Evaluation of corneal topography and tomography in fellow eyes of unilateral keratoconus patients for early detection of subclinical keratoconus

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Purpose: To analyse topographic and tomographic changes in fellow eyes of unilateral keratoconus patients by comparing them with normal eyes. Methods: This five-year retrospective observational comparative case study included 15 advanced keratoconus eyes of unilateral keratoconus (KCN group), 15 normal fellow eyes of unilateral keratoconus (Fellow eye group) and 34 eyes of normal refractive surgery candidates (Normal group). Topographic and tomographic data, data from enhanced elevation maps, and keratoconus indices were measured in all study eyes using Pentacam. Receiver operating characteristic (ROC) curves were used to evaluate the area under the curve (AUC), sensitivity and specificity of each parameter and identify cut-off points in discriminating between the fellow and normal eyes. Results: Corneal thickness at the apex (CTA, \( P = 0.001 \)) and at the thinnest point (CTT, \( P < 0.001 \)), corneal volume (CV, \( P = 0.007 \)), Belin/Ambrosio Enhanced Ectasia Display (BAD) - thinnest point (Dt, \( P = 0.002 \)) and thinnest point displacement (Da, \( P = 0.002 \)) were significantly lower in the fellow group compared to eyes of normal subjects. On ROC curve analysis, the most efficient distinguishing indices between the fellow group and normal controls were BAD - overall D value (AUC = 0.859), Dt (AUC =0.827), Da (AUC = 0.789) followed by pachymetric progression index maximum (AUC = 0.741). Conclusion: BAD-D value and pachymetric progression index could be useful in detecting the earliest form of subclinical keratoconus. However, every single parameter alone is not enough to detect early changes; a combination of different data is required to distinguish subclinical keratoconus.

Key words: Belin/Ambrosio enhanced ectasia display, Pentacam, tomography, topography, unilateral keratoconus

Detecting keratoconus in its earliest stage is one of the most important aspects of avoiding iatrogenic corneal ectasia after refractive surgery. Based on a large series of cases reported in the literature, Randleman et al. proposed a score that can be used to predict the risk of ectasia (Ectasia Risk Score) to prevent the development of post-refractive surgery corneal ectasia. This score takes into account the preoperative topographic appearance, the preoperative central corneal thickness, the residual posterior wall, the patient’s age, and the planned correction. Among these various parameters, the presence of undiagnosed early keratoconus is the leading risk factor for post-refractive surgery ectasia. Studies suggest that subclinical or clinical keratoconus is found in 1-6% of myopic patients undergoing refractive surgery. Advanced keratoconus can be diagnosed with typical biomicroscopic, retinoscopic, and topographic findings. However, detection of the disease in the preclinical stage is difficult.

In literature, there were multiple terms referring to the earliest stage of keratoconus, which were frequently misused and caused confusion, including subclinical keratoconus, keratoconus suspect (KCS), and forme fruste keratoconus (FFKC). The term KCS was reserved for the cornea with some anterior topographic changes of keratoconus but without evidence of clinical keratoconus in either eye. The term FFKC was first described by Amsler as an incomplete, abortive, or unusual form of a syndrome of disease, meaning corneas that have subtle topographic characteristics but do not reach the threshold of keratoconus suspect. However, due to the ambiguity of definition and significant overlap between these terms, there are no definitive criteria to distinguish subclinical keratoconus from normal.

Pentacam is considered to be the most sensitive device for detecting the early form of keratoconus using various parameters such as corneal thickness spatial profile, the percentage of thickness increase, and Belin/Ambrosio Enhanced Ectasia Display (BAD). The purpose of this study was to evaluate the characteristics of the subtle changes in subclinical keratoconus and compare it with normal eyes. Previous research shows that true unilateral keratoconus is rare and that the normal fellow eye is believed to have subclinical keratoconus. Hence, the normal fellow eye in unilateral keratoconus may be the ideal model for the earliest form of...
subclinical keratoconus. In the present study, normal fellow eyes in unilateral keratoconus patients were considered as the mildest form of subclinical keratoconus, and topographic and tomographic parameters were compared with normal eyes using Pentacam.

