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Research Article

The Prevalence of Keratoconus among Saudi Adults in Riyadh, Saudi Arabia; A Cross Sectional Study

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Abstract

Purpose: To determine the prevalence and associated risk factors for keratoconus (KC) in the Saudi population.

Methods: Cross-sectional study enrolled Saudi subjects between the ages of 20 - 40 who randomly participated at a mall in Riyadh, Saudi Arabia in December 2018. Volunteers were excluded if they had corneal or ocular pathology other than KC, a history of ocular surgery or trauma and contact lenses wear within 7 days of data collection. All subjects underwent bilateral corneal topography and auto-refraction. Keratoconus was defined and staged based on the Amsler-Krumeich criteria by two cornea specialists. Statistical analysis was performed to determine an association of KC with age, gender, and geographic location. A P-value less than 0.05 was considered statistically significant.

Results: A total of 400 individuals (768 eyes) with a mean age of 29 ± 5.8 years were included. More than half of the volunteers were females 260 (65%). Forty-six individuals had keratoconus indicating a prevalence of 9.89%. KC was significantly associated with a positive family history of the disease ($P < 0.0001$). The highest distribution of KC was in the central region (55.6%) followed by the southern region (24.4%).

Conclusion: The prevalence of keratoconus in Saudi Arabia was higher than other parts of the world. This may be associated with a combination of genetic and environmental factors and improved diagnostic methods. This study highlights the need for public health outreach programs to include screening and early intervention to manage visual disability due to keratoconus.

Keywords: *Keratoconus (KC); Corneal Collagen Cross-Linking (CXL); PKP*

Introduction

Keratoconus (KC) is one of the major corneal diseases that affect young adults causing significant visual morbidity. The etiology of keratoconus is multifactorial, consisting of genetic and environmental factors [1]. Keratoconus has also been documented in siblings [2]. A history of allergy and chronic eye rubbing is also associated with keratoconus, supporting the contribution of environmental factors. The onset of the disease is usually in the second or third decade of life but can also present in late adulthood [2-4]. Besides, Chronic irritation of the cornea by the use of apical-bearing contact lenses is an environmental factor that can lead to corneal apical scarring over time [3]. Early identification and treatment are imperative for limiting disease progression and the need for surgery. Patients with keratoconus

can be treated conservatively or surgically [2-4]. Leung., *et al*. described a comparison of the cost-effectiveness of Corneal Collagen Cross-Linking (CXL) compared to conventional penetrating keratoplasty (PKP) in the management of KC. They found a difference in costs where CXL is cost-effective compared with conventional management with PKP in the treatment of KC [1,2,5].

Keratoconus represents a particularly significant healthcare burden in Saudi Arabia and is the leading indication for corneal transplantation [6]. The prevalence of KC varies significantly based on the geographical region. For instance, the prevalence of keratoconus is higher in Asian and Middle Eastern countries compared to Europe and the US. In Russia, Finland, US and Denmark the prevalence is 0.0002%, 0.03%, 0.054% and 0.086%, respectively [7-10]. In central India, the prevalence of keratoconus is 2.3% [11]. In the Middle East, a similar prevalence of 2.34% and 3.3% has been reported [12]. The limited and variable data on the local prevalence of keratoconus necessitates a novel cross-sectional study on the adult population that accurately determines the true prevalence of keratoconus in Saudi Arabia. Establishing the exact prevalence will result in a better understanding of the causes and risk factors of this disease and aid in developing strategies to diagnose and treat the disease in the early stages.

