

Demographic and clinical characteristics of patients with ocular allergy in an outpatient clinic of a university hospital in São Paulo, southeastern Brazil

Características demográficas e clínicas de pacientes com alergia ocular em ambulatório de hospital universitário em São Paulo

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ABSTRACT

Introduction: Ocular allergy (OA) encompasses a group of diseases that can be classified into multiple phenotypes. Despite its common occurrence, there is limited data on OA in Brazil. This study aimed to outline the demographic and clinical characteristics of patients diagnosed with OA. **Methods:** We conducted a retrospective analysis of the medical records of patients with OA treated at a university hospital outpatient clinic between 2002 and 2022. Variables such as age, sex, clinical manifestations, associated atopic diseases, age of symptom onset, and treatment approaches were investigated. Statistical analysis was performed using STATA software, with a significance level of 5%. **Results:** The study included 100 patients, 57% of whom were male, with ages ranging from 5 to 66 years. Most patients (80%) reported the onset of symptoms during childhood. Perennial allergic conjunctivitis was the most common form of OA, and the most frequent symptoms were pruritus and hyperemia. Allergic rhinitis was the most commonly associated comorbidity. The most frequently used treatment strategy was a combination of olopatadine eye drops and artificial tears. Additionally, 61% of patients received immunotherapy. Ocular complications, including keratoconus and corneal ulcers, were observed in 26% of cases, and 7% required surgical intervention. No correlation was found between the studied variables and ocular complications.

RESUMO

Introdução: A alergia ocular (AO) engloba um conjunto de doenças que podem ser classificadas em diferentes fenótipos. Apesar de sua prevalência, existem poucos dados sobre AO no Brasil. Este estudo teve como objetivo descrever as características demográficas e clínicas de pacientes diagnosticados com AO. **Métodos:** Foi realizada uma análise retrospectiva dos prontuários de pacientes com AO atendidos entre 2002 e 2022 em um ambulatório de hospital universitário. Foram investigadas variáveis como idade, sexo, manifestações clínicas, doenças atópicas associadas, início dos sintomas e tipo de tratamento. A análise estatística foi conduzida utilizando o *software* STATA, adotando um nível de significância de 5%. **Resultados:** O estudo incluiu 100 pacientes, sendo 57% do sexo masculino, com idades variando entre 5 e 66 anos. Oito em cada dez pacientes relataram início dos sintomas na infância. A conjuntivite alérgica perene foi a forma mais comum da doença, e os sintomas mais frequentes foram prurido e hiperemia. A rinite alérgica foi a comorbidade mais associada à AO. O tratamento mais frequentemente utilizado foi a combinação de colírios de olopatadina e lágrimas artificiais. Além disso, 61% dos pacientes foram submetidos à imunoterapia. Complicações oftalmológicas, como ceratocone e úlcera de córnea, foram observadas em 26% dos casos, e 7% dos pacientes necessitaram de intervenção cirúrgica. Não foi encontrada correlação entre as variáveis estudadas

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Conclusions: OA was more prevalent in males, with symptom onset during childhood. Allergic rhinitis was the most common atopic comorbidity. The most frequently used treatment involved a combination of artificial tears and multi-action eye drops. Although more than a quarter of the patients experienced ocular complications, no significant correlation was identified between the variables and these complications.

Keywords: Allergic conjunctivitis, allergic rhinitis, phenotype, immunotherapy, demography.

e as complicações oftalmológicas. **Conclusões:** A AO foi mais prevalente no sexo masculino e teve início na infância, com a rinite alérgica sendo a comorbidade atópica mais comum. O tratamento mais utilizado foi a combinação de lágrimas artificiais e colírios de múltipla ação. Embora mais de um quarto dos pacientes tenha apresentado complicações oftalmológicas, não houve correlação significativa entre as variáveis e essas complicações.

Descritores: Conjuntivite alérgica, rinite alérgica, fenótipo, imunoterapia, demografia.

