J Chin Med Assoc

ORIGINAL ARTICLE

Serum level and clinical significance of vitamin E in pregnant women with allergic rhinitis

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Abstract

Background: Allergic rhinitis is a frequent disorder during pregnancy, while in children it is triggered by significantly lower serum vitamin E level. This research aimed to investigate whether serum vitamin E level exhibited clinical significance in pregnant women with allergic rhinitis.

Methods: In this study, 37 pregnant women with allergic rhinitis and 35 healthy pregnant women were recruited. Allergic rhinitis severity was analyzed by the Total Nasal Symptom Score (TNSS) questionnaire. Blood samples were collected to evaluate serum vitamin E, interleukin (IL), and total IgE levels.

Results: In pregnant women with allergic rhinitis, serum level of vitamin E was significantly lower than in healthy pregnant women. Serum vitamin E level in pregnant women with allergic rhinitis showed a negative correlation with TNSS, IL-13, IL-4, and total IgE levels.

Conclusion: In conclusion, this research has demonstrated that pregnant women with allergic rhinitis showed significantly lower serum level of vitamin E. The decreased vitamin E showed a correlation with the pathogenesis of allergic rhinitis in pregnant women.

Keywords: Allergic rhinitis; IgE; Pregnant women; Vitamin E

1. INTRODUCTION

As a common disorder, allergic rhinitis during pregnancy is characterized by nasal congestion with no respiratory tract infection and known allergic cause during the last 6 or more weeks of pregnancy.[1] The process of pregnancy may aggravate nasal obstruction, initiate nasal allergy, and cause allergic rhinitis.[2] In nasal mucosa, enhanced inflammatory response caused by allergic rhinitis induces the generation of several different clinical symptoms, including congestion, itching, sneezing, and nasal discharge.[3] As shown by epidemiological data, nearly 20% of pregnant women suffer from allergic rhinitis and the incidence rate of allergic rhinitis during pregnancy is predicted to increase in the next few years.[4,5] Although allergic rhinitis is a common disorder during pregnancy, it is often underestimated or ignored. After evaluating the symptoms of allergic rhinitis, research has illustrated that approximately 30% of patients have worsened situations during pregnancy.[6]

The therapeutic strategies of allergic rhinitis include avoidance of allergen, specific immunotherapy, and pharmacological therapy.[7] Although the elimination of allergen exposure is a direct treatment for allergic rhinitis, the efficiency of this strategy is limited, especially for outdoor allergens.[8] Antihistamines and corticosteroids are the two most commonly used medicines for allergic rhinitis, which provide temporary symptom relief with several side effects.[9] A simple alternative treatment for allergic rhinitis is nasal irrigation through isotonic solutions.[10] Since the performance of pharmacological therapy introduces additional risks, caution should be taken when administering drugs to pregnant women. Thus, understanding the molecular mechanism underlying pregnant-related allergic rhinitis pathogenesis is critical for developing novel therapeutic strategies.

Several studies have reported the mechanism of pregnancy allergic rhinitis. It is demonstrated that estrogen is the main cause of nasal epithelial cell receptor expression, vasodilation, and gland secretion.[11] Recently, evidence has illustrated the relationship between vitamin D deficiency and allergic diseases, and in particular a negative correlation between serum vitamin D and allergic rhinitis.[12,13] Another research has shown that the occurrence of allergic rhinitis in children is triggered by significantly lower serum vitamin E level.[14] However, the correlation between vitamin E and pregnancy allergic rhinitis is still unknown. In this study, we investigated whether the pathogenesis of allergic rhinitis during pregnancy was correlated with serum vitamin E level.

2. METHODS

2.1. Patient eligibility

In this randomized controlled trial, all pregnant women were recruited in the Maternal and Child Health Hospital of Wuxi, Nanjing Medical University from 2018 to 2019. This research was approved by the Ethics Committee of Maternal and Child

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Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2022) 85: 597-602.

