

Review article on VKC associated with ocular complication.

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Abstract: VKC is bilateral inflammatory condition. It occurs in pediatric age group. It is chronic, bilateral, inflammatory and allergic disorder. 90% percent Case resolved till the age of puberty with good prognosis, only 10 percent case affect the eye health. VKC is symptomatic allergic form, which create disturbance in day to day life such as irritation not able to open eyes, foreign body. There are three type of VKC such as Limbal, Palpebral and mixed form. There are many grading proposed by different researcher. VKC is mostly found in hot and dry area. It is characterized by the infiltration of conjunctiva by a different type of cells such as eosinophils. VKC is IgE mediated diseases and some other factor also affect it. Hypersensitivity of unknown pathogen is increased because there is chances of increased no of activated CD+4, lymphocytes. Tarntas spot, limbal thickening and papillae are common sign VKC. Photophobia, hypersensitivity and blurring of vision are the symptom of VKC. There are many corneal complication associated with VKC. Such as steroid induced glaucoma, shield ulcer, microbial keratitis, keratoconus, Corneal scarring, Superficial punctate keratitis, steroid induced cataract etc. The management may be conservative and surgical according to the presentation of disease.

Key words: VKC, Steroid induced glaucoma, Keratoconus and shield ulcer, ocular complication and Clinical grading.

Methodology: All thing that are written in this article searched with the term of VKC, clinical grading and ocular complication in Google Scholar, Pubmed and NCBI. At the end of this review article reference are written. Excluded article that is written in other language.

Inclusion Criteria: In this article we included those article which is only published on google scholar, pubmed and NCBI. This review article included only article which is published in between 1990 to 2021.

Exclusion article: This review article only included about VKC, clinical grading and ocular complication. This article not included VKC with any associated surgery, retinal complication and vision loss due to primary glaucoma.

Introduction: Keratoconjunctivitis define as an inflammatory condition in which both cornea and conjunctiva is included. There are five category of ocular allergy: Seasonal allergic conjunctivitis, perennial allergic conjunctivitis, Vernal keratoconjunctivitis (VKC), Atopic keratoconjunctivitis (AKC), Perennial keratoconjunctivitis (PKC) and giant papillary conjunctivitis (GPC) [17]. VKC is stand for Vernal keratoconjunctivitis. It is mostly found in pediatric age group. It is chronic, bilateral, inflammatory and allergic disorder [1]. It mainly found in first decade of life. 90% percent Case resolved till the age of puberty with good prognosis, only 10 percent case affect the eye health [2]. VKC is symptomatic allergic form, which create disturbance in day to day life such as irritation not able to open eyes, foreign body sensation, photophobia, watering, itching, discharge and rubbing. The prevalence of VKC is hot and dry area such as Mediterranean basin, the Middle East, Africa and the Indian subcontinent). It is relatively unusual in most of North America and Western Europe (Bremond-Gignac et al., 2008) [3]. It affect the conjunctival part such as palpebral, bulbar, limbal and also cornea [3]. The diagnosis is depend upon the sign and symptom, but in severe cases conjunctival scarring is best method to diagnosed VKC because in scarring we found out the infiltration of eosinophils [10].

Form of VKC: There are three division of VKC Palpebral (included both upper and lower tarsal conjunctiva), limbal and mixed (include both limbal and tarsal conjunctiva).

1. Palpebral division: It include the lower and upper tarsal conjunctiva. Papillae and cobble stone papillae found in palpebral form. This involves the upper tarsal conjunctiva.

2. Limbal Division: It affect on limbal area. It does not include both bulbar and palpebral conjunctiva [4].

3. Mixed Division: It involve the palpebral and limbal conjunctiva.

Etiology: There are several cause which is given below:

The main cause of allergic reaction and hypersensitivity that produce airborne allergens. It occur due to the complex exchange of information between tissue through cell communication, chemical mediators, cytokines and adhesion molecule [19].

Prevalence of VKC: In European countries the prevalence of VKC is 1.2-10.6 in 10000 population [5]. It is most commonly found in hot and dry area such as Tropical countries, subtropical countries, The middle east, latin america and asia. VKC is most commonly found in school going children. If we compare other diseases to VKC, the VKC is more prominent for referral pediatric eye clinic in east africa. VKC affect children daily activity.

Grading of VKC: On the basis of symptom VKC grade explained by some scientists.

Pucci et al define grading based upon symptom such as itching, photophobia, tearing, foreign body sensation grade [12].

Grade 1: Mild Discomfort without disturbing daily activities.

