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A Cross-sectional Study of Refractive Errors in Vernal Keratoconjunctivitis.

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Abstract

Vernal Keratoconjunctivitis (VKC) is an allergic disease that typically affects young individuals, of which males are predominant. The disease involves the lids, conjunctiva, limbus and the cornea. The corneal changes range from punctate keratitis to shield ulcers. High incidences of keratoconus and abnormal corneal topographic patterns have been reported in these cases. The configuration of the corneal surface and the abnormal pattern of corneal surface can lead to vernal keratoconjunctivitis. Hence, an association between refractive errors and vernal keratoconjunctivitis was needed to be made.In our study we compared the refractive error with the stage of vernal keratoconjunctivitits (acute or chronic). Also we have tried to compare the type (limbal, bulbar or mixed) with the refractive error. *Materials and methods:* Fifty patients, ages ranging between 3 and 20 years, with Vernal Keratoconjunctivitis attending the ophthalmology out-patient department at Sri Siddhartha Medical College from December 2015 to December 2016 were included in the Study. The demographic data were noted, slit lamp evaluation and refractive error assessment were done for all patients. The data was compiled on a percentile basis of the two variables. Chi–square and Fisher's exact statistical analysis was used to study the association. *Results:* We found a male preponderance (78%) for the disease. Hypermetropia was the commonest (48% of patients) refractive error. Maximum patients manifested with signs of chronic Vernal Keratoconjunctivitis (76% patients). Bulbar type of Vernal Keratoconjunctivitis was commonest in our study group, (76% of patients). On evaluating the association of refractive error type with stage of Vernal Keratoconjunctivitis, the P value was not significant, thus indicating their independence. Also on evaluating the type of refractive error with the clinical variant of Vernal Keratoconjunctivitis, the p- value was not significant suggesting that they were independent. *Conclusion:* We found hypermetropia to be the commonest refractive error associated with VKC, followed by myopia and astigmatism. Perilimbal pigmentation suggestive of chronic Vernal Keratoconjunctivitis was the commonest stage of manifestation seen. Bulbar Vernal Keratoconjunctivitis was the commonest clinical type. There was no conclusive evidence to show an association between the refractive error and the stage and type of Vernal Keratoconjunctivitis

Keywords: Vernal Keratoconjunctivitis; Bulbar; Palpebral; Hypermetropia; Astigmatism.

Introduction

Vernal Keratoconjunctivitis (VKC) is an allergic disease that typically affects young individuals [1,2].

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VKC is an ocular disease which has a broad racial and geographical distribution. It is most common and most severe in hot, arid environments such as the Mediterranean basin, West Africa, and the Indian subcontinent [3].

Differences in prevalence could be due to the diversity of gene pool, the environment (climate, socioeconomic status, and living styles), and gene-environment interaction [4].

The condition is more common in males, although this gender difference is less absolute in tropical climates. The gender discrepancy coupled with the tendency to spontaneously improve during puberty has prompted a possible role for hormonal influence on disease burden [4].

Patients from age 1 to 22 years old (mean 6±3.7 years) may present with signs and symptoms of VKC. Resolution has been noted to start as early as eight years of age, and as late as 22. The disease usually lasts 4 to 10 years and resolves after puberty [5,6].

Symptoms in Vernal Keratoconjunctivitis consist predominantly of eye itching, along with tearing, discharge, irritation, redness, blepharospasm and photophobia.

Clinically, lids may be erythematous and thickened; a reactive ptosis may be present due to photosensitivity. The tarsal conjunctiva develops a cobblestone appearance and, in active disease, can have mucus accumulation between the papillae. In the limbal form, the conjunctiva may show a fine papillary reaction. Here the predominant findings are gelatinous limbal papillae associated with epithelial infiltrates called Horner-Trantas dots. These are focal collections of degenerated eosinophils and epithelial cells.

The corneal changes range from mild (punctate epithelial erosions) to severe (macroerosions and ulcers). Superficial corneal neovascularization and macroerosions form the inciting agents (e.g., eosinophilic major basic protein) released from the epithelium of the upper tarsal conjunctiva progress to corneal epithelial necrosis [8].

Epithelial erosions may heal completely, however, mucus and calcium deposition can prevent re-epithelialization, and a shield ulcer develops. Waxing and waning gray-white lipid deposits in the peripheral, superficial stroma create an arcuate infiltrate known as pseudogerontoxon [3].

