

Association of Dry Eye with Vernal Keratoconjunctivitis: A Hospital-based Cross-sectional Study

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ABSTRACT

Introduction: Vernal Keratoconjunctivitis (VKC) is a common allergic disease seen in children. The allergic component is caused by Immunoglobulin E (IgE) and mast cell-mediated pathway. It is proposed to be a combination of immune system, genetic, and environmental factors. Secondary dry eye develops secondary to inflammatory disease namely vascular, allergic, environmental conditions like allergens, cigarette smoke, hormonal changes, systemic disorders, such as diabetes mellitus, eye surgeries such as refractive surgery and systemic medications, such as diuretics and antihistamines. Co-existence of dry eye and VKC can worsen the symptoms of the patient and may also lead to prolonged and unnecessary treatment of the disease.

Aim: To study the association of dry eye with VKC by Schirmer's test and Tear Film Breakup Time (TBUT).

Materials and Methods: A hospital-based cross-sectional study was conducted in the Department of Ophthalmology, Sri Siddhartha Medical College and Research Centre, Tumkur, Karnataka, India, from December 2020 to June 2022. Thirty-three patients of age group between 5-20 years with symptoms of VKC were evaluated for dry eye using Schirmer's test and TBUT, respectively. Each patient was subjected to detailed history taking, followed by ocular examination as per the predesigned proforma. The patients were subjected to the tear film analysis

using Schirmer's test and TBUT. The data was compiled and the association between categorical variables were analysed using Chi-square test. The data was analysed using Statistical Package for the Social Sciences (SPSS) software version 21.0. The parameters compared were the type of dry eye with the type of VKC.

Results: The mean±Standard Deviation (SD) age of the study group was found to be 11±1.5 years. Out of 33 patients, 69.69% of all the cases were seen in the 5-12 years age group. There was male preponderance in the present study with 63.63% of patients being male child. VKC was most commonly seen as mixed accounting for 57.57% of cases. In the current study, it was discovered that 60.6% of cases showed no sign of dry eye, whereas 39.82% of cases had dry eye. The dry eye was more commonly seen in mixed type of VKC. The p-value was statistically significant (p-value <0.001) for association of dry eye with mixed type of VKC.

Conclusion: The present study highlighted the co-existence of dry eye with VKC. There was a significant association of dry eye with VKC and type of VKC as well, which might have long-term effects on the ocular surface. These ocular surface alterations exist during active and the quiet phase of VKC. The patients of VKC may need a long-term follow-up and treatment for this ocular surface alteration.

Keywords: Allergy, Limbus, Palpebral, Schirmer's test, Tear breakup time

INTRODUCTION

The VKC is a recurrent, bilateral, seasonal and an external ocular inflammatory disease of unknown cause. VKC is known to have an allergic component caused by IgE and mast cell-mediated pathway. It is proposed to be a combination of immune system, genetic, and environmental factors [1]. The clinical picture of VKC is characterised by ocular symptoms such as ocular pruritus, tearing, burning, foreign body sensation and photophobia [2]. Clinical signs of VKC include a papillary reaction of the upper tarsal conjunctiva and throughout the limbus. The disease can be classified into three clinical subtypes based on the location of the papillae: tarsal (palpebral, limbal or bulbar and mixed form) [3].

The tarsal form is characterised by large, cobblestone like papillae on the upper tarsal conjunctiva. These can differ in shape and size, but are usually defined as >1.0 mm in diameter [1,3]. The limbal form typically involves Horner-Trantas dots, indicating lymphocytic and eosinophilic infiltration of the limbal conjunctiva [1,3]. The mixed form is characterised by the presence of both tarsal and limbal subtypes in only one eye (as signs are often heterogeneous between eyes). VKC occurs mainly in children and young adults with onset often occurring in the first decade of life (predominantly 5-10 years). While it is considered a long-term disease with an average duration

of 4-8 years [4], VKC generally subsides before or just after puberty, but can leave permanent lesions in patients with severe disease [4]. The disease is more common among males than females, with a ratio of 3:1, but this difference may become less at older ages of onset [4].

