Corneal topographic changes in healthy siblings of patients with keratoconus

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Abstract

AIM

To describe the involvement in relatives of keratoconus (KCN) patients with corneal topography map.

METHODS

A total of 150 siblings of 300 eyes of 75 KCN patients referred to corneal clinic were studied and experienced complete slit-lamp, refraction examinations and topographic cornea maps provided by videophotoker-atography. ANOVA, Fisher exact and Chi-square tests performed to compare of results.

RESULTS

Of 150 siblings, 56% were female and 44% were male with average age of 21 (range 15-39) years. KCN and suspect KCN diagnosed in 12.3% and 6.6% respectively. The central keratometry (CK) was 46.5±4.51 dioptr (D) in KCN and 45.66±1.52D in suspect KCN. Inferior-superior value (I-S) was 3.51±2.5D in KCN and 1.56±1.22D in suspect KCN. In KCN condition the oval pattern was 67.6% (*n*=25) and Round pattern detected 32.4% (*n*=12). In suspect KCN these patterns detected 90% and 10% respectively. Refractive errors in KCN were -7.5 to +1.25 dioptr (-1.25±1.83), in suspect

KCN 0.45 to -4.2 dioptr (-0.68±0.76) and in healthy group 2.75 to -7.5 dioptr (-0.6±1.12). Astigmatism was mild in 22.7%, moderate and sever astigmatism in 18.3% in KCN and suspect KCN

CONCLUSION

Increasing KCN condition in healthy siblings of KCN patients shows require to screening plan to early diagnose and cautionly treatment of contact lens in these individuals.
Keywords: keratoconus, topography, siblings, suspect KCN

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INTRODUCTION

Keratoconus (KCN) is a bilateral noninflammatory corneal degeneration with well-described clinical and histopathologic features and with differential diagnosis with other non-inflammatory corneal thinning disorders like keratoglobus, pellucid marginal degeneration and Terrien's marginal degeneration. It is mostly isolated disorder with approximately incidence of 1 per 2 000 in general population[1]. Despite the unknown etiology, pathogenesis or inheritance of KCN[1]-[3], Laboratory studies reports about role of degenerative enzymes, proteinase inhibitors, collagen genes and their regulatory products[1] and occur ness of KCN in about 6% of relatives of KCN patients totally provide strong indications of a major role for genes in its etiology. The early KCN condition has been able to rapid diagnosis by provided videokeratography results[1]. Similar and less severe corneal videokeratography maps of family members of patients with keratoconus, irregular corneal astigmatism with inferior corneal steepening. Central steepening, greater steepening of the cornea inferior to the apex, and substantial asymmetry in the central dioptric power are some of reported corneal changes which has been detected by computer-

assisted corneal topography in healthy family members of patients with KCN. This study was designed and carried out to provide and assess corneal topographic changes in healthy siblings of patients with KCN to find out early KCN variations in our region.

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MATERIALS AND METHODS

Patients

In a descriptive cross sectional study, with consideration of confidence level (1-α)=95% and delicacy level (d)=0.04, 300 eyes from 150 KCN patients siblings were estimitated; so, from all of 75 KCN patients who referred to cornea department of Shaheed Rahnemon hospital, we invited 2 siblings in one year (during July 2006-2007). They were couple of sister and brother or two isosexsual ones older than 15 years old. We excluded who were using soft and RGP contact lens in three pervious weeks or impossible to topography or with inflammatory corneal thinning. For all eyes, we used snellen panel to determine uncorrected VA, corrected VA, obvious corneal blur or Manson's sign. Complete slit-lamp examination and retinoscopy to discover cornea changes and scissor motion performed too. Refractive errors including myopia (was defined as a spherical equivalent less than 0.50DS)[2]hyperopia (was defined as spherical equivalent greater than + 0.50DS)[2], astigmatism (was defined d as a cylindrical error less than 0.50 diopter cylinder (DC) in any axis)[2] in with the rule (if the axis lay within 15° on either side of the horizontal meridian)[2], against the rule (if the axis lay within 15° on either side of the vertical meridian) and oblique pattern (if the axis lay between 15° to 75° or between 105° to 165°)[2] was done.