Introduction

Ocular allergy (OA) encompasses a set of diseases with common symptoms, such as ocular itching, hyperemia, edema, tearing, foreign body sensation, photophobia, and papillae formation in the upper tarsal conjunctiva.¹ The prevalence of OA is difficult to estimate, as ocular symptoms are often not spontaneously reported in medical consultations and can be neglected by physicians and patients.² In a review of medical records of 1,549 patients with asthma, 44% had symptoms suggestive of OA, but only 16% were diagnosed with allergic conjunctivitis.³ Most studies on OA focus on allergic rhinoconjunctivitis, which affects 30% to 70% of patients with allergic rhinitis.⁴

A study of 3,120 adolescents in Paraná, Brazil found a 51% prevalence of ocular itching, with the most frequent manifestation being tearing (74% of the cases).⁵ In the United States, it is estimated that 15%-20% of the general population has OA,² with some authors reporting that OA is involved in 25% of consultations with allergists, 10% of consultations with ophthalmologists, and 5% of consultations with pediatricians.⁶

OA can be classified into 3 types based on the immunological mechanism involved: immunoglobulin E (IgE)-mediated (seasonal and perennial allergic conjunctivitis), IgE- and non-IgE-mediated (vernal and atopic keratoconjunctivitis), and non-IgE-mediated (giant papillary conjunctivitis, eyelid dermatitis, and contact conjunctivitis). The main characteristics of the most frequent clinical forms (phenotypes) are summarized in Table 1.⁶⁻⁸

OA diagnosis is based on the patient's personal and family history, as well as a history of exposure

to an allergen capable of causing the symptoms. However, to confirm the allergic etiology, skin prick and patch tests are used to determine sensitization to a certain allergen, with conjunctival provocation tests used in certain cases.⁹⁻¹⁰

OA involves an inflammatory response caused by type I and/or IV hypersensitivity reactions following allergen exposure.¹¹ The severity of the reaction depends on the intensity of the inflammation, the patient's age, and genetic and geographic factors. Ocular changes, such as corneal opacities, keratoconus, and cataracts, can affect visual acuity, especially in patients with allergic keratoconjunctivitis.¹²

Given the lack of national data on OA and its ophthalmological consequences, this study aimed to present a demographic and clinical description of patients treated at a specialized university hospital outpatient clinic. The analyzed variables included age, sex, age at symptom onset, phenotypes, clinical manifestations, associated atopic diseases, ophthalmological alterations, and treatment. We also verified the associations between certain variables (age at symptom onset, number of symptoms, and medications used) and ophthalmological changes.

Methodology

Study design

This descriptive, retrospective, cross-sectional study was conducted with patients treated at the OA outpatient clinic of a specialized Allergy and Clinical Immunology Department of a university hospital in São Paulo, Brazil between January

Table 1Classification of clinical forms of ocular allergy⁷

Seasonal and perennial allergic conjunctivitis	This is the most prevalent form of ocular allergy, affecting 22% of the population. In the seasonal form, symptoms appear seasonally and last < 4 weeks. In the perennial form, it is characterized by signs and symptoms that persist for 4 days a week and for > 4 consecutive weeks.
Atopic keratoconjunctivitis	It is usually severe and chronic, mainly affecting men between 30 and 50 years of age. It is associated with atopic dermatitis in almost 100% of cases. Severe cases may result in reduced visual acuity due to epithelial defects, limbal deficiency and corneal opacity.
Vernal keratoconjunctivitis	This is a severe form that occurs prior to 10 years of age in approximately 80% of patients, being slightly more predominant in boys. It is associated with other atopic manifestations in approximately 50% of cases. Central involvement of the cornea may occur, with neovascularization and opacity.
Giant papillary conjunctivitis	It is induced by mechanical irritation from contact lenses, ocular prostheses, or ocular sutures. It usually presents as proliferative changes in the conjunctiva of the upper eyelid.
Allergic conjunctivitis (or eyelid dermatitis)	It occurs after sensitization of the eye through contact, for example, with topical medications. Eyelid dermatitis can be included when the edges of the eyelids are affected.

