

Evaluation of allergic sensitization in Lebanese patients with allergic conjunctivitis

Nicolas Arej  · Carla Irani · Youssef Abdelmassih · Elise Slim ·
Joelle Antoun · Riad Bejjani · Alexandre Schakal · Naji Waked

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Abstract

Purpose To describe the profile of patients with allergic conjunctivitis (AC) regarding their demographics, symptomatology and specific allergen sensitization, in a Lebanese tertiary hospital.

Methods Cross-sectional study conducted at the Hôtel-Dieu de France hospital (Beirut, Lebanon) during a period of 18 months. Patients with seasonal or perennial AC presenting for ophthalmic consultation had measurements of total and specific IgE. A matching group of patients with AC seen at the allergist office during the same period underwent skin prick tests (SPTs).

Results Forty-four patients were enrolled for blood work by their ophthalmologists. Seasonal and perennial forms were almost equivalent. In total, 56.8% had positive specific IgE, with higher prevalence in patients with seasonal AC ($p = 0.002$), other

associated allergies particularly allergic rhinitis ($p = 0.002$) or a family history of allergy ($p = 0.005$). Ocular surface severity scales were not shown as predictors. High levels of total IgE were commonly detected in those with positive specific IgE. Thirty-eight patients were assessed with SPT, and all had a positive result for at least one allergen. Dust mites were found to be the most frequent allergens based upon both specific IgE (72%) and SPT (92%), followed by Parietaria and other pollens.

Conclusion In our study, dust mites mono- or co-sensitization is present in the majority of patients with AC, with odds of positivity being higher using SPT than specific IgE. The latter are found more readily in seasonal AC and in the presence of personal and family history of allergy.

Keywords Airborne allergen · Allergen-specific IgE · Allergic conjunctivitis · Conjunctiva · Skin prick test

N. Arej · Y. Abdelmassih · E. Slim · J. Antoun ·
R. Bejjani · N. Waked
Department of Ophthalmology, Faculty of Medicine,
Saint Joseph University, Beirut, Lebanon

C. Irani
Department of Internal Medicine, Faculty of Medicine,
Saint Joseph University, Beirut, Lebanon

N. Arej (✉) · C. Irani · Y. Abdelmassih ·
R. Bejjani · A. Schakal · N. Waked
Hôtel-Dieu de France Hospital, Blvd. Alfred Naccache,
Achrafieh, P.O. Box: 166830, Beirut, Lebanon
e-mail: nicolas.arej@gmail.com

Introduction

The ocular surface, similarly to the skin or the respiratory system, can be the site of allergic reactions. The conjunctiva is the main tissue of concern since it covers most of the ocular surface as well as the inner side of the eyelids. It has similar anatomical and physiological features to those of the nasal mucosa;

hence, allergic symptoms often occur simultaneously at both sites [1]. Although allergic conjunctivitis (AC) can be associated with allergic rhinitis and asthma, it represents an independent nosological entity and a frequent complaint in medical and ophthalmological practice [2, 3]. It is a mostly benign condition, yet it has an important economic and quality-of-life impact [4].

Different types of AC are distinguished based on specific signs on ocular examination and degree of severity [5]. Seasonal and perennial conjunctivitis are the most frequent; they affect together 15–20% of the general population [6] and rely on an IgE-mediated hypersensitivity (Gell and Coombs type I) with degranulation of previously sensitized mastocytes. More severe forms of AC are able to produce corneal lesions such as those found in vernal keratoconjunctivitis and atopic keratoconjunctivitis; these two forms bring into play not only immediate (type I) hypersensitivity reactions, but also delayed (type IV) hypersensitivity. Noteworthy, giant papillary conjunctivitis can be regarded as a separate form of ocular allergy and is the prerogative of contact lens wearers.

The diagnosis of AC is made from the patient examination, reported symptoms, as well as his personal and familial past allergic history. Slit-lamp examination is essential to diagnose AC and helps to distinguish its different forms and rule out differential diagnoses [3]: infectious conjunctivitis, blepharitis, ocular dryness, and cases of nonspecific conjunctival irritation that are common in urban settings [7]. Given the quite common symptoms, it is not always easy to diagnose AC with certainty; therefore, an allergy assessment would be of interest to confirm the diagnosis and identify the allergens responsible for the disease.