Grade 2: Moderate discomfort without affecting daily activities.

Grade 3. Severe Symptom affecting daily activities and patient want to stay in house. According to Spadavecchia et al. They divided the clinical severity in two type one is ocular sign such as conjunctival hyperemia, tarntas dot and papillae another is based upon patient symptom. Recently Boini et al. [8] define new grading system based on clinical representation. Grade 0 is

define if patient has no symptom or papillae is present in the inactive form. Grade 2 is define when patient have same symptom including with patient have difficulty in day activities. Mild papillary reaction and conjunctival hyperemia is also present. In grade 3 daily activity is disturbing with severe conjunctival hyperemia and secretion may be due to Horner tarntal dot, In case of moderate to severe VKC cornea present with papillary reaction and superficial punctate keratitis. The symptom of grade 4 are itching, photophobia, mucous discharge on the ocular surface and papillae. The sign of grade 4 is included horner-Tarntas dot and other corneal complication. The grade 5 is define as occasional symptom (in seasonal period) and papillary reaction may or may not be present.

Shoji et al define clinical grading that is called 5-5-5- grading scale. There are grading which is define below:

Grade 1: He give 100 point for each observation of sign such as active giant papillae, gelatinous infiltrate, shielded ulcer, exfoliative epithelial keratopathy and papillary proliferation at lower conjunctiva.

Grade 2: In this grade 10 point is give for each that are papillary reaction, superficial punctate keratopathy and blepharitis.

Grade 3: 1 point for each sign. It include papillae at upper palpebral conjunctiva and follicle at lower conjunctiva, hyperemia of bulbar and palpebral, lacrimal effusion [9].

The recent grading system is based upon symptom:

Grade 0: In this patient has no symptom and therapy

Grade 1: In this patient is using allergic eye drop without any symptom of photophobia.

Grade 2: This grading include symptomatic patients those have photophobia etc.

Grade 3: Patients are using daily anti allergic medication and steroid.

Grade 4: Patients are present with corneal ulcer, keratoconus and punctate keratitis and patient is using high dose steroids.

The conclusion of all grading is there is no specific grading which is gold standard. Many researcher give clinical scoring according to sign and symptom, but there is no fixed criteria which help in clinical grading of VKC.

Pathophysiology:

It is characterized by the infiltration of conjunctiva by a different type of cells such as eosinophils. VKC is IgE mediated disease and some other factor also affect it [11]. Hypersensitivity of unknown pathogen is increased because there is chances of increased no of activated CD+4, lymphocytes [12].

A study done with the help of vivo confocal microscopy that show the corneal irregularity. Not only epithelium membrane affect but also basal epithelium and stromal layer also affect in VKC. Corneal nerve also affected in because of density of inflammatory cell is increased [13]. Other factor affect corneal involvement are eosinophils and some protein such as major basic protein (MBP) and cationic protein, neurotoxins, and collagenases, in particular matrix metalloproteinase (MMP)-9 [14]. An important role play in the development of IgE mediated reaction is mast cell. It release histamine and interleukins. It stimulate the activity of fibroblast and collagen 1 and 3 that formed giant papillae. The necessary vascular supply of the forming giant papillae is provided by capillary proliferation. Chronic conjunctival inflammation is due to increased staining via immunohistochemistry for mediators that may stimulate vascular proliferation [15].

Eosinophils are most commonly found in the biopsy of VKC, while basophils, neutrophils, and lymphocytes are rare. Cytologic examination of mucus secretions show the dominance of eosinophils [16].

Symptom: There are various symptom such as: Photophobia, Watering, Irritation, foreign body, sensation, rubbing, Mucous discharge, Blurred vision, Pain.

Sign: There are various sign of VKC which is describe given below.

Conjunctival signs: Giant papillae and infection are present in conjunctiva. These papillae approx >1mm in diameter is characterized with flattened tops that take fluorescein stain sometime. The giant papillae is sometime seen near limbus area and symblepharon formation and fibrosis of conjunctiva also occur [18]. White elevation near limbus area called Horner and Trantas dot. The Giberlins studied showed that their is conjunctival secretions and eosinophils are the main component in that secretions [19].

Limbal signs: The sign of limbal VKC are thickening, opacification of limbal conjunctiva, gelatinous appearance and limbal papillae. Horner dot are made from degenerated epithelial cell and eosinophils [2]. Pannus formation and neovascularization are formed due to LSCD [20].