Higher incidences of keratoconus (due to eye rubbng) and abnormal corneal topography patterns have been reported [9].

The role of IgE-mast cell activation in VKC comes from findings such as IgE in serum, tear cytology, increased number of mast cells in conjunctival tissue, clinical observations of allergen exposure and symptom exacerbation, and association with other atopic states. Overexpression of proinflammatory cytokines, chemokines, growth factors, and enzymes are found in VKC. Eosinophils and eosinophil-derived major basic protein (MBP) and cationic protein, neurotoxins, and collagenases, in particular matrix metallopeptidase (MMP)-9, have been shown to damage the corneal epithelium and the basement membrane, causing corneal involvement in VKC [10].

In our study, we tried to observe if there was an association between refractive errors and VKC, its clinical type and the stage of disease.

In a study by Sucheki et al., they tried to compare the clinical variant of vernal keratoconjuctivitis with refractive errors. The prevalence of allergic conjunctivitis is higher in the contact lens wearers with refractive errors than in the non-contact lens wearers. This result suggests that allergic conjunctivitis occurs more frequently in the contact lens wearers [11].

Mimura et al found the mean spherical equivalent and spherical power were significantly lower in patients with SAC than in patients without SAC. These results suggested that with respect to the non-contact lens wearers, patients with SAC were more myopic than healthy individuals. Therefore, myopes might have more association with vernal keratoconjunctivitis was their conclusion [12].

The configuration of the corneal surface leads to allergic conjunctivitis. Vernal conjunctivitis is related to the abnormal pattern of the corneal surface [9]. The abnormal ocular surface deteriorates the capacity of the fluid reservoir over the ocular surface. Tear film anomalies capture allergens in the conjunctival SAC and cause the conjunctival immune-based inflammation by inducing T-cell activation. Thus, refractive error may be a possible risk factor for the direct progression to allergic conjunctivitis. Second, myopic eyes, which have a longer axial eye length and wider palpebral fissures, may be liable to mediate intimate attachment of allergens by the close interaction between bulbar and palpebral conjunctiva. Third, myopia may be indirectly relevant to seasonal allergic conjunctivitis.

Six-patients with VKC experience significant morbidity, which affects the quality of life; [13] moreover, vision-threatening corneal complications in severe and chronic cases coupled with potential iatrogenic side effects makes VKC an ocular surface disorder with considerably sinister consequences if not treated optimally.

Materials and Methods

All patients in the age group of 3 years to 20 years with ocular features suggestive of Vernal Keratoconjunctivitis attending the Ophthalmology OPD at Sri Siddhartha Medical College from December 2015 to December 2016 were included in the Study. The children with systemic atopic dermatitis, phlyctenularconjunctivis and other seasonal allergic diseases were excluded.

The demographic data of these students were collected along with detailed anterior segment examination of the eye. This included Visual Acuity testing on Snellens Visual Acuity Chart,

Slit lamp examination of the eye on diffuse light and oblique illumination, Examination of the upper tarsal and the lower palpebral conjunctiva for papillae, Evaluation of the refractive error on autorefractometer (model UNIQUE –RK –URK800) testing and dilated acceptance of the refractive error.

The data was collected and is presented on a percentile basis.

A total of 40 patients' data was collected and evaluated.

Result

Table 1: Age Distribution of the patient

Age of the patient	Frequency of Distribution
0-5	10(20.00)
6-10	17(34.00)
11-15	16(32.00)
16-20	4(8.00)
21-25	2(4.00)
26-30	1(2.00)
Total	50(100.00)

Table 2: Gender Distribution of the Patients with Vernal Keratoconjunctivitis

Sex	Frequency
Male	39(78.00)
Female	11(22.00)
Total	50.(100.00)

Table 3: Distribution of Associated Refractive Error

Type of refractive error	Frequency
Myope	19 (38.00)
Hypermetrope	24 (48.00)
Astigmatism	7 (14.00)
Total	50 (100.00)

Table 4a: Type of VKC Stage

VKC Stage	Frequency
Acute	12 (24.00)
Chronic	38 (76.00)
Total	50 (100)

Table 4b: Clinical Variant of VKC

VKC Clinical Variant	Frequency
Bulbar	38(76.00)
Palpebral	8(16.00)
Both	4(8.00)
Total	50(100.00)

