle contraction.²⁷

The prevalence of serum vitamin D deficiency was significantly higher in patients with AR than the normal population. In a study performed by Moradzadeh et al the prevalence of severe vitamin D deficiency was significantly greater in patients with AR than the normal population (30% versus 5.1%; p=0.03) demonstrating that there is an association between serum vitamin D levels and allergic rhinitis status.²⁸

In our study, both groups had deficient levels of vitamin D. The study group with allergic rhinitis had significantly lower mean levels of serum vitamin D as compared to the control group. However, upon stratification of vitamin D3 levels into further sub groups, the results were not significant. Similar results were found in the study conducted by Dogru et al and Bener et al which didn't show positive correlation between levels of vitamin D3 and AR.^{29,30} There are few studies which contradict the outcome of above studies. In a study conducted by Wjst et al there was a positive association between levels of vitamin D3 and AR.³¹ Similar study known as third national health and nutrition examination survey III study in Germany found that AR prevalence increased with levels of 25 (OH) D3 in all subgroups.

Our study has certain limitations. Firstly, the sample size was small and a large proportion of the study sample was outdoors which was thought to bring a bias on higher vitamin D levels to the study (due to sun exposure). Secondly, the relationship between IgE and AR should be investigated in a large population so that it can be considered as a prognostic factor of AR severity.

CONCLUSION

The study group with AR had significantly higher mean level of serum IgE as compared to control group and having inverse relationship with serum vitamin D levels. The AR group had significantly lower mean levels of serum vitamin D than the control group. However, upon stratification, the differences were insignificant. Further studies with robust randomization and blinding including larger population and addition of more allergy parameters should be conducted to know the value of IgE as a prognostic factor of AR severity and to identify exact relation of vitamin D with AR.

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