Methods
This 5-year retrospective observational comparative study included patients with unilateral keratoconus diagnosed by Pentacam and candidates for refractive surgery with normal corneas. Clinical records of 49 patients (64 eyes) were retrospectively analysed at our eye institute between January 2014 and December 2018. The ethical committee approval was obtained, and the tenets of the Declaration of Helsinki were followed for all study procedures. The study was registered in Clinical Trials Registry - India (CTRI).

The study subjects were divided into 3 groups: 15 advanced keratoconus eyes of unilateral keratoconus patients (KCN group), 15 normal fellow eyes of unilateral keratoconus patients (Fellow eye group) and 34 eyes of normal refractive surgery candidates (Normal group). Eyes were diagnosed as keratoconus based on Pentacam rotating Scheimpflug camera–derived topographic/tomographic parameters and criteria used in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) study.[15] Patients with advanced keratoconus in 1 eye and a normal fellow eye were defined as unilateral keratoconus. In this study, fellow eyes in unilateral keratoconus should not only be clinically normal but also satisfy all of the following criteria determined by the Pentacam: normal index of topographic and tomographic keratoconus classification with final D value <1.6 standard deviation (SD) from the BAD. Normal control patients were myopic or myopic astigmatism candidates for refractive surgery with clinically normal corneas and topographic/tomographic characteristics within normal limits determined by the Pentacam. All normal control patients underwent uncomplicated refractive surgery, either Small incision lenticule extraction (SMILE) or Femto-laser-assisted in situ keratomileusis (LASIK) and had a 6-month follow-up without any evidence of ectatic corneal changes. In the normal group, only left eyes were used in the study analysis.

Exclusion criteria included a history of ocular surgery, history of ocular trauma, any other ocular pathology and significant corneal scarring that might potentially affect the outcomes.

All patients were asked to stop wearing soft contact lenses for at least 1 week and rigid gas-permeable contact lenses for at least 3 weeks before the examination. A complete ocular examination including slit lamp biomicroscopy, cycloplegic refraction, best corrected distance visual acuity (BCVA) using Snellen acuity chart, keratometry readings, intraocular pressure measurement and dilated fundus examination was performed.

Topographic and tomographic examinations were performed using the Pentacam rotating Scheimpflug camera (Oculus, Wetzlar, Germany). Image quality was checked, and for each eye, only one examination with a good quality factor was recorded. Various parameters were derived from topographic and tomographic maps and the BAD, as described below.

Data from topographic maps: flat keratometry (K1), steep keratometry (K2), mean keratometry (Km) for the central 3.0 mm of the cornea, maximum keratometry (Kmax), topographic astigmatism (A), asphericity for the anterior corneal surfaces (Q), keratometric asymmetry: inferior-superior asymmetry at 4 and 6 mm (4 mm I-S and 6 mm I-S), superotemporal-inferonasal asymmetry at 4 and 6 mm (4 mm ST-IN and 6 mm ST-IN), and superonasal-inferotemporal asymmetry at 4 and 6 mm (4 mm SN-JT and 6 mm SN-JT) radius ring of the cornea, corneal volume (CV) in 7 mm diameter centred on the anterior corneal apex, corneal thickness at the apex (CTA) and at the thinnest point of the cornea (CTT) with y coordinate of the thinnest local (Y).

Data from elevation maps: maximum elevations on anterior (AEmax) and posterior cornea (PEmax), minimum elevations on anterior (AEmin) and posterior cornea (PEmin), elevation differences (maximum-minimum) on anterior (AEdif) and posterior cornea (PEdif) in the central 3 mm zone.

Data from topometric maps: index of surface variance (ISV), index of vertical asymmetry (IVA), keratoconus-index (KI), centre keratoconus-index (CKI), index of height asymmetry (IHA), index of height decentration (IHD), and radii minimum (Rmin).

Data from the BAD: D values representing the front surface (Df), back surface (Db), pachymetric progression (Dp), thinnest point (Dt), thinnest point displacement (Da), and final (D), pachymetric progression indices – maximum (PImax), minimum (PImin) and average (PIavg).

