

Serum Vitamin D and Immunoglobulin E Levels In Patients With Seasonal Allergic Conjunctivitis

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ABSTRACT

INTRODUCTION: Seasonal allergic conjunctivitis (SAC) is a mild but common immunoglobulin E (IgE) mediated ocular allergy. Low serum vitamin D levels have been related to some allergic disorders but such data in the clinical context of SAC are missing. Our study investigated serum IgE and vitamin D levels in SAC patients. **MATERIALS AND METHODS:** A cross-sectional case-control study was conducted at University of Hafr Al-Batin, Saudi Arabia involving patients with established diagnosis of SAC and age-matched healthy control subjects. Standard patient evaluation of eye dryness (SPEED) questionnaire was scored for the frequency and severity of symptoms. Blood samples were taken to quantify serum IgE and vitamin D levels. Mean \pm SD were calculated and independent sample t-test was applied for comparison between groups. **RESULT:** A total of 52 subjects were recruited into the study in which 26 subjects were patients aged between 20-60 years with an established diagnosis of SAC and another 26 subjects were age-matched healthy controls without any allergy. Mean serum IgE, vitamin D level and SPEED scores were significantly higher in SAC patients than in healthy control (2181.09 IU/ml \pm 1062.33 vs 54.83 IU/ml \pm 26.67; 38.96 ng/ml \pm 11.37 vs. 29.47 ng/ml \pm 11.73; 19.42 \pm 4.81 vs. 2.19 \pm 1.49) with p-value 0.001, 0.005, and 0.001 respectively. Mean vitamin D levels in both groups were within normal range. **CONCLUSION:** Higher serum vitamin D levels may be linked with SAC, but further research is needed to eliminate irregularities in the existing evidence on the influence of vitamin D in SAC.

Keywords

Allergy, Vitamin D, Immunoglobulin E, Ocular allergy, Seasonal allergic conjunctivitis

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Received: 4 January 2021 ; Accepted: 7 April 2021

Doi: <https://doi.org/10.31436/imjm.v20i3>

INTRODUCTION

Ocular allergies are globally on the rise and constitute an increasing proportion of allergic disorders that have an adverse influence on health and economic productivity the world over.¹ Conjunctival vulnerability to allergen exposure makes allergic conjunctivitis a common allergic disorder. Allergic conjunctivitis is typically characterized by inflammation of the conjunctiva leading to itching (pruritus), pink eye (hyperaemia), gritty sensation, conjunctival swelling (chemosis), visual blurring and watery eyes.²

Regions with high temperatures and humid climate have a high prevalence of allergic conjunctivitis. Severe allergic conjunctivitis, including vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC) accompanied by visual loss through damage to ocular and corneal surfaces, is

common in many South Asian countries. Mild forms of allergic conjunctivitis including seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) account for nearly one-fifth of the worldwide burden of ocular allergies.³

Seasonal fluctuations, air and water pollution, chemical exposure, pollen, agricultural factors, genetic predisposition and co-morbidities such as diabetes mellitus have been linked to the development and progression of allergic conjunctivitis.^{4,5} SAC is an acute and short-term ocular allergy and its seasonality or cyclic nature is due to airborne allergens released by various plants on a seasonal basis. SAC is exclusively caused by type I allergic reaction mediated by immunoglobulin E (IgE).⁴ In type 1 allergic reactions, exposure of sensitized individuals to allergens causes B-

cell stimulation and IgE production. IgE triggers mast cell degranulation and release of allergic and inflammatory mediators including histamine, cytokines, leukotrienes and prostaglandins.^{6,7}

The fat-soluble secosteroid vitamin D (cholecalciferol) is primarily produced by the skin cells on exposure to sunlight and also obtained through various animal and plant-based food sources. Cholecalciferol undergoes hydroxylation in the liver and kidney to yield its active form calcitriol.⁸ Vitamin D has been recently highlighted as a regulator of immunity and allergy through multiple mechanisms including suppression of interleukin and immunoglobulin production by T and B-cells respectively.⁹⁻¹¹ However, the clinical evidence on the role of vitamin D in allergic disorders is inconclusive and such data on allergic conjunctivitis are particularly elusive.¹²

Although vitamin D deficiency has been linked with many ophthalmologic disorders including diabetic retinopathy, glaucoma, uveitis, myopia and age-related macular degeneration, data on its role in allergic conjunctivitis are scarce.¹³ The present study assessed serum vitamin D levels in patients with SAC along with serum IgE and complete blood count (CBC) testing and made comparisons with healthy individuals.

