·Clinical Research·

Topographic characteristics of keratoconus among a sample of Jordanian patients

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Abstract

• **AIM: To identify topographic characteristics of keratoconus in a Jordanian sample.**

• **METHODS: This study characterized 210 corneas affected with keratoconus presenting to Jordan University Hospital. Patients were diagnosed based on clinical examinations and Pentacam imaging. Eyes of males (*n* =101) were of a similar proportion to females (*n* =109). All of the 111 patients were affected bilaterally. Ages ranged between 13 and 44y with a mean age of 25.2y.**

• **RESULTS: Results revealed significant differences between males and females at the level of the flat curvature power, basement membrane thickness and size of the anterior chamber. Eyes were arranged in three groups based on severity levels: mild, moderate and severe determined by the mean curvature power (Km). Results show that the flat (K1) and steep (K2) curvature powers, corneal asphericity coefficient (QV), thinnest point, pachy apex and basement membrane thickness are significantly different among the three groups, but not the corneal and anterior chamber volumes. Morphological analyses, based on sagittal maps, show no differences in keratometric values between eyes with different sagittal patterns except for the vertical location of the pachy apex relative to the pupil center and the thinnest point. Eyes with the island front elevation map are significantly more affected than eyes with the U shape and the ridge pattern.**

• **CONCLUSION: All keratometric values measured except for corneal and anterior chamber volumes vary significantly with disease severity. The vertical pachy apex location correlates well with severity levels while the horizontal location seems to have no effect. Our study also indicates that front elevation maps may be a better predictor of the severity of keratoconus than sagittal maps.**

• **KEYWORDS:** keratoconus; morphology of keratoconus; topographic characteristics
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INTRODUCTION

Keratoconus is a progressive thinning and steepening of the cornea that has its onset at puberty. As the cornea steepens, the amount of astigmatism increases causing a distortion of the image which reduces visual acuity of affected patients [1]. Identifying keratoconus is an extensive process which is based on certain clinical signs in addition to corneal topographic values, when available. In the last decade, optical imaging systems such as Pentacam or Orbscan have made it possible for ophthalmologists to collect an extensive amount of data about the anterior segment[2]. As a result, corneal topography and pachymetry values are now playing an increasingly important role in the diagnosis of keratoconus and treatment options.

Keratoconus is a complex condition with an etiology involving both external factors, such as allergies and eye rubbing, and genetics factors [3-5]. Severity of the disease has been shown to be associated with family history and ethnic origin [6-8]. In the Middle East, consanguineous marriages are currently leading to a high prevalence of keratoconus [9]. Different optical and surgical options for Keratoconus management are available, although early treatment modalities focused on improving visual acuity, new treatment options aim at preventing the disease progression [10]. This study aims at characterizing topographic features of Jordanian patients with keratoconus in order to facilitate early diagnosis of this condition.

SUBJECTS AND METHODS

Participants Informed consents were obtained from all participants and an ethical approval was granted by the institutional review board at the Department of Ophthalmology of University of Jordan Hospital. Principles

Table 1 Gathered data and analysis by gender $\bar{x} \pm s$

Parameters	All	Males	Females
Age (a)	25.2±6.2 (13-44)	23.8±5.4	26.6±6.8
Mean curvature power, Km (D)	49.81±5.13 (40.8-70.8)	49.259±5.452	50.310±4.790
Flat curvature power, K1 (D)	47.55± 4.99 (39.0-68.5)	[1]46.9±5.22	[1]48.2±4.71
Steep curvature power, K2 (D)	52.35±5.60 (42.1-73.6)	52.05±6.11	52.62±5.10
Asphericity coefficient, QV	-0.899±0.608 (-2.53-0.71)	-0.884±0.617	-0.913±0.603
Thinnest corneal location (μm)	445.8±50.5 (297-574)	450.88±50.230	441.16±50.460
Corneal volume (mm^3)	57.32±3.49 (48.20-69.40)	57.149±3.350	57.487±3.621
Basement membrane thickness (μm)	24.40±5.18 (12.1-50.8)	[1]23.423 ±4.958	[1]25.311±5.237
Anterior chamber volume (mm^3)	199.5±36.6 (115-345)	[1]212.05±37.78	[1]187.86±31.324
Anterior chamber depth (mm)	3.470±0.366 (2.52-4.47)	[1]3.525 ±0.390	[1]3.418±0.335