Many studies explored epidemiological features of AC in different regions of the world through skin prick testing (SPT) or dosage of specific IgE in the serum of affected patients [8, 9]. However, there has not been, to our knowledge, any study on this subject in the Lebanese population. That being the case, we aim to describe the profile of patients with AC as they show for ophthalmological or allergological consultation in a Lebanese tertiary hospital, according to various parameters: demographic, clinical, biological and functional. This will also allow us to determine the frequency of the involved allergens in our region.

Methods

This is a cross-sectional study that included patients presenting for symptoms of AC at the ophthalmological consultations of Hôtel-Dieu de France University Hospital (HDF, Beirut, Lebanon) between July 2013 and January 2015. Only patients with seasonal or perennial types of AC were included. Those having a history of eczema, systemic illness or steroid intake during the preceding month were excluded, as well as contact lens wearers. No age restriction was made. The study protocol was approved by the HDF Ethics Committee, and it adhered to the Declaration of Helsinki. A written informed consent was obtained from all patients, and their anonymity was conserved.

Patients were asked to fill a questionnaire inquiring about their demographics, medical history, current and past ocular symptoms (see “Appendix 1”). They also subjectively graded the severity of their condition on a scale from 0 to 10 and then through answering some questions from the MiniRQLQ® questionnaire [10]. The latter is a standardized questionnaire initially validated to assess the impact of rhinoconjunctivitis on patients’ quality of life; questions regarding rhinitis were omitted; and a total score over 54 points was calculated. A slit-lamp examination was then performed for every patient by the same competent examiner, looking for objective signs of AC (hyperemia, follicles, papillae, chemosis, corneal staining, etc.) and grading each sign on a scale from 0 to 3 whether it was judged to be mild, moderate or severe, according to specific predefined criteria (maximum total score = 30) as shown in “Appendix 2” [11].

After the ophthalmic consult, patients underwent a blood workup comprising the dosage of both total and specific IgEs. Total IgEs were measured by immunonephelometry using the BN ProSpec® system (Siemens Healthcare Diagnostics Inc, Germany), whereas specific IgEs were sought by the AllergyScreen® kit (Lebanon inhalation panel) [12], which relies on an immunoblot technique to semiquantitatively detect the IgE serum concentrations against the 20 most widespread respiratory allergens in Lebanon. Sensitivity and specificity of this technique are known to be equal to 95.1 and 80.2%, respectively [13].

In another setting, records of patients presenting to the allergist office at the Hôtel-Dieu de France hospital during the same period were retrospectively reviewed. A matching sample of patients was selected among

those who had SPT as a workup for AC. SPTs looked for sensitization against 13 common respiratory allergens including dust mites, pollens, molds and animals. The choice of the skin prick test panel of aeroallergens is based upon two previous studies conducted to determine the most clinically relevant aeroallergens in Lebanon [14, 15]. Results were then compared to those obtained from specific IgE testing.

Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were reported as mean and standard deviation for continuous variables. Chi-square (or alternatively Fisher for small samples) and Student's *t* test were used to compare qualitative and quantitative variables, respectively. A *p* value of less than 0.05 was considered to be statistically significant. A bivariate correlation study was performed between the number of allergens detected by specific IgEs, total IgE levels and the various severity scores in patients who presented to ophthalmic consultation. Pearson's coefficients were calculated along with their 95% confidence intervals.

Results

Forty-four patients were enrolled from the ophthalmology department. Their characteristics are listed in

Table 1. The majority live in the cities (72.7%). Only 20.5% had contact with animals. The most prevalent socioeconomic categories were students (29.5%), followed by people in retirement or unemployment (22.7%).

Eye itching was the most common symptom noted by almost all the patients. It was followed by redness, tearing, foreign body sensation, secretions, dryness, blurred vision, eyelid edema and photophobia. SAC (59.1%) was slightly more prevalent than PAC (40.9%). In most cases (72.7%), AC was associated with one or more other forms of allergy: allergic rhinitis (47.7%), urticaria (31.8%), asthma (27.3%), whereas no other allergy was noted in 12 patients (27.3%). Twenty-five patients (56.8%) mentioned a positive family history of allergy.