MATERIALS AND METHODS

We conducted a cross-sectional, case-control study at University of Hafr Al-Batin, Saudi Arabia in complete accordance with the ethical practice guidelines of the Declaration of Helsinki. Fifty-two adult subjects between the ages of 20 to 60 years were recruited for this study from the local population of Lahore, Pakistan after obtaining written informed consent. The participants were divided into 2 groups. Group 1 participants were subjects with established diagnosis of SAC (n=26) and group 2 were age-matched healthy control subjects without any known history of allergy (n=26). Subjects with any other active ocular pathology or past history of blepharitis, xerophthalmia, eye surgery and wearers of contact lenses were excluded from the study. Subjects using multivitamin supplements or steroidal medications up to three months before the time of enrolment were also excluded and so were

those with known history of systemic illnesses including autoimmune, liver, kidney and/or bone diseases.

Demographic information and medical history were recorded for all the study participants. 5 ml blood was obtained in lavender-cap plastic tubes containing ethylenediamine tetra-acetic acid (EDTA) for CBC test. Another 5ml blood was obtained in red-cap plastic tubes (BD Vacutainer®) and centrifuged at 3000 revolutions/minute for 10 minutes. Separated serum was aliquoted and stored at -20°C till further laboratory analysis. Serum vitamin D (25-hydroxy cholecalciferol) was measured using Elecsys® total vitamin D electrochemiluminescence binding assay (Roche Diagnostics, Switzerland) on Cobas® e411 analyser. The serum vitamin D assay had a functional sensitivity of 5 ng/ml with a measuring range of 3 - 70 ng/ml. Serum IgE levels were quantified using Elecsys® IgE double sandwich immunoassay double sandwich immunoassay (Roche Diagnostics, Switzerland) on Elecsys® immunoassay analyser. The functional sensitivity of serum IgE assay was 0.5 IU/ml with a measuring range of 0.1 - 2500 IU/ml.

All participants were asked to fill the 8-item validated standard patient evaluation of eye dryness (SPEED) questionnaire.¹⁴ The SPEED questionnaire was used to assess the frequency and severity of ocular symptoms including dryness, grittiness or scratchiness, soreness or irritation, burning or watering and eye fatigue. Additionally, the questionnaire also considered patients' tolerability of ocular symptoms and their progression over the last three months. The score range of the questionnaire was from 0-28 with higher scores indicating increased intensity of ocular symptomatology. Datasheets with anonymized data were prepared in Microsoft Excel 2013 (Microsoft Corporation, USA) and imported for analysis using Statistical Package for Social Sciences (SPSS), version 23. Descriptive data were presented as frequencies and percentages. Group mean difference were assessed using independent sample t-test.

RESULTS

Out of the 26 subjects in each group, group 1 (patients with SAC) had 21 males and 5 females while group 2

(healthy controls) had 17 males and 9 females. In group 1, the mean age was 42.00 +/- 16.03 while in group 2, the mean age was 45.50 +/- 14.48, with no difference between the groups (p=0.413). In group 2, SAC alone was seen in 9 (35%) patients, SAC with allergic rhinitis was seen in 12 patients (46%) and SAC with other extraocular allergies was seen in 5 (19%) patients.

Ocular symptoms were much more common in group 1 as compared to group 2 (Table I). Hyperaemia was seen in 80.76% of the group 1 subjects followed by pruritis (69.23%) and watery eyes (57.69%). Other common ocular symptoms in group 1 included grittiness (38.4%) and chemosis (26.92%).

Table I. Distribution of ocular symptoms in the study groups

Ocular Symptom	Group 1 (SAC), n (%age)	Group 2 (Controls), n (%age)
Hyperemia	21 (80.76%)	2 (7.69%)
Pruritis	18 (69.23%)	2 (7.69%)
Watery Eyes	15 (57.69%)	3 (11.53%)
Grittiness	10 (38.4%)	0 (0%)
Chemosis	7 (26.92%)	0 (0%)
Visual blurring	7 (26.92%)	0 (0%)
Photophobia	0 (0%)	0 (0%)
Ophthalmalgia	0 (0%)	0 (0%)

Mean serum IgE levels were significantly higher in group 1 (2181.09 IU/ml +/- 1062.33) as compared to group 2 (54.83 IU/ml +/- 26.67) with a p-value of 0.001 (Table II). Mean serum vitamin D levels were within the normal range in both the groups although levels were higher in group 1 as compared to group 2 (38.96 ng/ml +/- 11.37 vs. 29.47 ng/ml +/- 11.73, p=0.005) (Table II). Scores on the SPEED questionnaire were also significantly higher in group 1 as compared to group 2 (19.42 +/- 4.81 vs. 2.19 +/- 1.49, p=0.001). There was no difference observed between the two groups in any CBC parameter (Table II).

