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COMPARISON OF ANTERIOR SEGMENT PARAMETERS IN NORMAL AND KERATOCONUS EYES USING COMBINED PLACIDO-DISK SCHIEMPFLUG IMAGING-BASED TOPOGRAPHY

Kurakula Madhuri, Pasumarthi Pavani Yelamanchili, Mannam Gitanjali, Kotagiri Srawanthy

The aims*: The purpose of this study was to evaluate and compare the anterior and posterior corneal surface parameters, keratoconus indices, thickness profile data, and data from enhanced elevation maps of keratoconus and normal corneas using Combined Placido-Schiempflug imaging-based topography, and to determine the sensitivity and specificity of these parameters in discriminating keratoconus from normal eyes.*

Materials and methods*: A retrospective comparative observational study of 100 normal eyes and 100 keratoconus eyes was done from April 2014 to May 2015 at MM Joshi Eye Institute, Hubli, Karnataka. We evaluated and compared the anterior and posterior corneal surface parameters, keratoconus indices, thickness profile data, and data from enhanced elevation maps of keratoconus and normal corneas using Combined Placido-Scheimpflug Imaging based Topography to determine the sensitivity and specificity of these parameters in discriminating keratoconus from normal eyes.*

Results*: Keratoconus indices (Sif, Sib, BCV-f, BCV-b, KVf, KVb, CCT, MinCT) showed Excellent AUROC values followed by K- steep in posterior curvature at 3 mm, 5 mm followed by K- steep in anterior curvature and other parameters in discriminating Normal from Keratoconus-Suspect eyes. Elevation indices- BCV-f, BCV-b, CCT, Min-CT, K-steep & K-flat in anterior and posterior curvature in 3 mm, 5 mm, 7 mm, and CV were significant in discriminating normal from mild keratoconus. All parameters except ACV and ICA were significant in discriminating normal from moderate keratoconus. All parameters were significant in discriminating normal from severe keratoconus eyes. Morphological indices were significant in differentiating mild, moderate and severe keratoconus.*

Conclusion*: Many parameters were statistically significant between keratoconus and normal eyes compared with early keratoconus eyes.*

The topography and corneal aberration results in this study are promising for detecting ectatic corneas. In our study, thickness indices-CCT, MinCT, Abberometry indices- BCVf, BCVb and keratometry in steep meridian at posterior curvature had the highest AUC scores in differentiating normal from sub-clinical keratoconus.

Elevation indices- Rbf-f, Rbf-b, thickness indices- CCT, MinCT, aberrometry indices, and keratometry-steep in anterior & posterior curvature had the highest AUC scores in differentiating moderate and severe keratoconus

Keywords*: keratoconus, Placido-Scheimpflug imaging-based topography, anterior curvature, posterior curvature, Fleischer ring, Vogt striae, anterior stromal scar on slit-lamp examination*

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1. Introduction

Keratoconus is a non-inflammatory ectatic corneal dystrophy characterised by a usually progressive corneal thinning that results in corneal steepening, protrusion, irregular astigmatism, and gradual impairment of vision. The estimated prevalence in the general population is 54 per 100 000 [1]. It is commonly an isolated ocular condition but sometimes coexists with other ocular conditions (Vernal Keratoconjunctivitis, Retinitis Pigmentosa and Leber's Congenital Amaurosis), and systemic associations include many of the connective tissue disorders (Ehler's Danlos, Marfan's Syndrome), mitral valve prolapse, Atopic Dermatitis & Down's Syndrome.

Keratoconus is usually bilateral but is often asymmetric. The incidence of unilateral keratoconus is very low. It has been shown that 50 % of unaffected eyes of persons with unilateral keratoconus subsequently will develop the disease [2]. Hence the unaffected eye of a unilateral keratoconus patient is considered susceptible to developing ectasia. These cases can be considered the mildest form of the disease (early keratoconus) and may help understand and develop diagnostic criteria for detecting early ectasia.

Frank keratoconus can be diagnosed clinically or by corneal topography; however, despite extensive efforts, definitive criteria for diagnosing subclinical ectasia remain elusive. Accurate detection of subclinical keratoconus or forme-frost keratoconus among refractive surgery candidates is important because keratorefractive procedures may worsen their condition. One major difficulty is detecting subclinical keratoconus in its earliest stage and not detected by routine clinical tests, such as maximal contrast visual acuity measurements or slit-lamp examination. Early keratoconus can benefit from

new therapeutic modalities that can stop or delay the evolution [3]. Until recently, one of the most important criteria for diagnosing keratoconus was based on anterior corneal curvature provided by Placido disk–based computerised corneal topography. With the advent of scanning-slit topography and Scheimpflug tomography systems, both the anterior and posterior curvatures are considered [4, 5].

Wavefront technology has also shown promising results in diagnosing and grading the severity of keratoconus. Combined Placido-Scheimpflug based Sirius Topography device, which is a non-invasive, noncontact excellent new tool for diagnosis & documentation of corneal pathologies, angle structures, surgeries and response to therapy. Scheimpflug imaging differs from conventional imaging techniques in that the object plane, lens plane, and image plane all intersect in a straight line. The advantage of this principle is that a wide depth of focus is achieved. The Scheimpflug principle has been applied in ophthalmology to obtain optical sections of the entire anterior segment of the eye, from the anterior surface of the cornea to the posterior surface of the lens. The Sirius system is a new topography device that uses the principles of Scheimpflug photography and enables the acquisition and processing of 25 radial sections of the cornea and anterior chamber.

The combination between 1 monochromatic 360-degree rotating Scheimpflug camera and a Placido disc allows analysis of the cornea and anterior segment, providing tangential and axial curvature data of the anterior and posterior corneal surfaces, the global refractive power of the cornea, a biometric estimation of various structures, a corneal wavefront map with an analysis of visual quality, and corneal pachymetry maps. Specifically, this system allows the measurement of 35,632 points of the anterior corneal surface and 30,000 points of the posterior corneal surface in a high-resolution mode in approximately less than 1 second. With this point-by-point information on the anterior and posterior corneal surfaces, a pachymetric map is reconstructed [6].

In corneal refractive surgery, early diagnosis of keratoconus (subclinical asymptomatic keratoconus) is of great importance in patients seeking surgery because it can prevent the progression of the pathology after surgery and make it symptomatic (corneal ectasia), thus creating the need for diagnostic tests that provide high sensitivity (ability to detect the disease in affected subjects)with the objective that no asymptomatic subclinical keratoconus ends up not being diagnosed and thus not undergo corneal refractive surgery.

2. Materials and methods

This was a retrospective case series study. Clinical data and corneal examination were retrieved from clinical records at M.M Joshi Eye Institute.

The study was conducted following the ethical standards & approved by the ethical committee (1522261029/NBE/6466 in January 2013) by the local clinical research ethics committee with informed consent obtained.

Inclusion criteria: Normal Patients with mild myopia (manifest refraction spherical equivalent of at most –1.00 to –6.00 diopters, with a cylinder of more than –1.00 diopters)**,** presence of keratoconus diagnosed using the standard criteria; (that is, corneal topography showing an asymmetric bowtie pattern with or without skewed axes) and at least 1 keratoconus sign (stromal thinning, conical protrusion of the cornea at the apex, Fleischer ring, Vogt striae, anterior stromal scar) on slit-lamp examination.

Exclusion Criteria: Eye with other ocular pathology, severe Dry eye, corneal scarring, pellucid marginal degeneration, eyes already underwent a specific treatment such as collagen cross-linkage, intra corneal rings, and keratoplasty, history of corneal or other ocular surgery, patients who had ever used contact lenses in the preceding week**, e**yes with previous acute corneal hydrops**,** pregnancy or Nursing**, g**laucoma**, c**orneal infections **and u**se of topical medications

Routine eye examinations, including visual acuity, best corrected visual acuity, slit-lamp examination, and ophthalmoscopy, were done for all the patients. The parameters provided by the Sirius Schiempflug imaging system in patients with 200 eyes were recorded and divided into two groups.

Group 1 includes a normal group comprised of 100 eyes of 50 patients evaluated for refractive surgery between March 2014 to May 2015 at M.M Joshi Eye Institute.

Eyes were considered Normal if they had no ocular pathology, no previous ocular surgery and no irregular corneal pattern.

Group 2 includes the keratoconus group comprised of patients with keratoconus diagnosed by a corneal specialist based on clinical and topographic signs.

The ocular findings that defined keratoconus included:

(a) an irregular cornea determined by distorted keratometry mires and distortion of the retinoscopic or ophthalmoscopic red reflex (or a combination of these);

(b) at least 1 of the following biomicroscopic signs: Vogt's striae, Fleischer's ring of greater than 2 mm arc, or corneal scarring consistent with keratoconus.

This group is Sub-grouped as Group-2a, 2b, 2c, and 2d.