Received March 9, 2021; accepted May 14, 2021.

doi: 10.1097/JCMA.0000000000000723.

Health Hospital of Wuxi, Nanjing Medical University. In this research, 37 pregnant women with allergic rhinitis were recruited. Meanwhile, the healthy control group was composed of 35 healthy pregnant women with matched age and gender.

Inclusion criteria were: (1) single pregnancy; (2) age >18 years; (3) written informed consent. Exclusion criteria were: (1) having acute or chronic respiratory diseases; (2) pregestational body mass index (BMI) >29.9 kg/m^2; (3) twin pregnancy; (4) having gestational hypertension or diabetes mellitus; (5) Having smoking and/or alcohol consumption during pregnancy.

2.2. Allergic rhinitis diagnosis

Allergic rhinitis in pregnant women was diagnosed through examination of the ear, nose, and throat, skin-prick test, and total serum IgE level measurement by ear nose and throat specialists. None of the patients were administrated with corticosteroids or other anti-inflammatory drugs.

2.3. Rhinitis symptoms

The Total Nasal Symptom Score (TNSS) questionnaire was employed to assess the degree of rhinitis symptoms. Four individual symptoms were scored, including sneezing, itching, rhinorrhea, and nasal congestion. The score for each symptom was 0 to 3, 0 = none, 1 = mild, 2 = moderate, and 3 = severe. Total nasal symptom score was the sum of four symptom scores and ranged from 0 to 12.

2.4. Blood sample

Venous blood samples were collected from relative participants. Blood samples were centrifuged at 1500 rpm for 15 min to collect the serum. All samples were stored at –80°C.

Serum vitamin E level was evaluated through LC-20AD high-performance liquid chromatography (Shimadzu, Japan). Serum vitamin E level was adjusted by total cholesterol and triglycerides.

The serum levels of interleukin (IL)-13 and IL-4 were measured by Human IL-13 ELISA Kit (ab178014, Abcam, Cambridge, MA, USA) and Human IL-4 ELISA Kit (ab215089, Abcam) based on the manufacturer's instructions.

The serum level of total IgE was measured by fluorescence enzyme immunoassay using Immuno-CAP 100 (Phadia, Uppsala, Sweden).

2.5. Statistical analyses

In this research, statistical analyses were performed by SPSS version 17.0 software. The data were presented as mean ± standard deviation (SD) or number (n) and proportion (%). The differences in continuous variables between different groups were compared by Mann–Whitney test. Fisher's exact test or chi-square test was used for assessing the distribution of phenomena or observations between different groups. Linear correlations were verified using Spearman's correlation analysis. The diagnostic value of serum vitamin E level was evaluated by nonparametric receiver operating characteristic (ROC) analyses. The area under the curve (AUC) showed the diagnostic accuracy. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns means no significance.

3. RESULTS

3.1. Comparison of demographic characteristics between pregnant women with allergic rhinitis and control

In total 37 pregnant women with allergic rhinitis and 35 healthy pregnant women were recruited in this research. The demographic characteristics of the participants in these two groups were shown in Table 1. Based on the results of statistical analyses, these two groups were homogenous for age, BMI, obstetrical history, and gestational age. In pregnant women with allergic rhinitis, the percentages of women with previous allergic rhinitis or use of nasal decongestants were significantly higher than in healthy pregnant women.

Table 1

Demographic characteristics of the study population.

Variable	Study group: Allergic Rhinitis (n = 37)	Study group: Control (n = 35)	*p*
Age (years)	28.57 ± 5.64	25.48 ± 4.77	0.371
BMI (kg/m^2)	23.7 ± 3.6	24.2 ± 4.1	0.663
Previous spontaneous delivery	8 (21.6 %)	6 (17.1 %)	0.768
Previous caesarean section	4 (10.8 %)	5 (14.3 %)	1
Gestational age			
I trimester	13 (35.1 %)	10 (28.6 %)	0.654
II trimester	14 (37.8 %)	17 (48.6 %)	
III trimester	10 (27.1 %)	8 (22.8 %)	
Previous allergic rhinitis	14 (37.8 %)	2 (5.7 %)	0.001
Previous use of nasal decongestants	8 (21.6 %)	0 (0 %)	0.004

Values were expressed as n (percentage, %) or mean ± SD. p values for each group were derived from Mann–Whitney test. Chi-square test or Fisher's exact test was used for assessing distribution of observations or phenomena between different groups.