2002 and December 2022. Only patients with a confirmed diagnosis of OA were included. Data were extracted from their electronic medical records, including demographic characteristics (age, sex), personal and family history of atopy, age at ocular symptom onset, clinical diagnosis of OA, treatment types, clinical course, and associated ophthalmological complications.

Ethical aspects

This study was approved by the institutional research ethics committee on November 24, 2023 (opinion 73221018.3.0000.0068). All included patients provided written informed consent for

the use of their clinical data, which was a limiting factor since, despite being a retrospective study, the ethics committee required an informed consent form to be signed, meaning that only patients who were still being followed up and responded to a phone call could be included.

Statistical analysis

The data were analyzed in STATA 13.1 (StataCorp, Texas, USA). Numerical variables (such as age) were described as mean, standard deviation, and 95% confidence interval (95% CI). Asymmetrically distributed variables were presented as median, with minimum and maximum

values. Associations between categorical variables were assessed using the chi-square or Fisher's exact test, as appropriate. Comparisons between groups were performed using the Mann-Whitney (for 2 independent samples) or Kruskal-Wallis test (for > 2 independent samples), depending on the number of groups and the nature of the variables considered: age at symptom onset, medications, use and duration of allergen-specific immunotherapy (ASIT), and ophthalmic changes.

Results

Between January 2002 and December 2022, 602 patients were screened at our allergy outpatient clinic, with an initial diagnostic hypothesis of

OA. After clinical evaluation, this diagnosis was confirmed in 472. Of the 148 patients who were contacted regarding study participation, 100 agreed and provided written informed consent (Figure 1).

The majority (57%) were male, aged 5-66 (mean, 26.4) years. Of this group, 8% were ≤ 12 years of age, 21% were 13-18 years of age, and 71% were > 19 years of age. The majority (80%) reported OA symptom onset before 12 years of age (Table 2).

The patients were diagnosed as follows: perennial allergic conjunctivitis (83%), atopic keratoconjunctivitis (12%), vernal keratoconjunctivitis (4%), and giant papillary conjunctivitis (1%). No cases of seasonal allergic

