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Ocular Allergy and Its Relationship with Dry Eye Disease in The Paediatric Age Group in A Tertiary Hospital

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Abstract

***Purpose*:** *This study aims to determine the relationship between vernal keratoconjunctivitis (VKC) and allergic conjunctivitis (AC) (seasonal and perennial types) with dry eye disease (DED).*

Method: *This is a hospital-based prospective case-control study, in which children 5-15 years of age who presented to the eye clinic with clinical features of either Vernal Keratoconjunctivitis or Allergic Conjunctivitis with no other ocular pathologies. The control group were children 5-15 years old with no complaints suggestive of ocular allergy. A detailed ocular examination was done. Schirmer's 1 test, Tear film break-up time (TBUT) and Keratometry were done. Analysis was done using International Business Machines (IBM) and Statistical Package for Social Sciences (SPSS) version 27 (SPSS Inc., Chicago, IL, USA).*

Results: *Two hundred and forty- two children (242) were included in the study. The case group had 59.5% of males. The most prevalent age group was 6-10 years among the cases. Schirmer's test showed a mean value of10.5±3.5mm in the case group, indicating mild dry eyes. TBUT was 10.52±3.4secs in the case group and 13.73±5.2secs. in the control group.The keratometry value in the case group (43.1±1.7D) was higher than that of the control group (42.2±5.3D).*

***Conclusion*:** *There is evidence of an association between vernal keratoconjunctivitis, allergic conjunctivitis, and dry eye disease.*

Keywords: Allergic conjunctivitis, Vernal Keratoconjunctivitis, Ocular surface disease, Ocular Allergy, Children, Dry Eye, Seasonal conjunctivitis, Perennial Conjunctivitis.

Introduction

Ocular allergic diseases are commonly found in every pediatric eye clinic, and their chronic and sometimes recurrent nature are causes of recurrent hospital visits. Allergic conjunctivitis (AC) and vernal keratoconjunctivitis (VKC) are type I hypersensitivity reactions with the hallmark symptom of ocular and peri-ocular itching [1]. These diseases are significant causes of ocular morbidity. Severe cases can compromise the quality of life of the patient and lead to vision loss.

The ocular surface disturbance caused by ocular allergic diseases like AC and VKC can precipitate and lead to the clinical features of dry eye disease. Children are poorly descriptive when the symptomatology issue arises, which could account for the possible low incidence and even the failure to detect dry eye disease seen in them.

Understanding the relationship between AC, VKC, and dry eye in pediatric patients is also very important for determining the most suitable and effective treatment modalities. Clinical studies on this relationship are sparse locally and there is a need to build on the existing knowledge to make recommendations that can improve treatment and diagnostic outcomes.

Allergic conjunctivitis (AC) is a type 1 IgE-mediated (Immunoglobulin E –mediated) hypersensitivity reaction common in children. There are two variants: The Seasonal Allergic Conjunctivitis (SAC) also called Hay fever conjunctivitis and the Perennial Allergic Conjunctivitis (PAC). They differ primarily in their symptomatic timing with SAC having short-lived symptoms which are more in summer and spring and PAC tending to occur all year round with varying degrees of severity. Causative allergens include tree and grass pollen, house mites, animal dander, and fungal spores. Vernal Keratoconjunctivitis (VKC) is a type 1 IgE-mediated and type 4 hypersensitivity reaction with cell-mediated immune mechanisms [2]. It is common in warm dry climates and seen more in boys.1 It can be found in either of 3 forms: limbal, palpebral, or mixed [2].

In the pathogenesis of AC and VKC, inflammatory agents in tears incite ocular surface inflammation and increase tear osmolarity, which can lead to some of the characteristic clinical features of dry eye disease [3]. Itching seen in these conditions can cause cornea changes, such as reduced density of basal epithelial membrane, alteration in thickness, cornea scars, ulcers, and keratoconus [4-6].

VKC and AC affected patients can present with intense itching, foreign body sensation, tearing with occasional mucoid discharge, photophobia, and increased blinking [7-9]. Both conditions are significant causes of reduced quality of life, especially when they are in their active forms [10].

Dry eye disease (DED) is defined as a multifactorial disease of the ocular surface characterized by various factors and clinical features, such as loss of homeostasis of the tear film, accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play significant roles. It is documented to be seen mostly in adults.

