

The relation between serum vitamin D deficiency and allergic rhinosinusitis

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Received 09 July 2020

Revised 20 August 2021

Accepted 04 October 2021

Published 31 March 2022

Pan Arab Journal of Rhinology
2021, 11:129–133

Background

It has been reported that the prevalence of allergic diseases, including asthma, food allergy, and allergic rhinitis (AR), is strongly associated with vitamin D deficiency. This study was conducted to evaluate the relation between vitamin D levels and AR in Egyptian patients.

Patients and methods

A total of 100 AR cases and 50 healthy controls were included. Cases were subjected to complete history taking and ENT examination. Vitamin D and immunoglobulin E levels were ordered for both cases and controls.

Results

No significant difference was detected between cases and controls regarding demographics. Regarding total nasal symptom score, it was mild in 44 cases, whereas 56 cases had moderate to severe scores. Serum vitamin D levels were significantly lower in cases compared with controls (16.9 vs. 28.3 ng/ml – $P < 0.001$). Besides, vitamin D had lower levels in cases with higher total nasal symptom score. Conversely, immunoglobulin E was significantly higher in rhinitis cases compared with controls (1071.4 vs. 208.7 IU/ml – $P < 0.001$). With a cutoff value of 13.6 ng/ml, lower vitamin D levels had sensitivity and specificity of 95.7 and 82.2%, respectively, to identify AR cases.

Conclusion

It is evident that low vitamin D levels are associated with AR. Moreover, the more deficiency detected in its levels, the more severe symptoms experienced by patients.

Keywords:

allergic rhinitis, immunoglobulin E, total nasal symptom score, vitamin D

Pan Arab J Rhinol 11:129–133

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Introduction

Allergic rhinitis (AR) affects ~10–20% of the general population, and its incidence keeps increasing. It is an inflammatory disorder affecting the nasal mucosa, and it is mediated by immunoglobulin E (IgE) after exposure to allergens [1].

The severity of symptoms in AR cases could be assessed subjectively via the total nasal symptom score (TNSS) or objectively via estimating serum IgE levels. Moderate to severe AR is present in ~67.5% of the AR population and affects the quality of life [2].

Multiple studies have pointed to the association between diminished vitamin D levels and allergic disorders. Vitamin D deficiency is considered one of the world health problems, and it can lead to acute and chronic morbidities [3].

Vitamin D can play a role in the pathogenesis of AR, as it has a crucial effect on the body's immune cells. A previous Indian research reported that vitamin D deficiency was detected in 91% of AR cases [4]; nevertheless, other studies failed to detect this relationship [5,6].

There is still a major controversy regarding this association. Most studies reported that there was a strong association between vitamin D deficiency and AR. Moreover, a strong negative correlation was also reported between serum vitamin D levels and TNSS [7,8].

Conversely, some other studies showed different results in the response of interleukin (IL)-4 and IL-13 in mice bronchoalveolar secrete after being given vitamin D [9,10].

In other words, the relationship between serum vitamin D levels with AR and TNSS is still unclear; hence, further study is needed to obtain more accurate results [11].

This study was conducted in Benha University Hospitals aiming to evaluate the relation between vitamin D levels and AR in Egyptian patients.

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Patients and methods

This is a case-control study that was conducted during the period of 1 year (from January 2019 till January 2020) at the Otorhinolaryngology Department of Benha University. We included 150 participants, comprising 100 cases with AR (cases group) and 50 healthy controls (control group).

Cases with liver disease, kidney disease, pregnancy, hypertension, paranasal sinusitis, septal deviation, or respiratory tract infections were excluded from our study.

An informed oral consent was obtained from all cases and controls before participating in the study. Besides, the study was approved by the local ethical committee of Benha University.

All cases were subjected to complete history taking and thorough ENT examination. The TNSS was assessed for all cases [11]. Moreover, serum vitamin D and IgE levels were ordered for both cases and controls.