Results of all eyes (n=210) and comparison of males (n=101) with females (n=209). [1]Differences are significant (P<0.05). Means±standard deviations; values in brackets represent the range.

outlined in the Declaration of Helsinki (2008) were followed. Data were collected from 99 patients consulting for keratoconus at the ophthalmology department of the University of Jordan between January 2008 and November 2011. All patients were affected with keratoconus bilaterally and did not have any surgical intervention for their keratoconus at the time of data collection. An additional 12 patients joined the study after one eye being grafted for keratoconus, thus a total of 210 eyes were included in this study.

Patients were diagnosed with keratoconus depending on the following clinical signs: scissoring of retinoscopic reflex with hard neutralization during refraction, stormal thinning, apical decentration and conical protrusion, a Feishar ring and Vogt lines (Striae). Patients wearing contact lenses removed them for at least two weeks before obtaining the optical imaging.

Procedures Corneal topographic imaging was made using the OCULUS Pentacam® HR rotating Scheimpflug camera at a time allocated between 11:00 and 12:00 a.m. The test was repeated whenever the quality specificity (Qs) indicates a poor quality until at least a moderate quality was obtained as indicated by the machine. Basement membrane thickness was obtained directly from the instrument (Pentacame) and added manually by the operator for final display. Sagittal and elevation patterns of the front part of the cornea as well as the elevation patterns of the back of the cornea were studied using colored printouts. Corneal volume and the anterior chamber volume depth were obtained at the central 10 mm. The numerical data were taken from the printouts. To study the distance from the pupil center, the data of the left eye were multiplied by-1 (adjusted for the right eye) so that positive values correspond to distance towards the temporal side and negative values towards the nasal side.

Statistical Analysis SPSS for Windows (Version 17) was used to perform statistical analysis. Descriptive analysis was conducted to calculate frequencies, percentages, means and standard deviations. Five sets of analysis were performed based on the front elevation patterns, back elevation patterns, severity levels, sagittal maps and gender. Kolmogorov-Smirnov's test were used to examine the normality of study variables; Levene's test was used to study homogeneity of variances; Kruskal-Walls' test was used to explore differences among variables; and finally post-hoc tests (Mann-Whitney) with a Bonferroni correction (P<0.0083, P<0.0167, P<0.0167, P<0.001 and P<0.05) were carried out to allocate differences between study groups (front elevation patterns, back elevation patterns, severity levels, sagittal maps and gender consecutively) while controlling for age as a covariate.

RESULTS

Keratometry Basic keratometric data for the 210 eyes are shown in Table 1. The parameters selected were those related to the morphology of the cornea including the mean curvature power (Km), flat (K1) and steep (K2) curvature powers, corneal asphericity coefficient (QV), corneal thinnest location, pachy apex, corneal volume, basement membrane thickness , anterior chamber volume and depth. Age of participants varied from 13 to 44 years old (average 25.2± 6.2). The population consisted of a similar proportion of males (n=101) and females (n=109). After adjusting for age, comparisons between values of males and females revealed significant differences in the flat curvature power (K1), the basement membrane thickness as well as the anterior chamber volume and depth (P<0.05). Males had smaller flat curvature power, thinner basement membrane, a larger anterior chamber depth and volume.