Methods

Videokeratography performed to provide the topographic maps by one experienced examiner in routine technique. The criteria were central keratometry (CK) value ≥47 dioptr and Inferior-Superior (IS) value ≥3 dioptr for each eye. We defined keratoconus was defined as central thinning of the stroma, with a Fleischer's ring, Vogt's striae, or both observed by slit-lamp examination. Patients with keratoconus suspect were defined as those with abnormal localized steepening observed in the axial power videokeratographic map, according to the 1.5D scale (Klyce/Wilson scale) for visual inspection[3].

Statistical Analysis

All included data were entered SPSS software version 11.5 (SPSS Inc., Chicago, IL). Correlation of topography indices with KCN condition evaluated with Chi-square test and presented as mean±SD. We explored correlation of visual acuity and KCN with ANOVA test, correlation of KCN with age and severity of astigmatism with fisher exact test and correlation of astigmatism pattern and topographic values with Chi-square test. We considered $P<0.05$ significant statistically.

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RESULTS

The studied population was ranged to healthy, KCN and suspect KCN groups who were with average age of 21 years (15-39 years). Among three hundred studied eyes, KCN diagnosed in 37 eyes (12.3%, male=43.2% and female=56.8%) and, suspect KCN in 20 eyes (6.6%, male=30% and female=70%). The most suspect KCN (*n*=11, 55%) and KCN (*n*=25, 67.5%) conditions were in age group of <20 years old which containing of 64% of participated siblings (Table 1). Clinical signs presented in 62.1% (*n*=23) with KCN

condition (*n*=37), but no evidence in anyone with suspect KCN condition. The mean of best-corrected visual acuity was less in KCN group (1.25) against suspect KCN and healthy groups (0.68, 0.6) significantly. Among 300 eyes, 198 eyes (66%) were myopia, 10 eyes (3.3%) were hyperopia and the reminders (*n*=92, 30.1%) didn't have any refractive error.

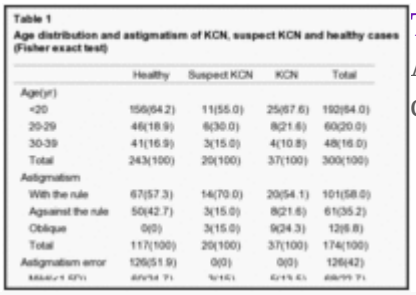

Table 1
Age distribution and astigmatism of KCN, suspect KCN and healthy cases (Fisher exact test)

	Healthy	Suspect KCN	KCN	Total
Age(yr)				
<20	156(64.2)	11(55.0)	25(67.6)	192(64.0)
20-29	46(18.9)	6(30.0)	8(21.6)	60(20.0)
30-39	41(16.9)	3(15.0)	4(10.8)	48(16.0)
Total	243(100)	20(100)	37(100)	300(100)
Astigmatism				
With the rule	67(57.3)	14(70.0)	20(54.1)	101(58.0)
Against the rule	50(42.7)	3(15.0)	8(21.6)	61(35.2)
Oblique	0(0)	3(15.0)	9(24.3)	12(6.8)
Total	117(100)	20(100)	37(100)	174(100)
Astigmatism error	126(51.9)	0(0)	0(0)	126(42)

Refractive errors in KCN group were from -7.5 to +1.25 dioptr (-1.25±1.83) where in suspect KCN were 0.45 to -4.2 dioptr (-0.68±0.76) and in healthy group were 2.75 to -7.5 dioptr (-0.6± 1.12). Astigmatism detected in all of KCN and suspect KCN cases and among 174 Astigmatic eyes, mild (≤1.5 dioptr) in 22.7%, moderate (1.5 to 3 dioptr) and sever astigmatism (≥3 dioptr) in 18.3% detected. We found sever astigmatism in 59.5% and 60% of KCN and suspect KCN cases. The mostly astigmatism in KCN group was sever (*n*=22, 59.5%) and in healthy group was mild (*n*=60, 24.7%; Table 1). Axis patterns of astigmatism were; with the rule pattern in 58%, against the rule in 53.2% and oblique pattern in 6.8%. With the rule pattern astigmatism was 54.1% in KCN and 70% in suspect KCN groups (it was the most astigmatism pattern in KCN and suspect KCN group), we didn't find oblique astigmatism in healthy group, but it was detected threefold in KCN group comparing suspect KCN group (Table 1) Topographic pattern of Round (central steepening) and Oval (asymmetrical bowtie) provided and compared. In KCN condition the oval pattern was 67.6% (*n*=25) and Round pattern detected 32.4% (*n*=12). In suspect KCN these patterns detected 90% and 10% respectively.