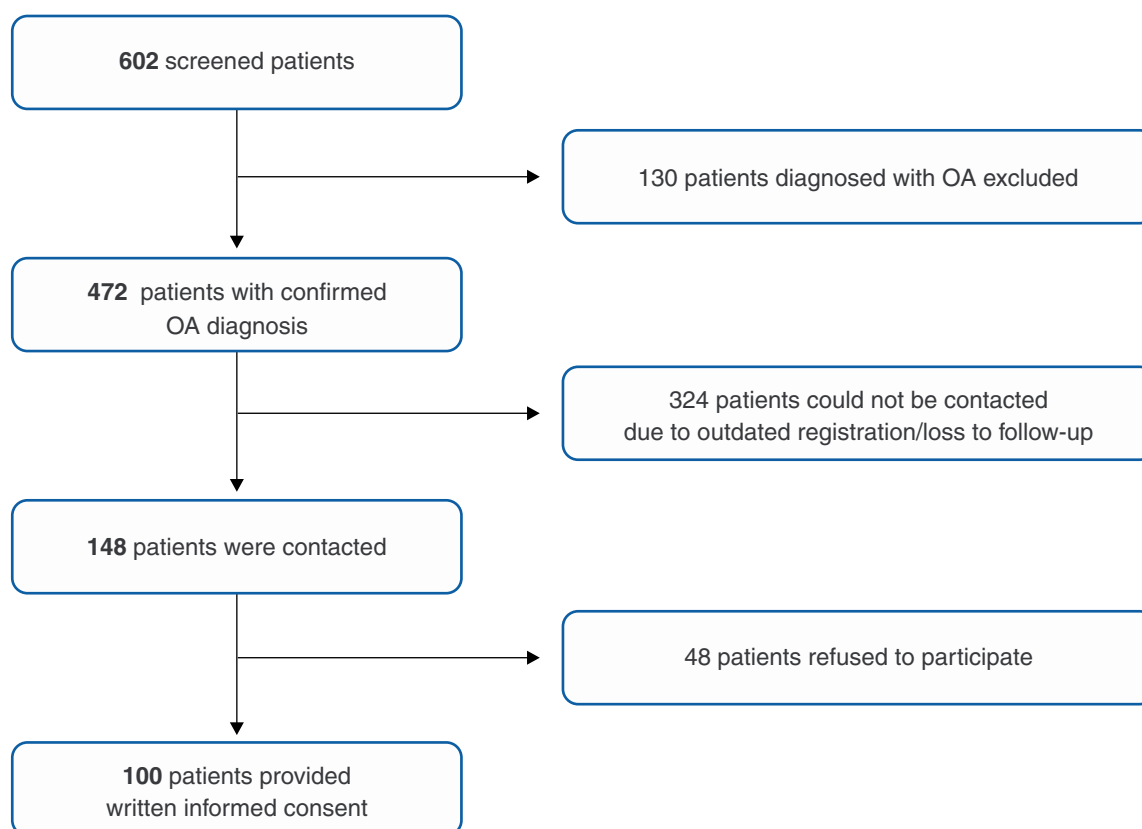


Figure 1

Patient screening and inclusion flowchart
OA = ocular allergy.

Table 2

Distribution of patients by sex, according to age group, and age of symptom onset in patients with ocular allergy included in this study

Children (0-12 years of age)	(n = 8)
Female	4
Male	4
Adolescents (13-18 years of age)	(n = 21)
Female	3
Male	18
Adults (>18 years of age)	(n = 71)
Female	35
Male	36
Age of onset	
Childhood (< 12 years)	80
Adolescence (13-18 years)	8
Adulthood (> 19 years)	12

conjunctivitis, periorbital contact dermatitis, or eyelid dermatitis occurred. The mean time of disease progression was 14.9 years.

The most common patient symptoms were pruritus (90%), hyperemia (65%), and lacrimation (42%). Only 2 patients reported impaired visual acuity. Ophthalmological changes occurred in 26% of the patients, including keratoconus (15%), corneal ulcer (9%), tarsal papillae (5%), Tantra spots (3%) and senile pseudo halo (2%).

In addition to OA, 93% of patients had allergic rhinitis, 55% had asthma, and 30% had atopic dermatitis. Only 1 patient reported a food allergy. The number of associated atopic diseases was higher among children (≤ 12 years of age), with an average of 3.5 diseases per patient, while adolescents and adults (≥ 13 years of age) had an average of 2 diseases.

The most common treatment was topical dual-action antihistamine (olopatadine, 86%

of cases), followed by lubricating eye drops (hydroxypropyl methylcellulose, 61% of cases). Other treatments included second-generation oral antihistamines (loratadine, 13% of cases), mast cell stabilizers (disodium cromoglycate, 6% of cases), topical ocular immunosuppressants (tacrolimus and cyclosporine, 7% of cases), and topical ocular corticosteroids (dexamethasone and fluorometholone acetate, 6% of cases). Most patients (73%) were regularly using topical nasal corticosteroids (budesonide 32 $\mu\text{g}/\text{puff}$) to treat associated allergic rhinitis.

ASIT was recommended for 61% of patients, and 39 (52%) underwent treatment for > 3 years. The mean ASIT treatment time was 41.6 months, and the mean age at initiation was 11.3 years. Patients treated with ASIT had more severe symptoms (pruritus [$p < 0.05$], hyperemia [$p = 0.004$], and lacrimation [$p < 0.05$] than those who were not. Most patients treated with ASIT were female and had concomitant asthma (step 1 severity).

All patients were referred for ophthalmologic evaluation, and 47% were followed up by an ophthalmologist. Surgical procedures were indicated for 7% of the patients, including corneal transplantation (3%), cataract surgery (1%), lacrimal duct surgery (1%), cosmetic surgery for papillary hypertrophy (1%), and lens placement (1%). The patients' clinical and demographic characteristics are shown in Table 3.