3.2. Correlative analysis of serum vitamin E level and TNSS

As shown in Fig. 1A, pregnant women with allergic rhinitis displayed significantly higher TNSS scores than healthy pregnant women. Meanwhile, the levels of serum vitamin E in pregnant women with allergic rhinitis were much lower than in healthy people (Fig. 1B). Spearman's correlations showed a negative correlation between TNSS and serum vitamin E levels in pregnant women with allergic rhinitis (Fig. 1C).

3.3. Correlative analysis of serum vitamin E level and serum IgE level

The pathogenesis of allergic rhinitis in pregnant women dramatically elevated the levels of serum IgE (Fig. 2A). Since serum vitamin E levels were decreased in patients with allergic rhinitis, serum IgE levels showed a negative correlation with vitamin E in pregnant women with allergic rhinitis (Fig. 2B).

3.4. Correlative analysis of serum vitamin E level and serum IL-13 and IL-4 levels

Allergic rhinitis induced the release of pro-inflammatory cytokines such as IL-13 and IL-4. As shown in Fig. 3A and 3B, pregnant women with allergic rhinitis showed significantly higher serum IL-13 and IL-4 levels than healthy pregnant women. Based on the results of Spearman's correlations, both serum IL-13 and IL-4 levels displayed negative correlation with serum vitamin E in pregnant women with allergic rhinitis (Fig. 3C and 3D).

3.5. Diagnostic accuracy of serum vitamin E level for allergic rhinitis in pregnant women

ROC analysis evaluated the diagnostic accuracy of serum vitamin E level. Results illustrated that the AUC for serum vitamin E level was 0.8494 (Fig. 4). Thus, serum vitamin E level was an effective marker in diagnosis of allergic rhinitis in pregnant women.

4. DISCUSSION

Allergic rhinitis is a chronic allergic inflammatory disease in the respiratory tract. Epidemiological investigations have shown that