Patients were divided as listed in Table 2 according to whether or not they had positive specific IgE, regardless of the level of positivity, the number of detected allergens or total IgE titers. In total, specific IgEs were found for at least one allergen in 25 patients (56.8%); none was found in the other 19 patients (43.2%). No statistically significant difference was found regarding gender (*p* = 0.361), age (*p* = 0.088) or living environment (*p* = 0.735). Likewise, all symptoms were comparable between the two groups, except for ocular dryness sensation that seemed to be

Table 1 Demographic characteristics, allergic history and current symptoms of patients presenting to the ophthalmology clinic (*n* = 44)

<i>Gender</i>		<i>Age</i>	
Men	25 (56.8%)	Mean ± SD	35.2 ± 21.46
Women	19 (43.2%)	Min–Max	5–80
<i>Living environment</i>		<i>Type of allergy</i>	
Urban	32 (72.7%)	SAC†	26 (59.1%)
Rural	12 (27.3%)	PAC‡	18 (40.9%)
<i>Socioeconomical class</i>		<i>Associated allergies</i>	
Students	13 (29.5%)	Rhinitis	23 (52.3%)
Retired/Unemployed	10 (22.7%)	Urticaria	14 (31.8%)
Office workers	6 (13.6%)	Asthma	12 (27.3%)
Educationists	6 (13.6%)	None	12 (27.3%)
Health workers	6 (13.6%)		
Artisans	3 (6.8%)	<i>Family allergies</i>	
<i>Symptoms</i>		Secretions	25 (56.8%)
Itching	43 (100%)	Ocular dryness	23 (52.3%)
Redness	35 (79.5%)	Blurred vision	20 (45.5%)
Tearing	35 (79.5%)	Eyelid edema	19 (43.2%)
Foreign body sensation	26 (59.1%)	Photophobia	10 (22.7%)

† Seasonal allergic conjunctivitis

‡ Perennial allergic conjunctivitis

Table 2 Comparison of patients' characteristics in terms of specific IgE results

	Specific serum IgE result		
	Positive ($n_1 = 25$)	Negative ($n_2 = 19$)	p value
<i>Gender</i>			
Men	16 (64%)	9 (47.4%)	0.361
Women	9 (36%)	10 (52.6%)	
<i>Age</i>			
Mean $\pm$ SD	30.1 $\pm$ 17.4	41.8 $\pm$ 24.7	0.088
Min–Max	5–70	11–80	
<i>Type of allergy</i>			
SAC†	20 (80%)	6 (31.6%)	0.002**
PAC‡	5 (20%)	13 (68.4%)	
<i>Associated allergies</i>			
Rhinitis	15 (60%)	6 (31.6%)	0.062
Asthma	10 (40%)	2 (10.5%)	0.030*
Urticaria	8 (32%)	6 (31.6%)	0.976
None	2 (8%)	10 (52.6%)	0.002**
Familial allergies	19 (76%)	6 (31.6%)	0.005**
<i>Living environment</i>			
Urban	19 (76%)	13 (68.4%)	0.735
Rural	6 (24%)	6 (31.6%)	
<i>Symptoms</i>			
Itching	25 (100%)	18 (94.7%)	0.432
Redness	21 (84%)	14 (73.7%)	0.467
Tearing	20 (80%)	15 (78.9%)	0.932
Secretions	13 (52%)	12 (63.2%)	0.547
Foreign body sensation	18 (72%)	8 (42.1%)	0.066
Blurred vision	13 (52%)	7 (36.8%)	0.248
Dryness	17 (68%)	4 (31.6%)	0.032*
Edema	12 (48%)	7 (36.8%)	0.547
Photophobia	8 (32%)	2 (10.5%)	0.148
<i>Subjective severity/10</i>			
Mean $\pm$ SD	7.1 $\pm$ 1.7	6.7 $\pm$ 1.9	0.544
Min–Max	3–10	3–10	
<i>MiniRQLQ© score/54</i>			
Mean $\pm$ SD	29.4 $\pm$ 8.8	22.2 $\pm$ 9.5	0.015*
Min–Max	9–43	6–48	
<i>Objective severity/30</i>			
Mean $\pm$ SD	7.1 $\pm$ 2.7	9 $\pm$ 3.4	0.045*
Min–Max	1–12	4–15	
<i>Total IgE (IU/mL)</i>			
Mean $\pm$ SD	288.3 $\pm$ 379.1	61.7 $\pm$ 73.3	0.007**
Min–Max	27.8–1530	16.4–280	
Total IgE $\geq$ 100 IU/mL	17 (68%)	3 (15.8%)	0.001**

[†] Seasonal allergic conjunctivitis

[‡] Perennial allergic conjunctivitis

* $p < 0.05$

** $p < 0.01$

more frequent in patients having positive specific IgE ($p = 0.032$).