Methods

This cross-sectional study was approved by the Institutional Review Board of King Abdullah International Medical Research Center (KAIMRC) in Riyadh, Saudi Arabia. The study enrolled 400 healthy Saudi subjects between the ages of 20 - 40 years who were invited to join a screening campaign at a shopping mall in the center of Riyadh city from December 2018 until January 2019. The sample size was chosen based on the calculation of the population of Saudi adults between the ages of 20 - 40 years in Riyadh which were 1,656,711 according to the latest estimation by the General Authority of Statistics (GASTAT) of 2017 and with a confidence interval of 95% and a margin of error of 5% a minimum of 385 participants was needed [13]. Volunteers were asked about their demographic data (age, gender, region), contact lens use, family history of KC, and ocular pathology or surgery. Exclusion criteria were age younger than 20 years or older than 40 years, corneal or ocular pathology other than keratoconus, a history of eye surgery or trauma and contact lenses wear within 7 days of data collection. After initial evaluation individuals underwent auto-keratometry and auto-refraction (KR-800; Topcon Corp; Tokyo, Japan).

Measurements of refractive error were based on spherical equivalent for myopia, hyperopia, and astigmatism. Subsequently, an anterior segment examination and Scheimpflug tomography and pachymetry (Pentacam; Oculus Optikgeräte GmbH, Wetzlar, Germany) were performed.

Individuals with abnormal tomography were instructed to follow up with their ophthalmologists. Later, two cornea consultants (TA and MT) reviewed the autorefraction and corneal topographies to determine individuals with keratoconus. These patients were then classified according to Amsler-Krumeich criteria as Stage 1 (Eccentric steepening, Myopia and astigmatism < 5 D, or mean central K readings < 48 D), Stage 2 (Myopia and astigmatism from 5.00 to 8.00 D, mean central K readings < 53.00 D, Corneal thickness > 400 microns and absence of scarring), Stage 3 (Myopia and astigmatism from 8.00 to 10.00 D, Mean central K readings > 53.00 D, Corneal thickness 300 to 400 micron and absence of scarring) and Stage 4 (refraction not measurable, mean central K readings > 55.00 D, central corneal scarring, corneal thickness < 200µ).

A data extraction sheet was developed by the authors and validated by KAIMRC to gather the patient variables needed. All the collected data were inserted in a Microsoft Excel sheet (Microsoft Excel 2013, Microsoft® Windows, USA) and the analysis was carried out using Paired T-test and Chi-square test for P-value. A P-value less than 0.05 was considered statistically significant. Data were expressed as means with standard deviations or as frequencies and percentages.

Results

A total of 400 healthy participants (768 eyes) were included in this study. Excluded eyes were due to contact lens wear unilaterally, corneal procedures, and/or pathology in one eye. The mean age of the study sample was 29 ± 5.8 years (range, 20 - 40 years). The majority of volunteers were females 260 (65%) and from the central region 225 (56.3%). Table 1 presents the demographics and clinical characteristics of the participants.

Demographics and clinical characteristics	Description
Eye	
Right eye	385 (50.1%)
Left eye	383 (49.9%)
Gender	
Male	140 (35%)
Female	260 (65%)
Age	
Range	20 - 40
Mean ± SD	29 ± 5.8
Age	
20 - 25	130 (32.5%)
26 - 30	109 (27.3%)
31 - 35	97 (24.3%)
36 - 40	64 (16%)
Origin	
Central	225 (56.3%)
Southern	77 (19.3%)
Northern	37 (9.3%)
Western	8 (2%)
Eastern	53 (13.3%)
CCT	
Range	433 - 650
Mean ± SD	543.6 ± 35.7

Table 1: *Demographics and clinical characteristics of the participants. SD denotes standard deviation; CCT denotes central corneal thickness.*

Keratoconus was identified in 46 (9.89%) individuals (keratoconus group). For the keratoconus group, the mean flat K was 44.61 ± 2.04 D, steep K was 47.83 ± 3.07 D and corneal astigmatism was 2.17 ± 1.93 D.

There were 51 females (69.0%) within the keratoconus group and 23 males (31.1%) Using chi-square test (P = 0.307). Therefore, no significant difference was observed between males and females in terms of keratoconus.