Statistical analysis
Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. The normality of data was tested by the Kolmogorov-Smirnov test. Qualitative variables were compared using Pearson’s Chi-Square test/Fisher’s exact test. One way ANOVA was used to test the mean values between the 3 groups, followed by Tukey HSD Post-hoc test for multiple comparisons. The receiver operating characteristic (ROC) curve with area under the curve (AUC) was plotted for Pentacam parameters between the 3 groups. The diagnostic specificity and sensitivity of the main parameters (AUC >0.7) for distinguishing fellow eyes from normal eyes were evaluated, and cut-off points were presented. A probability value (P value) less than 0.05 was considered as significant at 95% confidence level. The statistical package for social sciences (SPSS) version 24.0 was used in the analysis.

Results
Fifteen eyes of 15 unilateral keratoconus patients (10 males and 5 females) and 34 eyes of 34 normal refractive surgery candidates were analysed (17 males and 17 females). Out of 15 unilateral keratoconus eyes, advanced keratoconus manifested in 11 left eyes and 4 right eyes, which was statistically significant (P <0.001). The ratio of male to female patients was 2:1 in the unilateral KCN group and 1:1 in the Normal group, respectively. The mean age was 26.4 ± 4.08 (range: 18-33) years in the unilateral KCN and 25.22 ± 4.24 (range: 18-35) years in the normal, which was not statistically different.

KCN vs. Fellow eye group: There were significant differences (P ≤ 0.001) between the KCN and fellow eye group in almost all measured parameters except for corneal
volume (CV), superotemporal-inferonasal asymmetry at 4 mm (4 mm ST-IN) and y coordinate of the thinnest local point (Y) [Tables 1 and 2].

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KCN vs. Normal group: There were significant differences ($P \leq 0.001$) between the KCN and normal eye group in all measured parameters [Tables 1 and 2].

Table 1: Mean pentacam parameters in KCN, fellow eye, and normal groups

| Pentacam parameters | KCN group (n=15), mean (SD) | Fellow eye group (n=15), mean (SD) | Normal group (n=34), mean (SD) |
|---------------------|-----------------------------|-----------------------------------|-----------------------------|
| K1                  | 45.8 (4.11)                 | 42.73 (0.99)                      | 42.95 (1.37)                |
| K2                  | 49.89 (5.15)                | 43.68 (1.11)                      | 44.03 (1.49)                |
| Km                  | 47.74 (4.52)                | 43.21 (1.02)                      | 43.47 (1.4)                 |
| Kmax                | 57.68 (8.1)                 | 44.39 (1.15)                      | 44.57 (1.47)                |
| A                   | 4.09 (2.02)                 | 0.95 (0.47)                       | 1.08 (0.64)                 |
| Q                   | −0.76 (0.44)                | −0.3 (0.14)                       | −0.29 (0.09)                |
| 4 mm I-S            | 12.64 (5.91)                | 0.27 (0.94)                       | 0.06 (0.69)                 |
| 6 mm I-S            | 6.45 (4.83)                 | 0.58 (1.07)                       | 0.03 (1.09)                 |
| 4 mm ST-IN          | −3.07 (5.92)                | −0.04 (0.64)                      | −0.08 (0.54)                |
| 6 mm ST-IN          | −2.69 (4.39)                | 0.28 (0.59)                       | 0.1 (0.72)                  |
| 4 mm SN-IT          | −9.12 (6.77)                | −0.35 (0.47)                      | −0.2 (0.59)                 |
| 6 mm SN-IT          | −5.41 (3.1)                 | −0.21 (2.64)                      | −0.41 (0.66)                |
| CV                  | 56.99 (2.74)                | 58.37 (3.13)                      | 61.09 (2.62)                |
| CTA                 | 467.8 (28.41)               | 515.07 (26.64)                    | 546.24 (23.99)              |
| CTT                 | 455.13 (29.26)              | 512.2 (26.79)                     | 544.12 (23.46)              |
| Y                   | −0.64 (0.47)                | −0.45 (0.18)                      | −0.3 (0.18)                 |
| AEmax               | 29.67 (16.76)               | 3.13 (0.92)                       | 2.82 (1.03)                 |
| PEmax               | 57.27 (28.14)               | 5.27 (2.89)                       | 4.12 (2.28)                 |
| AEmin               | −10.93 (7.91)               | −0.47 (1.64)                      | −0.26 (0.99)                |
| PEmin               | −17.87 (14.98)              | −1.67 (2.69)                      | −2.18 (3.5)                 |
| AEdif               | 40.6 (20.24)                | 3.6 (1.55)                        | 3.09 (1.36)                 |
| PEdiff              | 75.13 (32.07)               | 6.93 (3.28)                       | 6.29 (3.08)                 |
| ISV                 | 102.8 (47.69)               | 16.13 (2.47)                      | 15.62 (4.05)                |
| IVA                 | 1.16 (0.56)                 | 0.11 (0.04)                       | 0.11 (0.04)                 |
| KI                  | 1.28 (0.18)                 | 1.02 (0.02)                       | 1.02 (0.02)                 |
| CKI                 | 1.08 (0.07)                 | 1 (0.01)                          | 1 (0.01)                    |
| IHA                 | 32.13 (34.55)               | 5.43 (5.43)                       | 6.9 (3.23)                  |
| IHD                 | 0.15 (0.09)                 | 0.01 (0.01)                       | 0.01 (0)                    |
| Rmin                | 5.96 (0.8)                  | 7.58 (0.18)                       | 7.58 (0.26)                 |
| Plmax               | 3.94 (2.34)                 | 1.31 (0.16)                       | 1.17 (0.16)                 |
| Plmin               | 1.35 (0.66)                 | 0.73 (0.11)                       | 0.65 (0.16)                 |
| Plavg               | 2.3 (1.11)                  | 1.03 (0.13)                       | 0.93 (0.12)                 |
| Df                  | 10.92 (7.14)                | 0.21 (0.93)                       | −0.08 (1.04)                |
| Db                  | 8.01 (5.78)                 | −0.04 (0.56)                      | −0.36 (0.82)                |
| Dp                  | 9.43 (7.5)                  | 0.83 (0.87)                       | 0.16 (0.83)                 |
| Dt                  | 2.87 (1.19)                 | 0.81 (0.85)                       | −0.15 (0.65)                |
| Da                  | 3.1 (0.68)                  | 0.82 (0.52)                       | 0.13 (0.64)                 |
| D                   | 9.18 (4.06)                 | 1.18 (0.32)                       | 0.54 (0.54)                 |

