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CORNEAL TOPOGRAPHIC CHANGES IN CHILDREN WITH VERNAL KERATOCONJUNCTIVITIS: TERTIARY HOSPITAL REPORT FROM JAMMU AND KASHMIR, INDIA

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ABSTRACT: BACKGROUND: Vernal keratoconjuctivitis has a known association with keratoconus. **OBJECTIVE:** Study was conducted to evaluate corneal topographic characteristics of patients with vernal keratoconjunctivitis (VKC) and compare the corneal topographic indices in VKC subjects with normal subjects. **STUDY DESIGN:** Prospective comparative study. **MATERIAL AND METHODS:** Videokeratography was done in 210 consecutive VKC patients and 201 age and sex matched normal subjects by Carl Zeiss meditec inc USA to evaluate corneal topography. Other tests included visual acuity testing with Snellens chart, slit lamp biomicroscopy, dilated fundus examination, measurement of central corneal thickness and intraocular pressure. Topographic indices were analyzed and compared using unpaired t-test among different groups. **RESULT:** Among 210 subjects with VKC, males comprised of 173 patients (82.3%) and mean age of presentation was 11.5±4.6 years with mixed VKC in 60%. Keratoconus-like topography was present in 64 patients (30.47%). **CONCLUSION:** Keratoconus-like topography was observed in very high proportion of patients of VKC.
KEYWORDS: Vernal Keratoconjuctivitis, Keratoconus.

INTRODUCTION: Vernal keratoconjunctivitis (VKC) is a chronic, bilateral, at times asymmetrical, seasonally exacerbated allergic inflammation of the ocular surface involving tarsal and/or bulbar conjunctiva.[1,2,3] The disease may present in three clinical forms: tarsal, limbal and the mixed form. Large papillae of different shape and size, usually greater than 1mm in diameter, on the upper tarsal conjunctiva characterize the tarsal form, while Trantas' dots and infiltrates on the limbus are typical of the limbal form. The mixed form is characterized by the presence of both forms in the same eye. VKC sufferers have a characteristic ropey, stringy mucous and/or serous discharge, and corneal complications, such as superficial punctate keratopathy (SPK), and shield ulcers are common.

Moderate to intense conjunctival hyperemia, intense itching, photophobia, mild to moderate chemosis, foreign-body sensation, and pain are typical signs and symptoms which may be very intense upon awakening, causing frequently what is called the morning misery. While it is considered a long-term disease with an average duration of 4–8 years, VKC generally subsides before or just after puberty.[1,2,4] Onset is usually in childhood. It is more common in boys than girls and usually resolves by late adolescence. Chronic ocular trauma and rubbing of eye due to pruritus could be the environmental factor ("Trigger") associated with keratoconus development in genetically predisposed individuals.[5,6] Videokeratography is one of the most commonly used method in practice for detecting keratoconus.[7,8] There is a high prevalence of both keratoconus and VKC in Sringar population as indicated by early trends in an ongoing study which has been conducted at GMC Medical College Srinagar and associated SMHS hospital, however the there is no previous data on there prevalence. The present study is subset of patients till now included in the study.

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Study has been undertaken to determine corneal topographic characteristics of children with vernal keratoconjunctivitis and compare the change in corneal topographic indices in VKC subjects with normal subjects.

MATERIALS AND METHODS:
Study Design: Prospective comparative study was carried out in Govt. Medical College Srinagar (J & K, India) and associated SMHS hospital among 210 consecutive subjects with VKC and 210 age and gender matched normal subjects from September 01, 2014 to August 30, 2015.

Patients with disease other than VKC, previous history of shield ulcer, corneal scars, history of surgery and unwilling to participate in the study were excluded. Age and gender matched subject with normal ocular finding were considered as a normal comparable group. The purpose and procedure of study were clearly explained to and verbal consent was received from all subjects.