The highest distribution of keratoconus was from the central region (55.6%) followed by the southern, eastern, and northern region accounted for 24.4%, 17.8% and 2.2%, respectively. There was no statistically significant association between the distribution of KC and local regions (P = 0.042).

The most prevalent stage of keratoconus was stage 1 (47%); where eccentric steepening (superior-inferior disparity > 1.40) has been found in 72% of the volunteers; while 27% of the KC cases had mean central K < 48 D, followed by stage 2 (37%), stage 4 (13%), and stage 3 (3%). More than half of the participants with stage 1 keratoconus were from the central region (56%). While most of the participants with stage 4 were from the southern region (67%) followed by the eastern region (34%). Nevertheless, the association between the regions and stages was not statistically significant (P = 0.139).

There was a greater number of keratoconus patients with a positive family history of keratoconus (24.4%) compared to patients without keratoconus who had a positive family history (3.3%). The association between family history and keratoconus is statistically significant (P < 0.0001).

Discussion

The current study determined the prevalence of keratoconus in the Saudi population. Countries with a higher prevalence of keratoconus have a greater social and financial burden in managing this disease. Due to the small number of studies on the prevalence or incidence of keratoconus in Saudi Arabia, there is insufficient data to accurately identify the population at risk or allocate resources appropriately, Furthermore, the data from previous local studies are variable. The reported prevalence of keratoconus is 4.79% in Saudi children and adolescents between 6 and 21 years [14]. Another study from Taif Area in Saudi Arabia described the prevalence of KC among patients seeking refractive laser surgery to be as high as 8.59% [15]. Additionally, incidences have been reported from Asir province; a southern region of Saudi Arabia by Alamri., *et al*. to be 18.5% [17]. However, all previous studies were hospital-based and were performed on patients with a refractive complaint and/or seeking refractive correction [14-16]. In our study, the prevalence of KC was 9.89% collected randomly from public gathering based on Scheimpflug corneal tomography and Amsler-Krumeich criteria. Compared to population-based local studies, the prevalence of the current study was found to be the highest reported to date.

KC reported prevalence varied broadly depending upon the geographical location, diagnostic criteria, and the cohort of patients selected. Internationally, a 48-year study of keratoconus in Minnesota reported the overall incidence and prevalence of keratoconus to be 0.002%. and 0.05%, respectively. Yet, this study relied solely on the examiner's description of retinoscopic reflexes as well as irregular keratometry mires [9]. The low prevalence from the previous study may be attributed to the under-detection of early-stage keratoconus that is only detected by modern corneal topography. Corneal topography facilitates the detection of early changes associated with keratoconus (forme fruste). The use of modern corneal topographers similar to our study may increase the diagnostic sensitivity and explain the higher prevalence of keratoconus reported in recent studies [18] (Table 2).

Author	Year of Publication	Location	Age (Years)	Sample Size	Source	Prevalence
Jonas JB [11]	2009	Maharashtra, India	30 and Older	4711	Population	2.3%
Waked' N [18]	2011	Lebanon	22-24	92	Medical Student Population	3.3%
Mohd-Ali [26]	2012	Lumpur, Malaysia	5-80	13000	Hospital Patients	1.2%
Liang Xu [27]	2012	Beijing, China	50-93	3468	Population	0.9 ± 0.2%
Hashemi H [28]	2013	Tehran, Iran	40- 64	6311	Hospital Patients	1.02%
Jorge E [29]	2014	Monterrey, México	10-20	500	Hospital Patients	1.8%
Shehadeh M [30]	2015	Nablus, Palestine	17- 27	1234	Tertiary Student Population	1.5%
Godefrooje DA [23]	2017	Utrecht, Netherlands	10-40	4.4 Million	Health Insurance Database.	0.26%
Al-Amri [16]	2018	Abha, Saudi Arabia	18-52	2931	Refractive surgery Patients	18.7%
Hashemi H [31]	2018	Tehran, Iran	1 and Older	2667	Rural Population	4%
Current Study	2018	Riyadh, Saudi Arabia	20-40	400	Population	9.8%