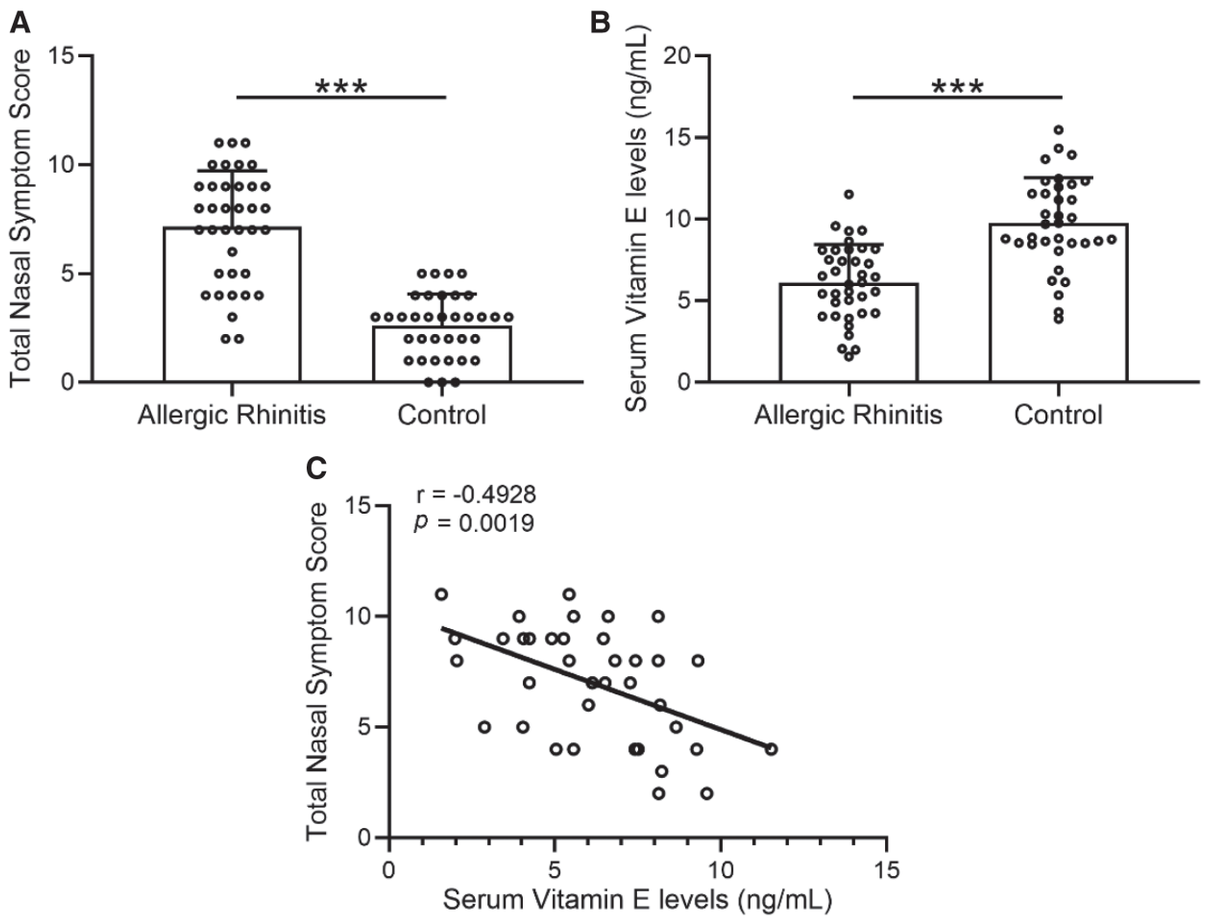

Fig. 1 Total nasal symptom score (TNSS) showed negative correlation with serum vitamin E level in pregnant women with allergic rhinitis. The comparisons of TNSS (A) and serum vitamin E levels (B) between pregnant women with allergic rhinitis and healthy pregnant women. Data were presented as mean ± SD. *** $p < 0.001$, Mann Whitney test. C. Spearman's correlations between total nasal symptom score and serum vitamin E levels in pregnant women with allergic rhinitis.

its incidence has increased recently, and the continuous deterioration of the environment in various countries is the main inducing factor. Due to the existence of various known or unknown allergens in the environment, long-term repeated episodes of allergic rhinitis are difficult to cure, and induce chronic complications such as asthma, sinusitis, and nasal polyps, causing inconveniences