Uncorrected and corrected distance visual acuity of each eye was assessed with the Snellens chart six meter distance in normal illumination for school going children. Detailed anterior segment examination was carried out with the help of a Slit lamp biomicroscopy (Haag–Streit 900 Ag., Switzerland).

Diagnosis of VKC was made on the basis of the typical clinical history of severe itching with characteristic signs, including giant papillae on the upper palpebral conjunctiva, limbal infiltrates, and eosinophilic concretions (Horner–Trantas'_dots). Slit-lamp biomicroscopic sign Vogt's striae, Fleischer's ring, stromal thinning, and stromal scarring and keratometric findings of irregular mires consistent with diagnosis of keratoconus were recorded for each subject. Fundus evaluation was performed using the Heine Beta 200 direct ophthalmoscope, slit lamp funduscopy using +90 D 'Volk'lens (U.S.A) and Indirect Ophthalmoscopy (Appaswamy, India) using +20 D 'Volk'_lens (U.S.A) after pupil dilatation with 0.5% cyclopentolate. Cycloplegic refraction was performed with the help of Heine streak retinoscope in each child after instilllation of eye ointment atropine 1% 3 times a day for 3 days. Videokeratography was performed with Atlas Model 9000 Corneal Topography System, from Carl Zeiss Meditec Inc (USA). Before initiation of corneal topography, a drop of artificial tears (Carboxymethylcellulose 0.5%) was instilled into the inferior fornix to ensure an adequate tear film.

Three Videokeratographic images ensuring proper fixation. One keratograph of each eye was chosen for analysis based on the criteria: the least eyelid shadow to allow proper centration, proper focusing with thin regular continuous rings that covered the cornea from limbus to limbus, and absence of any dry spots (Discontinuous rings) or excess pooling of tears along the inferior lid margin. Pathfinder II corneal analysis software was used to determine suspected keratoconus like topography. The clinical data captured by Pathfinder II makes it possible to compare findings in an individual patient to expected findings from different populations of individuals with eyes that have various known conditions or pathologies. Using a trained Support Vector Machine, or SVM algorithm, Pathfinder II displays the probability (From 0 to 99%) that the corneal topography matches each of the categories established in the PathFinder II clinical study database.[9] Path Finder II's aforementioned clinical database provide you with a probability that the topography falls into (It will report up to two category matches) the following five categories:

1. **Normal**. This includes corneas that have no corneal pathologies and no history of refractive surgery or other corneal surgery.

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2. **Suspect Keratoconus (KCN):** This includes forme fruste keratoconus (also known as subclinical keratoconus), long-standing keratoconus (patients in whom you've already established the condition) and pellucid marginal degeneration (PMD).
3. **Myopic Laser Vision Correction (LVC):** This includes patients who've undergone myopic laser vision correction, such as LASIK, photorefractive keratectomy (PRK) or laser epithelial keratomileusis (LASEK).
4. **Hyperopic Laser Vision Correction (LVC):** This includes patients who've undergone hyperopic LVC, such as LASIK, PRK or LASEK.
5. **Other:** This includes corneal pathologies, such as corneal scars and degenerations, and surgeries, such as post-penetrating keratoplasty (PKP) and LASIK that affect the anterior corneal surface.

This system determines the presence or absence of keratoconus based on the analysis of twelve topographic indexes derived from corneal topographic analysis of the twelve corneal parameters analyzed, three evaluate the irregularity (CIM = Corneal Irregularity Measurement), mean apical curvature (TKM = Toric Keratometric Mean), and shape of the cornea (Shape Factor).

The remaining nine parameters are derived from the Mean Curvature View namely Max Mean curvature, Max Mean Curvature Xmm, Max Mean curvature Ymm, Centroid Xmm, Centroid Ymm, Convexity Ymm, Convexity, Mean I-S,Mean IN-ST, Mean IN-SN.

Central corneal thickness was measured by TOPCON SP-3000 (USA). Intraocular pressure (IOP) was measured by Goldmann Applanation Tonometer attached to the Slit lamp Biomicroscope (Haag–Streit 900 Ag., Liebefeld, Switzerland).

