# Characteristics and associations of keratoconus patients

Mohammad Naderan*, Saeed Shoar, Farzaneh Rezagholizadeh, Masoome Zolfaghari, Morteza Naderan

*Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran*

### ARTICLE INFO

### ABSTRACT

*Purpose:* To determine the characteristics and risk factors of keratoconus (KC) patients and the possible associations between these characteristics and the severity of KC.

*Methods:* A prospective case–control study was performed in a referral eye hospital, recruiting KC patients and comparing their demographic and clinical characteristics with age and sex-matched control subjects to determine factors associated with KC. Mean keratometry (mean K) and central corneal thickness (CCT) of KC patients were recorded and compared. The severity of KC was further compared with the characteristics of KC patients.

*Results:* A total of 922 KC patients and controls were enrolled in the study. The mean age at the first presentation of KC patients was $21.03 \pm 6.17$ years. The most frequent presenting symptom was blurred vision. The multivariate analysis revealed that KC in relatives, eye rubbing, itchy eyes, and low educational level are independent predictors of KC. Severity of KC was moderate in 43.8% and severe in 41% of the patients. None of the proposed characteristics were significantly associated with mean K and CCT. KC patients with a higher frequency of eye rubbing, family history of KC and more KC members in their family had a more severe KC, while diabetic patients had a less severe KC.

*Conclusion:* This study presented an overview of a large population of KC patients in Iran, emphasizing the associated risk factors for this condition. Our findings add weights to the evidences that eye rubbing and positive family history of KC are independent risk factors for developing KC.

## 1. Introduction

Keratoconus (KC) is a bilateral chronic and asymmetric eye disease with a usual onset at puberty [1,2]. It is a condition in which the cornea steepens, protrudes, and takes on a conical shape which is progressive in the majority of cases [2,3].

KC has been linked to Down syndrome, Ehlers–Danlos syndrome, osteogenesis imperfecta and some other connective tissue disorders, though the underlying etiology has not been sufficiently described [4,5]. A common belief is that environmental factors may trigger the disease in genetically susceptible patients [6–9]. Although asymptomatic in the earlier stages, KC patients eventually present with visual impairment in the later stages, along with bio-microscopic signs of KC including marked stromal thinning, Fleischer's ring, Vogt's striae and corneal apical scarring [10,11].

The treatment of mild KC typically begins with spectacles or even soft contact lenses, whilst cases with more advanced disease usually require rigid gas-permeable (RGP) contact lenses [1,2,10–12]. RGP lenses offer superior visual correction over spectacles and soft contact lenses by providing superior masking of irregular astigmatism and correcting both cylindrical and coma aberrations [13]. Surgical keratoplasty is used for KC patients who do not tolerate RGP lenses or for severe cases with corneal scar who may not benefit from other treatment alternatives [14].

Though detecting of KC can be difficult in the early stages, awareness and consideration of the risk factors may help the diagnosis. A large number of studies have already reported the characteristics and factors associated with KC [6–9,15–22]. Very few studies, however, have compared KC patients with normal subjects [9,10]. Moreover, epidemiological and geographical studies may provide different factors associated with KC.

For this reason, we aimed to study the demographic, epidemiological and clinical characteristics of KC in our population and determine how the proposed risk factors are related to this condition and its severity.

* Corresponding author at: Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Qazvin Square, Tehran 1336616351, Iran.
Tel.: +98 21 55421006; fax: +98 21 55416134.
*E-mail address:* Moh@Naderan.com (M. Naderan).

## 2. Methods and materials

### 2.1. Study population

A prospective case–control study was conducted at Farabi Eye Hospital, Tehran, Iran, a major tertiary eye care center, recruiting 461 consecutive KC patients aged between 18 and 65 attending the corneal clinic of our hospital between January 2012 and January 2014. The KC diagnosis was made by a certified ophthalmologist based on clinical diagnostic signs of KC found by scanning-slit biomicroscopy such as conical protrusion of the cornea, Fleischer ring, corneal tilting, Vogt's striae, Munson's sign, Rizzuti's sign, corneal stromal thinning, or scissoring reflex on retinoscopy, and corneal topography mapping and anterior or posterior elevation map using the rotating Scheimpflug camera images (Pentacam, OCULUS Optikgerate GmbH, Wetzlar, Germany, software version 1.12). Patients with a history of ophthalmic surgery or trauma and any ophthalmic disease other than KC were excluded from the study. The KC and control groups were matched for age and sex. The Institutional Review Board of our hospital approved the research protocol and all the patients signed an informed consent to enroll in this study.

### 2.2. Study design

Demographic variables, clinical presentation of KC, keratometric and topographic findings, concurrent diseases, employed treatment options, and potential risk factors including eye rubbing, smoking and self-reported estimation of daily sun exposure were recorded for each KC patient. Similar data were recorded for the control group including 461 consecutive patients attending the screening clinic of our hospital for routine ophthalmological examination who were not diagnosed with or suspect for KC (astigmatism 2.00 diopters, slit-lamp or Pentacam imaging findings of KC). A person to person interview was performed for each subject and all variables of the two groups were compared to determine the predictors and risk factors of KC in this cohort of patients.

