Original Research Article

International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 22-11-2019; Accepted: 23-12-2019; Published: 25-01-2020
www.medicalsciencejournal.com
Volume 6; Issue 1; 2020; Page No. 187-190

Assessment of clinical profile of patients diagnosed with the venrnal keratoconjunctivitis in Bihar region

Dr. Richa Choudhary[1], Dr. Sony Sinha[2*]

[1] Senior Resident, Department of Ophthalmology Patna Medical College & Hospital, Patna, Bihar, India
[2] Associate Professor, Department of Ophthalmology, Patna Medical College & Hospital, Patna, Bihar, India
[*] Corresponding Author: Dr. Sony Sinha

Abstract
VKC differs from other ocular allergies for age of onset, clinical symptoms and scarce response to anti-allergic treatment. Typical symptoms are ocular itching, watering, foreign body sensation and mucoid discharge. The disease may involve upper tarsal or limbal conjunctiva characterised by papillary hypertrophy of the palpebral and/or the limbal conjunctiva giving a cobble stone appearance. These signs are associated with bulbar or perilimbal conjunctival pigmentation, bulbar hyperemia and corneal changes like superficial punctate keratopathy, corneal erosions and scarring. The disease has a good prognosis with spontaneous resolution after puberty, few sight–threatening complications due to corneal damage can occur. Patients with VKC experience significant morbidity, which affects the quality of life. Hence based on above findings the present study was planned for Assessment of Clinical Profile of Patients Diagnosed with the Venrnal Keratoconjunctivitis in Bihar region
The present study was planned in Department of Ophthalmology Patna Medical College, & Hospital, Patna, Bihar, India. The study was conducted from February 2019 to April 2019. Out of the total patients diagnosed with the hospital 50 cases of Venrnal Kerato Conjunctivitis (VKC) were enrolled in the present study. All those patients in age group coming to opd with complain of itching, redness, foreign body sensation, history of any associated allergy, mucoid discharge underwent proper clinical evaluation including slit lamp evaluation to look for associated signs including palpebral papillae, ropy discharge, horner-tranta spots, any corneal findings, best corrected visual acuity, fundus examination, signs of any recurrence. History was taken of all diagnosed cases of vkc including age of onset of disease, place of residence, any seasonal variations, associated allergic illnesses.
The data generated from present study concludes that Vernal keratoconjunctivitis primarily affects boys and onset is generally from about age of 5 years onwards and resolves around puberty. So, after knowing the geographical trend and clinical profile of VKC, we can make the treatment plan and preventing measures can be taken for recurring cases. Unfortunately, severe and chronic cases of this disease still remain a challenging threat. So, continued research, further detailed evaluation and studies are still required to understand the complex nature of this condition, so as to treat it fully and with less morbidity.

Keywords: palpebral, bulbar, allergic, atopic, keratoconjunctivitis, etc

Introduction
Vernal keratoconjunctivitis (VKC) is a recurrent, bilateral, and self-limiting inflammation of conjunctiva, having a periodic seasonal incidence. The ocular surface may exhibit a wide variety of immunologic responses resulting in inflammation of the conjunctiva and cornea. In the Gell and Coombs classification system for various immunologic hypersensitivity reactions, 5 types of reactions are recognized. The major type I hypersensitivity reactions involving the conjunctiva are commonly referred to as allergic conjunctivitis and are further subclassified into seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC). Far less common are the more severe forms of allergic conjunctivitis, including atopic keratoconjunctivitis (AKC), giant papillary conjunctivitis (GPC), and limbal and tarsal vernal keratoconjunctivitis (VKC).
Diagnosis of allergic conjunctivitis is generally made by thorough history and careful clinical observation (see Clinical). The presence of an antigen triggers the allergic cascade, and, thus, avoidance of the offending antigen is the primary behavioral modification for all types of allergic conjunctivitis. In other respects, management of allergic conjunctivitis varies somewhat according to the specific subtype. Allergic conjunctivitis can be treated with a variety of drugs, including topical antihistamines, mast cell stabilizers, nonsteroidal anti-inflammatory drugs, and corticosteroids [1].
Type I (immediate) hypersensitivity reactions occur when a sensitized individual comes in contact with a specific antigen. Immunoglobulin E (IgE) has a strong affinity for mast cells, and the cross-linking of 2 adjacent IgE molecules by the antigen triggers mast cell degranulation.
The mast cell's degranulation releases various preformed and newly formed mediators of the inflammatory cascade. Most notable of these inflammatory mediators are histamine, tryptase, chymase, heparin, chondroitin sulfate, prostaglandins, thromboxanes, and leukotrienes. These various inflammatory mediators, together with various chemotactic factors, result in an increase in vascular permeability and migration of eosinophils and neutrophils. This type I hypersensitivity reaction is the most common

allergic response of the eye. These immune-derived reactions may also be the underlying cause of more rare and serious ocular conditions, such as ocular cicatricial pemphigoid (OCP) and Mooren ulcer [2].