DED can present as a primary ocular disorder or a secondary ocular disorder. It is also marred with significant morbidity. The secondary dry eyes are mostly due to conditions that affect the ocular surface such as systemic allergy, and autoimmune diseases like Rheumatoid arthritis and Sjogren syndrome amongst several others [11].

Symptomatic diagnosis of allergic conjunctivitis conflicts very much with dry eye disease as both conditions share similar clinical presenting features. In a study relating allergic conjunctivitis with dry eye diseases, patients who reported itchiness redness, and dryness were evaluated using the subjective evaluation of symptoms of dry eye questionnaire. found that most patients with itchy eyes, which was consistent with allergic conjunctivitis also had dry eye disease. Hence, it was concluded that the patients could have concomitant ocular allergic disease and dry eye [12].

DED complicates VKC as shown in a Middle East study that assessed complications and causes of visual loss amongst patients with VKC. Of the 58 patients included in the study, 32 of them had dry eye disease, which according to the study, contributed to their visual loss. 5In another study carried out, dry eye disease in VKC was seen to have very strong associations, especially in the active VKC group where increased symptoms and signs of ocular surface disease was found [13]. In AC and VKC, diagnosis is mostly clinical. Additional investigations, such as blood count for eosinophil and basophil assay are mostly supportive in the clinical diagnosis. Cornea scrapping, conjunctiva impression cytology, and skin allergy testing are among other investigations that can be employed. DED involves both clinical and investigative procedures [14].

Subjective questionnaires are useful in the diagnosis of DED; however, they are not child-friendly, hence their limited use in the diagnosis of dry eye disease in the pediatric population [15,16]. in their study, employed visual analogue scale symptoms assessment, slit lamp biomicroscopy, tear film break-up time with fluorescein, conjunctiva lissamine green staining, corneal esthesiometry, Schirmer's test with anesthetic, and meibomian glands inspection and expression in their diagnosis of DED [13]. Other clinical investigations used in the diagnosis of DED include tear film break-up time lacrimal lake height, Tear Break-up time, cornea fluorescein staining, rose bengal staining, conjunctiva impression cytology, tear osmolarity, ocular tear ferning test, erythrocyte sedimentation rate, C- reactive protein, Lacrimal gland biopsy [17,18].

The subjective and objective nature of these investigations in the diagnosis of DED was shown by Onwubiko et al, to have a poor agreement but an almost equal correlation for DED diagnosis [19]. Newer biomarkers, such as matrix metalloproteinase 9(MMP-9), lactoferrin, and lysozyme are now being used in the diagnosis of DED and AC.These biomarkers show a significant correlation between clinical symptoms and signs. This article focuses on vernal keratoconjunctivitis (VKC) and Allergic conjunctivitis (AC) (seasonal and perennial types)

and assesses their relationship with dry eye disease [20].

Methods

This is a hospital–based prospective case-control study, in which children 5-15 years that presented to the eye clinic with clinical features of Vernal Keratoconjunctivitis or Allergic Conjunctivitis with no other ocular pathologies. The control group were children 5-15 years old with no complaints suggestive of ocular allergy. Ethical approval was obtained from the Lagos State University Teaching Hospital (LASUTH) Health Ethics and Research Committee. Schirmer's 1 test and Tear film break-up time (TBUT) were done and recorded [21]. Keratometry was done using the autorefractor-keratometer and recorded in diopters. Analysis was done using International Business Machines (IBM) and Statistical Package for Social Sciences (SPSS) version 27 (SPSS Inc., Chicago, IL, USA). A 95% confidence interval was used for all the statistical tests. P value < 0.05 was considered significant.

Results and Discussion

Allergic conjunctivitis is a common benign process that is rarely vision-threatening but can decrease the quality of life of the patient [22]. Dry eye disease (DED), which is a multifunctional disease, causes ocular discomfort and visual disturbance. It can interfere with the daily activities of the affected individuals [23]. The presence of both in the same individual could be devastating. One hundred and twenty-one children with cases of allergic conjunctivitis or VKC and 121children made up the control group. The case group had a higher proportion of males (59.5%). **Fig.1**.