### 2.3. Outcome measures

Data were collected on demographic characteristics (age, sex and education level), keratometric (flat, steep and mean keratometry) and topographic findings (central corneal thickness (CCT)) by Pentacam, the referral method to the hospital (ophthalmologist or optometrist), presented symptoms, refractive correction modality, mean age at the first presentation of KC patients, age at the enrolment in the study, family history of KC, and medical history including atopic disorders (eczema, asthma, and allergy), cardiac diseases, diabetes, hypertension, dyslipidemia, epilepsy, anemia, and certain environmental factors (smoking, self-reported estimation of daily sun exposure, and eye rubbing) and genetic disorders (glucose 6-phosphate deficiency [G6PD] and Down syndrome). So as to assess the frequency of eye rubbing similar to a study by Shneor et al. [12], the patients were asked to estimate their eye rubbing frequency on a scale of never, rarely, sometimes, often and always. It should be noted that all KC patients and the control group were of the Caucasian ethnicity.

The severity of KC was classified according to Zadnik et al. [1] where steep keratometry reading of the worse or more advanced eyes is categorized into mild (<45 D), moderate (45–52 D) and severe KC (>52 D). Severity groups, mean keratometry (mean K) and CCT were compared with the characteristics of KC patients in order to find out the possible relationships.

**Table 1**
Demographics, keratometric and topographic findings of the study patients.

| | Keratoconus group | Control group | p value |
|---|---|---|---|
| Age (years) | 24.50 ± 5.67 | 24.85 ± 6.08 | 0.190 |
| Sex | | | 1 |
| Male | 282 (61.2%) | 282 (61.2%) | |
| Female | 179 (38.8%) | 179 (38.8%) | |
| Mean age at first presentation | 21.03 ± 6.17 | N/A | – |
| BMI (kg/m$^2$) | 24.73 ± 4.5 | 25.11 ± 4.19 | 0.179 |
| Flat K (D) | 47.4 ± 4.5 | 42.6 ± 1.5 | <0.001 |
| Steep K (D) | 51.7 ± 5.4 | 44.2 ± 1.3 | <0.001 |
| Mean K (D) | 49.4 ± 4.9 | 43.2 ± 1.3 | <0.001 |
| CCT (μm) | 455.8 ± 45.4 | 561.5 ± 25.2 | <0.001 |

BMI: body mass index; N/A: not applicable; K: keratometry; D: diopter; CCT: central corneal thickness.

### 2.4. Statistical analysis

Data were analyzed using SPSS for windows (version 20, SPSS Inc., Chicago, US). The Kolmogorov–Smirnov test was performed in order to analyze the normal distribution of the variables where variables with a p value of more than 0.05 were considered normal and were further included in the remaining statistical analysis. The results of Kolmogorov–Smirnov test revealed that all variables were normal ($p > 0.05$). Chi square or Fisher's exact test was applied for categorical variables and Student's t-test for continuous variables. A logistic regression model was also performed so as to determine the potential risk factors of KC. Variables with p values <0.05 in the univariate analysis were included in a multivariate analysis for the detection of independent predictors of KC. Data were presented as mean ± standard deviation (SD) and number (%), 95% confidence interval was also provided, and a p value <0.05 was considered statistically significant.

## 3. Results

A total of 461 KC subjects and 461 controls were included in this study. Demographic characteristics and keratometric and topographic findings of each group are summarized in Table 1. Each group consisted of 282 males (61.17%) and 179 females (38.83%). The mean age was 21.03 ± 6.17 at the first presentation of KC patients (range, 5–49 years) where male patients had a lower mean age compared to females (20.45 ± 5.87 vs. 21.95 ± 6.53 years, p = 0.01). Mean keratometric findings (flat, steep and mean keratomerty) were significantly higher while CCT was significantly lower in KC patients than in the control group ($p < 0.001$). Bilateral KC was detected in 407 patients (88.3%). In those 54 patients with unilateral disease (11.7%) no sign of forme fruste keratoconus was evident in the contralateral eye.

The visual complaints of the KC patients and the control group are presented in Table 2. Blurred vision, poor visual acuity with

**Table 2**
Visual complaints of keratoconus patients.

| Visual manifestations | Keratoconus n (%) | Control n (%) | p value |
|---|---|---|---|
| Blurred vision | 179 (38.8%) | 22 (4.8%) | <0.001 |
| Poor visual acuity with spectacles | 140 (30.4%) | 42 (9.1%) | <0.001 |
| Itchy eyes | 85 (18.4%) | 6 (1.3%) | <0.001 |
| Frequent changes of spectacles | 80 (17.4%) | 50 (10.8%) | 0.006 |
| Pain | 49 (10.6%) | 7 (1.5%) | <0.001 |
| Foreign body sensation | 29 (6.3%) | 7 (1.5%) | <0.001 |
| Diplopia | 26 (5.6%) | 4 (0.9%) | <0.001 |
| Contact lens intolerance | 21 (4.5%) | 14 (3.0%) | 0.301 |
| Tearing | 20 (4.3%) | 1 (0.2%) | <0.001 |
| Redness | 20 (4.3%) | 0 (0.0%) | <0.001 |
| Photophobia | 19 (4.1%) | 0 (0.0%) | <0.001 |