SD=Standard deviation, n=Number of eyes, KCN=Keratoconus, K1=Flat keratometry, K2=Steep keratometry, Km=Mean keratometry, Kmax=Maximum keratometry, A=Topographic astigmatism, Q=Asphericity for the anterior corneal surface, 4 mm I-S=Keratometry inferior-superior asymmetry at 4 mm, 6 mm I-S=Keratometry inferior-superior asymmetry at 6 mm, 4 mm ST-IN=Superotemporal-inferonasal asymmetry at 4 mm, 6 mm ST-IN=Superotemporal-inferonasal asymmetry at 6 mm, 4 mm SN-IT=Superonasal-inferotemporal asymmetry at 4 mm, 6 mm SN-IT=Superonasal-inferotemporal asymmetry at 6 mm, CV=Corneal volume, CTA=Corneal thickness at the apex, CTT=Corneal thickness at the thinnest point, Y=Y coordinate of the thinnest local, AEmax=Maximum elevation on anterior cornea, PEmax=Maximum elevation on posterior cornea, AEmin=Minimum elevation on anterior cornea, PEmin= Minimum elevation on posterior cornea, AEdif=Elevation differences on anterior cornea, PEdiff=Elevation differences on posterior cornea, ISV=Index of surface variance, IVA=Index of vertical asymmetry, KI=Keratoconus-index, CKI=Centre keratoconus-index, IHA=Index of height asymmetry, IHD=Index of height decentration, Rmin=Radius minimum, Df=Belin/Ambrosio enhanced ectasia display value representing the front surface, Db=Back surface, Dp=Pachymetric progression, Dt=Thinnest point, Da=Thinnest point displacement, D=Overall deviation, Plmax=Pachymetric progression index maximum, Plmin=Pachymetric progression index minimum, Plavg=Pachymetric progression index average.
Table 2: Comparison of Pentacam parameters between KCN, Fellow eye and Normal groups

