Clinicians' perspectives on the management of vernal keratoconjunctivitis (VKC) in Indian Settings

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ABSTRACT

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| **Background:** Vernal keratoconjunctivitis (VKC) is a chronic, bilateral allergic inflammation of the conjunctiva that tends to recur over time. Globally, VKC represents around 1% of all eye diseases, whereas in tropical areas, it contributes to approximately 3% of serious ophthalmic cases.**Objective**: The present study assesses clinicians' perspectives and preferences on the diagnosis, treatment approaches, and therapeutic strategies in the management of vernal keratoconjunctivitis (VKC) conducted in Indian settings.**Methods**: The cross-sectional study was conducted using a multi-response questionnaire among ophthalmologists specialized in managing vernal keratoconjunctivitis across India. The questionnaire included 23 items designed to assess clinicians’ views on VKC management strategies and treatment preferences. Data were analyzed using descriptive statistical methods, and visual representations were generated using Microsoft Excel 2013.**Results**: The study included 151 participants. Approximately 64% reported that VKC most commonly affects children. About 61% identified the mixed form of VKC as the most frequently observed clinical presentation. Olopatadine was cited as the preferred treatment for children by 60% of respondents and for patients with giant papillary conjunctivitis by 49%. Additionally, 56% of participants indicated that ketorolac is the most commonly used topical nonsteroidal anti-inflammatory drug (NSAID) for VKC. For diagnostic evaluation, around 70% preferred assessing both serum IgE levels and absolute eosinophil counts. Allergic rhinitis (AR) was the most frequently associated comorbidity, reported by 89% of clinicians. Nearly 79% of respondents rated trehalose as effective or very effective in managing VKC.**Conclusion**: The study findings suggest that VKC predominantly affects children, with the mixed form being the most common presentation. Olopatadine, topical steroids, ketorolac, and trehalose are widely preferred for treatment. These insights emphasize the need for standardized, evidence-based management strategies to ensure optimal patient outcomes. |

***Keywords****: Vernal keratoconjunctivitis, Olopatadine, Ketorolac, Trehalose, Topical steroids*

1. INTRODUCTION

Vernal keratoconjunctivitis (VKC) is a chronic, bilateral allergic inflammation of the conjunctiva that tends to recur over time [1]. Although it accounts for less than 1% of ocular conditions in developed countries, its prevalence varies considerably across different regions [2]. In tropical countries, VKC is a significant cause of hospital visits, affecting 3% to 6% of patients across all age groups [3]. VKC is globally distributed, but its incidence varies based on geographic and climatic factors. It is relatively rare in Northern Europe and North America, yet more frequently observed in warm, dry regions such as the Mediterranean, Central and South America, Sub-Saharan Africa, and the Middle East. Globally, VKC represents around 1% of all eye diseases, whereas in tropical areas, it contributes to approximately 3% of serious ophthalmic cases [4]. In India, the community prevalence of VKC has been reported as 4.98% and 1.11% in different population subsets [5]. The heterogeneity of VKC prevalence has been attributed to a range of factors, including population characteristics (e.g., genetic differences, migration patterns of susceptible people, age distribution) and environmental influences (e.g., climate, socioeconomic status, and the interactions of lifestyle, genetic, and environmental factors) (Ali et al., 2024).

A range of pharmacologic agents is employed in the management of VKC, each targeting different aspects of the underlying allergic and inflammatory processes. Olopatadine is a dual-acting antihistamine and mast cell stabilizer that alleviates allergic symptoms by blocking histamine H1 receptors and preventing the release of inflammatory mediators from mast cells. It has shown effectiveness in alleviating VKC symptoms across a broad age range (18–70 years) and among both genders [6,7]. Topical steroids exert their anti-inflammatory effects by inhibiting phospholipase A2, thereby reducing the synthesis of pro-inflammatory cytokines and eicosanoids [8]. Ketorolac, a topical nonsteroidal anti-inflammatory drug (NSAID), works by inhibiting cyclooxygenase (COX) enzymes, leading to decreased prostaglandin production and inflammation [9]. Trehalose, a disaccharide with antioxidant and membrane-stabilising properties, protects ocular surface cells from oxidative stress and inflammation, aiding in epithelial healing and maintaining tear film stability [10]. VKC usually follows a seasonal pattern with onset in spring, exacerbation in summer, and remission during the autumn-winter period. Although VKC occurs more frequently in young boys within the first decade of life, it impacts both genders equally in tropical climates. The condition often resolves spontaneously after puberty but, in approximately 12% of patients, it persists beyond 20 years of age. Approximately 50% of patients with VKC have an atopic background as assessed by a skin prick test or serum-specific immunoglobulin E measurements (Babineaux et al., 2020).

This study aims to gather insights from ophthalmologists practicing in Indian settings regarding the diagnosis, treatment approaches, and therapeutic preferences in managing VKC.

2. materialS and methods

A cross-sectional study was conducted among ophthalmologists in managing VKC in Indian settings from June 2024 to December 2024. The study was performed after obtaining approval from Bangalore Ethics, an Independent Ethics Committee, which was recognized by the Indian Regulatory Authority, the Drug Controller General of India.

