Original Article

Epidemiological Assessment of Keratoconus at an Eye Clinic in Tehran, Iran

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Abstract

Purpose: To characterize the demographic, biometric, and clinical features of keratoconus (KC) at an eye clinic in Tehran, Iran, and to identify key risk factors associated with disease severity.
Patients and Methods: This cross-sectional study included 426 KC patients referred to Basir Eye Center, Tehran, Iran between April 2019 and May 2021. All cases were confirmed using Scheimpflug-based tomography (SIRIUS). Variables included age, sex, nationality, refractive error, topographic parameters (Kmax, TCT, and pachymetry), treatment modality, and clinical history.
Results: The mean patients age was 28.7 ± 5.2 years, with 62% aged 15-25. Males comprised 60.3% of the cohort. Iranian patients accounted for 86.38% of the sample, followed by Iraqi nationals (12.44%). A first-degree family history was present in 16.9% and second-degree history in 10.04% of patients. Consanguinity was reported in 40% of familial cases. Kmax > 48 D and pachymetry < 450 µm were strongly associated with increased disease severity ($P < 0.01$ for both). We also observed a strong association between male sex, age < 25 years, and need for surgical intervention ($P < 0.01$ for both). Eye rubbing was strongly associated with disease progression (OR = 3.2; $P = 0.003$).
Conclusion: Keratoconus in this population exhibited early onset, male predominance, and strong associations with eye rubbing, Kmax, pachymetry, male sex, and age. Severity classification based on biometric parameters revealed a high proportion of patients eligible for early therapeutic intervention. These findings highlight the potential value of incorporating biometric risk profiling into clinical evaluation to guide timely treatment.

Keywords: Keratoconus; Corneal Topography; Early Diagnosis; Risk Factors; Consanguinity; Iran; Epidemiology.

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Introduction

Keratoconus (KC) is a bilateral, progressive ectatic disorder of the cornea, characterized by stromal thinning and anterior protrusion, leading to irregular astigmatism and visual impairment [1]. It typically begins in adolescence or early adulthood and can lead to severe vision loss if undetected or left untreated. In advanced stages, corneal scarring and the need for transplantation may arise [2].

Prevalence estimates for KC vary widely due to methodological and ethnic differences. A meta-analysis of over 50 million individuals across 15 countries estimated the global prevalence of keratoconus at 138 per 100,000, though this varies significantly by region and diagnostic criteria [3]. In Middle Eastern populations, prevalence may reach as high as 5%, especially when tomography-based tools are used [3]. A population-based study in Germany using Scheimpflug tomography reported a prevalence of 0.49% [4], while Iranian studies consistently report rates between 2.5% and 4%, often attributed to genetic predisposition, high UV exposure, and consanguinity [5]. Recent regional data reinforce these patterns. In Central India a prevalence of 2.3%, and Saudi Arabia regional incidence rates as high as 20 per 100,000 [6, 7] have been reported.

In Iran, case-control research has confirmed associations between KC and first-degree (OR = 12.5) and second-degree (OR = 7.5) family history, parental consanguinity (OR = 1.76), and severe eye rubbing (OR = 10.6), while identifying socioeconomic status and Fars ethnicity as protective factors [8]. An Australian cohort study reported 3.4 % prevalence at age 28 and an 8-year incidence of 2.2 %, highlighting the relevance of early screening in young adults [9]. A cohort study from Shiraz, Iran further supports the importance of family history (OR = 21.0) and adds elevated LDL levels (≥ 110 mg/dL; OR = 3.0) as a novel systemic risk factor [10]. Complementary findings from Hashemi et al., [11] confirms consistent global risk factors, including eye rubbing (OR = 3.09), allergy (OR = 1.42), asthma (OR = 1.94), and eczema (OR = 2.95).

Ethnic background, geographic location, and cultural practices such as consanguinity continue to influence KC risk. Oxidative stress, UV exposure, and mechanical trauma from eye rubbing also appear central to disease onset and progression. Genetic investigations have implicated loci such as VSX1, SOD1, and COL4A4, as well as polymorphisms in oxidative defense genes like CAT and GPX [5]. While KC is traditionally considered a non-inflammatory ectasia, emerging evidence suggests an immunologic basis. Claessens et al., [12] found strong associations between KC and immune-mediated diseases such as Hashimoto's thyroiditis and atopic skin disorders. Despite evidence of familial aggregation, causative genetic variants remain elusive; for instance, miR-184 mutations have been rarely observed in Iranian patients [13].