Conversely, there was a fourfold predominance of SAC over PAC in patients with positive testing (80 vs. 20%, $p = 0.002$), as shown in Fig. 1. On the other hand, PAC is more prevalent in cases of negative specific IgE (68.4 vs. 31.6%).

Among the different types of allergy that may be associated with AC, only asthma was significantly more prevalent in cases of positive testing (40 vs. 10.53%, $p = 0.030$). Furthermore, a strong association was discovered between the presence of at least one of these allergies and the positivity of specific IgE: 92% of patients with positive specific IgE have at least one other type of allergy beside AC, whereas 47.4% of patients with negative testing do not have any associated allergy ($p = 0.002$). Family history of allergies is also significantly more frequent in patients with positive rather than negative testing (76 vs. 31.6%, $p = 0.005$). Subjective severity scores were comparable between the two groups, while the MiniRQLQ© and the objective scores were significantly higher in cases of positive testing. Specific IgE was more likely positive with higher total IgE titers, particularly greater than 100 IU/mL.

Table 3 reveals Pearson's correlation coefficients and their 95% confidence intervals for various continuous variables. Unsurprisingly, there was a positive correlation between the MiniRQLQ© and subjective severity scores ($r = 0.495$, [0.232; 0.690]). More importantly, the number of detected allergen showed a positive correlation ($r = 0.345$, [0.054; 0.582]) with total IgEs, but a negative correlation ($r = -0.316$) with the objective severity score.

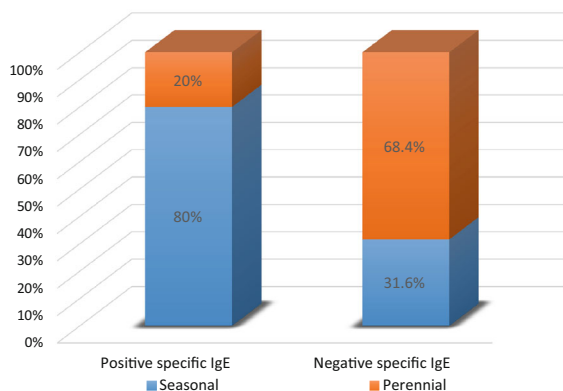


Fig. 1 Frequencies of the types of allergy depending upon specific IgE results ($n = 44$, $p = 0.002$)

The mean ($\pm$ SD) number of detected allergens per patient was 4.96 ($\pm$ 3.6) with a noticeable predominance of the two dust mite species *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (72%), followed by plants and pollens (60%), particularly Parietaria (Fig. 2). Six cases of latex allergy were detected despite the absence of evocative history. Allergies to animals and molds were the least detected (44 and 20%, respectively).

Among patients who presented to the allergist office during the same period, 38 were assessed with SPT and all had a positive result for at least one allergen. Their main characteristics are listed in Table 4 and are statistically comparable to those of patients assessed by specific IgE. Dust mites were found to be the most frequent allergens (92.10%), followed by pollens (89.47%), especially Parietaria, then molds (44.74%) and animals (15.79%). Compared to specific IgE results, SPT was significantly associated with more positive results (100 vs. 56.82%, $p < 0.001$) and higher odds of detecting dust mites and pollens, as listed in Table 5. Allergy to animals was more likely detected by specific IgE, whereas no statistically significant difference was found between the two tests regarding Latex allergy.

Discussion

Allergic conjunctivitis is a commonly encountered diagnosis in both ophthalmological and allergological practices. It has been well said that the diagnosis of allergy begins and ends with history and physical examination, but this does not always seem obvious in front of nonspecific manifestations overlapping with ocular irritation symptoms. Thus, AC has to be well differentiated from other forms of ocular diseases and allergies, knowing that these are distinguished more by their pathophysiological mechanisms (IgE-mediated or not) than by their clinical manifestations. In this regard, the dosage of specific IgE can acquire the merit of being not only an etiological examination, but also a diagnostic one.