Group 2a includes keratoconus Suspects, which comprises patients with 25 eyes with subtle signs of keratoconus topographically but without evidence of clinical keratoconus in either eye.

Group 2b includes patients of 25 eyes with Mild keratoconus, where k readings are less than 47D.

Group 2c includes patients of 25 eyes with Moderate Keratoconus, where k readings are between 47D and 55D.

Group 2d includes patients of 25 eyes with severe keratoconus, where k readings are more than 55D.

The same experienced examiner performed all the tests.

• Corneal curvature, elevation, and thickness measurements were obtained by means of a Scheimpflug camera combined with Placido corneal topography (Sirius, software version 1.2, CSO, Firenze, Italy).

• The scanning process acquires a series of 25 Scheimpflug images (meridians) and 1 Placido top

view image. The ring edges are detected on the Placido image so that height, slope, and curvature data are calculated using the arc-step method with conic curves. From the Scheimpflug images, the profiles of the anterior cornea, posterior cornea, anterior lens, and iris are derived. Anterior surface data from both Placido and Scheimpflug images are merged using a proprietary method. All the other measurements for internal structures (posterior corneal curvature, anterior lens surface, and iris) are derived solely from Scheimpflug data. Previous studies have reported that the system's pachymetric and shape measurements (curvature, eccentricity, elevation) have good repeatability.

• Measurements were performed by a single experienced examiner according to the manufacturer's guidelines. The examiner was unaware of the clinical diagnosis. The device was brought into focus, and the patient's eye was aligned along the visual axis using a central fixation light. One scan was obtained for each patient. Every examination was critically reviewed for the quality of the topographic image, alignment, and anterior and posterior coverage. In case of a poor-quality scan, a new scan was repeated, and the patient was excluded if the new scan was also poor quality.

The Sirius topography, based on a combined Placido and Schiempflug imaging system, is a non-invasive topography used to measure the anterior segment parameters. Data on numerous parameters are derived from the Scheimpflug and Placido images. Measurements with the Sirius Topography analyser were performed according to the manufacturer's guidelines. The following parameters provided by the Sirius topography system were used for analysis: anterior curvature-flat keratometry (K), anterior curvature steep K, Mean K reading anterior, posterior curvature flat K, posterior curvature-steep K, Mean K reading Posterior, Central pachymetry, thinnest pachymetry, Corneal Volume and anterior chamber depth (ACD),

Symmetry indices front & back, the anterior elevation and posterior elevation(best fit sphere), Baiocchi Calossi Versaci (BCV) front & back, root mean square of high order aberrations(RMS). The total corneal aberrations were obtained from the anterior and posterior surfaces, with measurements centred on the pupil (6.0 mm).

The following values were recorded:

Anterior curvature parameters (simulated keratometry [K]) is derived from the anterior axial curvature map. Simulated K-steep (anterior

curvature-steep K) and simulated K=flat (anterior curvature-flat K) is calculated from the pair of meridians 90 degrees apart, with the greatest difference in average power from 0.5 to 2.0 mm distance from the centre. The anterior curvature average is the arithmetic mean of the steep and the flat meridians. The power of the steep and flat meridians is calculated using the keratometric index (1.3375). Posterior curvature parameters (derived from the posterior axial curvature map) are calculated similarly to the ones from the anterior surface.

The only difference is that the K values are not simulated but are calculated with the real indices of refraction of the cornea (1.376) and the aqueous humour (1.336).

The dual Scheimpflug analyser automatically shows the average central corneal thickness (CCT) and thinnest CCT. Because keratoconus is characterised by stromal thinning in the protrusion region, an index based on the thinnest value of corneal pachymetry is likely to help discriminate between normal and keratoconus eyes. The thinnest corneal value was calculated over an 8-mm area. Corneal volume is reported as the volume of the cornea in a diameter of 10 mm, centred on the anterior corneal apex. Anterior chamber depth was defined as the distance from the corneal endothelium to the anterior surface of the lens capsule.

The anterior chamber volume is calculated from endothelium down to the iris and lens over a 12mm diameter centred on the anterior corneal apex. The default angle displayed is the smallest in the horizontal position calculated from the Scheimpflug image. Symmetry Index of Front (SIf) and Back Corneal Curvature (SIb). The symmetry index of front corneal curvature (SIf) was defined as the difference in mean anterior tangential curvature (expressed in diopters) between 2 circular zones centred on the vertical axis in the inferior and superior hemispheres (centre: x = 0 mm; y= +/-1.5 mm; radius: 1.5 mm). SIf measures the vertical asymmetry of anterior corneal curvature: Positive values indicate a steeper inferior hemisphere, whereas negative values indicate a steeper superior hemisphere. Likewise, the symmetry index of back curvature (SIb) was defined as the difference in mean posterior tangential curvature between 2 circular zones centred on the vertical axis in the inferior and superior hemispheres. Because SIb is measured in diopters and the difference between the refractive index of the cornea and that of the aqueous produces a value of the opposite sign relative to SIf (which is measured on the anterior corneal surface), the arithmetic sign of SIb was arbitrarily changed to make comparison with SIf easier.

Differences calculated from asphere-toric best fit reference surfaces were used to model the elevation data of anterior and posterior corneal surfaces over a diameter of 8 mm. The asphericity of the reference surface was set equal to the average value in the 8-mm zone, as measured in our sample of normal eyes. Elevation data were decomposed into Zernike polynomials up to the 7th order, centred on the corneal vertex, as previously done by Schwiegerling and Greivenkamp [7].

The best-fit radius of the anterior corneal surface (Rbf f): The best-fit radius of the anterior surface (Rbf f) was defined as the measurement (in millimetres) of the apical radius of the best-fit ellipsoid with the eccentricity of an average eye over an 8-mm diameter. The apical radius was calculated for the whole surface because this approach is less influenced by noise and artefacts than calculating the apical radius for a single meridian or a couple of meridians.

Baiocchi Calossi Versaci front index (BCVf) and BCV, back index (BCVb) following coefficients are the most relevant for keratoconus detection: vertical trefoil c3 _3, vertical coma c3 _1, horizontal coma c3 _1, primary spherical aberration c4 0, and second order vertical coma c5 _1. The BCVf, expressed in micrometres, was obtained by properly combining these coefficients (from the anterior corneal surface) and weighting them by a function of the coma axis. Likewise, a linear combination of c3 _3, c3 _1, c3 _1, c4 0, and c5 _1 and information

about the coma axis on the posterior Zernike decomposition were used to define the BCVb.

The root mean square of higher-order aberrations is based on previous studies showing that higher-order aberrations of the anterior corneal surface can be used to detect and grade keratoconus. Therefore, we measured the front and back corneal surface root mean square of higher-order aberrations.

Statistics. Eyes with keratoconus were compared with normal corneas in separate series of analyses. All numerical results were entered into a database, and statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 16.0.

Pairwise differences between groups (Keratoconus Suspects versus Normal eyes, Mild keratoconus versus Normal eyes, Moderate Keratoconus versus Normal eyes and Severe keratoconus versus Normal eyes) for demographic variables were analysed by the unpaired t-test. A p-value less than 0.05 was considered statistically significant.

The accuracy of the parameters was determined using receiver operating characteristic (ROC) curves. For the output values area under the curve (AUC), sensitivity (true positive/[true positive C false negative]), specificity (true negative/[true negative false positive]), and cut-off value that corresponded to the maximum AUC were calculated and compared between the groups. The AUC is a measure of test accuracy. Based on the magnitude of the AUC, the accuracy of a diagnostic test is classified as excellent (AUC 0.9 to 1.0), good (AUC 0.8 to 0.9), fair (AUC 0.7 to 0.8), poor (AUC 0.6 to 0.7), or fail (AUC 0.5 to 0.6).

3. Results

In the normal group, the study involved 100 eyes of 50 patients with a mean age of 24.11 ranging from 15–45 years; 40 eyes were male, and 60 were female. In the keratoconus group, the study involved 100 eyes. The keratoconus suspect group (group 2a) comprised 25 eyes with a mean age of 27.28 ranging from 15–45 years, 13 eyes were male, and 12 eyes were female. The mild keratoconus group(group 2b) comprised 25 eyes with a mean age of 24.72 ranging from 15–45 years, 12 eyes were male, and 13 were female. The moderate keratoconus group (group 2c) comprised 25 eyes with a mean age of 24.12 ranging from 15-45 years, 13 eyes were male, and 12 were female.

The severe keratoconus group (group 2d) comprised 25 eyes with a mean age of 22.80 ranging from 15-45 years, 13 were male, and 12 were female. The normal group and keratoconus (mild, moderate, severe) group did not differ significantly concerning age (p=0.98, p=0.99, p=0.76) (Table 1).