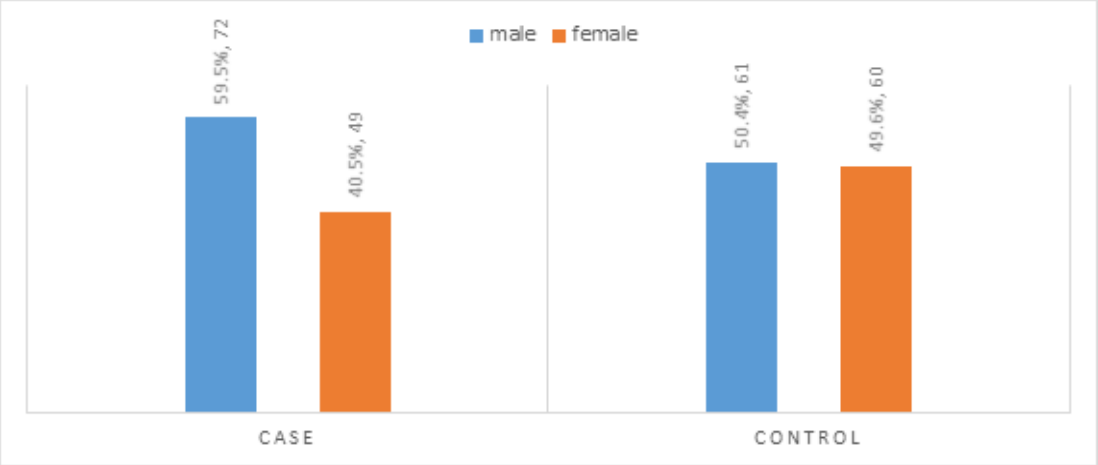

Figure1: Gender distribution

This aligns with several studies, in which there was an increase in the proportion of males as opposed to other studies that found more prevalence of females [24- 31]. While other studies showed equal distribution in males and females [32,33].

The high preponderance of males could be due to the more involvement of males in outdoor activities than girls and their more exposure to allergens that cause allergies. It could also be due to the influence of the hormone estradiol which may enhance mast cell activation and allergic sensitization causing a male preponderance before puberty and a reversal of this gender after adolescence. The most prevalent age group category among the cases was in the 6-10 years group (45.5%). **Fig.2 [34]**.

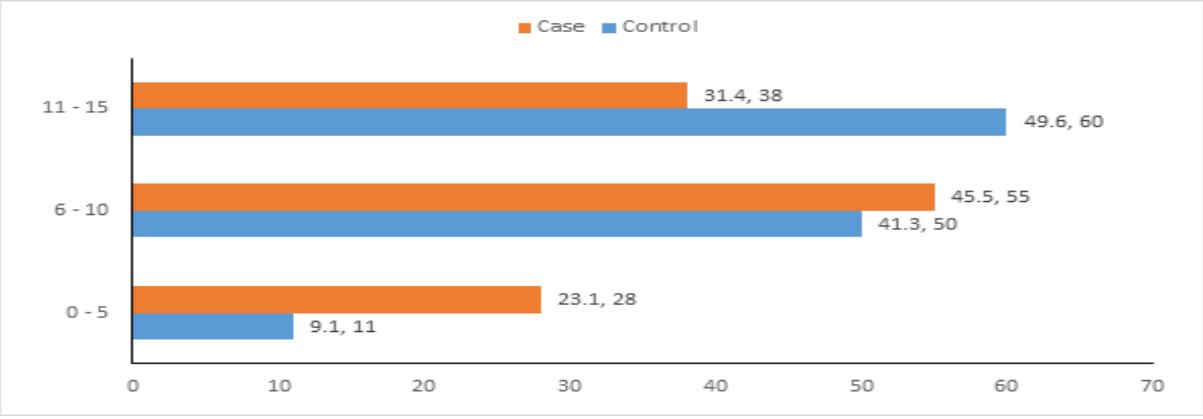

Figure 2: Age Distribution.

This is comparable to a study done, where most of the children seen with AC were within the 5-8 years age group (38.2%) and 9-11 age group (31.8%). However, contrary to other studies where older children were seen more to have ocular Allergies [26,25,27,32].

The ocular allergy classified among the participants in the study was divided into three categories: Seasonal Allergic Conjunctivitis (SAC), Perennial Allergic Conjunctivitis (PAC) and Vernal Keratoconjunctivitis (VKC). A notable proportion of the participants (55.4%) had VKC.**Fig. 3**.