Type III hypersensitivity reactions result in antigen-antibody immune complexes, which deposit in tissues and cause inflammation. A classic systemic type III reaction is the Arthus reaction, and ocular type III hypersensitivity reactions include Stevens-Johnson syndrome and marginal infiltrates of the cornea. These type III reactions can often induce a corneal immune (Wessely) ring that disintegrates as the inflammatory reaction subsides.

Type IV hypersensitivity reactions, also known as cell-mediated immunity, are facilitated by T lymphocytes, rather than merely antibodies. This inflammatory cell-driven reaction is also referred to as delayed-type hypersensitivity, since its onset is generally after 48 hours, in contrast to the type I reaction, which is an immediate hypersensitivity [3].

Type IV hypersensitivity reactions imply immunocompetence on the part of the individual since an intact immune system is required to mount the cell-mediated response. Ocular examples of type IV hypersensitivity include phlyctenular keratoconjunctivitis, corneal allograft rejection, contact dermatitis, and drug allergies, although drug sensitivities can lead to all four types of hypersensitivity reaction. Seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) are commonly grouped together.

Vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), and giant papillary conjunctivitis (GPC) constitute the remaining subtypes of allergic conjunctivitis. Early diagnosis and treatment will help prevent the rare complications that can occur with this disease [4].

Since allergic conjunctivitis generally clears up readily, the prognosis is favorable. Complications are very rare, with secondary corneal ulcers or keratoconus occurring rarely. Although SAC, PAC, and GPC commonly reoccur, they rarely cause any visual loss. Conversely, VKC and AKC are frequently associated with significant risk of progressive corneal damage and resultant visual loss.

Patients should make every attempt to identify the allergen causing the problem and to avoid the offending antigen. For patient education information, see the Eye and Vision Center, as well as Pinkeye, Eye Allergies, and How to Instill Your Eyedrops.

VKC is a chronic bilateral inflammation of the conjunctiva, commonly associated with a personal and/or family history of atopy. More than 90% of patients with VKC exhibit one or more atopic conditions, such as asthma, eczema, or seasonal allergic rhinitis. Corneal complications and conjunctival scarring frequently occur, particularly in more severe cases and in patients whose VKC onsets at a very young age.

Diagnosis of allergic conjunctivitis generally is made by taking a thorough history and by careful clinical observation. In seasonal and perennial allergic conjunctivitis, important features of the history include a personal or family history of atopic disease, such as allergic rhinitis, bronchial asthma, and/or atopic dermatitis. Perhaps the most important feature in the clinical history is the symptom of itching. Without itching, the diagnosis of allergic conjunctivitis becomes suspect.

With vernal keratoconjunctivitis (VKC), as with other allergic or type I hypersensitivity disorders, itching is the most important and most common symptom. Other commonly reported symptoms are photophobia, foreign body sensation, tearing, and blepharospasm. Photophobia due to chronic keratitis is also common. Ocular signs of VKC commonly are seen in the cornea and conjunctiva. In contrast to atopic keratoconjunctivitis (AKC), the eyelid skin usually is not as significantly involved [5].

Removal of any and all possible allergens as well as conservative management such as cool compresses and lid scrubs make up the first line of therapy. A topical antihistamine only may work in mild cases. Topical mast cell stabilizers (cromolyn sodium, nedocromil sodium, and lodoxamide) are typically used with topical antihistamines and have been shown to be effective in moderate presentations of VKC. Mast-cell stabilizers have a loading period to reach their full therapeutic effect. If seasonal recurrence is known, it is suggested that mast-cell stabilization therapy be initiated prior to the season in which symptoms are encountered and continued throughout the season. Dual-Action agents with both H1-blocking mechanism and mast-cell stabilization have the benefits of working immediately and having long-term disease modifying effects. Topical corticosteroids are typically the most effective. High pulse dose with quick tapering and use of low-absorptions corticosteroids (fluoromethelone, loteprednol, remexolone, etc.) is preferred when using topical corticosteroid therapy. Oral corticosteroids can be considered in sight threatening conditions. Injection of local corticosteroid into the upper tarsal papillae can sometimes offer short term relief as well.