Table 1

Comparison of male and female patients with a mean age in five study groups

Groups	Mean age	SD age
Normal	24.11	3.86
Group 2A	27.28	7.90
Group 2B	24.72	5.86
Group 2C	24.12	4.93
Group 2D	22.80	4.12
Total	24.42	5.05
F-value	2.8934	
P-value	0.0234*	
Pair-wise comparisons by multiple post-hoc procedures		
Normal vs Group 2A	P=0.0343*	
Normal vs Group 2B	P=0.9819	
Normal vs Group 2C	P=0.9999	
Normal vs Group 2D	P=0.7616	

*Note: *p<0.05*

There was no statistical difference in mean age between patients in 5 groups, and no gender preponderance was seen (Table 2).

Table 3 shows the parameters' mean values in all 5 groups.

Table 2

Summary statistics of all variables in five groups

Variables	Groups	Min	Max	Mean	SD
1	2	3	4	5	6
KF readings anterior (3mm)	Normal	39.43	46.76	43.40	1.68
	Group 2A	39.85	46.83	44.18	1.90
	Group 2B	40.55	45.83	43.59	1.23
	Group 2C	44.53	53.85	48.88	2.52
	Group 2D	52.99	84.60	62.88	7.88
	Total	39.43	84.60	46.64	7.16
KF readings anterior (5mm)	Normal	39.49	46.73	43.38	1.68
	Group 2A	39.92	47.12	44.19	1.81
	Group 2B	41.17	45.38	43.67	1.07
	Group 2C	44.27	52.65	48.19	2.13
	Group 2D	52.11	79.23	60.72	6.79
	Total	39.49	79.23	46.29	6.35
KF readings anterior (7mm)	Normal	39.46	46.53	43.26	1.68
	Group 2A	39.80	46.73	44.00	1.67
	Group 2B	41.64	45.53	43.59	0.99
	Group 2C	43.82	51.49	47.24	1.73
	Group 2D	50.39	71.69	57.63	5.76
	Total	39.46	71.69	45.68	5.32

Continuation of Table 2

1	2	3	4	5	6
KF readings posterior (3mm)	Normal	5.56	6.59	6.05	0.25
	Group 2A	4.15	7.31	6.11	0.54
	Group 2B	0.55	7.30	5.87	1.22
	Group 2C	0.66	9.10	7.17	1.52
	Group 2D	1.04	15.52	8.66	3.03
	Total	0.55	15.52	6.50	1.56
KF readings posterior (5mm)	Normal	5.57	6.66	6.08	0.25
	Group 2A	4.87	7.11	6.16	0.40
	Group 2B	0.88	6.99	5.93	1.11
	Group 2C	1.06	8.56	6.99	1.36
	Group 2D	1.50	13.07	8.37	2.27
	Total	0.88	13.07	6.47	1.29
KF readings posterior (7mm)	Normal	5.58	6.68	6.11	0.25
	Group 2A	5.20	6.96	6.17	0.35
	Group 2B	1.18	6.79	5.96	1.03
	Group 2C	1.40	7.77	6.73	1.18
	Group 2D	1.84	11.07	7.84	1.77
	Total	1.18	11.07	6.39	1.03
KS reading anterior (3mm)	Normal	39.76	49.29	44.80	1.91
	Group 2A	41.13	51.80	45.90	2.27
	Group 2B	43.23	51.32	47.53	1.84
	Group 2C	50.32	63.58	55.11	3.93
	Group 2D	62.00	98.28	71.88	9.31
	Total	39.76	98.28	49.95	9.75
KS reading anterior (5mm)	Normal	39.76	49.11	44.74	1.91
	Group 2A	41.09	50.65	45.69	2.08
	Group 2B	43.04	50.13	46.97	1.61
	Group 2C	49.28	60.70	53.50	3.29
	Group 2D	59.98	88.43	67.29	6.76
	Total	39.76	88.43	49.05	8.07
KS reading anterior (7mm)	Normal	39.66	48.64	44.58	1.87
	Group 2A	41.14	49.45	45.37	1.90
	Group 2B	42.76	49.70	46.30	1.58
	Group 2C	47.91	57.64	51.58	2.71
	Group 2D	56.56	77.76	62.61	5.42
	Total	39.66	77.76	48.02	6.51
KS reading posterior (3mm)	Normal	5.65	7.19	6.43	0.31
	Group 2A	6.01	7.82	6.71	0.41
	Group 2B	2.62	8.43	7.02	1.04
	Group 2C	3.03	11.21	8.71	1.53
	Group 2D	8.90	33.13	12.88	4.81
	Total	2.62	33.13	7.63	2.79
KS reading posterior (5mm)	Normal	5.66	7.22	6.44	0.31
	Group 2A	5.94	7.67	6.64	0.36
	Group 2B	6.25	7.73	6.94	0.37
	Group 2C	7.06	9.90	8.27	0.75
	Group 2D	8.93	31.08	11.61	4.31
	Total	5.66	31.08	7.40	2.30
KS reading posterior (7mm)	Normal	5.54	7.15	6.41	0.31
	Group 2A	5.88	7.43	6.56	0.31
	Group 2B	6.35	14.90	7.09	1.65
	Group 2C	6.94	17.93	8.17	2.10
	Group 2D	8.36	15.05	9.68	1.42
	Total	5.54	17.93	7.14	1.55

Continuation of Table 2

1	2	3	4	5	6
Mean readings anterior (3mm)	Normal	39.59	47.40	44.09	1.73
	Group 2A	40.48	49.62	45.03	1.96
	Group 2B	44.75	47.31	45.11	0.84
	Group 2C	44.75	44.75	44.75	0.00
	Group 2D	44.75	69.04	46.95	6.29
	Total	39.59	69.04	44.77	2.77
Mean readings anterior (5mm)	Normal	39.62	47.25	44.04	1.72
	Group 2A	40.50	48.82	44.92	1.83
	Group 2B	42.65	47.14	45.25	1.14
	Group 2C	47.51	55.25	50.69	2.45
	Group 2D	55.95	83.58	63.79	6.60
	Total	39.62	83.58	47.60	7.08
Mean readings anterior (7mm)	Normal	39.66	47.27	43.92	1.72
	Group 2A	40.46	47.90	44.67	1.69
	Group 2B	42.45	47.07	44.92	1.11
	Group 2C	46.63	53.26	49.30	2.01
	Group 2D	53.30	74.60	59.99	5.52
	Total	39.66	74.60	46.82	5.83
Mean readings posterior (3mm)	Normal	5.60	6.76	6.24	0.26
	Group 2A	5.30	7.56	6.38	0.42
	Group 2B	1.38	7.76	6.38	1.13
	Group 2C	1.69	10.04	7.88	1.50
	Group 2D	2.32	16.16	9.81	2.66
	Total	1.38	16.16	6.93	1.67
Mean readings posterior (5mm)	Normal	5.62	6.80	6.26	0.26
	Group 2A	5.65	7.38	6.39	0.34
	Group 2B	2.05	7.26	6.34	0.95
	Group 2C	2.50	9.01	7.51	1.19
	Group 2D	3.15	13.50	9.26	1.89
	Total	2.05	13.50	6.82	1.33
Mean readings posterior (7mm)	Normal	5.62	6.84	6.27	0.26
	Group 2A	5.72	7.19	6.36	0.30
	Group 2B	2.56	6.96	6.29	0.81
	Group 2C	3.05	8.34	7.19	0.96
	Group 2D	3.64	11.27	8.49	1.38
	Total	2.56	11.27	6.67	1.01
CCT	Normal	460.00	650.00	531.19	39.86
	Group 2A	438.00	574.00	496.64	31.75
	Group 2B	414.00	528.00	485.60	25.19
	Group 2C	350.00	523.00	441.16	40.53
	Group 2D	261.00	444.00	358.04	45.37
	Total	261.00	650.00	488.28	69.14
MIN CT	Normal	459.00	647.00	528.79	39.63
	Group 2A	431.00	555.00	488.08	32.77
	Group 2B	400.00	521.00	472.64	26.05
	Group 2C	338.00	513.00	427.72	43.30
	Group 2D	245.00	433.00	333.20	43.88
	Total	245.00	647.00	479.60	75.58
CV	Normal	49.70	68.40	58.16	3.71
	Group 2A	49.60	62.40	55.43	3.20
	Group 2B	49.60	61.40	55.28	2.90
	Group 2C	48.50	61.80	54.84	3.16
	Group 2D	39.00	60.00	54.07	4.00
	Total	39.00	68.40	56.53	3.87