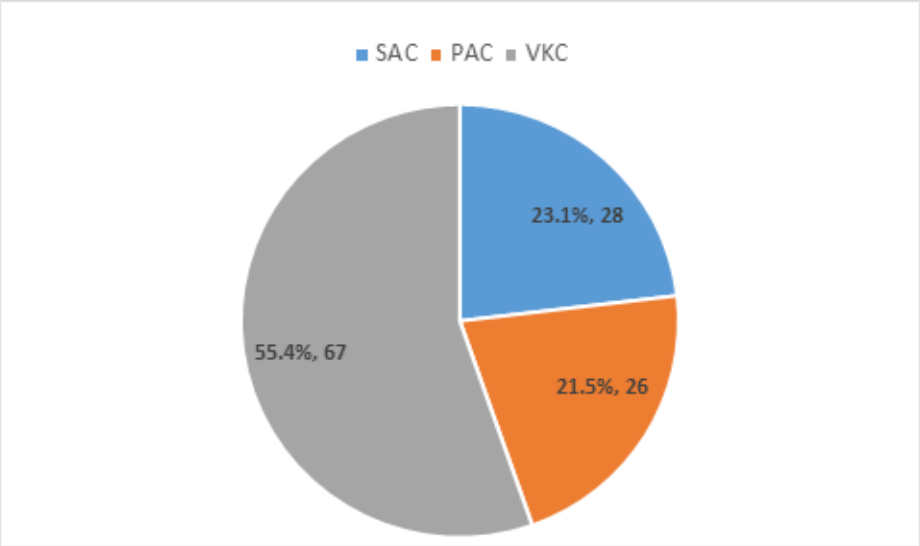

Figure 3: Classification of Ocular Allergy

This finding is comparable to a study done in Pakistan, where VKC was the most common type of allergic conjunctivitis followed by PAC [28]. A similar result was also seen in a study done by, where most of the cases seen had VKC [24]. The increase in the number of children with VKC could be a result of referral to a tertiary hospital because VKC can cause bilateral recurrent inflammatory disorder of the conjunctiva and cornea and visual impairment. Also, VKC is a disease of warm climates and the study location was in a warm environment. It is also said to be more prevalent in African countries and Japan. A contrary result was found in a study where 1502 children from 10 schools were examined [35]. Allergic conjunctivitis was seen in 29.16% of them, with SAC (56.36%) being the most common type of AC. PAC was more prevalent in a cross- sectional survey done in a semi-urban low-income community in India [25,26].

Symptoms like frequent itching (90.1%), watering (67.8%), and thick ropy discharge (58.7%) were more common among the cases than the controls. Table 1.

Variables	Group			X^2 (P-value)
	Total (242) (%)	Case (121)(%)	Control (121)(%)	
Frequent itching in the eye				
Yes	118 (48.8)	109 (90.1)	9 (7.4)	165.3 (<0.001)*
No	124 (51.2)	12 (9.9)	112 (92.6)	
Watering				
Yes	105 (43.4)	82 (67.8)	23 (19.0)	58.5 (<0.001)*
No	137 (56.6)	39 (32.2)	98 (81.0)	
Burning Sensation in the eyes				

Yes	37 (15.3)	33 (27.3)	4 (3.3)	26.8 (0.001)*
No	205 (84.7)	88 (72.7)	117 (96.7)	
Thick ropy Discharge				
Yes	73 (30.2)	71 (58.7)	2 (1.7)	93.3 (0.001)*
No	169 (69.8)	50 (41.3)	119 (98.3)	

Significant at p<0.05.

The hallmark of ocular allergy is itching [36]. This was seen in most studies done on ocular allergies 25 [26-32]. This could be a result of the release of cytokines and chemokines by the mast cells with the release of histamine and eosinophils thereby creating continued inflammation [37]. Watery of the eyes was more prominent after itching in some studies, while ropy discharge was more prominent after itching in others[36,27,25,30].

A significant majority (91.3%) of the participants demonstrated visual acuity (VA) within the range of 6/6 to 6/18. Notably among the case group. 5(4.1%) cases and 12(9.9%) of control presented with visual acuity of 6/18-6/60. This is contrary to a study done in Yemen where the majority of the participants had visual acuity between 6/24 and 6/60(32%) [38]. The participants seen in that study had mainly vernal keratoconjunctivitis which can cause visual impairment when there is cornea involvement.

