

Original Article

Keratoconus among patients seeking refractive surgery in Qassim, Saudi Arabia: A hospital record analysis

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ABSTRACT

Objectives: Keratoconus is a progressive ocular disease that may lead to severe visual loss. Screening patients seeking laser vision correction (LVC) might help in its early diagnosis, management, and prevention. The purpose of the study was to determine the prevalence of keratoconus among patients seeking refractive surgery in Qassim, Saudi Arabia.

Methods: Retrospective analysis of 1500 consecutive patients, 970 males and 530 females, who underwent routine refractive surgery work-up from January 2022 to December 2022 at a referral Ophthalmology clinic in Qassim. The mean age of subjects was 28.1 ± 7.3 (range 16-54) years. The diagnosis of keratoconus was based on corneal tomography with Pentacam HR.

Results: The overall prevalence rate of keratoconus was found to be 9.7% (145/1500) (95% confidence interval [CI] 8.2-11.2%), comprising manifest and subclinical keratoconus, which was 8.5% (128/1500) (95% CI 7.1-10.0%) and 1.2% (17/1500) (95% CI 0.6-1.7%), respectively. Keratoconus was found to be higher in males (11.0%) than in females (7.2%) ($P = 0.016$). The subgroup of patients with high astigmatism (≥ 2 D in either eye) had a much higher prevalence of keratoconus (31.2%) than the subgroup with ≤ 2 D (1.40%).

Conclusion: The prevalence of keratoconus in LVC patients of a clinic in Qassim is 9.7%. Our findings will serve as a reference for refractive surgeons while screening patients for LVC. Multi-center studies are warranted in Qassim to validate our findings. Wider screening programs in the general population may help determine the prevalence of keratoconus in the general population.

Keywords: Keratoconus, Manifest and subclinical keratoconus, Prevalence, Saudi Arabia

INTRODUCTION

Keratoconus is a progressive ocular disease characterized by corneal steepening, irregular stromal thinning, and decreased visual acuity.^[1,2] There is considerable variability in the worldwide prevalence of keratoconus. Population-based studies reported the prevalence of keratoconus as 0.05% in USA,^[3] 0.06% in UK,^[4] 0.09% in Denmark,^[5] 0.19% in Norway,^[6] and 0.9% in China.^[7] A review of literature from the Middle East reported a relatively high prevalence of keratoconus, ranging from 1.5% to 3.3%.^[8-12]

The literature reports that the prevalence of keratoconus among patients seeking laser refractive surgery/laser vision correction (LVC) is higher in some regions of Saudi Arabia and lower in

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others. For instance, studies from different regions of Saudi Arabia (Taif, Jazan, and Asir) reported keratoconus prevalence of 18-40% among patients seeking LVC.^[13-15] Due to variations in environmental factors and genetic predisposition among the population living in different regions of Saudi Arabia, it is important to find the prevalence of keratoconus in other regions as well. Information on the prevalence of keratoconus in the clinic's region is valuable for the surgeon evaluating patients for LVC. Surgeons in the high keratoconus prevalence regions should be extra cautious when assessing corneal tomography during pre-operative work-up. This is likely to decrease the risk of post-operative corneal ectasia.

To the best of the author's knowledge, the prevalence of keratoconus in Qassim has not been reported previously. In the present study, the purpose was to find the prevalence of keratoconus among patients seeking refractive surgery/LVC in Qassim, Saudi Arabia.

MATERIALS AND METHODS

Study design and subjects

This retrospective, cross-sectional study included 1500 consecutive patients who underwent keratoconus screening between January 2022 and December 2022 as a part of a routine pre-operative work-up before undergoing refractive surgery/LVC at a referral Ophthalmology clinic in Qassim, Saudi Arabia. Patients with incomplete medical records, pre-existing ocular disease other than keratoconus, and a history of refractive or corneal surgery were excluded. The study adhered to the tenets of the Declaration of Helsinki and was approved by the Committee of Health Research Ethics at Qassim University.

Data collection

The patient's demographic history, such as age, sex, and eye laterality was recorded. Keratoconus was diagnosed using corneal tomography with Pentacam HR (Oculus, GmbH, Wetzlar, Germany) using the Belin-Ambrosio enhanced ectasia display (BAD). BAD is a comprehensive refractive surgical screening tool to evaluate elevation data (anterior and posterior), pachymetry data, and keratometry. The final D value is based on regression analysis and maximizes accuracy in detecting normal and keratoconus corneas. In the Pentacam display system, each parameter is color-coded and is classified as normal if the value is <1.6 standard deviation (SD) from the population mean (white); subclinical keratoconus if ≥ 1.6 SD and <2.6 SD (yellow); abnormal (manifest keratoconus) if ≥ 2.6 SD (red).^[16-19]

Keratoconus prevalence was determined by the assessment of both eyes. Patients were classified as (a) manifest keratoconus

if at least one eye had manifest keratoconus and (b) subclinical keratoconus if there is subclinical keratoconus in both eyes or in one eye with normal topography in the fellow eye.

Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) Statistics version 27.0 (IBM SPSS Statistics for Windows, version 27.0, Armonk, NY: IBM Corp). Descriptive for continuous data included means and standard deviation. Frequency and prevalence data were presented as counts and percentages. The main outcome of the study was the prevalence of keratoconus within the study subjects. Chi-squared tests were used to compare the prevalence of keratoconus between males and females or between subjects with pre-operative astigmatism ≥ 2 D versus ≤ 2 D. A $P < 0.05$ was considered significant.

RESULTS

A total of 1500 consecutive patients were included in the present study. Of these, 64.7% ($n = 970$) were males, and 35.3% ($n = 530$) were females. The mean age of the subjects at the time of refractive surgery work-up was 28.1 ± 7.3 (range: 16-54) years. The mean age of males was 27.9 ± 7.4 (range: 16-50) years and of females was 28.3 ± 7.2 (range: 16-54) years. The mean age of patients with keratoconus was 29.2 ± 6.9 years and those without keratoconus were 27.9 ± 7.3 years ($P = 0.049$).

The overall prevalence of keratoconus was 9.7% (145/1500) (95% confidence interval [CI] 8.2-11.2%). Of the overall keratoconus prevalence, the prevalence of manifest and subclinical keratoconus was found to be 8.5% (128/1500) (95% CI 7.1-10.0%) and 1.2% (17/1500) (95% CI 0.-1.7%), respectively [Figure 1].

Keratoconus prevalence was assessed among males and females. Overall, keratoconus was diagnosed in 11.0% ($n = 107$) males and 7.2% ($n = 38$) females, representing

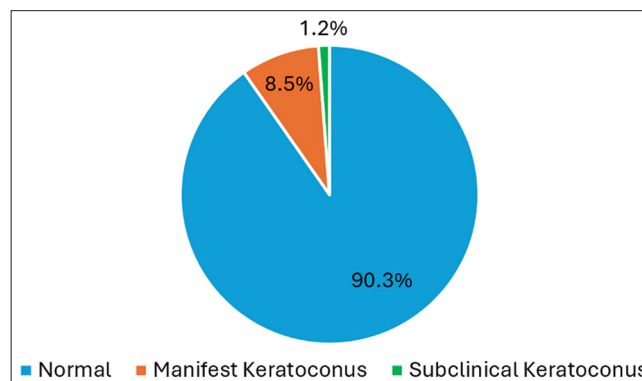


Figure 1: Pie chart depicting the overall prevalence rate of keratoconus in patients seeking laser refractive surgery in the referral ophthalmology clinics of Qassim, Saudi Arabia.

statistically significant differences ($P = 0.016$). The prevalence of manifest and subclinical keratoconus was analyzed in gender subgroups and results are summarized in Table 1.

The prevalence of keratoconus was also assessed in a subgroup of patients with pre-existing astigmatism ≥ 2 D and in a subgroup of patients with astigmatism ≤ 2 D. Overall, in a subgroup of patients with astigmatism ≥ 2 D ($n = 417$), the prevalence of keratoconus was found to be 31.2% ($n = 130$) whereas in a subgroup of patients with astigmatism ≤ 2 D ($n = 1083$), the prevalence rate was 1.40% ($n = 15$) ($P < 0.001$). The prevalence of keratoconus was analyzed in astigmatism subgroups (astigmatism: ≥ 2 D vs. ≤ 2 D) and results are summarized in Table 1. Demographically, the patients with astigmatism ≥ 2 D were 66.1% males and 33.9% females and had a mean age of 28.5 ± 7.2 years.

DISCUSSION

The present study was designed to assess the prevalence of keratoconus among patients seeking refractive surgery/LVC at our ophthalmology clinic in Qassim. The results showed that the overall prevalence of keratoconus was 9.7% among patients seeking refractive surgery/LVC. To the best of our knowledge, this is the first study reporting the prevalence of keratoconus among patients seeking refractive surgery/LVC in Qassim, Saudi Arabia.