Statistical Analysis: All data were recorded in proforma and entered in computer database for statistical analysis with the help of the computer software SPSS 17. Variation in distribution of subjects with age and bestcorrected visual acuity (BCVA) were analysed using ANOVA and with sex and suspected keratoconus-like topography were analyzed using the Chi-square test. Comparison of features between VKC subjects with suspected keratoconus-like topography and non-keratoconus-like topography and normal subjects were performed with unpaired t-test.Chi-square test was performed for gender comparison. Level of significance was considered at p value<0.05 for 95% confidence interval.

RESULTS: Among 210 (Table 1) with Vernal Keratoconjunctivitis (VKC), males comprised of 173 patients (82.3%) and females comprised of 37(17.61%) patients with mean age of presentation of 11.5±4.6 years. Majority of patients 126(60%) comprised of mixed VKC followed by palpebral VKC in 64 subjects (28.7%) and limbal VKC in 20 subjects (9.52%). Age of presentation was significantly different (p = 0.001) in various types of VKC having early presentation in limbal VKC (9.3±4.2 years). Among 210 VKC subjects, suspected keratoconus-like topography was present in 64 subjects (30.47%) 10 of whom had confirmed slit lamp signs.

Table 2 presents the comparison of presenting features between VKC subjects and normal subjects. The mean age (p=0.16), sex distribution (p=0.10) best spectacle corrected visual acuity (p=0.3) and corrected IOP (p=0.10) of VKC subjects was not significantly different with normal subjects. Central corneal thickness was found to be significantly decreased (p=0.00) in VKC subjects (490.2±8.7) compared to normal subjects (510.4±9.1).

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Central corneal thickness was even more significantly reduced (p=0.00) in VKC subjects with suspected keratoconus like topography (450.6 ±12.2).

Table 3 presents comparison of topographic indices in normal subjects, VKC subjects with suspected keratoconus like topography and with normal topography.

Max mean curvature, max mean curvature Xmm, max mean curvature Ymm topographic indices between normal and VKC subjects were higher in VKC subjects but were statistically insignificant.

However other topographic indices between normal subjects and VKC subjects was statistically significant.

There was marked increase in the topographic indices in suspected keratoconus like topography when compared to VKC subjects with normal topography and was statistically significant.

DISCUSSION: This study compares the videokeratographic patterns in children with VKC as compared to age and sex matched normal group. Studies has shown association of VKC with keratoconus and constant eye rubbing has been implicated as a causation factor.[10]

Corneal videokeratography is very important investigative tool in detecting keratoconus and helps in diagnosis of early or subclinical forms of keratoconus. Various corneal topographical indices were found to be altered in VKC patients in this study. The mean age of presentation of the patients with VKC was 11.5±4.6 years.

Early presentation was seen in limbal VKC 9.3±4.2 years and late presentation in palpebral VKC 14.3± 6.0 years. Both mean age of presentation and variation in age of presentation of various types of VKC were similar to previous studies. VKC was seen to be more commonly present in males (82.3%) similar to previous studies.[11-16]

All studies reported late presentation of keratoconus in VKC patients except Gortzak et al.[15] Dantas et al. report, palpebral VKC (97.81%) was more common in patients having keratoconus whereas mixed VKC (36.50%) was more common in our study.[17]

Sixty four (30.47%) were found to have suspected keratoconus-like topography as compared to 10.7% by clinical criteria in our study. Slit lamp confirmed cases account for 10 of the 30 cases. Both clinically and topographically prevalence of keratoconus was more in our study than the others. Shoja and Besharati detected keratoconus by videokeratography maps in 28% of VKC patients.[16]