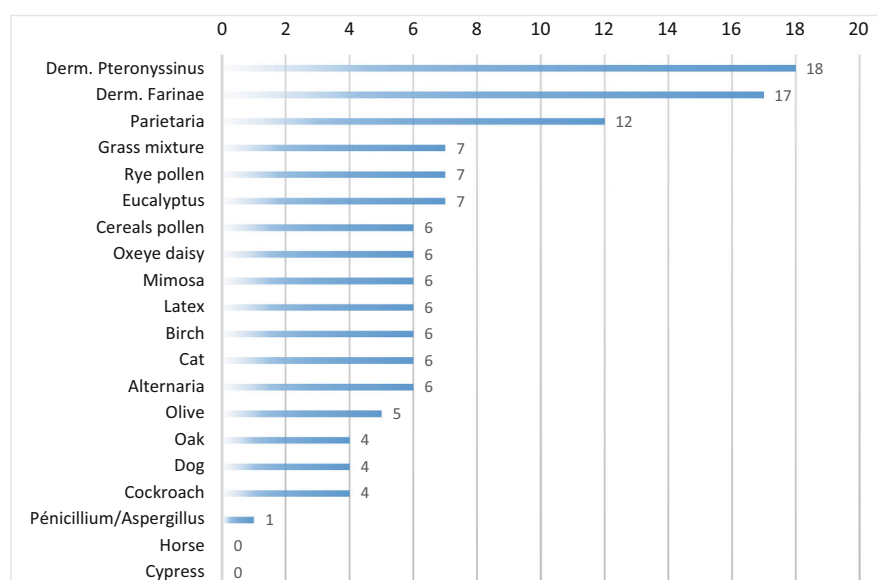
Itching is by far the most frequent symptom, in our study as in the medical literature, without it is being specific to AC. Moreover, no symptoms are known to be pathognomonic neither to diagnose AC nor to predict the positivity of specific IgE. The results of our study suggest that ocular dryness symptoms may be

Table 3 Pearson's correlation coefficient and its 95% confidence interval between severity scales, total IgE levels and the number of detected allergens by specific IgEs

Subjective severity				
MiniRQLQ[†]	0.495 [0.232; 0.690]*	MiniRQLQ[©]		
Objective severity	0.176 [− 0.128; 0.449]	0.130 [− 0.158; 0.464]	Objective severity	
Total IgE	0.011 [− 0.287; 0.307]	0.206 [− 0.174; 0.411]	−0.293 [− 0.543; 0.004]	Total IgE
Number of allergens	0.162 [− 0.142; 0.438]	0.171 [− 0.133; 0.445]	−0.316 [− 0.560; −0.021]*	0.345 [0.054; 0.582]*

[†] Mini Rhinoconjunctivitis Quality of Life Questionnaire

* $p < 0.05$

Fig. 2 Allergen sensitization detected by serum-specific IgEs ($n = 25$)**Table 4** Characteristics of patients having SPT compared to those who were enrolled for specific IgE testing

	Specific IgEs	Skin prick tests	<i>p</i> value
Mean age $\pm$ SD	35.2 $\pm$ 21.46	32 $\pm$ 18.7	0.483
M:F ratio	25:19	5:14	0.007
Type of allergy			
SAC [†]	59.1%	50%	0.409
PAC [‡]	40.9%	50%	
Associated allergies	72.7%	81.6%	0.343

[†] Seasonal allergic conjunctivitis

[‡] Perennial allergic conjunctivitis

associated with IgE-mediated allergy. Indeed, chronic allergic reactions are known to produce a significant loss of mucus cells; hence, an important intersection exists between dry eye syndrome and AC. Certain clinical forms of low inflammatory conjunctival allergy may even manifest mainly by intense dryness

symptoms and a very altered tear breakup time [7]. Therefore, it is important to identify the dry eye syndrome when it occurs, treat it with lacrimal substitutes and avoid unnecessary prolongation of antiallergic treatments, especially if they contain preservatives [16, 17].