In the present study, the prevalence of keratoconus among patients seeking LVC was lower when compared to similar published studies from different provinces of Saudi Arabia, such as Taif, Asir, and Jazan regions, where the reported prevalence of keratoconus among LVC patients was 18.05%,^[15] 41.5%,^[14] and 47.56%,^[13] respectively. A comparison of the present study results with similar studies conducted in other Middle Eastern countries showed wide variation. The studies from Egypt and Syria reported the prevalence of keratoconus to be 10.64%^[20] and 31.71%^[21] among patients seeking refractive surgery. In similar studies conducted outside the Middle East, the reported prevalence rate among LVC patients was 5.7% in the USA^[22] and 1.61% in India.^[23] The literature comparison of prevalence rates may not be directly comparable due to differences in screening tools, diagnostic criteria, and age/gender of LVC patients.

This worldwide variation in the prevalence rate of keratoconus (a multifactorial disease) has been attributed to various environmental (such as ultraviolet [UV] exposure and eye rubbing) and genetic risk factors (consanguinity) that have been found to contribute to its pathogenesis. For instance, the higher prevalence of keratoconus in countries with hot and dry climatic conditions, such as the Middle Eastern countries,^[2,24] has been attributed to excessive UV exposure of patients in these countries.^[24,25] Increased UV exposure has been linked with the formation of reactive oxygen species (ROS). Researchers have hypothesized that keratoconus corneas have a reduced ability to process ROS, and thereby, high levels of ROS result in oxidative damage, which has been implicated in the causation of keratoconus.^[26] In contrast, less keratoconus prevalence in countries with cold climatic conditions, such as the UK, USA, and Europe, has been postulated to be due to lower sun exposure.^[27]

Previous studies from the Middle East also reported a positive correlation of keratoconus with high altitude.^[13-15,21] For instance, the different regions of Saudi Arabia, such as Taif, Jazan, and Asir, which are situated at an elevation of 1700-2500 m, 2000 m, and 3000 m, respectively, above sea level, have reported a high prevalence rate of keratoconus. As UV radiation increases with height by about 10% for every 1000 meters of elevation,^[28] people living at high altitudes are probably more exposed to UV radiation. Thus, high exposure to UV radiation at high altitudes might act as a risk factor for the development of keratoconus.

Numerous studies also suggest the role of eye rubbing in the pathophysiology of keratoconus.^[20,21,27-31] A meta-analysis published in 2021 that included six studies across the world found an association between eye rubbing and keratoconus with pooled OR (95% CI) of 6.46 (4.12-10.1) in comparison to the controls with no eye rubbing.^[32] Eye rubbing, particularly vigorous knuckle-grinding type, has been associated with the severing of stromal collagen fibrils.^[33] Recurrent mechanical trauma releases matrix metalloproteinases (MMP-1 and MMP-13) and inflammatory mediators (interleukin-6 and tumor necrosis factor- α), which have been implicated in the keratoconus development.^[34] The duration of rubbing has been estimated to be significantly longer in

Table 1: Prevalence of keratoconus among males, females, and patients with preexisting corneal astigmatism of 2 D or higher.

	Males (n=970)		Females (n=530)		*P-value comparing male vs. female	Astigmatism ≥ 2 D (n=417)		Astigmatism ≤ 2 D (n=1083)		P-value comparing astigmatism ≥ 2 D vs. ≤ 2 D
	n	%	n	%		n	%	n	%	
Overall keratoconus	107	11.0	38	7.2	0.016	130	31.2	15	1.40	<0.001
Manifest keratoconus	96	9.9	32	6.0	0.011	119	28.5	9	0.80	<0.001
Subclinical keratoconus	11	1.1	6	1.1	0.997	11	2.6	6	0.60	<0.001

*The prevalence of manifest and subclinical keratoconus among females does not add to the overall prevalence due to rounding-off errors

keratoconus patients (10-180 s) than those without any ocular disorders (<5 s).^[24] Different environmental allergens and atopic conditions, such as asthma, eczema, and vernal catarrh, have been reported to induce eye rubbing that may contribute to the progression of keratoconus.^[24,30] Furthermore, regular use of rigid contact lenses is thought to be associated with rubbing-related trauma, which might lead to keratoconus.^[29,35-37]

Qassim is a relatively lower altitude region (600-750 m above sea level) with cool, rainy winters and hot, less humid summers. Compared to Taif, Jazan, and Asir, this region has milder climatic conditions. The authors believe that some of these factors may be contributing to the lower prevalence of keratoconus in Qassim.