Continuation of Table 2

1	2	3	4	5	6
ACV	Normal	89.00	266.00	179.20	35.75
	Group 2A	116.00	224.00	174.64	31.78
	Group 2B	143.00	260.00	190.92	31.35
	Group 2C	129.00	233.00	184.52	30.96
	Group 2D	133.00	255.00	195.44	33.49
	Total	89.00	266.00	182.79	34.21
ICA	Normal	24.00	59.00	44.61	7.26
	Group 2A	31.00	62.00	44.40	7.51
	Group 2B	33.00	60.00	46.60	6.58
	Group 2C	37.00	56.00	45.28	4.99
	Group 2D	37.00	61.00	48.32	6.00
	Total	24.00	62.00	45.38	6.88
ACD	Normal	2.32	4.04	3.23	0.34
	Group 2A	2.50	3.79	3.21	0.35
	Group 2B	2.84	3.84	3.41	0.29
	Group 2C	2.73	3.84	3.45	0.31
	Group 2D	3.00	4.58	3.84	0.40
	Total	2.32	4.58	3.35	0.40
Sif	Normal	-1.47	1.21	0.17	0.45
	Group 2A	-0.42	3.49	1.40	0.95
	Group 2B	2.13	8.71	4.78	1.97
	Group 2C	-2.18	12.09	4.27	4.19
	Group 2D	-6.31	18.72	4.60	6.28
	Total	-6.31	18.72	1.97	3.43
KVF	Normal	1.00	14.00	4.08	1.80
	Group 2A	4.00	16.00	9.80	3.33
	Group 2B	13.00	45.00	24.80	8.03
	Group 2C	17.00	65.00	36.16	11.97
	Group 2D	40.00	174.00	77.84	33.66
	Total	1.00	174.00	20.62	27.58
BCVf	Normal	0.00	1.17	0.20	0.20
	Group 2A	0.05	1.42	0.80	0.37
	Group 2B	1.29	3.57	2.27	0.66
	Group 2C	0.93	6.34	3.14	1.57
	Group 2D	2.45	13.20	6.71	2.78
	Total	0.00	13.20	1.72	2.45
Sib	Normal	-0.44	0.12	-0.05	0.10
	Group 2A	-0.13	1.09	0.37	0.31
	Group 2B	0.54	2.26	1.22	0.46
	Group 2C	-0.79	2.61	1.17	0.84
	Group 2D	-1.03	3.66	1.49	1.28
	Total	-1.03	3.66	0.51	0.85
KVb	Normal	7.00	28.00	13.49	3.65
	Group 2A	10.00	36.00	23.80	7.35
	Group 2B	30.00	93.00	53.72	16.97
	Group 2C	39.00	133.00	84.68	25.48
	Group 2D	84.00	249.00	161.72	45.23
	Total	7.00	249.00	47.24	53.31
BCVb	Normal	0.00	0.43	0.03	0.07
	Group 2A	0.00	2.40	0.81	0.61
	Group 2B	1.30	3.78	2.35	0.79
	Group 2C	0.52	6.12	3.05	1.44
	Group 2D	1.26	10.37	6.15	2.65
	Total	0.00	10.37	1.56	2.34

Continuation of Table 2

1	2	3	4	5	6
Rbf-f	Normal	39.54	46.74	43.78	1.69
	Group 2A	40.48	47.05	44.46	1.56
	Group 2B	42.42	47.68	44.71	1.21
	Group 2C	46.19	52.43	48.51	1.75
	Group 2D	51.72	69.71	57.94	4.72
	Total	39.54	69.71	46.34	5.15
Rbf-b	Normal	47.06	57.71	52.52	2.14
	Group 2A	48.17	58.60	53.23	1.99
	Group 2B	50.80	57.86	53.92	1.55
	Group 2C	54.53	66.23	59.77	2.91
	Group 2D	64.35	87.80	71.13	5.42
	Total	47.06	87.80	56.01	6.76

Table 3

Comparison of normal and group 2A groups with respect to different variables

Variables	Normal	Group 2A	t–value	p–value
	Mean ± SD	Mean±SD		
KF readings anterior (3mm)	43.40 ±1.68	44.18±1.9	–2.0177	0.0458*
KF readings anterior (5mm)	43.38±1.68	44.19±1.81	–2.1201	0.0360*
KF readings anterior (7mm)	43.26±1.68	44.00±1.67	–1.9770	0.0500*
KF readings posterior (3mm)	6.05±0.25	6.11±0.54	–0.7842	0.4344
KF readings posterior (5mm)	6.08±0.25	6.16±0.4	–1.2864	0.2007
KF readings posterior (7mm)	6.11±0.25	6.17±0.35	–0.9026	0.3685
KS reading anterior (3mm)	44.80±1.91	45.90±2.27	–2.4698	0.0149*
KS reading anterior (5mm)	44.74±1.91	45.69±2.08	–2.1907	0.0304*
KS reading anterior (7mm)	44.58±1.87	45.37±1.9	–1.8809	0.0624
KS reading posterior (3mm)	6.43±0.31	6.71±0.41	–3.7886	0.0002*
KS reading posterior (5mm)	6.44±0.31	6.64±0.36	–2.8159	0.0057*
KS reading posterior (7mm)	6.41±0.31	6.56±0.31	–2.0922	0.0385*
Mean readings anterior (3mm)	44.09±1.73	45.03±1.96	–2.3807	0.0188*
Mean readings anterior (5mm)	44.04±1.72	44.92±1.83	–2.2411	0.0268*
Mean readings anterior (7mm)	43.92±1.72	44.67±1.69	–1.9387	0.0548
Mean readings posterior (3mm)	6.24±0.26	6.38±0.42	–2.1745	0.0316*
Mean readings posterior (5mm)	6.26±0.26	6.39±0.34	–2.0646	0.0411*
Mean readings posterior (7mm)	6.27±0.26	6.36±0.3	–1.4471	0.1504
CCT	531.19±39.86	496.64±31.75	4.0226	0.0001*
MIN CT	528.79±39.63	488.08±32.77	4.7425	0.00001*
CV	58.16±3.71	55.43±3.2	3.3789	0.0010*
ACV	179.20±35.75	174.64±31.78	0.5825	0.5613
ICA	44.61±7.26	44.40±7.51	0.1284	0.8980
ACD	3.23±0.34	3.21±0.35	0.2647	0.7917
Sif	0.17±0.45	1.40±0.95	–9.4250	0.00001*
KVF	4.08±1.8	9.80±3.33	–11.7061	0.00001*
BCVf	0.20±0.20	0.80±0.37	–11.0027	0.00001*
Sib	–0.05±0.10	0.37±0.31	–11.4368	0.00001*
KVb	13.49±3.65	23.80±7.35	–9.9998	0.00001*
BCVb	0.03±0.07	0.81±0.61	–12.6158	0.00001*
Rbf–f	43.78±1.69	44.46±1.56	–1.8388	0.0684
Rbf–b	52.52±2.14	53.23±1.99	–1.5064	0.1345

*Note: * p<0.05*

It was found that K-steep in anterior curvature at 3mm,5mm, K- steep in posterior curvature at 3 mm, 5 mm, 7 mm, CCT, thinnest pachymetry, elevation-based indices(Bcv, best fit radius), keratometry vertex and symmetry indices(sif, sib) showed significance (p<0.05). It was found that K readings at 7 mm in the steep axis in anterior curvature (p=0.06), K reading in the flat axis at 3 mm, 5 mm, and 7 mm in posterior curvature(its p values are p=0.06, p=0.41, p=0.34) were not significant. ACV, ICA, ACD (p=0.56, p=0.89, p=0.79) RMS values (p=0.06) are not significant (Table 4).

Table 4

Comparison of normal and group 2B groups concerning different variables by unpaired t-test