Topographic pattern of oval from inferior steepening in KCN and suspect KCN groups was 51.4% and 70% respectively (*P*=0.017).

The mean central keratometry (CK) was 46.5 with SD=±4.51 dioptr in KCN and 45.66 with SD ± 1.52 dioptr in suspect KCN (Table 2). The mean inferior-superior value (I-S) was 3.51±2.5 dioptr in KCN and 1.56±1.22 dioptr in suspect KCN (Table 2). Topographic indices containing central keratometry (CK) and inferior-superior value (I-S) were significantly high in suspect KCN and KCN groups respectively.

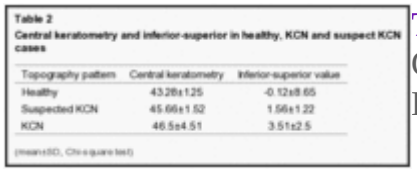
Table 2
Central keratometry and inferior-superior in healthy, KCN and suspect KCN cases

Topography pattern	Central keratometry	Inferior-superior value
Healthy	43.28±1.25	-0.12±0.65
Suspected KCN	45.66±1.52	1.56±1.22
KCN	46.5±4.51	3.51±2.5

(mean±SD, Chi-square test)

Table 2
Central keratometry and inferior-superior in healthy, KCN and suspect KCN cases

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DISCUSSION

There is a positive family history of KCN in 6% to 8% of patients and corneal topography can help to diagnosis of KCN and KCN suspects in first degree relatives of patients with KCN[4],[5]. In our study, the most affected persons were lower than 20 years old. Also in study of *et al*[6], the clinical natural history of patients was mostly in age range of 11 to 15 years old (67.1%). These can show degenerative corneal identity of KCN which mostly occurs in young patients. In study of Pobelle-Frasson C *et al*[7] about KCN in older patients, only 9 patients were older than 50 years old suggesting a relatively early age onset for KCN as a collagen disorder of corneal stroma. Although we didn't find any sexual predominance in KCN presentation similar to 1984 reported dominancy of female (15.7%) versus male (3.6%)[7]. In a similar study by Karimian F *et al*[5], KCN was diagnosed in 14% of the subjects and suspect KCN in 7.3%. Levy D *et al*[8] also reported suspect KCN in 9% of studied

subjects and we found 6.6% in suspect KCN and 12.3% in KCN condition. More presentation of suspect KCN rather than KCN in topography and no presence of obvious ophthalmologic signs for clinical diagnosis of suspect KCN condition (non of our diagnosed suspect KCN had clinical signs) suggest to provide map topographies as screening plan to discover suspect KCN conditions before developed clinical signs or switching to KCN condition. In our study, the high presentation of KCN condition can describe delay in diagnosis of conditions before KCN because of no specific symptom or clinical signs.

In a study by Salabert D *et al*[9], the inferior cornea markedly was steeper than the superior cornea (I-S - 0.86±-0.44 D). Zarnowski also showed, the inferior mid peripheral cornea was steeper than superior cornea (as quantified by an I-S value) in all of patients (71% with peripheral steeping and 29% with central steeping). Rabinowitz YS[1] observed and reported central steepening and greater steepening of the cornea inferior to the apex, in KCN patient relatives too In our study, Inferior steeping with the most oval topographic pattern and astigmatism detected in all of affected cases (*n*=19, 51.4%). In KCN condition, 32.4% had central steeping and 51.4% had inferior steeping (I-S 3.51±2.5D), it higher than suspect KCN cases). In a Prospective study showed KCN patient relatives whom appeared healthy had topography map abnormalities suggestive of early or mild KCN. These proportions of KCN condition in first-degree relatives of patients with KCN may represent the incomplete expression of a gene contributing to the development of KCN. In a Pedigree analysis an autosomal dominant inheritance pattern reported in 9 of the 11 families. These positive evidences of hereditary identity of KCN make videokeratography as a valuable step to accurate family pedigree analysis resulting to KCN diagnosis. Some studies like Kaya *et*

al[10] reported abnormal corneal topographic values despite of normal topographic pattern in first degree relatives of patients with KCN.

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