Table 5: Correlating VKC Stage with Age

	VKC Stage			Chi square =3.62 P=0.6
Age	Acute	Chronic	Total	
0-5	1 (8.33)	9 (23.68)	10 (18.37)	
6-10	4 (33.33)	13 (34.21)	17 (34.69)	
11-15	6 (50.00)	10 (26.32)	16 (32.65)	
16-20	1 (8.33)	3 (7.89)	4 (8.16)	
21-25	-	2 (5.26)	2 (4.08)	
26-30	-	1 (2.63)	1 (2.04)	
Total	12 (100.00)	38 (100.)	50 (100.0)	

Table 6: Correlation of VKC Stage with Gender

	VKC stage			Fisher's exact 0.07 p=0.10
Sex	Acute	Chronic	Total	
Male	7 (58.33)	32 (84.21)	39 (78.00)	
Female	5 (41.67)	6 (15.79)	10 (22.00)	
Total	12 (100.00)	38 (100.00)	50 (100.00)	

Table 7: Correlation of VKC Stage with Refractive Error

	VKC Stage			Chi square =0.26 P=0.87
Type of refractive error	Acute	Chronic	Total	
Myopia	5(41.67)	14 (36.84)	19 (38.00)	
Hypermetropia	5 (41.67)	19 (50.00	24(48..00)	
Astigmatism	2 (16.67)	5 (13.16)	7(14.00)	
Total	12 (100.00)	38 (100.00)	50(100.00)	

Table 8: Correlation of VKC Stage With Type of Astigmatism

	VKC Stage			Chi square =0.74 P=0.86
Type of Astigmatism	Acute	Chronic	Total	
None	5 (41.67)	12 (31.58)	17 (34.00)	
Simple Astigmatism	2 (16.67)	5 (13.16)	7 (12.00)	
Compound Astigmatism	2 (16.67)	7 (18.42)	9 (20.00)	
Mixed Astigmatism	3 (25.00)	14 (36.84)	17 (34.00)	
Total	12 (100.00)	38 (100.00)	50 (100.00)	

Table 9: Correlation of VKC Variant Type with Age

	VKC Type				Chi square =6.1 P=0.81
Age	Bulbar	Palpebral	Both	Total	
0-5	7(18.42)	2 (25.00)	19(25.00)	9 (18.18)	
6-10	11(28.95)	4 (50.00)	2 (50.00)	17938.64)	
11-15	14(36.84)	2 (25.00)	-	14(31.82)	
16-20	3 (7.89)	-	1(25.00)	2(4.55)	
21-25	2 (5.26)	-	-	2(4.55)	
26-30	1 (2.63)	-	-	1(2.27)	
Total	38 (100.00)	8 (100.00)	4(100.0)	50(100.00)	

Table 10: Correlation of VKC type with Gender

	VKC Type				Chi square =0.50 P=0.87
SEX	Bulbar	Palpebral	Both	Total	
Male	29 (76.32)	7 (87.50)	3 (75.00)	39(77.78)	
Female	9 (23.68)	1 (12.50)	1 (25.00)	11(22.22)	
Total	38 (100)	8 (100.00)	4 (100.00)	50(100.0)	

Table 11: Correlation of VKC Type with Refractive Error

	VKC Type				
Type of Refractive error	**Bulbar**	**Palpebral**	**Both**	**Total**	Chi square=2.67 P=0.61
Myope	16 (42.11)	2 (25.00)	1 (25.00)	19(38.00)	
Hypermetrope	17 (44.74)	4 (50.00)	3 (75.00)	24(48.00)	
Astigmatism	5 (13.16)	2 (25.00)	-	7(14.00)	
Total	38 (100.00)	8 (100.00)	4 (100.0)	50(100.0)	

Table 12: Correlation of VKC Type with Astigmatism Variant

	VKC Type				
Type of Astigmatism	**Bulbar**	**Palpebral**	**Both**	**Total**	Chi square =5.40 P=0.49
Simple Astigmatism	5 (13.16)	2 (25.00)	-	7 (14.00)	
Compound Myopic astigmatism	7 (18.42)	2 (25.00)	-	9 (18.00)	
Mixed Astigmatism	13 (34.21)	1 (12.50)	3 (75.00)	17 (34.00)	
None	13 (34.21)	3 (37.50)	1 (25.00)	17 (34.00)	
Total	389 (100.00)	8 (100.00)	4 (100.00)	50 (100.00)	

Discussion

The male:female ratio in our study was found to be 3.5:1, (Table 1). A similar study which was a cross sectional school study conducted by Roseline Duke et al. found the male: female ratio as 1.8:1 [14].