An invitation was sent to clinical professionals across India based on their expertise and experience in treating VKC in the month of March 2024 for participation in this Indian survey. About 151 clinicians from major cities of all Indian states, representing the geographical distribution, shared their willingness to participate and provide necessary data. Clinicians had the discretion to skip questions they did not wish to answer. Written informed consent was obtained from all participants, who were required to independently complete the questionnaire without consulting peers. Unanswered questions were treated as non-attempts.

The questionnaire booklet titled EXCEL (Expert Perspective Study on Allergic Conjunctivitis Management) was sent to the doctors who were interested in participating in this study. The EXCEL study questionnaire comprised 23 structured questions that covered demographics, clinical patterns, treatment preferences, investigations, supportive therapies, and associated systemic conditions.

**Statistical analysis**

Descriptive statistics were used to analyze the data. Categorical variables were presented as frequencies and percentages. Microsoft Excel 2013 (version 16.0.13901.20400) was used to generate bar charts and other visual representations to support data interpretation.

3. results

Out of 151 study participants, approximately 56% of respondents reported that the monthly average number of patients treated for VKC in clinical practice is between 11-20 patients. More than half (52.98%) of respondents reported that VKC affects males and females equally. About 64% of respondents reported that children are the age group most commonly affected by VKC (Table 1).

**Table 1: Distribution of responses on the age group more commonly affected by VKC**

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| **Age group** | **Response rate (n = 151)** |
| Children | 63.58% |
| Adolescent age group | 17.22% |
| Middle-aged population | 17.88% |
| Elderly population | 1.32% |

Around 38% of experts reported that VKC cases are more commonly seen in suburban regions. Approximately 55% indicated that summer is the predominant season for seasonal allergic conjunctivitis (SAC)/perennial allergic conjunctivitis (PAC). More than half (60.93%) of respondents reported that the mixed form of VKC is most commonly encountered in clinical practice (Fig. 1). Around 52% of respondents stated that the prevalence of keratoconus in VKC is less than 5%. The majority (60%) of respondents reported that olopatadine is the preferred drug for VKC in children (Fig. 2).

**Fig. 1: Distribution of responses on the type of VKC most commonly encountered in routine practice**



**Fig. 2: Distribution of responses on the preferred drug for VKC in children**



About 54% of participants opined that olopatadine is the preferred drug for VKC in young adults. According to 48% of respondents, olopatadine is the preferred antihistamine for VKC in pregnant women. A significant majority (62.91%) of respondents indicated that topical steroids like fluorometholone and loteprednol are the preferred add-on drugs for patients with severe signs and symptoms of VKC. Many clinicians (58.28%) stated that less than 10% of patients have giant papillary conjunctivitis (GPC) in clinical practice. According to 49% of experts, olopatadine is the preferred drug for patients with GPC (Fig. 3).

**Fig. 3: Distribution of responses regarding the preferred drug for patients with giant papillary conjunctivitis**



Approximately 54% of respondents reported frequently prescribing topical steroids to control conjunctival inflammation in VKC. Half (50%) of respondents indicated that less than 10% of patients are steroid responders once started on topical steroids for VKC. More than half (56.29%) of respondents stated that they occasionally prescribe topical immunomodulators like cyclosporine and tacrolimus to control conjunctival inflammation in VKC. Around 58% preferred both a short pulse of topical steroids and topical immunomodulators for refractory cases of VKC. Nearly 40% of respondents favored trehalose eye drops as artificial tears/lubricants in the management of VKC. Approximately 56% of clinicians reported that ketorolac is the preferred topical NSAID in patients with VKC (Fig. 4).

**Fig. 4: Distribution of responses on the topical NSAIDs preferred in patients with VKC**

Approximately 70% of clinicians preferred both serum IgE levels and absolute eosinophil counts as laboratory investigations in VKC (Table 2). According to 42% of respondents, yearly corneal topography is preferred for patients with VKC. Approximately 89% of respondents reported that allergic rhinitis (AR) is the condition most commonly associated with VKC (Table 3). As per 52% of respondents, trehalose is considered effective as a lubricant in the management of VKC.

**Table 2: Distribution of responses regarding the lab investigations preferred in VKC**

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| **Preference** | **Response rate****(n = 151)** |
| Serum IgE levels | 9.93% |
| Absolute eosinophil counts | 5.96% |
| All of the above | 69.54% |
| None of the above | 14.57% |

**Table 3: Distribution of responses on the conditions commonly associated with VKC patients**

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| **Condition** | **Response rate****(n = 151)** |
| Thyroid dysfunction | 3.31% |
| Vitamin D deficiency | 7.28% |
| Allergic rhinitis | 89.4% |

4. discussion

The study findings offer valuable insights into clinicians' perspectives on VKC management in India. The predominance of VKC among children and its higher occurrence in suburban areas during the summer months highlight the need for region- and season-specific awareness strategies. These observations align with existing literature. Doan et al. described VKC as a severe ocular allergic condition that predominantly occurs in children. It is characterized by bilateral, recurrent, and chronic inflammation of the cornea and conjunctiva, which can potentially lead to reduced visual acuity or even blindness [11]. Zicari et al. also noted that VKC is a rare chronic ocular inflammatory disease that primarily affects boys in their first decade of life and is often associated with atopic and autoimmune disorders [12].