Serum vitamin D was measured using the electrochemiluminescence immunoassays method via Cobas E411 (fully automated) hormone-immunoassay analyzer. For IgE levels, a 1470 Wizard gamma-counter (PerkinElmer, Helsinki, Finland), along with ImmunoCAP 100 (Phadia, Sweden), was utilized.

Statistical analysis

The collected data were coded, processed, and analyzed using the Statistical Package for Social Sciences, version 22 for Windows (IBM SPSS Inc., Chicago, Illinois, USA). Data were tested for normal distribution using the Shapiro-Wilk test. Qualitative data were represented as frequencies and relative percentages. χ^2 test was used to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean \pm SD. Independent samples *t* test was used to compare between two independent groups of normally distributed variables (parametric data). Receiver operator characteristic curve was tested to calculate the diagnostic ability of quantitative variable in prediction of categorical outcome. *P* value less than 0.05 was considered significant.

Results

The mean age of the included cases was 29.4 years, whereas it was 28.3 years for controls. We included 68 and 30 female cases in case and control groups,

respectively. No significant difference was detected between cases and controls regarding these parameters ($P > 0.05$). Table 1 illustrates these data.

In the case group, most cases had persistent AR symptoms (82%), whereas the rest of the cases had intermittent symptoms. These data are illustrated in Table 2.

Regarding TNSS, it was mild in 44 cases, whereas 56 cases had moderate to severe scores (Table 3).

It was evident that serum vitamin D levels was significantly lower in cases compared with controls (16.9 vs. 28.3 ng/ml – $P < 0.001$). Table 4 shows these data.

Conversely, IgE was significantly higher in rhinitis cases compared with controls (1071.4 vs. 208.7 IU/ml – $P < 0.001$). Table 5 illustrates these data.

As illustrated in Table 6, on analyzing vitamin D and IgE levels according to TNSS, it was evident that cases with moderate to severe symptoms had significantly higher IgE levels, and significantly lower vitamin D levels, compared with cases with mild disease.

With a cutoff value of 13.6 ng/ml, lower vitamin D levels had sensitivity and specificity of 95.7 and 82.2%, respectively, to identify AR cases, with an accuracy of 88.6%. Table 7 and Fig. 1 illustrate these data.

Table 1 Comparison of the demographic data in the two study groups

	Groups [n (%)]		Test of significance	<i>P</i>
	Allergic rhinitis (n=100)	Control group (n=50)		
Sex				
Males	32 (32)	20 (40)	$\chi^2=2.106$	0.124
Females	68 (68)	30 (60)		
Age (years)				
Mean \pm SD	29.4 \pm 6.65	28.3 \pm 5.32	<i>t</i> =1.087	0.275
Range	21-43	219-39		

Table 2 Analysis of allergic rhinitis classification in the cases included in the study

Items	Cases with allergic rhinitis (n=100) [n (%)]
Intermittent	18 (18)
Persistent	82 (82)

Table 3 Analysis of total nasal symptom score in the cases included in the study

Items	Cases with allergic rhinitis (n=100) [n (%)]
Mild	44 (44)
Moderate-severe	56 (56)

Table 4 Comparison of serum levels of vitamin D in the two study groups

	Groups		Test of significance	P
	Allergic rhinitis (n=100)	Control group (n=50)		
Vitamin D Levels (ng/ml)				
Mean±SD	16.9±6.18	28.3±6.32	t=-6.043	<0.001**
Range	8.3-29.5	14.1-43.4		

Table 5 Comparison of serum levels of immunoglobulin E in the two study groups

	Groups		Test of significance	P
	Allergic rhinitis (n=100)	Control group (n=50)		
IgE (IU/ml)				
Mean±SD	1071.4±673.75	208.7±38.76	t=11.765	
Range	503-3006	161.4-295.8		<0.001**
IgE, immunoglobulin E.				

Discussion

This study was conducted at Benha University Hospitals aiming to evaluate the relation between vitamin D levels and AR in Egyptian patients. We included a total of 100 cases with AR in addition to 50 healthy controls.

Another study handling the same perspective included a total of 50 AR cases together with 50 controls [12].