Variables	Normal	Group 2B	t-value	p-value
	Mean±SD	Mean±SD		
KF readings anterior (3mm)	43.40±1.68	43.59±1.23	0.5237	0.6014
KF readings anterior (5mm)	43.38±1.68	43.67±1.07	0.8096	0.4197
KF readings anterior (7mm)	43.26±1.68	43.59±0.99	0.9401	0.3490
KF readings posterior (3mm)	6.05±0.25	5.87±1.22	1.4271	0.1561
KF readings posterior (5mm)	6.08±0.25	5.93±1.11	1.2581	0.2108
KF readings posterior (7mm)	6.11±0.25	5.96±1.03	1.3829	0.1692
KS reading anterior (3mm)	44.80±1.91	47.53±1.84	6.4151	0.00001*
KS reading anterior (5mm)	44.74±1.91	46.97±1.61	5.3990	0.00001*
KS reading anterior (7mm)	44.58±1.87	46.30±1.58	4.2368	0.00001*
KS reading posterior (3mm)	6.43±0.31	7.02±1.04	4.9208	0.00001*
KS reading posterior (5mm)	6.44±0.31	6.94±0.37	7.0037	0.00001*
KS reading posterior (7mm)	6.41±0.31	7.09±1.65	3.8851	0.0002*
Mean readings anterior (3mm)	44.09±1.73	45.11±0.84	2.8579	0.0050*
Mean readings anterior (5mm)	44.04±1.72	45.25±1.14	3.3252	0.0012*
Mean readings anterior (7mm)	43.92±1.72	44.92±1.11	2.7554	0.0068*
Mean readings posterior (3mm)	6.24±0.26	6.38±1.13	1.1529	0.2512
Mean readings posterior (5mm)	6.26±0.26	6.34±0.95	0.7887	0.4318
Mean readings posterior (7mm)	6.27±0.26	6.29±0.81	0.2009	0.8411
CCT	531.19±39.86	485.60±25.19	5.4441	0.00001*
MIN CT	528.79±39.63	472.64±26.05	6.7194	0.00001*
CV	58.16±3.71	55.28±2.90	3.6075	0.0004*
ACV	179.20±35.75	190.92±31.35	1.5004	0.1361
ICA	44.61±7.26	46.60±6.58	1.2473	0.2147
ACD	3.23±0.34	3.41±0.29	2.4011	0.0178*
Sif	0.17±0.45	4.78±1.97	21.4879	0.00001*
KVF	4.08±1.8	24.80±8.03	23.7690	0.00001*
BCVf	0.20±0.20	2.27±0.66	27.0472	0.00001*
Sib	-0.05±0.10	1.22±0.46	25.4684	0.00001*
KVb	13.49±3.65	53.72±16.97	21.9973	0.00001*
BCVb	0.03±0.07	2.35±0.79	29.2271	0.00001*
Rbf-f	43.78±1.69	44.71±1.21	2.6038	0.0104*
Rbf-b	52.52±2.14	53.92±1.55	3.0797	0.0026*

*Note: * $p<0.05$*

In this comparison, it was found that K-steep in anterior curvature at 3mm,5mm, K- steep in posterior curvature at 3 mm, 5 mm, and 7 mm, K flat in 3 mm, 5 mm, 7 mm in anterior and posterior curvature, CCT, thinnest pachymetry, ACD, elevation based indices (Bcv, best fit radius), keratometry vertex, symmetry indices (sif, sib) and aberrometry indices (RMS) showed significance ($p<0.05$). In addition, K readings at 7mm in the steep axis in anterior curvature (p 0.16), Mean reading at 3 mm, 5 mm, and 7 mm in posterior curvature (p=0.25, p=0.43, p=0.84). ACV, ICA (p=0.13, p=0.21) are not significant. Rest all the parameters are significant (Table 5).

Table 5

Comparison of normal and group 2C groups with respect to different variables.

Variables	Normal	Group 2C	t–value	p–value
	Mean±SD	Mean±SD		
1	2	3	4	5
KF readings anterior (3mm)	43.40±1.68	48.88±2.52	–13.0740	0.00001*
KF readings anterior (5mm)	43.38±1.68	48.19±2.13	–12.1180	0.00001*
KF readings anterior (7mm)	43.26±1.68	47.24±1.73	–10.5737	0.00001*
KF readings posterior (3mm)	6.05±0.25	7.17±1.52	–7.0404	0.00001*
KF readings posterior (5mm)	6.08±0.25	6.99±1.36	–6.3007	0.00001*
KF readings posterior (7mm)	6.11±0.25	6.73±1.18	–4.8864	0.00001*
KS reading anterior (3mm)	44.80±1.91	55.11±3.93	–18.8800	0.00001*
KS reading anterior (5mm)	44.74±1.91	53.50±3.29	–17.4558	0.00001*
KS reading anterior (7mm)	44.58±1.87	51.58±2.71	–15.2066	0.00001*

Continuation of Table 5

1	2	3	4	5
KS reading posterior (3 mm)	6.43±0.31	8.71±1.53	–13.9417	0.00001*
KS reading posterior (5 mm)	6.44±0.31	8.27±0.75	–18.8591	0.00001*
KS reading posterior (7 mm)	6.41±0.31	8.17±2.10	–8.0954	0.00001*
Mean readings anterior (3 mm)	44.09±1.73	44.75±0.00	–1.9114	0.0583
Mean readings anterior (5 mm)	44.04±1.72	50.69±2.45	–15.7345	0.00001*
Mean readings anterior (7 mm)	43.92±1.72	49.30±2.01	–13.5262	0.00001*
Mean readings posterior (3 mm)	6.24±0.26	7.88±1.50	–10.3934	0.00001*
Mean readings posterior (5 mm)	6.26±0.26	7.51±1.19	–9.7228	0.00001*
Mean readings posterior (7 mm)	6.27±0.26	7.19±0.96	–8.5093	0.00001*
CCT	531.19±39.86	441.16±40.53	10.0679	0.00001*
MIN CT	528.79±39.63	427.72±43.30	11.1954	0.00001*
CV	58.16±3.71	54.84±3.16	4.1094	0.0001*
ACV	179.20±35.75	184.52±30.96	–0.6824	0.4963
ICA	44.61±7.26	45.28±4.99	–0.4356	0.6639
ACD	3.23±0.34	3.45±0.31	–2.9839	0.0034*
Sif	0.17±0.45	4.27±4.19	–9.6638	0.00001*
KVF	4.08±1.80	36.16±11.97	–25.9389	0.00001*
BCVf	0.20±0.20	3.14±1.57	–18.3598	0.00001*
Sib	–0.05±0.10	1.17±0.84	–14.2086	0.00001*
KVb	13.49±3.65	84.68±25.48	–27.1653	0.00001*
BCVb	0.03±0.07	3.05±1.44	–21.2033	0.00001*
Rbf–f	43.78±1.69	48.51±1.75	–12.4190	0.00001*
Rbf–b	52.52±2.14	59.77±2.91	–14.0368	0.00001*

*Note: * $p<0.05$*

In this comparison, it was found that all the parameters except ACV and ICA (p=0.49, 0.66) were found to be significant. In addition, K readings in steep and flat axis both in anterior curvature and posterior curvature at 3 mm, 5 mm, 7 mm, CCT, ACD, keratoconus indices (sif, sib, Bcv thinnest pachymetry, keratometry vertex values) and aberrometry indices (RMS) showed significance ($p<0.05$) (Table 6).

Table 6

Comparison of normal and group 2D groups concerning different variables

Variables	Normal	Group 2D	t–value	p–value
	Mean±SD	Mean±SD		
1	2	3	4	5
KF readings anterior (3 mm)	43.40±1.68	62.88±7.88	–22.9543	0.00001*
KF readings anterior (5 mm)	43.38±1.68	60.72±6.79	–23.1066	0.00001*
KF readings anterior (7 mm)	43.26±1.68	57.63±5.76	–21.7333	0.00001*
KF readings posterior (3 mm)	6.05±0.25	8.66±3.03	–8.5738	0.00001*
KF readings posterior (5 mm)	6.08±0.25	8.37±2.27	–9.9284	0.00001*
KF readings posterior (7 mm)	6.11±0.25	7.84±1.77	–9.5321	0.00001*
KS reading anterior (3 mm)	44.80±1.91	71.88±9.31	–27.1776	0.00001*
KS reading anterior (5 mm)	44.74±1.91	67.29±6.67	–29.3108	0.00001*
KS reading anterior (7 mm)	44.58±1.87	62.61±5.42	–27.5905	0.00001*
KS reading posterior (3 mm)	6.43±0.31	12.88±4.81	–13.4734	0.00001*
KS reading posterior (5 mm)	6.44±0.31	11.61±4.31	–12.0179	0.00001*
KS reading posterior (7 mm)	6.41±0.31	9.68±1.42	–21.3411	0.00001*
Mean readings anterior (3 mm)	44.09±1.73	46.95±6.29	–4.0213	0.00001*
Mean readings anterior (5 mm)	44.04±1.72	63.79±6.6	–26.7652	0.00001*
Mean readings anterior (7 mm)	43.92±1.72	59.99±5.52	–24.9140	0.00001*
Mean readings posterior (3 mm)	6.24±0.26	9.81±2.66	–13.3332	0.00001*
Mean readings posterior (5 mm)	6.26±0.26	9.26±1.89	–15.4563	0.00001*
Mean readings posterior (7 mm)	6.27±0.26	8.49±1.38	–15.1623	0.00001*
CCT	531.19±39.86	358.04±45.3	18.8895	0.00001*
MIN CT	528.79±39.63	333.20±43.88	21.5995	0.00001*
CV	58.16±3.71	54.07±4.00	4.8497	0.00001*
ACV	179.20±35.75	195.44±33.49	–2.0563	0.0419*

Continuation of Table 6

1	2	3	4	5
ICA	44.61±7.26	48.32±6.00	–2.3585	0.0199*
ACD	3.23±0.34	3.84±0.40	–7.6238	0.00001*
Sif	0.17±0.45	4.60±6.28	–7.0629	0.00001*
KVF	4.08±1.8	77.84	–22.0557	0.00001*
BCVf	0.20±0.2	6.71±2.78	–23.4791	0.00001*
Sib	–0.05±0.1	1.49±1.28	–12.0567	0.00001*
KVb	13.49±3.65	161.72±45.23	–32.7457	0.00001*
BCVb	0.03±0.07	6.15±2.65	–23.3665	0.00001*
Rbf–f	43.78±1.69	57.94±4.72	–24.5452	0.00001*
Rbf–b	52.52±2.14	71.13±5.42	–27.1208	0.00001*

*Note: * p<0.05*

AUC was good to excellent for most of the measured parameters. In discriminating normal from keratoconus suspects (Group 2a) symmetrical indices (sif, sib), (AUROC values 0.88, 0.94) keratometry vertex (KVf, KVb), (AUROC values 0.94,0.88), BCV (AUROC values 0.92, 0.95), CCT, MinCT (AUROC 0.86, 0.92) had highest AUROC scores and excellent sensitivity & specificity followed by keratometry readings in the flat and steep axis in anterior and posterior curvatures, best-fit sphere readings, central pachymetry and thinnest pachymetry. The cut-off values derived from ROC curve analysis were 2.08,1.07 for Sif, Sib, 13.50,28.50 for Kvf, Kvb and 1.16,1.68 for Bcvf, Bcvb respectively (Tables 7–9).