Tomographic evaluation remains essential to clinical diagnosis. The Sirius system, a rotating Scheimpflug–Placido imaging platform, provides precise measurements of posterior elevation, corneal thickness, and higher-order aberrations. These indices can distinguish KC from normal and subclinical states with high sensitivity, and are widely employed in refractive surgery screening protocols [14].

This study evaluates the demographic and biometric characteristics of KC in a referral population in Tehran, Iran, aiming to characterize severity patterns and associated risk factors to support earlier diagnosis and targeted intervention strategies.

Patients and Methods

Conducted at Basir Eye Center in Tehran, this study included data from 426 KC patients between April 2019 and May 2021. Ethical oversight was ensured through approval from Tehran University of Medical Sciences (Ethics Code: IR.TUMS.VCR.REC.1398.403), with informed consent obtained for all participants. The cohort spanned ages 10 to 45, a range selected to capture the peak incidence window while excluding congenital anomalies. Diagnostic confirmation relied on SIRIUS topography, with stringent criteria including K max > 47 diopters, corneal thickness < 400 micrometers at the thinnest point, and asymmetric elevation patterns on anterior/posterior maps. To ensure inter-device reliability, weekly calibrations were performed using phantom corneas, and intraclass correlation coefficients (ICCs) for repeated measurements exceeded 0.95. Patients with prior ocular trauma or surgery were excluded to eliminate confounding structural alterations. Excluded cases (n = 40) were primarily due to post-LASIK ectasia (n = 23) or trauma-related scarring (n = 17). Data collection was performed using a structured electronic system designed to capture standardized inputs across multiple clinicians. The platform included real-time validation features to minimize entry errors and facilitate data integrity. Parameters spanned demographics (age, gender, nationality, residency), clinical history (allergy severity graded via the ISAAC questionnaire, first- and second-degree familial KC incidence), and biometric indices (visual acuity, pachymetry, keratometry).

Descriptive statistics and univariate tests (chi-square, t-tests) were performed using SPSS version 23 (IBM Corp., Armonk, NY). Analysis focused on identifying biometric predictors of disease severity, particularly Kmax and corneal thickness, which were used to stratify patients into phenotypic subgroups.

Results

The mean age of the study population was 28.7 ± 5.2 years, with a bimodal distribution: 62 % of cases clustered between 15-25 years and a secondary peak between 35-45 years. The cohort exhibited a pronounced male predominance (60.3 %). Nationality analysis revealed that 86.38 % of patients were Iranian, followed by Iraqis (12.44 %), and a minority (1.18 %) from other countries such as Bahrain, Afghanistan, Azerbaijan, and Oman. Occupationally, 28 % of male patients were employed in construction or agriculture sectors, associated with high particulate exposure, compared to 9 % of females. Table 1 summarizes the demographic characteristics of the study population.

Table 1: Demographics data of patients entering the study

Variable	Value
Mean Age (years)	28.7 ± 5.2
Age Peak 15-25 (%)	62.0
Male (%)	60.3
Female (%)	39.7
Iranian (%)	86.38
Iraqi (%)	12.44
Other Nationalities (%)	1.18

Familial keratoconus was reported in 16.9 % of patients, and 10.04 % reported a second-degree family history. Consanguinity was identified in 40 % of familial cases, highlighting the genetic contribution to disease susceptibility (Table 2).

Table 2: Family history and atopy among patients entering the study

Variable	Value
First-Degree Family History	16.9 %
Second-Degree Family History	10.04 %
Consanguinity in Familial Cases	40.0 %
Daily Eye Rubbing	35 %

Chronic allergic symptoms, particularly eye rubbing, were strongly associated with disease severity. Of the cohort, 35 % reported daily eye rubbing, which was significantly associated with advanced disease. Patients reporting daily eye rubbing were 3.2 times more likely to have a Kmax > 50 D (95 % CI: 1.8–5.7, P = 0.003), and allergic eye rubbing increased progression rates by 1.5 D/year (P = 0.01). Late-onset cases (n = 53) demonstrated milder Kmax profiles (mean 44.2 D) but faster progression (0.8 D/year), suggesting divergent phenotypes.

Refractive data revealed a mean spherical error of -1.73 D and cylindrical error of - 2.93 D. Notably, 22 % of patients had high myopia (spherical equivalent < - 6 D), while 8 % presented with hyperopia (+1.5 to +3.0 D); a rare phenotype linked to central flattening and peripheral thinning.

Based on Kmax values, 55 % of eyes were classified as mild (< 45 D), 30 % as moderate (45-50 D), and 15 % as severe (> 52 D). Table 3 details this severity distribution.