| Pentacam parameters | KCN vs Fellow P | KCN vs Normal P | Fellow vs Normal P |
|---------------------|----------------|----------------|-------------------|
| K1                  | 0.001          | <0.001         | 0.949             |
| K2                  | <0.001         | <0.001         | 0.912             |
| Km                  | <0.001         | <0.001         | 0.934             |
| Kmax                | <0.001         | <0.001         | 0.989             |
| A                   | <0.001         | <0.001         | 0.931             |
| Q                   | <0.001         | <0.001         | 0.999             |
| 4 mm I-S            | <0.001         | <0.001         | 0.97              |
| 6 mm I-S            | <0.001         | <0.001         | 0.756             |
| 4 mm ST-IN          | 0.15           | 0.001          | 0.999             |
| 6 mm ST-IN          | 0.001          | <0.001         | 0.962             |
| 4 mm SN-IT          | <0.001         | <0.001         | 0.988             |
| 6 mm SN-IT          | <0.001         | <0.001         | 0.947             |
| CV                  | 0.366          | <0.001         | 0.007             |
| CTA                 | <0.001         | <0.001         | 0.001             |
| CTT                 | <0.001         | <0.001         | <0.001            |
| Y                   | 0.138          | <0.001         | 0.189             |
| AEmin               | <0.001         | <0.001         | 0.992             |
| PEmax               | <0.001         | <0.001         | 0.96              |
| AEdiff              | <0.001         | <0.001         | 0.984             |
| PEDiff              | <0.001         | <0.001         | 0.99              |
| ISV                 | <0.001         | <0.001         | 0.997             |
| IVA                 | <0.001         | <0.001         | 0.999             |
| KI                  | <0.001         | <0.001         | 0.98              |
| C Kl                | <0.001         | <0.001         | 0.997             |
| IHA                 | <0.001         | <0.001         | 0.958             |
| IHD                 | <0.001         | <0.001         | 0.995             |
| Rmin                | <0.001         | <0.001         | 1                 |
| Plmax               | <0.001         | <0.001         | 0.918             |
| Pmin                | <0.001         | <0.001         | 0.697             |
| Plavg               | <0.001         | <0.001         | 0.828             |
| Df                  | <0.001         | <0.001         | 0.963             |
| Db                  | <0.001         | <0.001         | 0.93              |
| Dp                  | <0.001         | <0.001         | 0.826             |
| Dt                  | <0.001         | <0.001         | 0.002             |
| Da                  | <0.001         | <0.001         | 0.002             |
| D                   | <0.001         | <0.001         | 0.552             |

Fellow eye vs Normal group: There were significant differences between the fellow eye and normal group in 5 parameters: corneal thickness at the apex (CTA, \( P = 0.001 \)) and at the thinnest point of the cornea (CTT, \( P < 0.001 \)), corneal volume (CV, \( P = 0.007 \)), BAD - thinnest point (Dt, \( P = 0.002 \)) and thinnest point displacement (Da, \( P = 0.002 \)) [Tables 1 and 2].

Receiver operating characteristic (ROC) curve analysis

When discriminating Fellow eye group from Normal group, the D value showed the highest AUC (0.859), followed by Dt (0.827) and Da (0.789) [Table 3]. In discriminating between KCN group and Normal group, most parameters had high AUCs [Table 3].

Table 4 shows the cut-off points and sensitivity and specificity values of the main Pentacam parameters derived from ROC curve analysis used to discriminate between Fellow eye in unilateral keratoconus and Normal groups. Fig. 1 presents the graphical representation of the ROC curve of Pentacam parameters between Fellow eye and Normal groups.

### Discussion

Many studies investigated early screening and diagnosis of keratoconus using the Pentacam device in different ethnic populations. Results varied in different populations related to race, geographic location, and size of the study population. Most such studies differed from each other by the criteria used to diagnose subclinical/FFKC. To the best of our knowledge, the present study is the first and only study to identify characteristics of the subtle morphologic changes in the fellow eyes of unilateral keratoconus patients in Indian population.

In the present study, fellow eyes of unilateral keratoconus patients showed normal values with respect to not only topographic but also tomographic parameters in Pentacam. This may be explained by the fact that fellow eye in our study was defined as the earliest form, with normal elevation and pachymetric values, including the final D value in BAD.