In a second series of analysis (Table 2), eyes were arranged based on Km values: less than 45 D (mild), between 45 and 52 D (moderate) or more than 52 D (severe). Comparing results of the three groups showed significant differences in the UVA, K1, K2 , QV, corneal thickness (at thinnest location and apex) and the basement membrane thickness. To summarize, results show that the more severe the keratoconus, the higher the curvature power, the thinner the cornea and the thicker the basement membrane. The corneal

Table 2 Analysis based on severity $\bar{x} \pm s$

Parameters	Mild	Moderate	Severe
UVA (decimal)	[1]0.48±0.29	[1]0.21±0.17	[1]0.15±0.12
Flat curvature power, K1 (D)	[1]42.11±1.51	[1]46.26±2.20	[1]53.54±4.63
Steep curvature power, K2 (D)	[1]45.41±3.34	[1]51.30±2.60	[1]58.71±4.60
Asphericity coefficient, QV	[1]-0.331±0.265	[1]-0.845±0.589	[1]-1.358±0.433
Thinnest corneal location (μm)	[1]493.9±40.2	[1]455.3±36.7	[1]397.2±39.7
Thickness at Pachy apex (μm)	[1]502.2±39.5	[1]470.5±37.2	[1]415.0±39.2
Corneal volume (mm^3)	57.14±3.75	57.22±3.20	57.63±3.91
Basement membrane thickness (μm)	[1]21.02±4.34	[1]24.46±4.77	[1]26.39±5.41
Anterior chamber volume (mm^3)	196.5±40.4	196.6±33.8	206.81±38.9
Anterior chamber depth (mm)	[1]3.202±0.351	[1]3.426±0.292	[1]3.723±0.358

Eyes with Km less than 45 D were considered mild (n=36), Km 45-52 D moderate (n=114), and eyes with Km values larger than 52 D severe (n=60). [1]Indicates where differences are significant (P<0.05). Means±standard deviations.

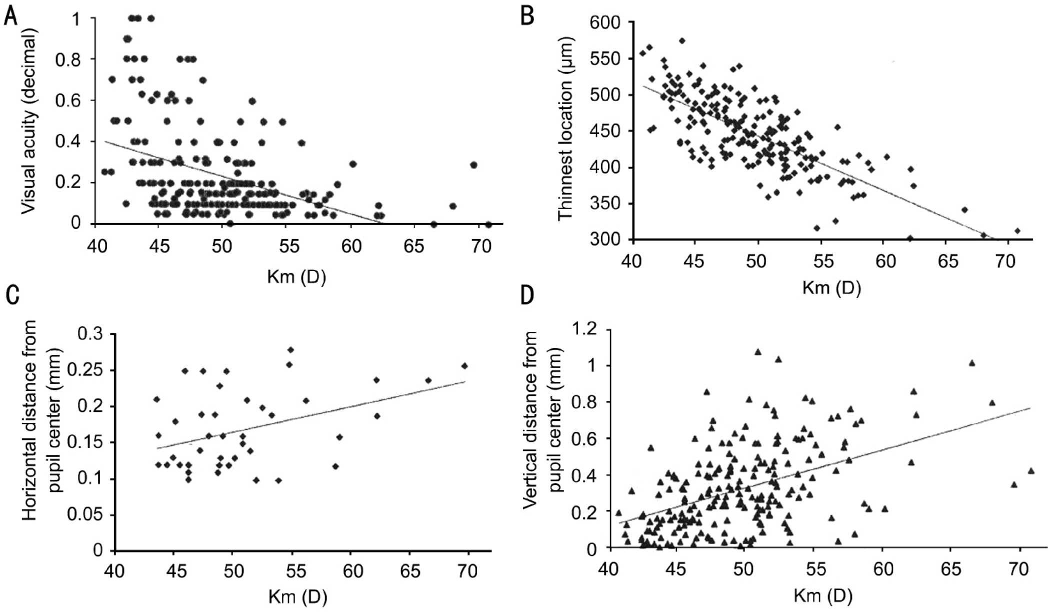

Figure 1 Correlations between Km and different parameters showed in clustered graphs.

volume, on the other hand, was not significantly different between the three groups. The depth of the anterior chamber increased significantly with the severity of the keratoconus, but not the volume.