The eyelids within the cases revealed a 68.6% of hyperpigmentation. Dermatitis was observed in 17.4% of those in the case group, while 13.2% exhibited superior tarsal papillae. This can be caused by rubbing and scratching the skin around the eyes and by fluid accumulation due to allergy [39]

On the conjunctiva, 53.7% of children with allergic conjunctivitis had brown discoloration of the conjunctiva. This is similar to a study done on Chinese patients with vernal keratoconjunctivitis that showed all the patients examined to have perilimbal conjunctiva pigmentation [40]. The pathogenesis is multifactorial. Abundant melanocytes and mast cells around the limbus, growth factors, or interleukins may stimulate the melanocytes producing such pigments around the limbus. Limbal/Palpebral papillae were not a common finding in this study as opposed to a study done by where it was found to be the most frequent sign [25]. Among the children with allergic conjunctivitis, 95.9% exhibited a clear cornea. Three of the children (1.2%) in the case group exhibited punctuate epithelial keratitis while 2 (0.8%) had shield ulcers. Table 2.

Table 2: Visual Acuity and Clinical signs of Allergic conjunctivitis

Symptoms	Total (%)	Group		X^2 (P-value)
		Case (%)	Control (%)	
Visual Acuity				
6/6-6/18	221 (91.3)	116 (95.9)	105 (86.8)	7.430 (0.59)
6/18-6/60	17 (7.0)	5 (4.1)	12 (9.9)	
<6/60-3/60	3 (1.2)	0 (0.0)	3 (2.5)	
<3/60-NLP	1 (0.4)	0 (0.0)	1 (0.4)	
Lids				
Normal	118 (48.8)	0 (0.0)	118 (97.5)	232.18 (<0.001)*
Hyperpigmentation	85 (35.1)	83 (68.6)	2 (1.7)	
Dermatitis	21 (8.7)	21 (17.4)	0 (0.0)	
Ptosis	2 (0.8)	1 (0.8)	1 (0.8)	
Superior tarsal papillae	16 (6.6)	16 (13.2)	0 (0.0)	

Conjunctiva				
White	150 (62.0)	32 (26.4)	118 (97.5)	129.71 (<0.001)*
Injected (Red)	24 (9.9)	23 (19.0)	1 (0.8)	
Brown	67 (27.7)	65 (53.7)	2 (1.7)	
Limbal/Bulbar papillae	1 (0.4)	1 (0.8)	0 (0.0)	
Cornea				
Clear	237 (97.9)	116 (95.9)	121 (100.0)	5.10 (0.78)
Punctate Epithelial Keratitis	3 (1.2)	3 (2.5)	0 (0.0)	
Shield ulcer	2 (0.8)	2 (1.7)	0 (0.0)	

*** Significant at p<0.05.**

This aligns with a study where the majority of those examined had clear cornea but contrary to study, where cornea scarring was observed in 59(20.3%) of those examined, and in Behera et al's study, where superficial punctate keratitis was observed in 31.79% of the patients. Otherwise, corneal involvement is said to be rare (25,28,41,25,43].

The quantity of tears assessed using Schirmer's test showed a mean value of 10.5±3.5mm in the case group, indicating they have mild dry eyes. While 26.5±9.1mm in control group indicating a normal range. Mild dry eyes were observed in 43.0% of the cases and moderate dry eyes in 42.1%.

Most cases in the VKC group showed mild to moderate dry eyes, while severe dry eyes were predominant in the SAC group. This is contrary to a study done by Mazumdar et al43 where severe dry eye was observed more in 45.45% of patients with PAC and least in those with VKC. In another study, only 5 of the 50 eyes with allergic conjunctivitis had abnormal Schirmer's test [44].

Tear-film Breakup time (TBUT) was 10.52±3.4secs. in the case group and 13.73±5.2secs. in the control group. The case group (53.7%) exhibited normal TBUT, while 46.3% had dry eyes. **Table 3.**