Table 7

Summary statistics of Akf, Akb, RMSf/A and RMSb/A in Group 2B, Group 2C and Group 2D

Variables	Groups	Minimum	Maximum	Mean±SD
Akf	Group 2B	47.89	61.57	52.33±3.69
	Group 2C	50.45	66.38	58.24±4.30
	Group 2D	64.26	111.17	80.46±14.49
	Total	47.89	111.17	63.68±15.07
Akb	Group 2B	43.93	84.67	70.22±8.83
	Group 2C	66.16	106.65	86.65±11.31
	Group 2D	89.39	168.63	120.12±20
	Total	43.93	168.63	92.33±25.17
RMSf/A	Group 2B	0.11	0.37	0.20±0.06
	Group 2C	0.13	0.46	0.26±0.09
	Group 2D	0.29	0.97	0.51±0.18
	Total	0.11	0.97	0.32±0.18
RMSb/A	Group 2B	0.23	0.64	0.40±0.11
	Group 2C	0.33	0.78	0.53±0.13
	Group 2D	0.58	1.41	0.96±0.28
	Total	0.23	1.41	0.63±0.30

Table 8

Receiver-operating-characteristic curve analysis of parameters and normal versus Group 2a

Variables	AUC	Std. Error	95 %CI		Sensitivity	Specificity	Cut off valve
			Lower Bound	Upper Bound			
1	2	3	4	5	6	7	8
KF readings anterior (3 mm)	0.63	0.07	0.51	0.76	0.99	0.96	46.75
KF readings anterior (5 mm)	0.64	0.06	0.52	0.76	0.99	0.92	46.68
KF readings anterior (7 mm)	0.63	0.06	0.51	0.75	0.90	0.80	45.45
KF readings posterior (3 mm)	0.62	0.07	0.49	0.75	0.90	0.84	6.44
KF readings posterior (5 mm)	0.63	0.06	0.51	0.75	0.93	0.88	6.50
KF readings posterior (7 mm)	0.60	0.06	0.47	0.72	0.92	0.92	6.51
KS reading anterior (3 mm)	0.64	0.06	0.52	0.76	0.99	0.92	49.10
KS reading anterior (5 mm)	0.64	0.06	0.52	0.76	0.98	0.92	48.48
KS reading anterior (7 mm)	0.61	0.06	0.49	0.73	1	1	50.50
KS reading posterior (3 mm)	0.70	0.06	0.58	0.82	1	0.96	7.56
KS reading posterior (5 mm)	0.66	0.06	0.54	0.78	0.97	0.93	6.97
KS reading posterior (7 mm)	0.63	0.06	0.51	0.74	0.97	0.96	6.95

Continuation of Table 8

1	2	3	4	5	6	7	8
Mean readings anterior (3mm)	0.64	0.06	0.52	0.77	0.99	0.88	47.42
Mean readings anterior (5 mm)	0.64	0.06	0.52	0.76	0.95	0.84	46.63
Mean readings anterior (7 mm)	0.62	0.06	0.50	0.74	0.87	0.84	46.17
Mean readings posterior (3 mm)	0.64	0.07	0.51	0.77	0.96	0.84	6.67
Mean readings posterior (5 mm)	0.63	0.06	0.51	0.75	0.97	0.92	6.72
Mean readings posterior (7 mm)	0.59	0.06	0.47	0.71	0.87	0.88	6.63
CCT	0.86	0.05	0.78	0.96	0.74	1	496.64
MIN CT	0.92	0.03	0.88	0.99	0.80	1	488.08
CV	0.27	0.06	0.16	0.38	0.84	0.96	62.30
ACV	0.46	0.06	0.34	0.59	0.94	0.96	223.50
ICA	0.47	0.07	0.33	0.60	0.96	0.96	58.58
ACD	0.49	0.07	0.36	0.63	0.94	0.96	3.72
Sif	0.88	0.05	0.79	0.98	1	0.76	2.08
KVF	0.94	0.03	0.89	0.99	0.99	0.80	13.50
BCVf	0.92	0.03	0.85	0.99	0.99	0.84	1.16
Sib	0.94	0.03	0.88	1.01	1	0.96	1.07
KVb	0.88	0.05	0.78	0.97	1	0.68	28.50
BCVb	0.95	0.04	0.88	1.02	1	0.88	1.68
Rbf-f	0.62	0.06	0.50	0.74	0.99	0.96	46.73
Rbf-b	0.60	0.06	0.49	0.71	0.98	0.96	56.67

Table 9

Receiver-operating-characteristic curve analysis of parameters and Group 2B versus normal group

Variables	AUC	Std. Error	95 %CI		Sensitivity	Specificity	Cut off value
			Lower Bound	Upper Bound			
KF readings anterior (3 mm)	0.54	0.06	0.43	0.65	0.91	1	45.85
KF readings anterior (5 mm)	0.57	0.06	0.46	0.68	0.87	0.96	45.25
KF readings anterior (7 mm)	0.56	0.06	0.46	0.67	0.91	0.96	45.45
KF readings posterior (3 mm)	0.52	0.07	0.38	0.67	0.99	0.92	6.89
KF readings posterior (5 mm)	0.55	0.07	0.41	0.68	0.98	0.92	6.59
KF readings posterior (7 mm)	0.53	0.07	0.40	0.66	0.99	0.96	6.57
KS reading anterior (3 mm)	0.85	0.04	0.77	0.93	1	0.84	49.51
KS reading anterior (5 mm)	0.81	0.04	0.73	0.90	0.98	0.80	48.72
KS reading anterior (7 mm)	0.75	0.05	0.65	0.84	0.99	0.88	48.52
KS reading posterior (3 mm)	0.88	0.05	0.79	0.98	1	0.60	7.23
KS reading posterior (5mm)	0.85	0.04	0.77	0.94	1	0.76	7.17
KS reading posterior (7 mm)	0.82	0.04	0.73	0.90	0.97	0.80	6.95
Mean readings anterior (3 mm)	0.67	0.05	0.57	0.76	0.98	0.92	47.05
Mean readings anterior (5 mm)	0.71	0.05	0.62	0.81	0.98	0.88	46.97
Mean readings anterior (7 mm)	0.68	0.05	0.58	0.78	0.91	0.92	46.41
Mean readings posterior (3 mm)	0.73	0.07	0.60	0.86	0.98	0.72	6.72
Mean readings posterior (5 mm)	0.71	0.06	0.58	0.83	0.98	0.84	6.74
Mean readings posterior (7 mm)	0.66	0.06	0.54	0.77	0.90	0.88	6.56
CCT	1.00	0.00	1.00	1.00	0.82	0.92	485.60
MIN CT	1.00	0.00	1.00	1.00	0.86	0.96	472.64
CV	0.27	0.05	0.17	0.37	0.80	0.92	61.35
ACV	0.58	0.06	0.46	0.70	0.96	0.96	245.50
ICA	0.58	0.07	0.45	0.71	0.96	0.96	56.5
ACD	0.65	0.06	0.53	0.78	0.97	0.96	3.83
Sif	1.00	0.00	1.00	1.00	1	0.96	8.62
KVF	1.00	0.00	1.00	1.00	1	0.80	14.5
BCVf	1.00	0.00	1.00	1.00	1	0.96	3.55
Sib	1.00	0.00	1.00	1.00	1	0.52	1.20
KVb	1.00	0.00	1.00	1.00	1	0.39	29
BCVb	1.00	0.00	1.00	1.00	1	0.76	1.94
Rbf-f	0.66	0.05	0.56	0.76	0.69	0.68	44.89
Rbf-b	0.69	0.05	0.60	0.79	0.86	0.88	55.31

AUC was good to excellent for most of the measured parameters. In discriminating normal from mild keratoconus (Group 2b) symmetrical indices (sif, sib)(AUROC 1.00, 1.00), keratometry vertex (AUROC 1.00), apical keratometry (AUROC 1.00), BCV (AUROC 1.00), CCT(AUROC 1.00) and MinCT (AUROC 1.00) had highest AUROC scores and excellent Sensitivity & Specificity followed by K-steep posterior (AUROC 0.88), K-steep anterior (AUROC 0.85), best-fit sphere readings (AUROC 0.69), K-flat posterior (AUROC 0.55), K-flat anterior (AUROC 0.54). The cut-off values derived from the ROC curve were 8.62, 1.20 for Sif, Sib, 0.80, 14.50 for Kvf, Kvb and 3.55, 1.94 for BCVf, BCVb, respectively (Table 10).