Long term immunomodulation with steroid sparing agents such as cyclosporine and tacrolimus is often needed. Topical cyclosporin-A in concentrations of 0.05% to 2% has been shown to decrease inflammatory cytokines and the signs and symptoms of treated VKC patients. Tacrolimus 0.1% topically has also shown to improved signs and symptoms of disease, with one study showing improvement even in patients unresponsive to 0.1% topical cyclosporine. Additionally, adult patients with VKC may respond more favorably to topical cyclosporin therapy.

Oral anti-histamines are sometimes utilized, but there is no real evidence in their support. There is at least one report of the successful use of omalizumab, an anti-IgE monoclonal antibody, in a patient with VKC recalcitrant to other treatment modalities.

VKC differs from other ocular allergies for age of onset, clinical symptoms and scarce response to anti-allergic treatment. Typical symptoms are ocular itching, watering, foreign body sensation and mucoid discharge. The disease may involve upper tarsal or limbal conjunctiva characterised by papillary hypertrophy of the palpebral and/or the limbal conjunctiva giving a cobble stone appearance. These signs are associated with bulbar or perilimbal conjunctival pigmentation, bulbar hyperemia and corneal changes like superficial punctate keratopathy, corneal erosions and scarring. The disease has a good prognosis with spontaneous resolution after puberty, few sight–threatening complications due to corneal damage can occur. Patients with VKC experience significant morbidity, which affects the quality of life. Hence based on above findings the present study was planned for Assessment of Clinical Profile of Patients Diagnosed with the Venrnal Keratoconjunctivitis in Patna Medical College & Hospital,

Patna, Bihar.

Methodology

The present study was planned in Department of Ophthalmology Patna Medical College, & Hospital, Patna, Bihar, India. The study was conducted from February 2019 to April 2019. Out of the total patients diagnosed with the hospital 50 cases of Venrnal Kerato Conjunctivitis (VKC) were enrolled in the present study. All those patients in age group coming to opd with complain of itching, redness, foreign body sensation, history of any associated allergy, mucoid discharge underwent proper clinical evaluation including slit lamp evaluation to look for associated signs including palpebral papillae, ropy discharge, horner-tranta spots, any corneal findings, best corrected visual acuity, fundus examination, signs of any recurrence. History was taken of all diagnosed cases of vkc including age of onset of disease, place of residence, any seasonal variations, associated allergic illnesses.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: All patients who had history of itching, redness, photophobia, lacrimation and mucous discharge were included in the study. Age 1 year to 25 years of either sex.

Exclusion Criteria: Patients with history of contact lens induced conjunctivitis, other ocular diseases and trauma were excluded from the study.

Results & Discussion

Vernal keratoconjunctivitis (VKC) or spring catarrh is a chronic, recurrent, bilateral, at times asymmetrical, seasonally exacerbated external ocular inflammation affecting children and young adults. VKC usually begins before the age of 10 years. It generally resolves around puberty, usually about 4-10 years after onset and only rarely may persist beyond the age of 25 years.

It is more common in males than in females. The male preponderance is prominent below 20 years of age but thereafter, male and female ratio of involvement becomes almost equal.

The exact aetiology and pathogenesis is still unclear, although allergic nature of this disease is being accepted for long. Role of genetic predisposition and environmental factors in onset, progression and resolution of this self-limiting disease, but incapacitating at times, is not clear. Occurrence of this disease is not limited to spring, with episodes of reactivity being quite common in winter. Initial seasonal feature turn into perennial (occurring throughout the year) disease after few years.

Patients may have associated atopy (genetic tendency to develop allergic disease) or have a close family history of atopy. Atopic patients often develop asthma, eczema and seasonal allergic rhinitis during infancy.

There is a higher predilection for warm, dry climates, as inflammation trends to decrease in the cooler months of the year. VKC is self-relenting and typically lasts 5-11 years with remission at puberty. The immune pathogenesis is multifactorial and has more environmental causes. Classically, it has been thought of as a type I IgE-mediated hypersensitivity reaction; though it is accepted that there is cell-mediated the involvement also. Vernal conjunctivitis has a varied spectrum of presentation from itching, ropy discharge, redness watering to severe forms of Corneal opacities leading to loss of vision. Palpebral form, Limbal form and Mixed variety are the three types of this disease described. Most common is palpebral form which is associated with thickened epithelial flat lesions like the Cobblestones on footpath in the palpebral conjunctiva. Limbal and the Mixed varieties come next in prevalence and have the characteristic ropy discharge. Vernal conjunctivitis with itching and subsequent rubbing of eyes leads rarely to corneal curvature problems like Keratoconus, corneal vascularisation called pannus and in extreme cases to loss of vision. 30% of series were found to be atopic based on the history of hay fever, asthma, and eczema etc. Studies by Lambiase *et al*. [6] and Bonini *et al*. [7] reported associated systemic allergies in 41.6% patients in different series.