The preponderance towards males in the population in this study is consistent with other keratoconus incidence studies. CTA, CTT, CV, BAD-Dt, and Da were significantly different in the fellow group and normal group; these results are very comparable to those of other studies. However, the fellow eye in the present study was defined as normal, not only in the anterior curvature, but also in the elevation, pachymetric, and BAD maps.

In this study, D value was the most characteristic index between the fellow and normal groups and showed the highest area under the ROC curve. The cut-off for D value to differentiate fellow eyes from normal eyes was found to be 0.835, with 93.3% sensitivity but limited specificity. On the other hand, the cut-off for D value in differentiating keratoconus from normal eyes was found to be 1.965, with a specificity of 100%. The D value is a multimetric combination parameter composed of keratometric, pachymetric, pachymetric progression, and posterior elevation parameters. Similar to this study, D value had the highest area under the ROC curve to differentiate between the fellow and normal eyes was found to be 1.155, with 93.3% sensitivity but limited specificity.

Pinero et al. reported progressively lower pachymetric readings in eyes with subclinical, early, or moderate keratoconus (\( P < 0.01 \)) and significantly lower CV in the moderate keratoconus group than in the subclinical and mild groups (\( P = 0.04 \)). A possible explanation for this finding may...
Table 3: Receiver operating characteristic curve (ROC) analysis for KCN and Fellow eye versus Normal groups

| Pentacam parameters | KCN vs Normal AUC (CI 95%) | Fellow eye vs Normal AUC (CI 95%) |
|---------------------|---------------------------|----------------------------------|
| K1                  | 0.74 (0.562-0.919)        | 0.431 (0.266-0.597)              |
| K2                  | 0.892 (0.77-1.014)        | 0.411 (0.244-0.577)              |
| Km                  | 0.833 (0.692-0.975)       | 0.427 (0.261-0.593)              |
| Kmax                | 0.981 (0.946-1.016)       | 0.45 (0.281-0.619)               |
| A                   | 0.969 (0.928-1.01)        | 0.457 (0.274-0.639)              |
| Q                   | 0.148 (−0.13-0.309)      | 0.387 (0.204-0.571)              |
| 4 mm I-S            | 1 (1)                     | 0.519 (0.334-0.703)              |
| 6 mm I-S            | 0.989 (0.969-1.01)        | 0.629 (0.46-0.799)               |
| 4 mm ST-IN          | 0.206 (0.004-0.407)       | 0.512 (0.325-0.698)              |
| 6 mm ST-IN          | 0.195 (0.018-0.372)       | 0.598 (0.432-0.764)              |
| 4 mm SN-IT          | 0.005 (−0.007-0.017)      | 0.457 (0.287-0.627)              |
| 6 mm SN-IT          | 0.025 (−0.022-0.073)      | 0.377 (0.185-0.57)               |
| CV                  | 0.138 (0.035-0.242)       | 0.249 (0.1-0.398)                |
| CTA                 | 0.008 (−0.01-0.026)       | 0.187 (0.05-0.324)               |
| CTT                 | 0 (0)                     | 0.171 (0.036-0.305)              |
| Y                   | 0.233 (0.089-0.378)       | 0.28 (0.13-0.431)                |
| AEmax               | 1 (1)                     | 0.605 (0.435-0.775)              |
| PEmax               | 1 (1)                     | 0.636 (0.452-0.821)              |
| AEmin               | 0.005 (−0.008-0.018)      | 0.485 (0.291-0.679)              |
| PEmin               | 0.122 (−0.003-0.246)      | 0.544 (0.369-0.719)              |
| AEdif               | 1 (1)                     | 0.584 (0.407-0.762)              |
| PEDif               | 1 (1)                     | 0.564 (0.382-0.745)              |
| ISV                 | 0.998 (0.992-1.004)       | 0.605 (0.435-0.775)              |
| IVA                 | 1 (1)                     | 0.508 (0.322-0.694)              |
| Kl                  | 1 (1)                     | 0.589 (0.418-0.76)               |
| CKI                 | 0.846 (0.682-1.01)        | 0.533 (0.342-0.724)              |
| IHA                 | 0.846 (0.689-1.004)       | 0.327 (0.131-0.524)              |
| IHD                 | 0.989 (0.966-1.013)       | 0.336 (0.133-0.54)               |
| Rmin                | 0.017 (−0.15-0.048)       | 0.53 (0.363-0.698)               |
| Plmax               | 0.997 (0.989-1.005)       | 0.741 (0.602-0.88)               |
| Plmin               | 0.947 (0.882-1.012)       | 0.689 (0.532-0.846)              |
| Plavg               | 0.998 (0.992-1.004)       | 0.693 (0.536-0.851)              |
| Df                  | 0.986 (0.957-1.015)       | 0.598 (0.432-0.764)              |
| Db                  | 0.988 (0.963-1.013)       | 0.648 (0.495-0.801)              |
| Dp                  | 0.998 (0.992-1.004)       | 0.695 (0.538-0.852)              |
| Dt                  | 1 (1)                     | 0.827 (0.693-0.962)              |
| Da                  | 0.998 (0.992-1.004)       | 0.789 (0.66-0.919)               |
| D                  | 1 (1)                     | 0.859 (0.756-0.961)              |