Table 10

Receiver-operating-characteristic curve analysis of parameters and group 2C versus normal group

Variables	AUC	Std. Error	95 %CI		Sensitivity	Specificity	Cut off value
			Lower Bound	Upper Bound			
KF readings anterior (3mm)	0.97	0.01	0.95	1.00	0.99	0.20	46.77
KF readings anterior (5mm)	0.97	0.02	0.94	1.00	1	0.28	46.82
KF readings anterior (7 mm)	0.96	0.02	0.92	1.00	1	0.36	46.46
KF readings posterior (3 mm)	0.96	0.04	0.88	1.03	0.99	0.28	6.68
KF readings posterior (5 mm)	0.95	0.04	0.88	1.03	0.99	0.28	6.67
KF readings posterior (7 mm)	0.94	0.04	0.86	1.02	0.99	0.29	6.67
KS reading anterior (3 mm)	1.00	0.00	1.00	1.00	1	0.56	56.18
KS reading anterior (5 mm)	1.00	0.00	1.00	1.00	1	0.60	54.76
KS reading anterior (7 mm)	1.00	0.00	1.00	1.00	1	0.64	52.75
KS reading posterior (3 mm)	0.96	0.04	0.88	1.04	1	0.72	9.33
KS reading posterior (5 mm)	1.00	0.00	1.00	1.00	1	0.68	8.85
KS reading posterior (7 mm)	1.00	0.00	0.99	1.00	1	0.24	7.31
Mean readings anterior (3 mm)	0.61	0.05	0.51	0.71	0.61	1	44.76
Mean readings anterior (5 mm)	1.00	0.00	1.00	1.00	0.92	0.73	43.14
Mean readings anterior (7 mm)	1.00	0.00	0.99	1.00	1	0.96	54.28
Mean readings posterior (3 mm)	0.96	0.04	0.88	1.04	0.99	0.80	7.74
Mean readings posterior (5 mm)	0.96	0.04	0.88	1.04	1	0.68	7.82
Mean readings posterior (7 mm)	0.96	0.04	0.88	1.03	1	0.16	6.88
CCT	1.00	0.00	1.00	1.00	0.84	0.96	441.16
MIN CT	1.00	0.00	1.00	1.00	0.86	0.96	427.72
CV	0.25	0.05	0.15	0.35	0.63	0.92	59.45
ACV	0.54	0.06	0.42	0.67	0.64	0.64	196.50
ICA	0.50	0.06	0.38	0.62	0.84	0.84	50.50
ACD	0.71	0.06	0.60	0.83	0.96	0.76	3.73
Sif	0.89	0.06	0.78	1.00	1	0.32	1.32
KVF	1.00	0.00	1.00	1.00	1	0.68	42
BCVf	1.00	0.00	1.00	1.00	0.99	0.32	2.26
Sib	0.96	0.04	0.88	1.04	1	0.60	1.29
KVb	1.00	0.00	1.00	1.00	1	0.60	90
BCVb	1.00	0.00	1.00	1.00	1	0.84	4.41
Rbf-f	0.99	0.01	0.98	1.00	1	0.96	52.38
Rbf-b	0.99	0.01	0.97	1.01	1	0.28	57.72

AUC was good to excellent for most of the measured parameters. In discriminating normal from moderate keratoconus (Group 2c). K readings in the steep axis in anterior and posterior curvature (AUROC 1.00), keratometry vertex (AUROC 1.00), BCV (AUROC 1.00). Best fit sphere readings (AUROC 1.00), CCT, MinCT (AUROC 1.00, 1.00) had the highest AUROC scores with excellent Sensitivity & Specificity, followed by the rest of the symmetrical indices (Sif, Sib) (AUROC 0.89, 0.96), K readings in the flat axis in anterior and posterior curvature (AUROC 0.96) and other parameters (Table 11).

AUC was good to excellent for most of the measured parameters. In discriminating normal from severe keratoconus (Group 2d). K readings in steep & flat axis in anterior and posterior curvature (AUROC 1.00) keratometry vertex (AUROC 1.00), BCV (AUROC 1.00), Best fit sphere readings (AUROC 1.00), CCT, Min CT (AUROC 1.00, 1.00) had highest AUROC scores with excellent Sensitivity & Specificity followed by rest of the symmetrical indices (Sif, Sib), and other parameters (Fig. 1).

Table 11

Receiver-operating-characteristic curve analysis of parameters and Group 2D versus normal group

Variables	AUC	Std. Error	95 %CI		Sensitivity	Specificity	Cut off value
			Lower Bound	Upper Bound			
KF readings anterior (3 mm)	1.00	0.000	1.00	1.00	1	0.60	62.53
KF readings anterior (5 mm)	1.00	0.000	1.00	1.00	1	0.96	77.89
KF readings anterior (7 mm)	1.00	0.000	1.00	1.00	1	0.68	57.99
KF readings posterior (3 mm)	0.83	0.000	0.69	0.98	1	0.20	6.74
KF readings posterior (5 mm)	0.91	0.000	0.80	1.02	1	0.48	8.55
KF readings posterior (7 mm)	0.92	0.000	0.81	1.02	1	0.12	6.75
KS reading anterior (3 mm)	1.00	0.000	1.00	1.00	1	0.80	76.43
KS reading anterior (5 mm)	1.00	0.000	1.00	1.00	1	0.32	63.69
KS reading anterior (7 mm)	1.00	0.000	1.00	1.00	1	0.28	59.25
KS reading posterior (3mm)	1.00	0.000	1.00	1.00	1	0.56	12.09
KS reading posterior (5 mm)	1.00	0.000	1.00	1.00	1	0.28	9.98
KS reading posterior (7 mm)	1.00	0.000	1.00	1.00	1	0.36	8.96
Mean readings anterior (3 mm)	0.66	0.016	0.56	0.76	0.61	0.88	44.76
Mean readings anterior (5 mm)	1.00	0.000	1.00	1.00	1	0.20	59.20
Mean readings anterior (7 mm)	1.00	0.000	1.00	1.00	1	0.36	57.06
Mean readings posterior (3 mm)	0.91	0.000	0.81	1.02	1	0.76	11.02
Mean readings posterior (5 mm)	0.95	0.000	0.88	1.03	1	0.08	8.02
Mean readings posterior (7 mm)	0.96	0.000	0.88	1.04	1	0.48	8.53
CCT	1.00	0.000	1.00	1.00	0.88	1	358.04
MIN CT	1.00	0.000	1.00	1.00	0.88	1	333.20
CV	0.22	0.000	0.12	0.31	0.44	0.88	57.25
ACV	0.63	0.047	0.50	0.76	0.65	0.48	197.50
ICA	0.64	0.028	0.52	0.76	0.99	0.96	58.50
ACD	0.87	0.000	0.77	0.97	0.99	0.64	3.97
Sif	0.72	0.001	0.55	0.90	0.98	0.28	1.03
KVF	1.00	0.000	1.00	1.00	1	0.28	55
BCVf	1.00	0.000	1.00	1.00	1	0.68	7.79
Sib	0.84	0.000	0.70	0.98	1	0.48	1.56
KVb	1.00	0.000	1.00	1.00	0.99	0.20	120
BCVb	1.00	0.000	1.00	1.00	1	0.40	5.62
Rbf-f	1.00	0.000	1.00	1.00	1	0.64	57.70
Rbf-b	1.00	0.000	1.00	1.00	1	0.44	69.93