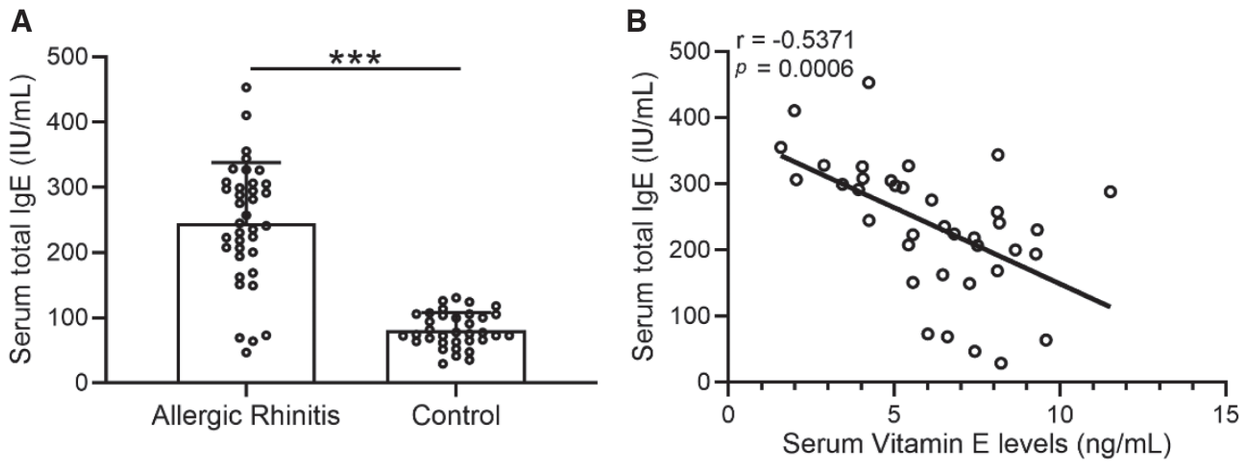

Fig. 2 Serum total IgE level showed negative correlation with serum vitamin E level in pregnant women with allergic rhinitis. A, The comparison of serum total IgE levels between pregnant women with allergic rhinitis and healthy pregnant women. Data were presented as mean ± SD. *** $p < 0.001$, Mann Whitney test. B, Spearman's correlations between serum total IgE levels and serum vitamin E levels in pregnant women with allergic rhinitis.