Gortzak et al. detected 22.5% of keratoconus by videokeratography maps and 3.75% clinically by slitlamp examination in VKC patients.[15] Dantas et al. reported 22.53% of keratoconus by videokeratographic maps and 9.85% clinically by slit lamp examination in VKC patients.[17] Total et al. detected 26.8% of keratoconus by videokeratography maps and 8.5% clinically by slit lamp examination in VKC.[14]

These studies used the modified Rabinowitz-McDonnell criteria.[15-17] whereas, we used pathfinder II corneal analysis using machine Carl zeiss meditec inc USA model ATLAS 9000 specially sensitive to early detection of keratoconus. Pathfinder II corneal analysis has sensitivity and specificity of >90% to detect abnormal corneas as reported by preliminary report in large multicentric clinical trials.[9]

Other studies used central corneal power, difference in central corneal power between fellow eyes, and the Inferior–Superior (I–S) value. These three parameters were significantly different in patients with suspected keratoconus-like topography than in normal controls. Rabinowitz et al. reported the sensitivity of I–S ratio at 95.7% in the sample tested with KPI index and KISA% index.[18]

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To have significant different clinical and topographic keratoconus among VKC subjects, various factors may be attributable such as age of presentation, population difference, type of VKC apart from the different criteria adopted to detect keratoconus pattern clinically as well as topographically. Keratoconus-like topography can be characterized by an area of localized, abnormal steepening often located in inferior quadrant. But sometimes, it is seen in the center or superior portion of the cornea.

This abrupt steepening in cornea results in asymmetry and a large refractive power difference across the corneal surface.[8] Pathfinder II corneal analysis software helps in detection of these characteristics using 12 different topographic indices (Table 3) to detect any abnormality in cornea and helps in early detection of subclinical cases of keratoconus. It also helps to differentiate keratoconus with other corneal abnormalities. As compared to Rabinowitz criteria which only measures inferior-superior asymmetry, pathfinder II analysis measures inferior nasal-superio temporal asymmetry and inferior temporal -superior nasal asymmetry and can detect keratoconus causing steeping in atypical quadrants.

Apart from steeping, early corneal abnormal irregularities can be detected by topographic indices like corneal irregularity measurement (CIMμm), toric keratometric measurement (TKM), Shape factor (SF), Centroid Xmm, Centriod Ymm and Convexity. Between normal control group and the VKC patient group all the topographic indices were statistically significant except Max mean curvature, Max mean curvature Xmm and Max mean curvature Ymm. This indicates that in all VKC patients there occurs some change in the corneal contour and some of these cases it may progress to keratoconus like topography.

CONCLUSION: This study is a preliminary data of ongoing prevalence studies on Vernal keratoconjuctivitis and Keratoconus showing early indication of very high prevalence of Keratoconus in Vernal keratoconjuctivitis patients of Kashmir population.

This study also shows that a very high number of subclinical keratoconus can be detected by videokeratography as compared to clinical examination.

	Total VKC n=210	Mixed n=126 (60%)	Palpebral n=64 (30.47%)	Limbal n=20 (9.52%)	p value
Age (yrs.)	11.5±4.6	10.8±4.2	14.3±6	9.3±4.2	0.001
Sex (%)					
Males	173(82.3%)	110(87.3%)	48(75%)	15(75%)	0.86
Females	37(17.61%)	16(12.69%)	16(25%)	5(25%)	
BCVA(Log MAR)	0.04±0.15	0.05±0.18	0.03±0.04	0.02±0.07	0.55
Keratoconus	64(30.47%)	46(36.50%)	15(23.43%)	3(15%)	0.02
Table 1: Comparison between different types of VKC patients					

VKC=Vernal keratoconjuctivitis, BCVA=Best corrected visual acuity.

p value ≤ 0.05 is considered significant by ANOVA.

p value ≤ 0.05 is considered significant by Chi-square test.