Vernal and atopic conjunctivitis are also hypothesised to be the causes of dry eye disease and dry eye like symptoms [5]. Dry eye syndrome is a disease of the ocular surface and it is multifactorial. Dry eye is characterised by inflammation of the ocular surface and reduction in tear production [5]. The definition of Dry Eye Disease (DED) as per Dry Eye Workshop (DEWS) II of the Tear Film Ocular Surface Society (TFOS) was identified as a multifactorial ocular surface illness that is characterised by a vicious cycle of tear film instability and hyperosmolarity [6,7].

Secondary dry eye arises as a result of inflammatory disease, specifically vascular, allergy, and environmental factors like allergens, tobacco smoke and hormone changes. Systemic disorders including diabetes mellitus, refractive eye surgery, and systemic drugs like diuretics and antihistamines [8]. Studies have shown an overlap of dry eye and allergic conjunctivitis, but recent reports show the synergic effect of these both conditions in affecting tear film dynamics, and ocular surface maintenance [8,9].

Inflammations in the eye can be a causative factor for goblet cell damage, Mucin 5AC, Oligomeric Mucus/Gel-forming (MUC5AC) messenger Ribonucleic Acid (mRNA), expression, and corneal nerves damage, contributing to dry eye [9]. Hence, the present study was pursued to evaluate the association between dry eye and VKC. It exacerbates the symptoms of allergy and may also alleviate the complications of VKC. In the present study, association between Schirmer's graded dry eye and with VKC was also made. This study also tried to grade the severity of the dry eye (TBUT) with the subtype of VKC.

MATERIALS AND METHODS

A hospital-based cross-sectional study conducted in the Department of Ophthalmology, Sri Siddhartha Medical College and Research Centre, Tumkur, Karnataka, India, from December 2020 to June 2022. The study was approved by Institutional Ethics Committee (SSMC/MED/IEC-42/ JAN-2021). All patients who presented with symptoms of VKC at Sri Siddhartha Medical Hospital were selected and evaluated for dry eye with Schirmer's and TBUT tests in the study.

Inclusion criteria: Patients of age group between five to 20 years as it typically affects first decade of the life presenting with symptoms like ocular pruritus, tearing, burning, foreign body sensation and Photophobia, tear film instability were included in the study.

Exclusion criteria: Patients with pre-existing dry eye, pre-existing keratoconjunctivitis sicca, meibominitis, patients having vitamin A deficiency and patients with history of atopy were excluded from the study.

Study Procedure

A total of 33 patients were sequentially collected after considering inclusion and exclusion criteria. Informed consent was obtained from all subjects after the nature of the study was explained to them. A comprehensive ophthalmic examination, including Best-Corrected Visual Acuity (BCVA), slit-lamp examination, was undertaken for all participants. Snellen's chart was used to assess VA and improvement with pinhole, if any was noted. The patients were subjected to the tear film analysis using Schirmer's test and tear film breakup time. The Schirmer's test was carried out as follows, to evaluate the production of aqueous tears. Sterilised paper strips were placed in the inferior temporal area of the conjunctival sac in both eyes.

The patient was instructed to close their eyes, the room was softly light, and the length of wetness was measured in millimetres after five minutes. Wetness of <15 mm after three minutes was considered abnormal. A value of less than 6 mm of strip wetting in three minutes was accepted as diagnostic marker of aqueous tear deficiency. The time before tear film breaks up following a blink is referred to as TBUT. The normal TBUT is between 15 and 20 seconds. A fluorescein strip that has been moistened with saline covers the inferior cul-de-sac. After several blinks, the tear film was examined using a broad-beam slit lamp with a blue filter to check for the appearance of the first dry spots on the cornea. Less than 5 to 10 second TBUT values were indicative of a tear deficiency. Severity of dry eye was categorised with TBUT <10 seconds, moderate <5-10 seconds, severe <5 seconds [10,11] and according to the Schirmer's test, mild <10 mm, moderate <5-10 mm, severe <5 mm [12,13].