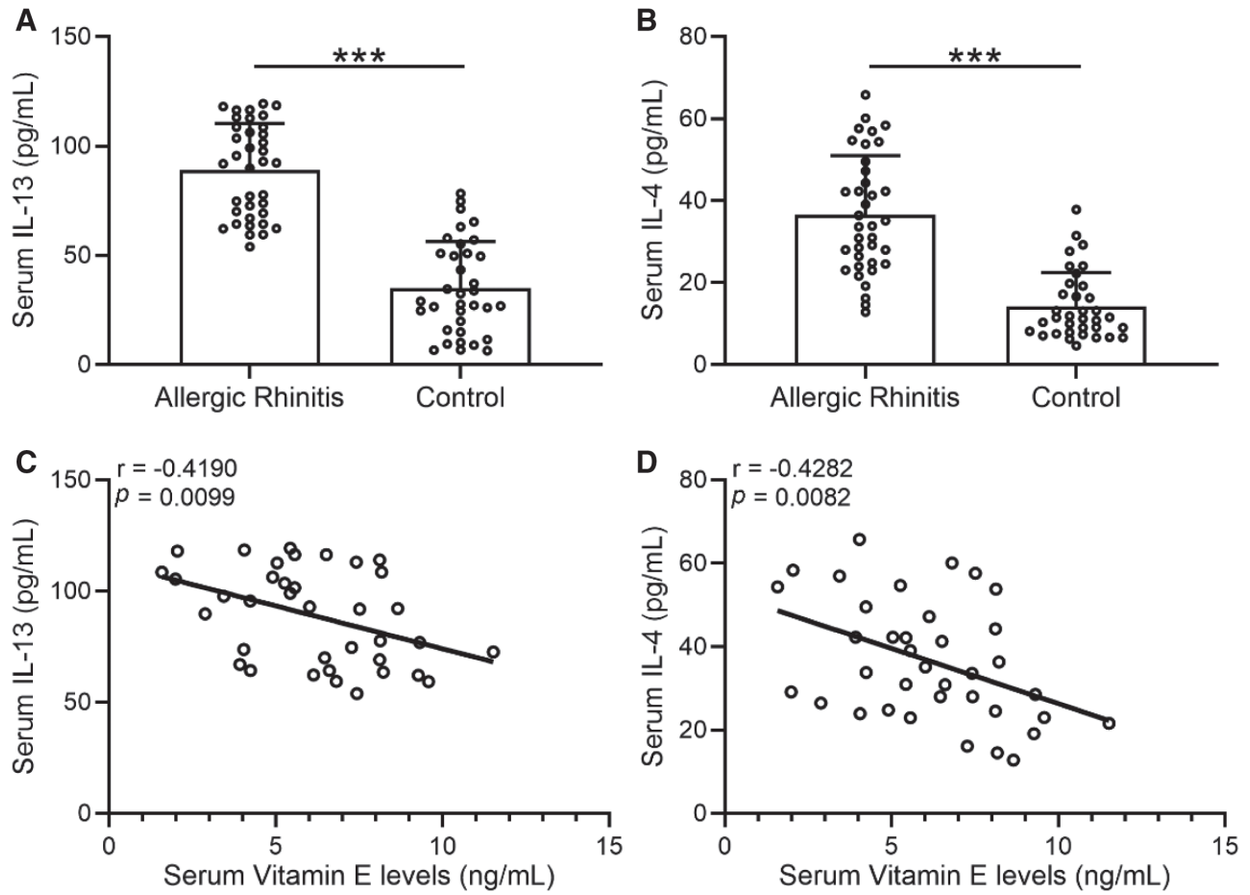

Fig. 3 Serum IL-13 and IL-4 levels showed negative correlation with serum vitamin E level in pregnant women with allergic rhinitis. The comparisons of serum IL-13 (A) and serum IL-4 (B) levels between pregnant women with allergic rhinitis and healthy pregnant women. Data were presented as mean ± SD. *** $p < 0.001$, Mann Whitney test. C. Spearman's correlations between serum IL-13 levels and serum vitamin E levels in pregnant women with allergic rhinitis. D. Spearman's correlations between serum IL-4 levels and serum vitamin E levels in pregnant women with allergic rhinitis.

to daily life.[15,16] Approximately 20%-30% of women of childbearing age suffer from allergic rhinitis, which makes allergic rhinitis one of the most common nasal diseases that complicate the pregnancy process.[7] Studies have shown that the original symptoms of allergic rhinitis in women after pregnancy could be changed due to physiological changes (such as hormone secretion changes), psychological changes (such as emotional stress) and changes in the external environment (such as health protection, etc.) during pregnancy.[17,18] Simultaneously, medication restriction during pregnancy also have a certain impact on the degree of allergic rhinitis symptoms.[19] So far, there are few research reports on the appearance of allergic rhinitis during pregnancy and its impact on the quality of life. Mabry et al. found that found that the overall incidence of allergic rhinitis during pregnancy was 30% in 66 pregnant women.[18] Understanding the molecular mechanism of allergic rhinitis pathogenesis in pregnant women has benefits on the development of novel and safe therapeutic strategies. Vitamin E levels in children with allergic rhinitis are significantly lower than that in healthy children and correlated with the occurrence of allergic rhinitis in children.[14] Thus, we investigated whether vitamin E level was also decreased by the pathogenesis of allergic rhinitis in pregnant women.

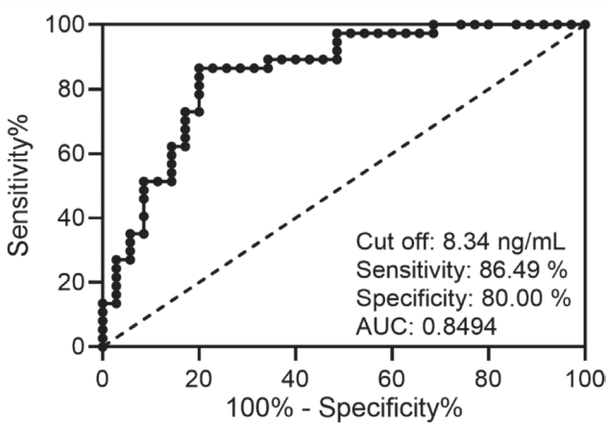

Fig. 4 ROC analysis of serum vitamin E levels in pregnant women with allergic rhinitis.