AUC=Area under the receiver operating characteristic curve; CI=Confidence interval

Table 4: Cut-off points, sensitivity, and specificity of the main Pentacam parameters derived from receiver operating characteristic curve (ROC) analysis used to discriminate between Fellow eye in unilateral keratoconus and Normal groups

| Pentacam parameters | Cut-off value | Sensitivity | Specificity |
|---------------------|---------------|-------------|-------------|
| D                   | 0.835         | 0.933       | 0.324       |
| Dt                  | 0.105         | 0.867       | 0.294       |
| Da                  | 0.515         | 0.8          | 0.353       |
| Plmax               | 1.155         | 0.933       | 0.471       |

Figure 1: Receiver operating characteristic (ROC) curve of Pentacam parameters between Fellow eye and Normal groups

be that at the early stages of keratoconus, a redistribution of CV occurs with no loss of tissue.\[11\] As discussed, we found significant differences in CCT, CTA, and CV between normal eyes and fellow eyes of unilateral keratoconus.

Uçakhan et al. evaluated Pentacam parameters in mild to moderate keratoconus, subclinical keratoconus, and normal eyes with myopic astigmatism. They defined subclinical keratoconus as the fellow eye of keratoconus with abnormal topographic features (inferior-superior asymmetry or bow-tie pattern with skewed radial axis) and found that corneal thickness distribution indices and posterior elevation data were more helpful than anterior elevation data in identifying eyes with subclinical keratoconus.\[16\] This is similar to the observations of the present study. Bae et al., on the other hand, found that keratometric asymmetry, topometric index and anterior/posterior elevation difference had a higher discriminative ability than pachymetric parameters in detecting the earliest form of subclinical keratoconus.\[18\]

Huseynli et al. evaluated scheimpflug tomography parameters in subclinical keratoconus, clinical keratoconus, and normal Caucasian eyes. They defined subclinical keratoconus as clinically normal eyes with abnormal topographic features and observed that D value, elevation parameters, and pachymetric progression indices could effectively differentiate subclinical keratoconus from normal corneas in a Caucasian population.\[23\] This is in comparison with the results of the present study.

As discussed above, our study is the first and only study to identify early topometric and tomographic changes in the fellow eyes of unilateral keratoconus patients in the Indian population, and we had included only those fellow eyes which were normal in the anterior curvature, elevation, pachymetric, and the BAD maps.
The limitation of this study was its relatively small sample size. The incidence of true unilateral keratoconus is rare, and thus, this is unlikely to skew the results of this study. Further studies with larger sample size and simultaneous evaluation of the corneal biomechanics and wave front aberrations may be more useful for early detection of subclinical keratoconus.

**Conclusion**

Our study showed that the BAD-D value and pachymetric progression index were more effective than other Pentacam parameters in detecting the earliest form of subclinical keratoconus. The present study supports findings previously reported on the usefulness of Scheimpflug imaging to assess subclinical keratoconus in different populations and confirms results indicating that any single parameter alone is not enough to detect early changes. A combination of different data is required to distinguish subclinical keratoconus.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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