Table 1: Demographic Details

Parameters	No. of Cases
Age	
1 – 10 years	23
11 – 20 years	19
21 – 30 years	8
Sex	
Males	44
Females	6
Total	50

Table 2: Symptoms Details

Symptoms	No. of Cases
Itching	5
Redness	25
Photophobia	12
Ropy discharge	4
Foreign body sensation	4

Table 3: Clinical types of VKC

Clinical types	No. of Cases
Palpebral	36
Limbal	3
Mixed	11
Total	50

Table 4: Ocular signs

Ocular signs	No. of Cases
Papillae on upper palpebral conjunctiva	29
Conjunctival congestion	10
SPKs and limbal papillae	4
Horner tranta's spots	7

The prevalence of subtypes of VKC is different in various parts of the world. The multi centric study from Italy [8]. reported predominance of limbal presentation (53.8%) whereas Ukponmwan reported 82.6% cases with palpebral presentation in Nigeria [10]. De Smedt *et al* in a School Survey on VKC in central Africa reported predominance of limbal presentation (98.4%), In contrast, majority of our cases (74.0%) had a mixed presentation comprising of both limbal as well as palpebral involvement, followed by isolated palpebral involvement in 17.5% and limbal involvement in 8.4% of the patients. This pattern was similar to the Saboo. U.S *et al*. [9] study in south India.

Perilimbal conjunctival pigmentation is a new clinical sign described in VKC [11, 13]. In this series, perilimbal conjunctival pigmentation was documented in 16% of the patients. Rao *et al*., described perilimbal pigmentation as a consistent finding in VKC [12].

Classically, it has been thought of as a type I IgE-mediated hypersensitivity reaction; however, it has been suggested that there is cell-mediated Th2 involvement. The major symptom is ocular itching. Minor symptoms include photophobia, burning, tearing, mild ptosis, and a thick, ropy, yellow, mucoid discharge. Clinically, there are three forms of conjunctivitis: palpebral, limbal, and mixed. The palpebral form is characterized by polygonal, flat-topped, giant cobblestone papillae of the superior tarsal conjunctiva. Most of the cases from our study showed a palpebral presentation. Complications of visual loss from corneal neovascularization, corneal scars, keratoconus and steroid-induced cataracts, and glaucoma are found in 7% of patients. 36% of subjects in our study were found to be atopic based on the history of hay fever, asthma, and eczema. Studies by Lambiase *et al*. [14] and Bonini *et al*. [15] reported associated systemic allergies in 41.6% patients in different series

Pharmacologic therapy is the mainstay of treatment and in that Topical treatments are more effective than systemic. The mainstay of drugs in treating this condition is Antihistamines like Olopatidine and Bepotastine. Mast cell stabilizers like Sodium chromoglycate are also useful in controlling the allergy cycle. Beyond this when patients have very severe allergy then short-term weak steroids like Fluorometholone and Loteprednol are used under frequent followup. Non-steroidal anti-inflammatory drugs like Ketorolac, Bromfenac and Nepafenac can be used in maintenance dose. Unfortunately, in certain cases who are fast steroid responders then IOP spikes have to be immediately addressed. If not judiciously used Steroids can lead to more harm than good. Patients have to be clearly explained not to self-medicate or refill prescriptions by themselves especially when they have exacerbations due to allergy triggers. Final resort in refractory cases is the use of topical cyclosporine. General Hygiene, cold compresses, and even shifting to a location with cooler temperate climate will help in fighting this malady of Vernal Catarrh.

Limitations of our study include a cross-sectional study design and sample size also needs to be large. Further research is needed with larger samples from diverse geographical areas and longitudinal studies to further the knowledge regarding epidemiology and natural course of vernal kerato-conjunctivitis which can help in better prevention and management of the disease.

Conclusion

The data generated from present study concludes that Vernal keratoconjunctivitis primarily affects boys and onset is generally from about age of 5 years onwards and resolves around puberty. So, after knowing the geographical trend and clinical profile of VKC, we can make the treatment plan and preventing measures can be taken for recurring cases. Unfortunately, severe and chronic cases of this disease still remain a challenging threat. So, continued research, further detailed evaluation and studies are still required to understand the complex nature of this condition, so as to treat it fully and with less morbidity.

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