Age of symptom onset was not associated with ophthalmological changes ($p = 0.23$). The number of symptoms and medications was also not significantly associated with ophthalmological changes ($p > 0.05$). There were no significant differences in ASIT treatment time in relation to the number of medication classes used ($p = 0.69$), although the number of medications decreased during treatment. Medication use was significantly lower in patients with a mean of 17.3 years since diagnosis ($p = 0.03$).

Discussion

Studies suggest that OA is more common in boys during childhood and in girls after puberty.¹³ In our study, up to 12 years of age and in those over

Table 3

Clinical characteristics of patients with ocular allergy evaluated in this study

Characteristic	(n = 100)
Clinical form of ocular allergy	
Allergic conjunctivitis	83
Atopic keratoconjunctivitis	12
Vernal keratoconjunctivitis	4
Giant papillary conjunctivitis	1
Contact dermatitis	0
Ocular signs/symptoms	
Ocular pruritus	90
Conjunctival hyperemia	65
Tearing	42
Photophobia	6
Eyelid edema	5
Decreased visual acuity	2
Morning eyelid stickiness	2
Ophthalmological changes	
Keratoconus	15
Corneal ulcer	9
Tarsal papillae	5
Tantra Points	3
Pseudo senile halo	2
Associated atopic diseases	
Rhinitis	93
Asthma	55
Atopic dermatitis	30
Drug treatment	
Dual-action topical ocular antihistamine	86
Topical ocular lubricant	61
Oral antihistamine	13
Mast cell stabilizer	6
Topical ocular corticosteroid	6
Topical immunosuppressant	7
Immunotherapy with dust mite extracts	61
Surgical treatment	
Corneal transplant	3
Cataract surgery	1
Tear duct surgery	1
Cosmetic surgery for papillary hypertrophy	1
Lens placement	1

18 years of age, the sex distribution was similar. However, among adolescents (13 to 18 years of age), there was a higher prevalence of males. This profile may be partly explained by the organization of care, since children are preferably treated at the institution's pediatric allergy outpatient clinic.

Although the literature describes OA onset in young adults (mean age 20 years),^{14,15} In our study, 80% of participants reported symptom onset in childhood. This is in line with the profile of our patients, who often have atopic comorbidities, and early symptom onset is characteristic of atopic individuals. This divergence may also be attributed to the different phenotypes prevalent in different case series.

Regarding the OA phenotypes in our case series, there was a predominance of perennial allergic conjunctivitis (83%), which agrees with the literature, since perennial and/or seasonal conjunctivitis is considered the most prevalent clinical form of OA.^{11,16} The lack of cases of seasonal allergic conjunctivitis could be explained by the characteristics of the metropolitan region in which the study was conducted. Patients with perennial allergic conjunctivitis showed a high association with rhinitis and, in practice, this phenotype can be called allergic rhinoconjunctivitis.

Patients with OA often present other associated atopic diseases, and we observed concomitant allergic rhinitis, asthma, and atopic dermatitis. These data are in agreement with the literature.¹⁷ Furthermore, our participants had an average of 3.5 atopic diseases in childhood, 2 in adolescence, and 2 in adulthood. The higher prevalence of atopic diseases in childhood can be explained by the atopic march, which characterizes the progression of diseases such as atopic dermatitis, rhinitis, asthma, and in some cases, food allergies. The immaturity of the immune system in childhood can also favor the development of several atopic conditions.¹⁸

Of the signs and symptoms presented by these patients, pruritus, conjunctival hyperemia, and tearing were the most frequent, followed by photophobia, eyelid edema, secretion, and decreased visual acuity. Ocular pruritus is the most characteristic symptom of OA and is present

in the vast majority of cases. In fact, its absence makes a diagnosis of OA less likely.⁸ Hyperemia, although present in most cases, is not specific to OA. The association between the above-mentioned symptoms and age of onset, duration, seasonality, symptom severity, and location of involvement helps differentiate the type of OA.^{19,20}