The majority of the study participants reported that the mixed form of VKC is commonly encountered in routine practice. However, literature findings indicate that the prevalence of different clinical forms of VKC varies across studies and geographic regions. For instance, a study conducted at a tertiary eye care center in South India found that the mixed form was the most prevalent, observed in 72% of patients, followed by the palpebral form in 15.6% and the limbal form in 12.6% [13]. Similarly, a study from Gujarat reported the mixed form as the most common, accounting for 72% of cases, with palpebral and bulbar forms comprising 16% and 11%, respectively [14]. In contrast, a retrospective study conducted by Nagpal et al. at a tertiary care hospital in India reported that the palpebral form was the most common, followed by the mixed and bulbar forms [15].

Many study participants identified olopatadine as their preferred treatment for VKC and GPC. This preference is supported by Sharma et al., who reported that olopatadine was more effective than other agents, showing a significant reduction in both itching and discharge [16]. Similarly, Mohan et al. found that 0.1% olopatadine showed a moderate improvement in VKC symptoms over a 6-month follow-up period [17]. Khurana et al. observed that olopatadine was found to be particularly effective in managing papillary conjunctivitis, especially in cases induced by contact lens use. The study concluded that olopatadine significantly reduces the signs and symptoms of mild to moderate contact lens-related GPC [18]. Leonardi and Zafirakis also favored olopatadine over ketotifen for allergic conjunctivitis, citing its superior efficacy and better patient comfort [19].

In the present study, the majority of the participants reported ketorolac as their preferred topical NSAID for managing VKC. This aligns with findings from Sharma et al., who demonstrated that ketorolac significantly reduced itching symptoms by 50.7% compared to 33.3% in the placebo group, after just two weeks of treatment (P <0.01) [20]. Similarly, Hasan et al. confirmed that 0.5% ketorolac tromethamine ophthalmic solution is both safe and effective in alleviating the signs and symptoms of VKC, offering a comparable efficacy and safety profile to other treatment options [21].

Many participants indicated that serum IgE levels and absolute eosinophil counts are commonly preferred laboratory investigations for diagnosing VKC. In line with this finding, Pokharel et al. reported a notably high concentration of tear IgE levels in VKC patients [22]. Similarly, Bozkurt et al. found that IgE-mediated mechanisms play a role in approximately 40% of VKC cases, and they also observed a higher incidence of immunoglobulin deficiency as a novel finding [23]. Furthermore, Bonini et al. highlighted that activated eosinophils are consistently present in VKC, both in the bloodstream (as shown by cytofluorimetry) and in ocular tissues (evident through tear cytology and conjunctival scrapings) [24].

In the present study, numerous participants indicated a strong association between AR and VKC. Similarly, Bozkurt et al. reported that AR is frequently linked with VKC, noting that individuals with AR are nearly three times more likely to experience Eustachian tube dysfunction compared to those without AR [25]. Additionally, Kaur and Gurnani et al. Reported that VKC is often linked with other atopic conditions such as asthma, allergic rhinitis, and dermatitis [1].

In addition to anti-inflammatory and antihistamine treatments, several participants emphasized the role of trehalose as an effective lubricant in VKC management. In a study by Cagini et al., trehalose was also found to exert protective effects on both corneal and conjunctival epithelial cells. It was shown to promote corneal healing, lower levels of inflammatory cytokines in the conjunctiva, and contribute to the restoration of osmotic balance on the ocular surface [26].

The study holds significant relevance in providing real-world data on the clinical patterns, preferred treatments, and diagnostic practices for VKC across a broad spectrum of practitioners. It highlights real-world trends such as the preference for olopatadine and the perceived effectiveness of trehalose. Another major strength is the use of a structured questionnaire to gather the data. However, the study has limitations, including its reliance on self-reported data, which may introduce recall or reporting bias. Additionally, regional variations and differences in clinical training may influence responses, potentially limiting generalizability. The absence of patient outcomes or direct clinical correlations also restricts conclusions about treatment efficacy.

4. Conclusion

The study confirms that VKC predominantly affects children and is most prevalent in suburban and rural regions during summer. The mixed form of VKC is most frequently encountered, with olopatadine, topical steroids, and ketorolac being the preferred treatment options. Trehalose has emerged as an effective supportive therapy. Laboratory investigations such as serum IgE levels and eosinophil counts are widely used, and AR remains the most common comorbidity. These findings underscore the need for continued awareness and standardized protocols in VKC management.

**Ethical Approval:**

The study was performed after obtaining approval from Bangalore Ethics, an Independent Ethics Committee, which was recognized by the Indian Regulatory Authority, the Drug Controller General of India.

**Consent:**

Written informed consent was obtained from all participants, who were required to independently complete the questionnaire without consulting peers.

**COMPETING INTERESTS DISCLAIMER:**

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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