In the current study, no significant difference was detected between cases and controls regarding age ($P=0.275$). The mean age was 29.4 and 28.3 years for cases and controls, respectively.

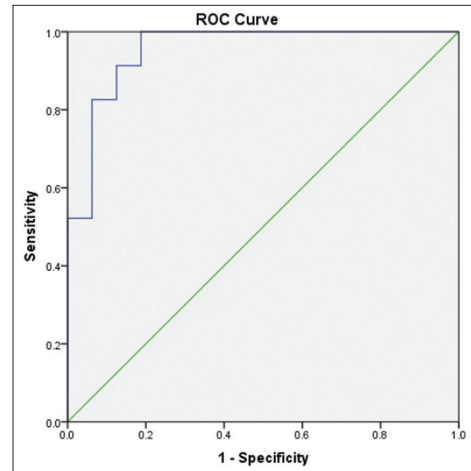
Another study also reported no significant difference between cases and controls regarding age ($P>0.05$). Age ranged between 8 and 64 years in cases, whereas it ranged between 20 and 69 years in the control group [13].

In another study, age was significantly different between cases and controls ($P<0.001$). It had a mean of 28.387 and 35.33 years in cases and controls, respectively [11].

In our study, no significant difference was detected between the two groups regarding sex ($P=0.124$). Males represented 32 and 40% of cases and controls, respectively.

In another study, there was no significant difference between cases and controls regarding sex ($P=0.20$). Males represented 76 and 86% of cases and controls, respectively [12]. The study reported no significance like ours. However, there was male predominance in contrast to ours.

Regarding TNSS in the current study, it was mild in 44 (44%) cases, whereas 56 (56%) cases had moderate to severe scores.

Figure 1

ROC curve for vitamin D levels to identify AR. AR, allergic rhinitis; ROC, receiver operator characteristic.

In another study, mild TNSS score was detected in five (33.33%) cases, whereas 10 (66.67%) cases had moderate–severe TNSS score [11].

In our study, IgE was significantly higher in rhinitis cases compared with controls (1071.4 vs. 208.7 IU/ml – $P<0.001$).

In another study, raised IgE was detected in 76% of AR cases, whereas it increased in only 12% of controls. There was a significant increase in IgE levels in cases compared with controls (553.5 vs. 219.4 IU/ml – $P<0.001$) [12]. This comes in line with our findings.

IgE, which mediates allergic immune responses, 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 [14].

Milovanovic *et al.* [15] stated that there was a significant negative correlation between serum vitamin D levels and IgE. That study result was from the study conducted by Yip *et al.* [7], which found that vitamin D could suppress the activity of IgE-mediated mast cells.

Regarding vitamin D levels in the current study, it was evident that serum vitamin D levels were significantly lower in cases compared with controls (16.9 vs. 28.3 ng/ml – $P<0.001$). With a cutoff value of 13.6 ng/ml, lower vitamin D levels had sensitivity and

Table 6 Correlation between total nasal symptom score and vitamin D and immunoglobulin E levels

	Groups		Test of significance	P
	Mild ART (n=44)	Moderate to severe (n=56)		
Vitamin D levels (ng/ml)	21.56±4.25	14.76±3.87	t=3.165	0.019*
IgE (IU/ml)	698.76±216.98	1043.76±450.87	t=-8.188	<0.001**

IgE, immunoglobulin E.

Table 7 Analysis of the diagnostic ability of vitamin D levels to identify allergic rhinitis

Diagnostic criteria	Data
AUC	0.954
Cut off point	<13.6
Sensitivity	95.7%
Specificity	82.2%
PPV	96.4%
NPV	94.3%
Accuracy	88.6%
P	0.001*

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.

specificity of 95.7 and 82.2%, respectively, to identify AR cases, with an accuracy of 88.6%.

There have been various reports of AR in children and adults with low levels of vitamin D [16,17]. Similarly, there have been reports of antenatal maternal vitamin D deficiency with a higher incidence of atopy in newborns [18].