Corticosteroids are widely used to treat asthma, chronic sinusitis, and allergic rhinitis. However, the duration of symptoms in most patients is related to high-dose or long-term use of steroids.[20] In addition, studies on the side effects of corticosteroids have found that 100% of patients have adverse reactions.[21] Vitamin E is a kind of steroid hormone that mainly plays an anti-inflammatory effect similar to glucocorticoids during treatment and regulates various types of immune and nonimmune cells.[22] Therefore, lack of vitamin E will exacerbate the deficiencies in the

immune function of the lower and upper respiratory tracts.[22] In studying the association between allergic rhinitis and vitamin E deficiency, there are few consistent conclusions. A study reported a potential association between low vitamin E level and allergic rhinitis, whereas another study reported no association.[23] In this research, we investigated the serum level of vitamin E in pregnant women with allergic rhinitis and healthy pregnant women. Results demonstrated that the pathogenesis of allergic rhinitis in pregnant women significantly decreased the serum level of vitamin E. Meanwhile, we also illustrated that the serum vitamin E level exhibited a negative correlation with allergic rhinitis severity in pregnant women. Thus, decreased vitamin E participated in the pathogenesis of allergic rhinitis in pregnant women.

The pathogenesis of allergic rhinitis is complex, and the imbalance of the ratio of helper T cells (Th1/Th2) is the main cause of allergic rhinitis.[24] After the allergen enters the nasal cavity, Th0 cells are stimulated to differentiate into Th1 and Th2 cells.[25] In the pathogenesis of allergic rhinitis, the expression of cytokines, such as thymic stromal lymphopoietin increases, which induces Th0 cells to differentiate in the direction of Th2 and cause the imbalance of Th1/Th2, resulting in a dominant Th2 immune response.[26] Hyperfunction of Th2 cytokines inhibits Th1 cell function, resulting in increased secretion of Th2, production of IL-13, IL-4, and other cytokines, thereby promoting the activation of B lymphocytes to produce IgE.[27] The specific IgE antibody could bind to mast cell surface receptors through the Fc segment, causing the patient to be in a sensitive state. When the patient comes into contact with the mutagen again, the mutagen binds to the specific IgE antibody and degranulates the mast cells through the signal transduction system, thereby releasing a series of cytokines, such as histamine, leukotriene, and so on, which triggers the contraction of capillary endothelial cells, expansion of the capillary network space, nasal mucosa edema, and finally causing allergic rhinitis.[28] Therefore, the genetic research of related Th2 cytokines IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13 has also received extensive attention. Evidences have shown that the polymorphism of IL-4 and IL-13 genes in allergic rhinitis patients related to the risk of allergic rhinitis.[29–31]

We also evaluated the level of IL-13, IL-4, and the total level of IgE in the serum of pregnant women with allergic rhinitis. The pathogenesis of allergic rhinitis significantly elevated the levels of IL-13, IL-4, and total IgE in the serum of pregnant women. Further analysis also showed a negative correlation between serum levels of vitamin E and IL-13, IL-4, and total IgE in pregnant women. ROC analysis of serum vitamin E levels in pregnant women with allergic rhinitis demonstrated that serum vitamin E level was an effective marker in the diagnosis of allergic rhinitis in pregnant women. Vitamin E promotes Th1 cytokine production and inhibits Th2 cytokine production, thus exhibiting a protective function against allergic sensitization.[32,33] In this research, we found a negative correlation between vitamin E level and the pathogenesis of allergic rhinitis in pregnant women. Oral and parenteral vitamin E supplements have been widely used to reduce vitamin E deficiencies and have few adverse effects.[34] Thus, vitamin E supplementation might be beneficial in alleviating the pathogenesis of allergic rhinitis.

A limitation in this research was that the sample size of the patients was relatively small, and future study with a larger sample size is needed to verify observations made in our current investigation.

In conclusion, this research demonstrated that pregnant women with allergic rhinitis have significantly lower serum level of vitamin E. The decreased vitamin E showed a correlation with the pathogenesis of allergic rhinitis in pregnant women.

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