A study by Leonardi et al., had a similar male: female ratio between 3.3 and 3.5 [15].

In a study at a Tertiary Eye Care Institute in South India, showed a male female ratio of 6.4:1.16

Our study conforms to the global preponderance.

In our study maximum patients were in the age group of 6 to 10 years, which is up to 34% in our study. The second majority of patients were found in the age group of 11 to 15 years amounting up to 32%. (Table 2)

Hence, in our study almost 66% of patients were found in the age group of 6 to 15 years.

In a study by Saleh et al., they found 49.2% patients were less than 10 years of age. While they also found that the disease persists till the age of 20 years [17].

In Table 3, we tried to correlate the distribution of the refractive error in the Vernal Keratoconjunctivitis patients. We found that 24 patients (48%) of the patients had Hypermetropia as the associated refractive error. Whereas in 19 patients (38%), we found Myopia as the associated refractive error, Astigmatism was found to exist in 7 patients (14%).

In a study by T Mimura et al., they found that Seasonal allergic conjunctivitis was found to be more common in myopes than hypermetropes, though the study was conducted in contact lens and non contact lens users by them [12].

However we found more of hypermetropes, these were uncorrected hyperopes. Further commenting on the refractive status, we found that among the astigmatism group the maximum had a mixed type of astigmatism; that is hyperopic as well as myopic component co-existed in 17 (34%) of the patients (Table 4).

In our study we have considered perilimbal pigmentation as a manifestation of chronic VKC. Presence of degenerating eosinophils and epithelial debris suggestive of Horner Trantas spots were considered as a sign of acute VKC. We found 12 patients (24%) with acute VKC and 38(76%) patient with Chronic VKC. (Table 5)

According to a study by Rao et al., which was a cohort of Asian patients suffering from VKC perilimbal conjunctival pigmentation has been reported to be a constant finding. They found that no correlation existed between the extent of pigmentation and the severity of the VKC [23].

In a study by Faisal et al., the perilimbal pigmentation also extends along the conjunctiva and helps differentiating seasonal and perennial allergic conjunctivitis [27].

On comparing VKC stage with the age (Table 5), the commonest age group of manifestation was 6-10 years of age, of whom 34% patients had chronic VKC. The second commonest age group was 11-15 years of which 50% patient had acute VKC manifestations. The chi-square test for independence of the variable showed value of 3.62, P value 0.6 which is not significant.

Also number of patients in above 20 years was only 7.89% and all were under chronic stage suggesting that the disease manifestation reduces by 20 years of age.

In a study by Saleh et al they found 49.2%, maximum patient in the less than 10 years age group [17]. Similarly we also had maximum study population in the 6- 10 years age group. Also the maximum patients were in the chronic VKC stage.

Comparing the VKC stage with the gender, (Table 6) showed that the two variables are independent with a fisher's exact of 0.07 and p=0.1. which is not significant. So we did not find a correlation between VKC stage and gender.

On comparing the type of refractive error with the stage of vernal keratoconjunctivitis (Table 7), we found that most patients were in the hypermetropic group i.e. 24 (48.0%) and most of them were in the Chronic VKC stage about 19 (79%). The Fischer's exact test value was p=0.87 and chi square was 0.26, which was not significant, showing no correlation between the two variables.

In a study by T Mimura et al., the mean spherical equivalent refraction, was lower in patients with seasonal allergic conjunctivitis than in patients without seasonal allergic conjunctivitis ($p<0.05$). Hence they concluded that patients with seasonal allergic conjunctivitis are more myopic than healthy individuals. However their inclusion criteria included population with age group of 20 to 40 years and population with seasonal allergic conjunctivitis [12].

Recent investigations have demonstrated that vernal conjunctivitis, classified under the term allergic conjunctivitis, is related to the abnormal pattern of the corneal surface [6]. The abnormal ocular surface deteriorates the capacity of the fluid reservoir over the ocular surface. Tear film anomalies capture allergens in the conjunctival seasonal allergic conjunctivitis and cause the conjunctival immune-based inflammation by inducing T-cell activation. Thus, refractive error may be a possible risk factor for the direct progression to allergic conjunctivitis. Second, myopic eyes, which have a longer axial eye length and wider palpebral fissures, may be liable to mediate intimate attachment of allergens by the close interaction between bulbar and palpebral conjunctiva [12].