Figure 1A illustrates the correlation between the mean curvature power (Km), which is widely used to determine the severity of keratoconus, and uncorrected visual acuity (UVA)[11]. In general, the highest the Km value (the more affected the eye), the poorest visual acuity (R^2=0.176). However, for each Km value, the UVA can vary widely. For example, of the 3 eyes with a Km value of 42.5 (considered mild keratoconus), two had a good vision (VA=0.8 and 0.9) while the third eye was severely impaired (VA=0.1). On the other hand, there is a clear correlation between Km and the thickness of the cornea at the thinnest point (Figure 1B.): the thinner the cornea, the higher the Km value (R^2=0.567). The last two cluster graphs show the effect of the position of the cone (pachy apex) relative to the centre of the pupil on the Km value. Figure 1C shows the position of the cone (pachy apex) on the vertical axis in relation to Km (R^2=0.232) for all eyes. When the values of all the samples were plotted, no correlation was found between the cone apex (pachy apex) and pupil centre on the horizontal axis, even after correction for the laterality (not illustrated). However, when considering only those eyes with a cone located 1 mm and more from the pupil centre on the temporal side, a positive correlation with the Km was seen (Figure 1D) (R^2=0.1752).

Morphology The sagittal curvature of the front of the cornea was also studied. Nine different patterns were recognized, falling into two main categories: bowtie (n = 111) and global shape (n=99). The most common sagittal configuration is the inferior steepening (n=86), followed by the asymmetric bowtie with skewed axis (n =48), the asymmetric bowtie with inferior steepening (n=39) and the symmetric bowtie (n=18). Other sagittal patterns were found less frequently: irregular (n =6), asymmetric bowtie with superior steepening (n=4), superior steepening (n=4), round (n=3), and the least common pattern is symmetrical bowtie with skewed axis (n=2) (Figures 2, 3). Comparisons between parameters available for the nine groups show no significant differences in age, visual acuity, K1, K2, Km, Qv, thinnest point and pachy apex. However, the position of the cone

Table 3 Analysis based on the front elevation pattern

Parameters	Island	U shaped	Ridge
UVA	[1]0.20±0.19	[1]0.24±0.21	[1]0.31±0.27
Mean curvature power, Km (D)	[1]52.60 ±6.77	[1]49.48±3.84	[1]46.98±4.02
Asphericity coefficient (QV)	[1]-1.060±0.710	[1]-0.947±0.507	[1]-0.543±0.605
Thinnest corneal location (μm)	[1]419.2±52.2	[1]450.3±42.7	[1]468.9±54.6
Corneal thickness at pachy apex (μm)	[1]437.7±53.8	[1]465.1±42.2	[1]478.6±49.1
Corneal volume (mm^3)	57.11±3.90	57.44±3.19	57.28±3.81

[1]Differences are significant (P<0.05). Means±standard deviations.

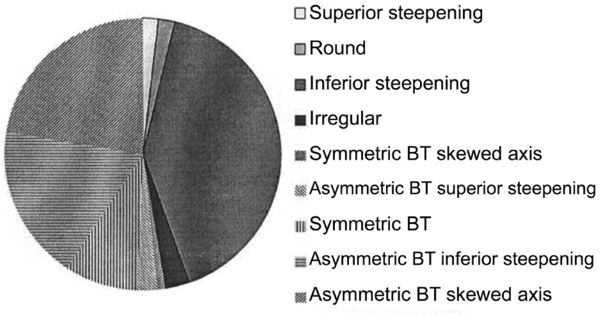

Figure 2 Distribution of the sagittal patterns.

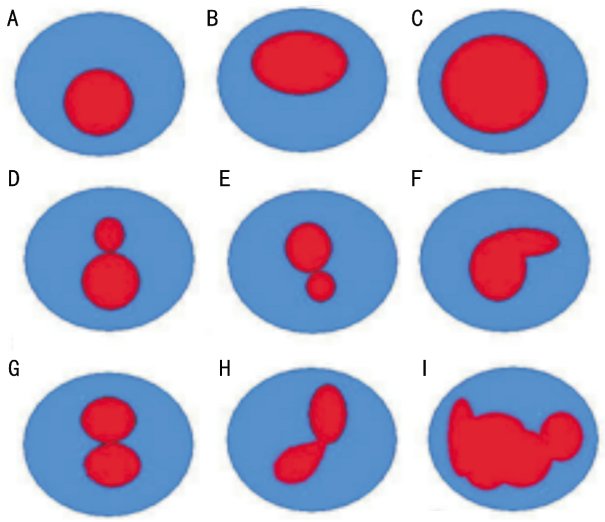

Figure 3 Front sagittal curvature maps showing the nine different sagittal patterns A: Inferior steepening; B: Superior steepening; C: Round; D:Asymmetric bowtie with inferior steepening; E: Asymmetric bowtie with superior steepening; F: Asymmetric bowtie with skewed axis; G: Symmetric bowtie; H: Symmetric bowtie with skewed axis; I: Irregular pattern.