The Nord-Trøndelag Health Study (HUNT) was a longitudinal cohort conducted in Norway. It collected serum vitamin D levels at baseline and then followed the individuals for around 11 years. In men, 9% developed AR; the adjusted odds ratio was 2.55 at vitamin D less than 50 nmol/l. In women, 15% developed AR; however, the adjusted odds ratio was 0.83 for each 25 nmol/l reduction in vitamin D levels [19].

Another study also confirmed these findings, as the mean levels of vitamin D were 9.13 and 26.22 ng/ml in both cases and controls, respectively ($P<0.001$). The receiver operator characteristic analysis curve showed that the cutoff points related to AR were 12.83 ng/ml, with 100% sensitivity and 80% specificity [11].

In a similar study, serum vitamin D levels were significantly higher in controls compared with cases (19.1 vs. 14.8 ng/ml – $P=0.002$) [12].

Another study has reported most AR cases had vitamin D deficiency. The mean vitamin D levels in the study group was found to be 14.7 ng/ml and 68% of patients had vitamin D deficiency [20].

In a study performed in Iran, vitamin D levels were assessed in 50 patients with AR, 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 AR than in normal population (30 and 5.1%, respectively) [13].

Some interventional studies have highlighted the role of supplementation of vitamin D in the alleviation of AR symptoms. In Heine *et al.* [21], vitamin D supplementation in vitamin D-deficient mice resulted in immunomodulation, which favored protection against allergic triggers. Production of pro-inflammatory cytokines was reduced and that of anti-inflammatory cytokines was increased by vitamin D supplementation. Jerzyńska *et al.* [22] supplemented children with vitamin D during the pollen season and observed fewer manifestations of AR as compared with the placebo group.

Furthermore, a study in India found that vitamin D deficiency occurred in 91% of the total AR samples and a significant improvement shown in TNSS after vitamin D supplementation [23].

The mechanism of action of vitamin D can be explained by its ability to control Th2-mediated cell regulation. It controls the APC by decreasing lipopolysaccharide activity, enhancing the tolerogenic phenotype of dendritic cells, and inhibiting APC differentiation [24]. Vitamin D inhibits mast cell differentiation and can cause mast cell apoptosis within 30–40 days. The inhibitory pathway of other mast cells was by inhibiting IgE and IL-4 [25].

On the contrary, in a study with Turkish children, the mean levels of vitamin D were significantly higher in AR cases compared with non-allergic cases and controls (18.07±6.1 ng/ml in AR vs. 14.81±4.86 ng/ml in the non-AR group, and 24.03±9.43 ng/ml in controls – $P=0.001$). More children in non-AR were vitamin D deficient as compared with (AR 67 vs. 89%). Vitamin D levels did not statistically correlate with allergen sensitivity and AR duration and severity [5]. This contradicts with our findings.

Furthermore, a previous meta-analysis has concluded that vitamin D level may not relate with neither the prevalence of the current AR nor the development of AR [6].

In the current study, on analyzing vitamin D and IgE levels according to TNSS, it was evident that cases with moderate to severe symptoms had significantly higher IgE levels, and significantly lower vitamin D levels, compared with cases with mild disease. Vitamin D had a mean level of 21.56 and 14.76 in mild and moderate to severe cases, respectively ($P=0.019$).

In another study, there was a significant negative relationship between serum vitamin D levels and TNSS of the patients with AR ($P<0.001$). The correlation coefficient (r) between the two variables was -0.8 , which indicated that the two variables had a strong negative correlation [11]. This agrees with our findings.

Furthermore, the results of this study were similarly reported by the study by Thakkar *et al.* [8], which also found a negative relationship between serum vitamin D levels and TNSS with moderate correlation strength.

This study has some limitations. First of all, the sample size was relatively small. Therefore, more studies including more cases should be conducted in the future. Second, cases with vitamin D deficiency should have been treated with vitamin D to determine its effect on AR improvement.

Conclusion

Based on our findings, it is evident that low vitamin D levels are associated with AR. Moreover, the more deficiency detected in its levels, the more severe symptoms experienced by patients. These findings encourage practitioners to correct vitamin D levels in such cases.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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