Corneal signs: Corneal sign depend upon the severity of disease. vary according to the severity of the disease process. Punctate epithelial erosions or keratitis can coalesce into macro-erosions of the epithelium. Plaques containing fibrin and mucous can accumulate into macro-erosions forming shield ulcers. Corneal neovascularization can ensue and resolution can leave a characteristic ring-like scar [21]. A waxing and waning gray-white lipid depositing in the peripheral, superficial stroma can occur and is known as pseudogerontoxon. Keratoconus has been shown to be more prominent in VKC patients as well; possibly due to increased eye rubbing of chronically irritated patient: Microbial keratitis is most severe complication, because of greater chances of infection in eyes.

Ocular complication: There are many corneal complication associated with VKC. Such as steroid induced glaucoma, shield ulcer, microbial keratitis, keratoconus, Corneal scarring, Superficial punctate keratitis, steroid induced cataract etc.

Steroid induced glaucoma: Steroid induced glaucoma is primary angle glaucoma. That is caused by increased resistance to the outflow of aqueous at the level of the trabecular meshwork. This condition is define in the increased production and decreased in extracellular matrix of trabecular meshwork [22].

Superficial punctate keratitis: Thygeson describe the superficial keratitis. TSPK is an chronic and recurrent disorder, that is characterized by tarntas dot extending to the entire anterior surface of the cornea of both eyes [23].

Shield ulcer: It is most commonly found in case of VKC. It occur 3 to 11% of VKC. superficial keratitis break in the corneal epithelium. If a patient have shield ulcer then they present with itching, discharge and light sensitivity [24].

Steroid induced cataract: It is due to the steroid which is prescribed in case of severe VKC. It is reversible condition of VKC.

Pseudogerontoxon: Pseudogerontoxon is defined as a small segment of arcus senilis or gerontoxon and is seen in many individuals with limbal vernal or atopic keratoconjunctivitis. It is an important clinical finding because pseudogerontoxon is often times the only clinical evidence of previous allergic eye disease.

Hydrops: It forms due to corneal ectatic nature, that involves the rupture of the corneal descemet membrane and it causes pain and loss of vision. The patient with symptoms such as pain, photophobia, loss of vision and corneal ectasia associated with eye rubbing in case of VKC. It is due to leakage of aqueous humor [25].

Corneal scarring: VKC is an allergic eye disease that causes damage to the ocular surface that leads to corneal scarring and vision loss, if it is not treated properly [26].

Keratoconus: VKC leads to keratoconus at any point. The prevalence of keratoconus in VKC is 26.8%. The corneal topography shows up to 71% of them. It shows most severe progression in VKC ($p < 0.05$) with severe changes in visual acuity that need keratoplasty, as compared to normal cases. Crosslinking treatment and corneal transplantation are required in keratoconus cases that are associated with VKC, but postoperative care is required because there is a high chance of inflammation and tell to avoid eye rubbing in the case of VKC [28].

Management: The management may be conservative and surgical according to the presentation of disease.

Conservative: First and foremost management of VKC is removal of any type of allergens with the help of protection or minimal exposure. Cold compresses are an effective way to manage VKC [28]. Lid scrub is also an effective method. Dark goggles are used for protection purposes, which help to reduce glare, photophobia and from allergen exposure. Another management is migration from hot and windy areas to cold areas, all management which helps to reduce minimum exposure to allergens.

Medical treatment: Topical mast cell stabilizers are required in the case of moderate severity such as sodium nedocromil (2%), sodium cromoglycate (2%) and lodoxamide [15]. It can be used with antihistamine eye drops that act on H1 receptors such as olopatadine and alcaftadine. Dual action drops are required with H-1 blocker and mast cell stabilizer in case of moderate to severe cases.

Advantage of dual action drop is immediate action and long term action. Topical non-steroidal and anti-inflammatory drugs are required in the case of VKC [29].

Fluorometholone, loteprednol and remexolone are low absorption steroids, the safest treatment for VKC. Dexamethasone or betamethasone are used as alternates that are required in severe cases. Topical steroids need a quick taper and close monitoring for intraocular pressure.

Steroid sparing is a better option in case of recurrent VKC. Cyclosporin (0.05 to 2%) and tacrolimus (0.1%) are the most commonly used in these cases. These act by decreasing the inflammatory cytokines. Cyclosporine plays a role in blocking the T helper two cells, that's why blocking results in lymphocyte proliferation. It also acts as an inhibitor of histamine release from mast cells and basophils and reduces the conjunctival fibroblast proliferation and interleukin 1b production [30].