OA treatment is divided into 4 lines of action. The first is preventive measures, such as avoiding causative agents, and using cold compresses and artificial tears. The second is antihistamines, which stabilize mast cells, and multi-action drugs. The third is topical corticosteroids for flare-ups and immunomodulators, such as cyclosporine and tacrolimus, for chronic inflammation. The fourth is surgical treatment (papillary excision, grafts) and systemic therapies, such as short courses of oral corticosteroids, in addition to the above mentioned immunomodulators. These approaches aim to alleviate symptoms and avoid complications from prolonged corticosteroid use.^{2,8,21} Among the therapies used in our sample, a combination of olopatadine eye drops and artificial tears was the most common. Olopatadine, which belongs to a group of multi-action drugs, has been shown to be effective both as an antihistamine and a mast cell stabilizer. Artificial tears are used to promote lubrication and hydration of the cornea and conjunctiva.^{2,8}

In more severe cases, topical immunomodulatory medications, such as tacrolimus, fluorometholone, and cyclosporine, were used. A small number of patients presented complications such as keratoconus, corneal ulcers, and giant papillae, for which surgical treatment was required in some cases, including corneal transplant and papillary hypertrophy surgery. In these patients, follow-up was performed in conjunction with the ophthalmology department, which indicated and performed the aforementioned procedures.

Just over a quarter of the patients evaluated in this study presented ophthalmic changes, with keratoconus being the most frequent, which agrees with the literature²² and reinforces national and international recommendations that individuals with OA should undergo a joint assessment by an allergist and an ophthalmologist for a more appropriate therapeutic approach and better quality

of life. Since most patients presented the perennial allergic conjunctivitis phenotype, we expected a lower incidence of ophthalmic changes, which in the literature are more associated with more severe clinical forms, such as vernal keratoconjunctivitis and atopic keratoconjunctivitis.^{7,22} In general, the therapeutic approach used in this group of patients agrees with other studies and follows current treatment guidelines, but was limited to medications provided by the Brazilian Unified Health System.

Most patients received ASIT for dust mite allergens (*Dermatophagoides pteronyssinus* and *Blomia tropicalis*) as additional treatment. According to the literature, the minimum recommended time for ASIT is 36 months,²³ and our patients received ASIT for an average of 41.6 months. In most of our patients, symptom onset occurred in childhood, and ASIT was initiated at an average age of 11.3 years, ie, our patients' immunotherapy was indicated early in the course of the condition. For resource management purposes, our department prioritizes ASIT as an additional treatment for the most severe patients. For this reason, patients who underwent ASIT had more intense symptoms (pruritus, hyperemia, and tearing) and a higher prevalence of asthma than the group that did not receive ASIT. According to the literature, immunotherapy with allergens is efficacious for reducing symptoms and exacerbations in patients with allergic rhinoconjunctivitis, with evidence suggesting that these benefits continue after the conclusion of treatment.²³

We observed no association between ASIT treatment duration and the number of medication classes used. Although reduced medication use during treatment suggests that ASIT is efficacious, it should be noted that the cross-sectional design of our study did not allow robust assessment of treatment efficacy. For a more accurate assessment of ASIT efficacy, longitudinal monitoring tools would be necessary.

Moreover, we observed no association between age of symptom onset and the occurrence of ophthalmic changes or between the number of symptoms, the classes of medications used, and the occurrence of ophthalmological changes.

Conclusions

In this sample of patients with OA treated at a specialized outpatient clinic in São Paulo, males predominated, with symptom onset generally occurring before 12 years of the age. The most common phenotypes were perennial allergic conjunctivitis and atopic keratoconjunctivitis, including symptoms such as pruritus, hyperemia, and tearing. Rhinitis and asthma were frequently associated, especially in children. The usual treatment included dual-action ocular antihistamines and artificial tears, with immunotherapy indicated in most cases. Ophthalmic changes, such as keratoconus and corneal ulcer, affected more than a quarter of the patients, with no significant correlations among symptoms or treatments.

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