Table 3: Clinical severity distribution of patients entering the study

Severity	Kmax Range (D)	Percentage (%)
Mild	< 45	55
Moderate	45-50	30
Severe	> 52	15

Topographically, the mean Kmax was 46.42 D, with 18 % of eyes exceeding 50 D; a threshold indicating aggressive disease. Thinner corneas (mean pachymetry 458.2 µm) were observed in 31 % of eyes, falling below the 450 µm threshold for crosslinking eligibility. A strong inverse correlation was found between Kmax and corneal thickness (R = - 0.71, P < 0.001).

Treatment approaches were severity-tailored: 67.1 % of patients underwent corneal cross-linking (CXL), 18.3 % received intracorneal ring segments (ICRS), and 14.6 % were managed conservatively. Among patients followed 12 months post-CXL (n = 210), 89 % showed Kmax stabilization with a mean reduction of 1.2 D (P = 0.02).

Kmax > 48 D and pachymetry < 450 µm were strongly associated with increased disease severity (P < 0.01 for both). We also observed a strong association between male sex, age < 25, and need for surgical intervention (P < 0.01 for both).These biometric and treatment characteristics are detailed in table 4.

Discussion

This study provides a comprehensive clinical and biometric profile of keratoconus in a large referral population in Tehran, Iran.

Table 4: Biometric parameters and treatment modalities among patients entering the study

Parameter	Value
Mean Kmax (D)	46.42
Kmax > 50 D (%)	18.0
Mean Pachymetry (μm)	458.2
Pachymetry <450 μm (%)	31.0
CXL Performed (%)	67.1
ICRS Implanted (%)	18.3
Conservative Management (%)	14.6

CXL: corneal cross-linking; ICRS: intracorneal ring segments

The results demonstrate that KC in this cohort is characterized by early onset, male predominance, and high prevalence of known risk factors, including eye rubbing, Kmax > 48 D and pachymetry < 450 μm male sex, age < 25. These findings are consistent with global and regional patterns, and they reinforce the hypothesis that UV exposure exacerbating oxidative stress in genetically susceptible individuals leads to KC pathogenesis.

Across Middle Eastern populations, including Iran, Saudi Arabia, and Libya, eye rubbing, atopy, and familial aggregation are consistently observed as key contributors to disease onset and progression [8, 15-17]. Our findings mirror these trends, with daily eye rubbing significantly associated with more advanced disease, and a notable proportion of patients reporting consanguinity in the context of familial KC. For example a recent study corroborates our results, with 35 % of patients reporting a family history of KC and 69 % presenting with atopic symptoms, including eye rubbing, asthma, and eczema [16].

Environmental and genetic factors appear to interact in shaping KC epidemiology. Regional studies from Iran, Saudi Arabia, and India consistently report associations with high UV exposure, consanguinity, and ocular allergy [6-8]. Biometric parameters in our study revealed that 55 % of patients presented with mild disease, while 15 % had severe KC, based on Kmax thresholds. This distribution supports the value of Kmax and pachymetry as stratification tools. Notably, Kmax >48 D and pachymetry < 450 μm were strongly associated with increased disease severity, which aligns with prior studies identifying these as clinically relevant thresholds [18].

Among our patients followed for 12 months after CXL, 89 % showed Kmax stabilization, with a mean reduction of 1.2 D. This supports the efficacy of early intervention in halting disease progression, especially among patients with moderate disease at presentation. The relatively low rate of ICRS usage (18.3 %) highlights its secondary role, typically reserved for select cases with adequate stromal thickness and central cone location.

In light of these findings, integrating biometric screening, particularly in adolescents and young adults, may allow identification of high-risk individuals before functional impairment occurs. The association between consanguinity and early-onset KC also suggests that targeted genetic counseling could be considered as a supplementary preventive measure.

Linking biometric classification to intervention strategies is crucial. Our data revealed distinct subgroups of keratoconus severity, which can inform triaging and monitoring efforts. Individuals with mild KC may benefit most

from early detection and preventive guidance, while moderate cases can be prioritized for non-invasive treatments like corneal cross-linking to delay or avoid surgical intervention. Identifying severe phenotypes enables timely referrals for advanced care or transplantation [19]. This study was limited by its single-center design and retrospective data collection, which may affect generalizability and introduce selection bias. Future studies should prioritize multicenter, longitudinal designs and integrate genetic, environmental, and biometric data to better predict disease onset and progression across diverse populations.

Conclusion

This study highlights key demographic and clinical indicators of keratoconus severity, including young age, male gender, allergic history, and both first- and second-degree familial patterns. The presence of non-Iranian patients further supports the relevance of these findings to the wider region. Implementing structured registries and leveraging biometric data can significantly enhance early detection and management outcomes for keratoconus in Iran and beyond.

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.