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	Normal n=201	VKC n=210	p value	VKC (N) n=146	VKC(K) n=64	p value
Age(yrs)	11.2±4.8	11.5±4.6	0.28	8.8±4.6	14.9±3.8	0.001
Sex (%)						
Males	146(72.6%)	173(82.31%)		112(76.71%)	48(75%)	
Females	55(27.3%)	37(17.61%)	0.18	34(23.28%)	16(25%)	0.5
BCVA (LogMAR)	0.02±0.10	0.04±0.15	0.26	0.02±0.12	0.28±0.38	0.01
Spherical equivalent(DS)	-1.8±0.6	-2.3±1.8	0.03	-1.6±1.9	-3.8±2.8	0.001
Cylinder(DC)	-1.01±0.5	-1.8±1.2	0.02	-1.1±1.4	-2.4±1.9	0.01
Corneal thickness(μm)	510±9.4	490.2±8.7	0.01	501.3±8.1	450.6±12.2	0.03
Corrected IOP(mmHg)	16.4±1.8	15.8±1.4	0.10	15.4±2.3	15.1±3.1	0.15
Table 2: Comparison between normal and VKC patients						

VKC=Vernal keratoconjuctivitis, BCVA=Best corrected visual acuity.

VKC (N)=Vernal keratoconjuctivitis with normal topography.

VKC (K)=Vernal keratoconjuctivitis with suspected keratoconus like topography.

p value ≤ 0.05 is considered significant by unpaired t-test.

p value ≤0.05 is considered significant by Chi-square test.

Normal Range	Normal Group n=201	VKC n=210	p value	VKC(N) n=180	VKC(K) n=30	p value
CIM μm(0.49 to1.68)	1.2±0.5	1.5±0.7	0.01	1.35±0.02	2.8±0.03	0.02
TKM(42.19 to 47.26D)	44.64±2.6	45.68±2.9	0.02	44.98±2.1	48.01±0.04	0.001
SF (0.26 to 0.64)	0.4±1.8	0.6±0.7	0.04	0.52±0.6	0.82±0.5	0.01
Max mean (41.97 to 47.36D) curvature	43.26±2.1	45.28±1.8	0.08	44.12±1.6	49.18±1.8	0.01
Max mean(-1.39 to 1.27) curvature Xmm	-0.8±0.6	1.1±0.5	0.18	1.01±0.6	2.01±0.7	0.001
Max mean(-2.42 to 0.72) curvature Ymm	-1.3±1.2	1.2±0.7	0.07	-0.1±0.5	1.87±0.5	0.01
Centroid Xmm (-0.72 to 0.71)	-0.2±0.5	0.4±0.3	0.04	0.2±0.3	1.61±0.6	0.001
Centroid Ymm (-1.24 to 0.31)	-1.1±0.2	-0.2±0.4	0.02	0.2±0.2	0.5±0.3	0.001
Convexity (0.777 to 0.981)	0.81±0.2	0.89±0.4	0.03	0.82±0.3	0.98±0.4	0.00

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Mean I-S(-0.78 to 1.77)	1.2±0.4	1.4±0.2	0.01	1.3±0.2	2.33±0.5	0.01
Mean IN-ST (-1.00 to 1.20 D)	-0.5±0.6	1.0±0.3	0.01	-0.2±0.5	1.8±0.5	0.01
Mean IT-SN (-0.51 to 1.45D)	1.1±0.4	1.3±0.5	0.11	1.2±0.3	3.05±1.2	0.01
Table 3: Topographic indices in normal patients, VKC patients with normal topography and suspected keratoconus like topography						

VKC= Vernal keratoconjuctivitis, BCVA.

VKC (N) =Vernal keratoconjuctivitis with normal topography.

VKC (K) =Vernal keratoconjuctivitis with suspected keratoconus like topography.

p value ≤ 0.05 is considered significant by unpaired t-test.

CIM=Corneal Irregularity Measurement, TKM = toric keratometric measurement, SF=Shape factor.

I-S=Inferior and superior keratometric difference.

IN-ST=Inferionasal and superiotemporal keratometric difference.

IT-ST=Inferiotemporal and superiotemporal keratometric difference.

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