(pachy apex) on the vertical axis (distance between pachy apex and both pupil centre and thinnest location) was significantly different between the inferior steepening, asymmetric bowtie with skewed axis, and the asymmetric bowtie with inferior steepening.

Fewer patterns were recognized on the elevation maps. In the front of the cornea, the U shape was the most common (n=116), followed by the island (n =54) and the least common was the ridge (n =40). In five eyes, the frontal elevation maps that had the shape of an hourglass or incomplete ridge were considered belonging to the ridge group. There were also fewer variations within each pattern in the elevation maps than in sagittal maps. In the front elevation, the opening of the U was towards the infero-temporal side in all but 4 eyes. Eyes with the island pattern had always their highest elevation located on the inferior half of the cornea. The ridge pattern was usually horizontal; in four eyes it was vertical. Back elevation maps showed the same patterns in similar proportions: U shape (n=98), island (n =76) and ridge (n=36). At the vast majority of the time (respectively 73.3%, 85.2% and 77.5%), the pattern of the front elevation was the same as that of the elevation pattern in the back of the cornea.

The visual acuity and keratometric values of eyes were analyzed based on the pattern of the frontal elevation map. Statistical analysis shows that eyes with the island elevation pattern are significantly more affected than those with the U shape, which are significantly more affected than the ridge elevation pattern (Table 3). Analysis of UVA, Km, QV, corneal thickness at both the thinnest point and pachy apex showed significant differences between the three groups but not for the corneal volume. Comparing the vertical (y) and horizontal (x) distances between the cone centre (pachy apex) and the centre of the pupil, revealed significant differences on the vertical axis, but not horizontally (not illustrated).

Finally, the co-occurrence in each eye of a sagittal pattern (global or bowtie) with the front elevation pattern was studied. Results show that when eyes had the island elevation pattern, the most commonly occurring sagittal map was the global shape with the inferior steepening (78%). The U shape elevation pattern, on the other hand, could exist with the global shape (43%) or the bowtie (56%). The ridge was seen more often with the bowtie pattern (80%) than global shape (20%; Figure 4).

DISCUSSION

In this study, the keratometric and morphological data of 210 eyes with keratoconus from Jordan were analyzed. All participants had both eyes affected, suggesting a lower percentage of unilateral keratoconus among Arab patients compared to other populations. According to previous studies, the incidence of unilateral keratoconus ranges from 4.5% in China to 12% in the UK[12-14].

As expected, our results show that pachymetry and corneal keratometric values vary according to the severity of

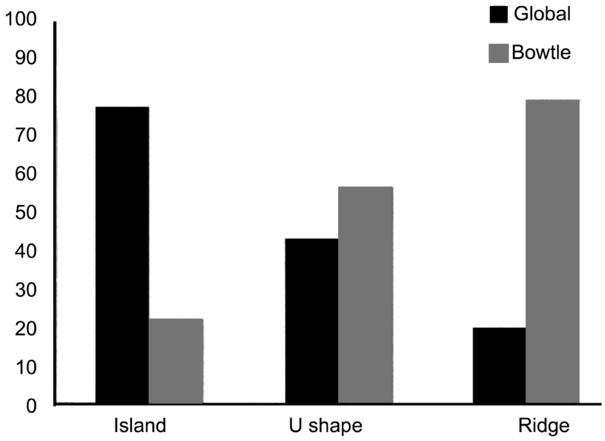

Figure 4 Co–occurrence of sagittal and front elevation patterns.

keratoconus. The thickness of the cornea has been known to decrease as the disease progresses [15]. On the other hand, the severity of the disease as determined by the Km value did not significantly have an effect on the corneal volume. This is consistent with the findings of Mannion *et al* [16], who found that the corneal volume of mild, moderate and severely affected patients with keratoconus were significantly different for the central part only (3 and 5 mm). Our results regarding the anterior chamber depth were also similar to previous findings [17]. In relation to the keratoconus severity, there was a significant difference in the anterior chamber depth but no statistically significant difference detected in the chamber volume, although the eyes affected more severely showed increased values.