Differential diagnosis: There are many similar differential diagnoses of allergic conjunctivitis such as atopic seasonal, perennial, giant papillary, seasonal allergic conjunctivitis. Except giant papillary conjunctivitis, all are IgE mediated allergic. The most similar diagnosis of VKC is AKC. The difference is VKC is found in early teenagers and AKC is found in 20 to 50 years old patients associated with rhinitis, asthma and dermatitis. The atopic is more chronic as compared to VKC. In VKC goblet cell count is increased whereas in AKC it is decreased [31].

2. Literature Review: Ocular complication of vernal keratoconjunctivitis:

Aim: The purpose of this study is to identify patients with severe vernal keratoconjunctivitis who have ocular problems and vision loss (VKC).

Methodology: This study involved 431 VKC patients who were treated at the Ibn Al-Hathim Eye Center. The study spans the period from January 1 to December 31, 2002. Snellen and KAY picture optotype are used in this study to measure visual acuity. The key characteristic of this condition, enormous papillae formation in the superior tarsal limbus, are included in this study. Recurrent bilateral symptoms of VKC with conjunctival giant papillae development were the inclusion criteria. The clinical score developed by Bonini et al. allowed for the classification of the disease's severity (2004). The patient included in this study showed persistent signs and symptoms such as large papillary conjunctivitis, limbal infiltration of 180° or more, thickening with papillary hypertrophy, and diffuse palpebral conjunctival edema. Cases with allergic conjunctivitis other than VKC were excluded from the study.

The best spectacle corrected visual acuity (BSCVA) for each eye is measured in this study using Snellen's optotype. With the aid of the KAY image, visual acuity in youngsters is measured (under the age of 5 years). Using guidelines from the World Health Organization (WHO), visual impairment is evaluated. According to the WHO's recommended standards of normal vision, mild visual impairment, severe visual impairment, and blindness, respectively, were defined as visual acuity (VA) of 6/6 to 6/18, 6/24-6/60, 6/60 to 3/60, and 3/60. The eye with the greater corrected visual acuity was used.

The Haag Struggle Slitlamp by Haag Streit is used for Zeiss Goldmann applanation tonometry and anterior segment evaluation +90 Dioptre Volk lens. If the patient's visual acuity is in the range of 3/60 to 6/60: severely impaired vision 3/60 blind

The information was gathered using a Microsoft Excel® spreadsheet 2003, and descriptive analysis was done on it (Microsoft Corporation, Seattle, USA)

Consequently, males ($n = 327$) and females ($n = 104$) made up the majority of VKC patients ($n = 431$), with a male:female ratio of 3.1:1. (32).

Results: Severe VKC affected 68 patients in total (54 boys and 14 girls; 15.7%). The 68 patients with severe VKC's visual acuity. Among 20 patients with blindness and severe visual impairment, keratoconus (7 cases), steroid-induced cataract (5 cases), central corneal scars (5 cases), and steroid-induced glaucoma were all associated with visual loss [3]. Many patients with keratoconus

experienced progressive vision loss that was frequently unrecoverable with the use of glasses or contact lenses. In two of the keratoconus patients, acute hydrops ensued.

Review: Corneal complication in case of VKC.

Aim: Finding out the corneal complication in cases of VKC is the goal of this investigation.

Method: From March 1999 to May 2000, a cross-sectional study was conducted in Peshwar, Pakistan.

Results: The most typical corneal consequence was superficial punctate keratitis, which affected 45% of patients. Cases with corneal plaques and shield ulcers (14 percent) had more severe visual impairment (8 percent). Also noted was a substantial relationship with keratoconus (15%). Hydrops (6%), pseudogerontoxon (3%) and corneal opacification (9%) were also seen.

Conclusion: Corneal complications, which might impair vision, are frequent in cases of VKC.

Prognosis: VKC is often a very good visual prognosis. If a patient is not treated, they are more likely to experience severe complications. In cases with VKC, early treatment and refraining from rubbing the eyes are crucial. A successful treatment is essential for the treatment of VKC.

Abbervation: VKC,AKC and KC

Conclusion: VKC is bilateral inflammatory diseases. It is a highly serious illness that, if not treated in a timely manner, can cause eyesight loss and other serious complications. Rubbing is crucial in VKC corneal complications.

The most frequent side effect is glaucoma caused by keratosis and steroids. There isn't a standard clinical grading system like goldstard. Keratosis is a condition that can be treated. IOP is crucial in the case of VKC. Patient receiving steroids has a greater risk of developing steroids-induced glaucoma [33].

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