STATISTICAL ANALYSIS

Descriptive statistical analysis was done by mean and standard deviation for quantitative variables and frequency/percentage for

categorical variables. The association between categorical variables were analysed by using Chi-square test. The data was analysed by using SPSS software version 21.0 and p-value <0.05 has been considered as level of significance.

RESULTS

The mean±SD age in the present study was found to be 11±1.5 years. The age-wise distribution is mentioned in the [Table/Fig-1].

Age groups (years)	Frequency (n)	Percentage (%)
5-8	12	36.36
9-12	11	33.33
13-16	6	18.18
17-20	4	12.12

[Table/Fig-1]: Age-wise distribution.

The patients were distributed according to gender as shown in the [Table/Fig-2]. Males 21 (63.63%) were found to be more frequently affected by VKC than females 12 (36.36%).

Gender	Frequency (n)	Percentage (%)
Female	12	36.36
Male	21	63.63

[Table/Fig-2]: Gender-wise distribution.

Patients were distributed according to the type of VKC as shown in [Table/Fig-3]. Mixed type accounted for 57.57% of instances of VKC, which was the most prevalent kind, followed by 8 (24.24%) patients with bulbar type and 6 (18.18%) patients with palpebral type.

The frequency distribution of deranged TBUT in patients with VKC is shown in [Table/Fig-4].

Type of VKC	Frequency (n)	Percentage (%)
Bulbar	8	24.24
Mixed	19	57.57
Palpebral	6	18.18

[Table/Fig-3]: Distribution of patients according to type of Vernal Keratoconjunctivitis (VKC).

Tear breakup time	Frequency (n)	Percentage (%)
Mild	9	27.27
Moderate	3	9.09
Severe	1	3.03
Normal	20	60.6

[Table/Fig-4]: Frequency distribution of VKC patients with deranged TBUT.

In the present study, it was found that 39.82% of cases showed dry eye with mild (27.27%), moderate (9.09%), and severe (3.03%). Schirmer's test results were shown in [Table/Fig-5] for the evaluation of dry eyes in VKC. In the current study, dry eye was present in 30.3% of patients and 69.69% of cases had no evidence of dry eye.

Schirmer's graded dry eye	Frequency (n)	Percentage (%)
Mild	8	24.24
Moderate	2	6.06
Normal	23	69.69

[Table/Fig-5]: Frequency distribution of VKC patients with Schirmer's graded dry eye.

[Table/Fig-6] compares the kind of VKC with the TBUT-related dry eye. In the present study, dry eye was more commonly seen in mixed type 6 (66.7%) of VKC. The p-value was statistically significant (p-value <0.001) for association with mixed type of VKC.

TBUT	Palpebral	Bulbar	Mixed	Total, n
Mild, n (%)	3 (33.3)	0	6 (66.7%)	9
Moderate, n (%)	0	1 (33.3)	2 (66.7)	3
Severe, n (%)	0	0	1 (100)	1

[Table/Fig-6]: Comparison between type of VKC and TBUT-related dry eye.

Comparison of the type of VKC with the Schirmer's associated dry eye is shown in [Table/Fig-7]. Schirmer's test results for mixed types of VKC revealed the presence of both mild 7 (87.5%) and moderate 2 (100%) dry eyes. There was a statistically significant association with p-value <0.001. Both the Schirmer's test for dry eyes and the TBUT test for dry eyes show statistically significant differences in the proportion of the various types of VKC with the grades of dry eye.

Schirmer's associated dry eye	Palpebral	Bulbar	Mixed	Total, n
Mild, n (%)	0	1 (12.5)	7 (87.5)	8
Moderate, n (%)	0	0	2 (100)	2
Severe, n (%)	0	0	0	0

[Table/Fig-7]: Comparison between type of VKC and Schirmer's associated dry eye.