In a study by Paulo et al. data obtained by the topographic analysis of the corneal anterior surface of both groups clearly demonstrated that patients with VKC presented corneal contour changes when compared to patients with normal corneal asphericity. Of evident clinical interest, is the fact that the mean anterior corneal curvature of patients with VKC was more accentuated than in the control group ($p<0.05$). The parameters that verify anterior corneal contour such as AK and ERP, presented significantly higher values in patients with VKC ($p<0.05$) [18].

In Table 8, on comparing the VKC stage with astigmatism, maximum patients, 17 (34%) patients showed to have mixed astigmatism. And 34% patients did not have astigmatism, only spherical refractive error was found.

The chi-square test was found to be 0.7 and p value was found to be 0.86. It was found that the two variables are independent.

In Table 9, 10, 11, we are comparing the variables of vernal keratoconjunctivitis type in terms of bulbar type, palpebral type and both type withage, gender, refractive error, and astigmatism respectively.

In a study by Keziah N Malu conducted in Nigeria, they found limbal VKC in 46.5% cases and mixed subtype in 45.7% [19].

In Table 9, we found 25 patients with bulbar VKC out of 31 patients in the age group of 6 to 15 years; this is the commonest age group of manifestation. Bulbar VKC was the commonest variant amongst them. Bulbar VKC type was the only type of manifestation seen in all age groups, from below 5 years to 30 years of age. In our study we found no manifestation of palpebral VKC beyond 16 years of age. On applying the chi-square, the value was found to be 6.1 with p value of 0.81. The values were not significant suggesting that the variable were independent.

In a study by Keziah N Malu, they found that the prevalence of the limbal (46.5%) and mixed (45.7%) subtypes of VKC were almost equal. The most frequently associated ocular conditions were refractive error (6.7%) and eye lid disorders (3.3%). Limbal VKC includes the bulbar variety in their study [19].

The limbal (bulbar) and mixed forms of VKC are seen more commonly in Africans and Asians, whereas the palpebral form occur more among the Europeans and the Americas [20,21,22,23].

In Table 10, on comparing VKC type with gender, 29 male patients out of 39 were having bulbar VKC and 9 females out of 11 females were having bulbar VKC. Hence bulbar VKC were the commonest among both the gender. On applying fisher's exact, the value was 0.07 and p value of 0.77 and chi-square of 0.50, showing that the variables are independent.

The sex distribution of VKC is not uniform; whereas in European and Asiatic populations the male to female ratios are as high as 3:1 with sex predilection decreasing with age; [2] in most African studies there is a less marked male sex predominance [20,24,25,26].

In Table 11, on comparing VKC type with refractive error, we found that 16 (42.11%) of the myopes had bulbar VKC and 17 (44.74%) of the hyperopes had bulbar VKC. Both the refractive errors showed predisposition to bulbar VKC. Papillae on the lid can worsen the astigmatic error, however bulbar VKC is only more prevalent amongst astigmatics.

In Table 12, we have further tried to analyze the VKC type with the type of astigmatism. 34.21% patients amongst the bulbar VKC did not have any astigmatism and another 34.21% patients had mixed astigmatism. However, the palpebral variant showed maximum patients with no astigmatism, and equal distribution with simple astigmatism and myopic astigmatism with least in the mixed Astigmatism.

In a study by Tahir et al, they found 66% of cases with multiple signs of VKC including the bulbar variety. 24% of the cases had only follicles while in 10% cases only papillae were found. In their study out of 50 patients, 22 (55%) patients had astigmatism, 10 (25%) patients had myopia and 8 (20%) patients had hyperopia, whereas 10 patients were emmetrope [26].

Conclusion

In our study we found a male predilection for vernal keratoconjunctivities, male to female ratio was 3.5:1 with maximum patients in 6 to 15 years of age to be about 73.33%. We found hypermetropia as the commonest associated refractive error in 48% of the cases followed by myopia (38% cases) and astigmatism (14% of cases). Chronic vernal keratoconjunctivitis characterized by perilimbal pigmentation was the commonest stage of manifestation seen in 76% of cases.

In our study, most of the hyperopes (50%) manifested with the chronic VKC stage. We found that the commonest clinical variant was the Bulbar VKC type seen in 76% of the cases. Bulbar VKC was found to be the commonest association in hyperopes (44.74%), in myopes (42.11% cases) and in astigmatics (13.16% Cases).

We didn't find a significant association of the refractive error with the stage and type of the Vernal Keratoconjunctivitis. Probably a larger population of study might help us determine the association of these parameters.

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