Table 5 Specific IgEs and skin prick tests compared in terms of overall positivity, main categories of detected allergens, and the mean number of allergens per patient

	Specific IgEs	Skin prick tests	<i>p</i> value
Positive results	25/44 (56.82%)	38/38 (100%)	<0.001**
Dust mites	18/25 (72%)	35/38 (92.10%)	0.033*
Pollens	15/25 (60%)	34/38 (89.47%)	0.006**
Animals	11/25 (44%)	6/38 (15.79%)	0.014*
Molds	5/25 (20%)	17/38 (44.74%)	0.044*
Latex	6/25 (24%)	4/38 (10.53%)	0.152
Mean number of allergens per patient (±SD)	4.96 (±3.56)	4.47 (±1.72)	0.472

* $p < 0.05$ ** $p < 0.01$

Although there is no immunopathological difference between SAC and PAC [18], our results show that seasonal forms are associated with positive specific IgE more than perennial forms. Yet, sensitization to dust mites, the main allergens of PAC, has been detected in a large number of patients. This discrepancy could be explained either by the presence of other untested perennial allergens or by the confusion between allergy and chronic irritation of the ocular surface in patients sensitized (but not allergic) to the mites, i.e., having specific IgEs that do not account for their symptoms.

The presence of associated allergies (rhinitis, asthma or urticaria) comforts the diagnosis of AC; they were found in more than 70% of patients in this study. The association between rhinitis and conjunctivitis appears to be slightly lower (52.3%) compared to the literature (65–70%) [19]. This suggests that ophthalmologists often see conjunctivitis without rhinitis, the latter being more easily taken in charge by general practitioners or ENT specialists. Another noteworthy fact is that isolated forms are significantly associated with negative specific IgE testing; this may be explained by the theory of local production of specific IgEs in tissues. A limited immune response appears to occur sometimes at the level of the conjunctiva without leaving detectable traces in the systemic circulation. The dosage of specific IgE in tears may then be more likely to be positive in particular cases of isolated AC [20]. Family history of allergy, being significantly associated with positive specific IgEs, helps in establishing the diagnosis of AC and increases the probability of identifying its etiology.

The correlational study demonstrates that biology does not predict the clinical situation, due to the

absence of a significant correlation between total IgE levels and the different modalities of severity evaluation. The negative relationship between the number of allergens and the objective severity score is a further evidence. However, the allergens tend to be more numerous when total IgE titers are high.

There is no common profile to all patients with AC, since allergens vary in time and space depending on climatic and geographic factors, as well as population lifestyle and biological susceptibility. To our knowledge, no previous attempt was made to study the allergological profile of Lebanese patients with AC. Attention is more often turned to other allergies such as asthma and allergic rhinitis. In fact, the profile of allergic rhinitis in Lebanon was the subject of a study carried out in 2002, showing that dust mites are the main involved allergens [21]. Similarly, dust mites were also the most frequent allergens in our study by both means of testing. Indeed, the survival and the growth of mites are maintained by hot and humid climates [22, 23], conditions that are fulfilled in the Lebanese littoral regions. Pollens and molds have lower frequencies than mites; this is probably due to the period of recruitment of patients that was not limited to the flowering season in Lebanon and to the fact that the majority of patients come from an urban environment. On the other hand, pollution in an urban setting favors the development of nonspecific hypersensitivity by cellular mechanisms involving complement activation and histamine release, without IgE production [24]; this may account at least for a part of the negative specific IgE results.

Based on the results of this study, we encourage prescribing specific IgE testing in patients with clinically manifest SAC and those with a personal and familial history of allergy. It is undoubtedly an

easy in vitro diagnostic tool, which can be used by ophthalmologists if they choose to perform an allergy workup themselves. Otherwise, SPT performed in an allergist clinic seems to provide at least equivalent information regarding allergic sensitization in patients with AC, with even higher odds of positivity. This confirms the findings of the specific IgE-based analyses and recalls the unquestionable value of in vivo testing in allergic patients.

The ultimate challenge of identifying the causative allergens of AC is to be able to implement measures of eviction or avoidance and possibly a specific immunotherapy so as to improve the quality of life of the patients. In order to better achieve this goal, a collaboration between ophthalmologists and allergy specialists seems to be of central importance.

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Compliance with ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Informed consent was obtained from all individual participants included in the study.