DISCUSSION

The present study was designed to determine the association of dry eyes with VKC. Majority of the patients belonged to 5-8 years age group. The results of the present study were in accordance with Saboo US et al., where, the mean age of presentation of VKC was 12 years [14]. In a study conducted in Ethiopia, Alemayehu AM et al., discovered that the average age of presentation was eight years [15]. VKC was reported to affect males (63.63%) more frequently than females (36.36%). The findings of the current study were consistent with those of investigations by Alemayehu AM et al., and Saboo US et al., in which 87% of cases and 55.6% of cases, respectively, were males [14,15].

In the current study, majority of patients had bulbar VKC, followed by mixed VKC. The study's findings agreed with those of Alemayehu AM et al., with mixed type of VKC of about 53.1% followed by palpebral type of VKC of about 43.8% [15]. In a study conducted by Ujwala S et al., showed 72% of mixed type VKC [14]. Dry eye was shown to co-occur in VKC patients as determined by the TBUT test, with mild dry eye detected in maximum cases and severe dry eye in least cases. In the current study, mild dry eye was defined as a TBUT of 10 seconds or less, moderate dry eye as a TBUT of 5-10 seconds, and severe dry eye as a TBUT of less than five seconds [14]. Villani E et al., studies revealed that VKC cases had a deranged TBUT rather than a lack of tearing. They found that the TBUT time reduced to 6.31 ± 2.60 seconds in their cases as compared to controls, who had 13.37 ± 2.93 seconds [16].

Another study by Tibrewal S et al., found that, TBUT was lower in VKC children with TBUT around (8.8±4.5 secs) as compared to the controls, which was 10.8±5.5 seconds. In the same study, the non invasive TBUT was found to be low but not statistically significant, (7±3 secs vs 8±2 secs). Thus, their study found that children with VKC had more prevalence of dry eyes and lower TBUT [17]. Based on the Schirmer's test values, it was found that mild dry eye in most of cases, followed by moderate dry eye in 6.06%, and no dry eye in 69.69% of the cases. Thus, it was found that only moderate and mild dry eye were recorded, with maximum patients showing on dry eye. It was found that there was a statistically significant association with a p-value <0.001 when compared type of VKC with type of dry eye, in accordance

with TBUT where it was found that the dry eye was more of mild type, predominantly seen in mixed type of VKC [17].

It was also noticed that it was a statistically significant association with p-value <0.001, when compared the type of VKC with type of dry eye in accordance with Schirmer's test, where in it was found that mild type of dry eye was predominantly seen in mixed type of VKC. Thus, the dry eye was significantly seen to be associated with mixed type of vernal conjunctivitis. Study by Villani E et al., showed association between short TBUT dry eyes and VKC [16], and also a study by Tibrewal S et al., showed prevalence of dry eye in accordance to dry eye tests like Ocular Surface Disease Index (OSDI), TBUT and Ocular Surface analyser (OSA). However, none of the studies compared the type of VKC with the severity of dry, as done in this study [17]. Thus, dry eyes are found to be present in VKC cases, and treatment should take account of this for better patient outcome.

Limitation(s)

The lack of follow-up of the study population and small sample size are the limitations of the study. Hence, studies with a larger sample size can be conducted in future.

CONCLUSION(S)

The present study highlighted the co-existence of dry eye with VKC. There was a significant association of dry eye with VKC and type of VKC as well. VKC is an under diagnosed and under recognised ocular surface disease, this is because the clinical form is generally mild and self-limiting, and access to care varies significantly, meaning that many patients do not present to a clinic. If VKC is not treated properly, the cornea and conjunctiva may suffer substantial damage and potential for visual impairment. VKC treatment should be adequate and continuous through patient or caregivers education on good ocular health and regular, long-term follow-up are essential. The treatment of VKC should also include the management of dry eye without which the ocular surface may never improve completely. Further studies on medical management of the VKC associated dry eye can be persued.

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