Table 3: Examination of Clinical Outcome

Parameters	Total (%)	Case (%)	Control (%)	X^2 (P-value)
Schirmer's test (mm)				
Mean ± SD	18.5 ± 10.5	10.5 ± 3.5	26.5 ± 9.1	
Severe dry eyes	8 (3.3)	5 (4.1)	3 (2.5)	130.09 (<0.001)*
Moderate eyes	60 (24.8)	51 (42.1)	9 (7.4)	
Mild dry eyes	60 (24.8)	52 (43.0)	8 (6.6)	
Normal tear function	114 (47.1)	13 (10.7)	101 (83.5)	
Keratometry				
Mean ± SD	42.2 ± 5.3	43.1 ± 1.7	41.4 ± 7.2	
40.5 – 46.5 D	231 (95.5)	118 (97.5)	113 (93.4)	4.70 (0.95)
47 – 48 D	10 (4.1)	2 (1.7)	8 (6.6)	
49 – 53 D	1 (0.4)	1 (0.8)	0 (0.0)	
TBUT (s)				
Mean ± SD	12.1 ± 4.60	10.52 ± 3.4	13.73 ± 5.2	
Dry eyes	85 (35.1)	56 (46.3)	29 (24.0)	132.22 (<0.001)*
Normal	157 (64.9)	65 (53.7)	92 (76.0)	

*** Significant at p<0.05.**

This is similar to a study done by in China, where mean TBUT was found to be 6.54±1.48 secs. in the case group and 10.04±1.79 secs. in the control group [45]. The mean TBUT was higher in other studies than in this study [44,]. Analysis of TBUT among the different types of allergic conjunctivitis studied showed TBUT to be less than 10sec in 48.2% of VKC cases, 26.8% of SAC, and 25.0% of PAC cases. This is contrary to a study done by, where 45.45% of those with PAC had TBUT less than 10 sec, SAC-30.43%, and the least was seen in those with VKC-10%, though the difference was not statistically significant [43]. Reduced TBUT which also indicates tear instability is a significant objective sign of dry eye disease.

Schirmer's test showing severe dry eyes were predominant in participants aged 11-15 years (62.5%), while moderate dry eyes were seen more in children of 6-10 years old (48.3%) and mild dry eyes in 40.0%. This age-related association was statistically significant (0.02). In the gender distribution, severe dry eyes were dominant among males (62.5%), with similar findings with moderate dry eyes (55.0%) and mild dry eyes (40.0%). The association between TBUT and socio-demographic factors indicates that dry eyes were predominant in age group 6-10(43.5%) and among male children (57.6%). — Table 4.

Table 4: Schirmer's Test Association with Ocular Allergies Classification

Parameters	Total (%)	Severe dry eyes (%)	Moderate dry eyes (%)	Mild dry eyes (%)	Normal tear function (%)	X^2(P-value)
Ocular allergies classification						
Seasonal allergic conjunctivitis (SAC)	28 (23.1)	3 (60.0)	12 (23.5)	10 (19.72)	3 (23.1)	15.08 (0.02)*
Perennial allergic conjunctivitis (PAC)	26 (21.5)	0 (0.0)	14 (27.5)	6 (11.5)	6 (46.2)	
Vernal Kera conjunctivitis (VKC)	67 (55.4)	2 (40.0)	25 (49.0)	36 (69.2)	4 (30.8)	

The relationship between TBUT and different types of ocular allergies showed dry eyes to be predominant in vernal keratoconjunctivitis (48.2%)—Table 5. The keratometry value in the case group (43.1±1.7D) was higher. Most of the children (95.5%) exhibited a keratometry reading within the 40.5 to 46.5 diopters range. Among those diagnosed with ocular allergy, a significant proportion (97.5%) fell within this range.This is similar to the study done by, which showed a higher K value in the allergic conjunctivitis group compared to the control group [44].

The Schirmer's test and TBUT were lower in the ocular allergy cases compared to the control group and the difference was statistically significant.

Table 5: TBUT (Tear Break-Up Time) Association with Ocular Allergies Classification

Parameters TBUT	Total (%)	Dry eyes (%)	Normal eyes (%)	X^2 (P-value)
Ocular allergies classification				
Seasonal allergic conjunctivitis (SAC)	28 (23.1)	15 (26.8)	13 (20.0)	2.162 (0.339)
Perennial allergic conjunctivitis (PAC)	26 (21.5)	14 (25.0)	12 (18.5)	
Vernal Keratoconjunctivitis(VKC)	67 (55.4)	27 (48.2)	40 (61.5)	

Conclusion

There is evidence of an association between allergic conjunctivitis, vernal keratoconjunctivitis with dry eye disease.Though mild dry eyes were more prominent in patients with VKC,tests for dry eyes should be incorporated into the management of allergic conjunctivitis and VKC in the pediatric population as they may not be able to complain of the symptoms of dry eye.

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Disclosure

SThe authors report no conflict of interest in the work.

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