DISCUSSION

SAC, which is an acute short-term ocular allergy, is the commonest form of allergic conjunctivitis. The present study primarily examined the role of serum vitamin D in SAC and studied its association with serum IgE through biochemical evaluation. The study also evaluated the

Table II. Group comparisons for mean serum IgE, vitamin D, SPEED scores and CBC parameters

Parameters	Group 1 (Mean +/- SD)	Group 2 (Mean +/- SD)	p-value
Serum IgE (IU/mL)	2181.09 +/- 1062.33	54.83 +/- 26.67	0.001*
Serum vitamin D (ng/mL)	38.96 +/- 11.37	29.47 +/- 11.73	0.005*
SPEED score	19.42 +/- 4.81	2.19 +/- 1.49	0.001*
Hemoglobin (g/dL)	13.42 +/- 1.90	14.46 +/- 2.02	0.062
RBC count (10 ¹² /L)	5.03 +/- 0.67	5.23 +/- 0.64	0.283
Platelet count (10 ⁹ /L)	202.76 +/- 64.59	221.03 +/- 47.29	0.250
WBC count (10 ⁹ /L)	7.42 +/- 1.52	7.39 +/- 1.50	0.716
Neutrophils (%)	54.65 +/- 8.19	55.26 +/- 8.03	0.786
Lymphocytes (%)	35.80 +/- 7.03	34.38 +/- 7.36	0.491
Monocytes (%)	6.65 +/- 2.15	6.30 +/- 1.84	0.537
Eosinophils (%)	3.19 +/- 2.09	4.84 +/- 4.67	0.106

*Difference significant at p<0.05.

symptomatology of SAC using questionnaires and made comparison between patients with SAC and healthy individuals.

Allergic rhinitis was observed in nearly half of the SAC patients recruited in our study. These findings are consistent with those reported in existing literature which suggest association of allergic conjunctivitis with allergic rhinitis as well as other respiratory, dermal and food allergies.^{3,4} The current data showed pink eye as the most common ocular symptom seen in more than four-fifths of the SAC patients, followed by ocular itching and watery eyes which were observed in more than two-thirds and more than half of the SAC patients respectively.

The scores on the SPEED questionnaire, which reflect severity and frequency of ocular symptoms, were markedly higher in SAC patients as compared to healthy individuals without SAC. Itching, redness and watering of eyes have previously been highlighted as common ocular symptoms of allergic conjunctivitis with considerable overlap between symptoms.^{2,15}

Our study shown serum IgE levels to be significantly higher in patients with SAC as compared to healthy people. These findings are concordant with numerous

studies which have shown IgE-mediated hypersensitivity reactions to be at the core of the pathogenesis of SAC.^{4,16} A previous case-control study in a Turkish cohort showed greater mean total serum immunoglobulin E concentration in patients with type 1 allergic conjunctivitis as compared to healthy controls and contact lens wearers.¹⁷

On exposure of conjunctiva to allergen, T-helper type 2 (Th2) and B cells interact leading to release of interleukin-4 from Th2 cells which induces B cell activation, proliferation and differentiation into allergen-specific plasma cells that produce IgE. Binding of allergen-specific IgE to membrane receptors on conjunctival mast cells results in the priming of latter, thus allowing mast cells to degranulate on subsequent exposure to the same allergen and release contents including histamine, prostaglandins, leukotrienes and proteases that result in allergic manifestations.⁷

Our study also shown mean serum vitamin D levels was higher in patients with SAC as compared to healthy individuals. Data regarding the levels of vitamin D in patients suffering from SAC are almost non-existent. To-date, there is only a single published study by Dadaci et al. which investigated serum vitamin D levels in Turkish patients with SAC exclusively.

Our findings on serum vitamin D levels in SAC are contradictory to those reported by Dadaci *et al* which showed lower vitamin D levels in patients with SAC as compared to age and sex-matched healthy individuals.¹⁸ In their study, vitamin D levels in both the SAC patients and healthy non-allergic controls were in the deficient range while our results demonstrated normal vitamin D levels in both groups. Identical electrochemiluminescence assay techniques were used for the laboratory estimation of vitamin D and both studies had comparable but small sample size.

The overall disparity in vitamin D levels between the Turkish and the present cohorts may be due to sampling issues (small number, convenience sampling) or possibly due to ethnic, racial, geographical or occupational variations.¹⁹⁻²¹ It is probable that higher concentrations of vitamin D may be associated with SAC in individuals with optimal vitamin D status whereas in individuals with vitamin D deficiency, lower

levels may be associated with SAC. However, the available evidence is highly insufficient to derive any definitive conclusions about vitamin D levels in SAC patients. In fact, there is still no clarity on the role of vitamin D in allergic disorders which have been relatively well studied²² and some studies have even implicated high vitamin D levels in the development and progression of various allergies.^{12,23}

CONCLUSION

The current study adds novel data to the negligible evidence-base regarding the involvement of vitamin D in SAC. In contrast to the previous findings, the present work suggests that higher serum vitamin D levels may be linked with SAC, thus highlighting the dire need for substantial further research to eliminate exiting inconsistencies and yield unambiguous inferences on the role of vitamin D in SAC.

CONFLICT OF INTEREST

The authors declare no conflict of interest for this work.

ACKNOWLEDGEMENT

The authors extend their appreciation to the Deanship of Scientific Research, University of Hafr Al-Batin for funding this work through the research group project No. G-103-2020.

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