In our population, thickness of the basement membrane, the anterior chamber volume and depth were significantly affected by gender. The depth of the anterior chamber was previously reported to vary with gender and the severity of keratoconus [18]. Values for the flat curvature were also significantly different between males and females, but neither the steep nor the mean curvature were.

Modern imaging systems allow an evaluation of the global morphology of corneas, in particular the sagittal and elevations maps[19]. We recognized three patterns of front and back elevation maps among corneas in our sample: island, U shape and ridge patterns. Keratometric values of each group were significantly different from the other. We were able to recognize nine different axial (sagittal) morphologies in our population, falling into either one of two nearly equal groups: global cone (48%) or bowtie (52%). Ertan *et al* [20] studied the sagittal maps of a Turkish population, finding a higher proportion of global cones (62%) compared to bowties (38%). The authors, however, did not refer to the severity of the disease, which makes it difficult to compare the two samples. Sagittal patterns are also similar to those seen by Jordan *et al* [6] in New Zealand, but in different proportions. On the other hand, elevation maps in the same population had altogether different patterns than ours; the most common anterior elevation map, the spur morphology, was not recognized in our population.

Comparison of keratometric data between the nine groups of eyes with different patterns revealed that the only significant difference was the absolute vertical distance of the cone apex (pachy apex) relative to the pupil center and to the thinnest point in the cornea. This result suggests that the distance of pachy apex from the pupil center on the vertical axis is correlated with the severity of the disease. On the horizontal axis, this was true only when the distance between the pupil center and the pachy apex was 1 mm or more on the temporal side, suggesting that cones located on the inferior and temporal side of the center of the pupil induce more severely affected. The location of the cone apex is expected to play a role in the severity of the disease[20]. For this reason, a number of studies have characterized morphological patterns of the cornea in both normal and keratoconus patients[6, 19, 21].

Although in the current study we focused primarily on assessment of corneal topography in a sample of keratoconus patients among our Jordanian population, we still believe that assessment of central cones thickness (CCT) is of a paramount importance in making the correct surgical decision. Currently CCT can be measured using different modalities such as, a novel rotating Scheimpflug camera (Pentacam; Oculus), scanning slit topography (Orbscan; Bausch & Lomb) and ultrasound pachymetry (USP). Vishal Jhanji and colleagues compared corneal thickness and corneal elevation in normal and keratoconic eyes using swept source optical coherence tomography (Casia SS-1000, Tomey, Nagoya, Japan) and slit scanning topography (Orbscan IIz, Bausch & Lomb). There results suggested that Swept source optical coherence tomography (SS-OCT) had better reproducibility coefficients and intraclass correlation coefficients as compared with Orbscan and may provide a reliable alternative for measurement of corneal parameters[22].

In conclusion, keratoconus in the population studied is a bilateral condition. Anatomical differences between males and females are reflected in the thickness of the basement membrane (thicker for women) and in the size of the anterior chamber (deeper and larger volume for men). The severity of the disease as determined by the mean curvature power of the cornea is better correlated with the corneal thickness than with the visual acuity. Similarly, the position of the cone in the vertical axis is better correlated with the severity of the disease than the position in the horizontal axis. The information on the morphology of the corneas obtained by imaging technique revealed that the elevation maps showed a better relationship with the severity of keratoconus than the sagittal maps. The maps with island shape correspond to the patients most severely affected by the disease, followed by the U shape. On the other hand, the nine sagittal patterns recognized did not have statistically significant differences in most of the keratometric values. These results may indicate that elevation maps are better indicators of the severity of keratoconus than sagittal maps.

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