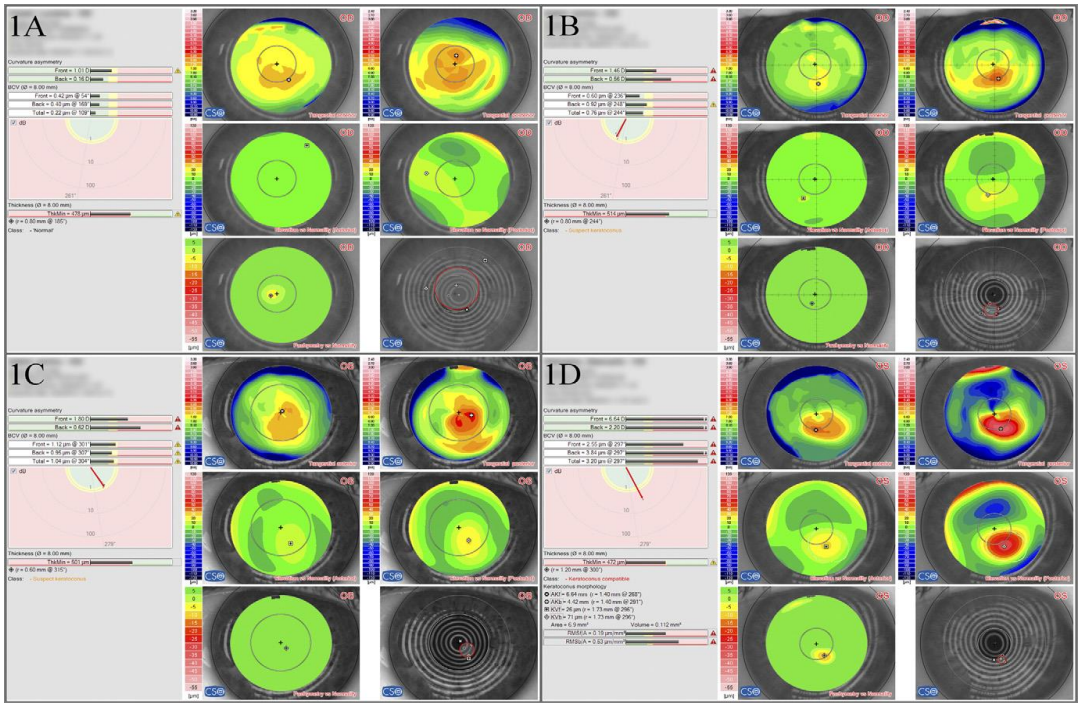

Fig. 1. Keratoconus screening display, as shown by Sirius: A – Normal case with no elevation anomalies but with anterior corneal surface asymmetry and high curvature and a low corneal thickness that may resemble keratoconus; B – Keratoconus suspect with slightly skewed astigmatism on the anterior surface and markedly asymmetric curvature, and abnormal elevation on the posterior corneal curvature; C – Keratoconus suspect with slightly asymmetric curvature and elevation of both corneal surfaces; D – Keratoconus with markedly asymmetric curvature and elevation of both corneal surfaces

4. Discussion

In our study, out of 32 parameters derived from topographic maps obtained from normal and all the groups of keratoconus, CCT and MinCT had the highest AUROC values in discriminating normal from all the groups of keratoconus. Being a well-known pathophysiological feature of KC, corneal thickness is an important marker for both detection of KC and the severity level of the disease. In this study, a cut-off value of 488 μ had 80.0 % sensitivity and 99.2 % specificity for discriminating normal eyes from keratoconus Suspects, a cut-off value of 472 μ had 86.2 % sensitivity and 96.2 % specificity for discriminating normal eyes from Mild Keratoconus, a cut-off value of 427 μ had 84.2 % sensitivity and 96.2 % specificity for discriminating normal eyes from Moderate Keratoconus, a cut-off value of 333 μ had 88.2 % sensitivity and 99.8 % specificity for discriminating normal eyes from moderate keratoconus. In previous studies, the cut-off point of MinCT ranged from 489 to 493 μ in keratoconus [7]. In all the parameters, symmetry indices (sif, sib) (AUROC 0.88, 0.94), CCT (AUROC 0.86), minimum CT (AUROC 0.92), Kvf, Kvb (AUROC 0.94, 0.88) has highest AUROC values in discriminating normal from keratoconus suspects. The AUROC values of posterior steep K readings (AUROC 0.70) are highest than the best fit radius (AUROC 0.62) in differentiating keratoconus suspects from normal eyes. The cut-off values may have been different between the studies reported by de Sanctis et al. [8] (35 mm), Uc akhan et al. [9] (26.5 mm), and Mihaltz et al. [10] (15.5 mm) because of differences in the study populations and settings of the imaging units. De Sanctis et al. [8] used 9.0 mm fit for posterior elevation, whereas Mih altz et al. [10] used the BFS as a reference body using the float option and automatic diameter setting. It may not be appropriate to compare the degree of elevation between our study and those in the literature directly. As with other imaging devices, the changes in posterior curvature measured with the dual Scheimpflug imaging system also showed significant differences between ectatic and normal eyes.

Using the Scheimpflug analyser, Smadja et al. [11] found that using the best-fit toric and aspheric reference surface for calculating elevation was better than using the BFS for discriminating between normal eyes and keratoconus eye and between normal eyes and eyes with forme fruste keratoconus. Due to variable corneal toricity and asphericity, a reference surface that is both toric and aspheric would fit better to the original corneal shape and, therefore might help enhance irregularities more sensitively. In the study by Smadja et al. [11], the importance of elevation parameters has been emphasised in different ways; however, in our study, we showed the role of the dual Scheimpflug analyser in differentiating ectatic corneas from normal corneas using curvature details. In a recent study using an automated decision-tree classifier, Smadja et al. [12] found that the algorithm selected parameters related to posterior surface asymmetry and spatial thickness distribution as the most discriminant variables. However, it is not possible to directly compare the results in these studies with those in the present study because we considered only a few parameters related to the posterior surface and corneal thickness instead of corneal volume, which showed high specificity and sensitivity in differentiating ectatic corneas from normal corneas.

Of the anterior curvature parameters using a single Scheimpflug system, Pinero et al. [13] found an AUC of 1.00 for the anterior steepest meridian and Uc akhan et al. [9] an AUC of 0.93 for the maximum anterior corneal elevation above the BFS for differentiating keratoconus eyes from normal eyes.

Along with keratoconus indices (sif, sib, bcvf, bcvb, Kvf, Kvb, Rbf-f, Rbf-b), morphological indices (akf, akb, RMS values, kvf, kvb) also shows statistical significance in discriminating Mild from Moderate and Severe Keratoconus.

Limitations of the study.

• The parameters were not correlated with other established Imaging systems like Pentacam, Orbscan.

• Wavefront analysis parameters were not included in the study, which is also one of the important parameters for differentiating normal from keratoconus and grading keratoconus.

• Sample sizes were taken less due to a shortage of time.

Prospects for further research. Further studies are needed to better identify a universal set of criteria to identify subclinical keratoconus. Technologies such as polarisation sensitivity OCT, atomic force microscopy, Brillouin light-scattering microscopy, and optical coherence elastography may be promising new modalities that can be adapted into clinical practice.

5. Conclusion

1. Many parameters were statistically significantly different between keratoconus and normal eyes compared with early keratoconus eyes ($p<.05$).

2. This study's topography and corneal aberration results are promising for detecting ectatic corneas. In our study, thickness indices - CCT, MinCT (AUC 0.86, 0.92), aberrometry indices - BCVf, BCVb (AUC 0.92, 0.95) and Keratometry in steep meridian at posterior curvature (0.88) had the highest AUC scores in differentiating normal from subclinical KC.

3. Elevation indices (Rbf-f, Rbf-b), thickness indices-CCT, MinCT, aberrometry indices and keratometry-steep in anterior & posterior curvature had the highest AUC scores (0.99) in differentiating normal from moderate and severe keratoconus.

4. The purpose of the study is to verify and analyse different parameters given by Sirius topography, especially elevation indices, aberrometry indices & thickness indices apart from keratometry indices help detect early keratoconus and also in preoperative screening for refractive surgery.

Conflict of interest

The authors declare that they have no conflict of interest concerning this study, including financial, personal, authorship, or any other, that could affect the study and its results presented in this article.

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Pasumarthi Pavani Yelamanchili, Assistant Professor, Department of Ophthalmology, Maheshwara Medical College and Hospital, Isnapur, Patancheruvu, Telangana, India, 502307

Madhuri Kurakula, Assistant Professor, Department of Ophthalmology, Malla Reddy Medical College for Women, Jeedimetla, Suraram, X Road, Quthbullapur, Hyderabad, Telangana, India, 500055

Mannam Gitanjali, Assistant Professor, Department of Ophthalmology
Osmania Medical College, Koti, Hyderabad, Telangana, India, 500095

Kotagiri Srawanthy*, Assistant Professor, Department of Ophthalmology, Malla Reddy Medical College for Women, Jeedimetla, Suraram, X Road, Quthbullapur, Hyderabad, Telangana, India, 500055

***Corresponding author:** Kotagiri Srawanthy, e-mail: drkotagirisrawanthy@gmail.com*