Apart from environmental factors, it is believed that genetics also play a major role in the pathogenesis of keratoconus.^[27,38,39] There are reports of high concordance of keratoconus in monozygotic twins,^[40] and a family-based study from Brazil showed the association of 19 genetic loci with keratoconus.^[41] Studies from the Middle East^[8,15,20,42] and some parts of India have linked consanguinity with keratoconus.^[43] Consanguineous couples are at increased risk for autosomal recessive disorders due to their increased homozygosity by descent.^[44] The rate of consanguinity varies in different ethnicities and has been reported to be as high as 57.7% in Saudi Arabia.^[45] A study from the UK evaluating population-based keratoconus prevalence reported a four-fold higher prevalence among Asians (0.23%) as compared to Caucasians (0.05%).^[4] Similarly, in Iran, population-based keratoconus prevalence was found to be three times less in Persians (2.5%) than in non-Persians (7.9%).^[9] Variations in the keratoconus prevalence among different ethnic groups have been hypothesized to be due to the “genetic effect of consanguinity.”^[24]

The effect of genetic factors has not been studied previously in Qassim. The present study provides information about the low prevalence of keratoconus in Qassim as compared to other regions of Saudi Arabia. Future studies are warranted to evaluate the association of genetic risk factors with the prevalence of keratoconus in this region.

Two recent studies elucidated the interplay between genetic and environmental risk factors, which could be responsible for variations in the prevalence of keratoconus. A study from North Macedonia reported the prevalence of keratoconus among LVC patients as 12.5%, and after stratification into ethnic groups, Turk LVC patients showed a 40.8% prevalence rate.^[46] This much higher prevalence than other ethnicities living in the same area was hypothesized due to higher consanguinity among Turks compared with other ethnicities. A study from different regions of Syria found a higher rate of keratoconus among LVC patients of Damascus (24.22%) as compared to coastal cities.^[21] This was also hypothesized to be

due to the higher proportion of Armenians in the Damascus region who have higher levels of consanguinity. Damascus's geographical location, i.e., its high altitude, might also have contributed to the region's higher prevalence of keratoconus.

A review of the literature reveals conflicting trends in the gender predisposition to keratoconus. In the present study, the prevalence of keratoconus was higher in males (11.0%) compared to females (7.1%). This gender distribution agrees with three prior studies, which also found that males are more likely to be affected by keratoconus than females.^[11,47,48] However, a study from Mexico observed that females are twice as likely to have keratoconus as males,^[49] and the other two studies from the Middle East showed no gender predisposition in the keratoconus disease process.^[15,21] The differences between male and female proportions in keratoconus may be attributed to the sex hormones.^[50] Males have higher levels of androgens while females have a higher estrogen level.^[51,52] Sampling errors and different diagnostic criteria used in different studies could also affect these differences.^[24]

Pre-existing astigmatism has also been found to be linked to keratoconus prevalence. There are studies documenting a higher prevalence of keratoconus in patients with ≥ 2 D of astigmatism.^[7,53,54] In the present dataset, the patients with high astigmatism (≥ 2 D) had a statistically significantly higher prevalence of keratoconus (31.2%) than those with ≤ 2 D (1.40%). The patients with ≥ 2 D were demographically similar to the overall sample population. These findings suggest that patients attending outpatient clinics with astigmatism of 2 D or higher should be carefully screened for early diagnosis of keratoconus.

This study has some limitations. Due to the retrospective study design, different risk factors, clinical determinants, family history, etc., were not collected and analyzed in the present study. The association of environmental and genetic risk factors with keratoconus prevalence in Qassim was not studied due to the lack of such information in the literature. Future studies are expected to fill this gap.

CONCLUSION

In the present study, the prevalence of keratoconus in Qassim was found to be 9.7% among patients seeking refractive surgery. This was lower than previous publications from Taif, Asir, and Jazan. A review of the literature revealed large variations in keratoconus prevalence between different provinces of Saudi Arabia, which could be attributed to differences in UV exposure, eye rubbing, and consanguinity. Our findings will be a reference for clinical ophthalmologists while screening patients for refractive surgery in Qassim. Wider screening programs in the general population may help determine the prevalence of keratoconus in the general population.

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Ethical approval: The research/study was approved by the Committee of Health Research Ethics at Qassim University, number 220503, dated 28 September 2023 and adhered to the tenets of the Declaration of Helsinki.

Declaration of patient consent: Patient's consent is not required as patients identity is not disclosed or compromised.

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Conflicts of interest: There are no conflicts of interest.

Availability of data and material: The data supporting the findings of this study are available within the article.

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