Table 2: *Epidemiology of keratoconus worldwide.*

As keratoconus is a multifactorial disease, there may be several different reasons for the relatively high prevalence in Saudi Arabia. Different genetic factors have been associated with keratoconus that is supported by twin studies [19,20]. The southern region of Saudi Arabia has the second-highest prevalence and the most severe cases of keratoconus (66.7% of stage 4 patients). In the current study, family history was the only factor that had a statistically significant correlation with keratoconus. Consanguinity, which is quite common in Saudi Arabia, might increase the risk of the genetic contribution to disease development [19].

A meta-analysis of keratoconus risk factors showed that eye rubbing particularly when rubbing is performed with the knuckles, allergy, asthma, eczema, sleep position, night-time work, and screen time were the most imperative risk factors for keratoconus [21,22].

The hot dry weather for most of the year with frequent dusty days in Saudi Arabia may lead to eye rubbing which has been described as a risk factor that increases the risk of developing keratoconus [4]. Further studies are necessary to investigate the various risk factors for the high prevalence of keratoconus in the Saudi population.

The high prevalence of Keratoconus in our study indicates the importance of having a local screening program that detects the disease earlier, preventing vision loss and corneal transplants at later stages. Keratoconus can dramatically affect patient quality of life and negatively impact some critical milestones in the development of young age groups such as education since most of the patients are young adults who are still in schools or universities [23]. In our study, the majority (82.3%) of patients with keratoconus had stages 1 and 2 diseases. Early detection and treatment by using glasses, soft or rigid contact lenses, and cross-linking would be expected to reduce the burden and overall healthcare costs and provide more favorable outcomes. The lifetime cost of keratoconus treatment is significant to the patients and can have a major impact on governmental healthcare expenses. The greatest factor that contributes to the higher cost is a corneal transplant [5,24]. The difference in lifetime health outcomes (ICER) per Quality-Adjusted Life Year (QALY) of Can$9090/QALY descends below the range of Can$20 000 to Can$100 000/QALY and below US$50 000/QALY which is a threshold used to determine the cost-effectiveness of health interventions in Canada and the United States. Early detection and treatment by corneal cross-linking drastically improve vision-related quality of life and results in better outcomes before the progression of corneal changes that necessitate corneal transplant [5,9,24]. Further studies to determine the cost-effectiveness of a keratoconus screening program in this region with such high prevalence, with appropriate treatment with cross-linking as well as visual rehabilitation, are indicated.

Several factors could have influenced the findings of this study. The participants in our study were randomly invited to participate in a non-clinical gathering to minimize selection bias, but those with visual complaints may have been more likely to participate, possibly increasing the observed incidence of disease. The location and method of recruiting participants also allow the possibility that these results may not apply to other populations that differ in terms of ethnicity, age, and socioeconomic status.

Moreover, factors that could have artificially decreased the observed incidence include exclusion of participants with other ocular conditions or previous surgery, exclusion of contact lens wearers, and utilization of well-validated but potentially less sensitive diagnostic criteria (Amsler-Kreimich). Newer diagnostic criteria utilizing posterior elevation, pachymetric progression indices, epithelial thickness mapping, and other variables may have included participants without overt anterior topographical findings [25]. These alternative criteria may diagnose KC at earlier stages, but to find a disease that requires intervention, and for purposes of comparing epidemiologic findings to previous studies, we elected to use the Amsler-Krumeich criteria.

Conclusion

To conclude, the prevalence of keratoconus in Saudi Arabia was much higher than reported in other parts of the world. This may be related to a combination of genetic and environmental factors, as well as improved diagnostic methods. Positive family history was a significant predictor of keratoconus. Keratoconus is a significant burden on the public health of the region; the results of this study highlight the need for public health outreach programs to include aggressive screening and early intervention to manage visual disability due to keratoconus.

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