Appendix 1: Questionnaire

Appendix 1: Questionnaire

Name: _____ **Date of visit:** _____

Gender: ☐ M ☐ F **Date of birth:** _____

Profession: _____

Address: _____

Exposure to plants: ☐ No ☐ Yes

Exposure to animals: ☐ No ☐ Yes

Ocular symptoms:

☐ Redness	☐ Ocular dryness
☐ Itching	☐ Foreign body sensation
☐ Eyelid swelling	☐ Blurred vision
☐ Tearing	☐ Photophobia
☐ Secretions	

Type of allergy: ☐ Seasonal ☐ Perennial

Past medical history: _____

Associated allergies:

☐ Asthma	☐ Eczema / atopic dermatitis
☐ Rhinitis	☐ Other, specify: _____
☐ Urticaria	☐ None

Family allergies: ☐ No ☐ Yes, specify: _____

Contact lens wear: ☐ No ☐ Yes

Systemic steroid intake during the past month: ☐ No ☐ Yes

Quality of life:

Please estimate, on a scale from 0 to 10, the severity of your ocular symptoms

1 2 3 4 5 6 7 8 9 10

MiniRQLQ® simplified questionnaire:

Please complete all questions by circling the number that best describes how troubled you have been during the last week as a result of your eye symptoms

0 = not troubled

1 = hardly troubled at all

2 = somewhat troubled

3 = moderately troubled

4 = quite a bit troubled

5 = very troubled

6 = extremely troubled

Regular activities at home and at work (your occupation or tasks that you have to do regularly around your home and/or garden)	0	1	2	3	4	5	6
Recreational activities (indoor and outdoor activities with friends and family, sports, social activities, hobbies)	0	1	2	3	4	5	6
Sleep (difficulties getting a good night's sleep and/or getting to sleep at night)	0	1	2	3	4	5	6
Need to rub eyes repeatedly	0	1	2	3	4	5	6
Itchy eyes	0	1	2	3	4	5	6
Sore eyes	0	1	2	3	4	5	6
Watery eyes	0	1	2	3	4	5	6
Tiredness and/or fatigue	0	1	2	3	4	5	6
Feeling irritable	0	1	2	3	4	5	6

Juniper EF, Thompson AK, Ferrie PJ, Roberts JN. Development and validation of the mini Rhinoconjunctivitis Quality of Life Questionnaire. *Clin Exp Allergy* 2000 ; 30 : 132-40

Juniper et al. [10].

Appendix 2: Objective criteria evaluating AC severity

Ten objective ocular clinical findings of conjunctival, limbal and corneal lesions were graded on a four-point

scale (0 = none, 1 = mild, 2 = moderate, 3 = severe; left and right eye separately in each case; see Table 6 for details). The total score of ten findings, with a maximum of 30, taking the score of the more severe side in bilateral cases, was used as the clinical score [11].

Table 6 Criteria for clinical evaluation of allergic ocular findings

Descriptions			
Palpebral conjunctiva	Hyperemia	Severe	Impossible to distinguish individual blood vessels
		Moderate	Dilatation of many vessels
		Mild	Dilatation of several vessels
		None	No manifestations
	Edema	Severe	Diffuse marked edema
		Moderate	Diffuse mild edema
		Mild	Localized edema
		None	No manifestations
	Follicles	Severe	20 or more follicles
		Moderate	10–19 follicles
		Mild	1–9 follicles
		None	No manifestations
	Papillae	Severe	Diameter ≥ 0.6 mm
		Moderate	Diameter 0.3–0.5 mm
		Mild	Diameter 0.1–0.2 mm
		None	No manifestations
	Giant papillae	Severe	Elevated papillae in 1/2 or more of upper palpebral conjunctiva
		Moderate	Elevated papillae in less than 1/2 of upper palpebral conjunctiva
		Mild	Flat giant papillae
		None	No manifestations
Bulbar conjunctiva	Hyperemia	Severe	Vasodilatation of all vessels
		Moderate	Dilation of many vessels
		Mild	Dilation of several vessels
		None	No manifestations
	Chemosis	Severe	Cyst-like chemosis of entire conjunctiva
		Moderate	Diffuse thin chemosis
		Mild	Partial conjunctival swelling
		None	No manifestations
Limbus	Limbal edema	Severe	In $\geq 2/3$ of circumference
		Moderate	In 1/3 to 2/3 of circumference
		Mild	In less than 1/3 of circumference
		None	No manifestations
	Trantas' dots	Severe	≥ 9 dots
		Moderate	5–8 dots
		Mild	1–4 dots

Table 6 continued

Descriptions			
Cornea	Epithelial lesions	None	No manifestations
		Severe	Shield ulcer or epithelial erosion
		Moderate	Superficial punctate keratitis with filamentary debris
		Mild	Superficial punctate keratitis
		None	No manifestations

In cases having giant papillae, papillae and giant papillae should be graded simultaneously

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