Original Article

Assessing the Relationship of Keratocunus to Consanguinity

Abdul Rafe, Mohammed Tariq Munawar, Zaheer ud Din Babar and Kainaat Talat

ABSTRACT

Objective: The purpose of this research is to evaluate the relationship between consanguinity and the prevalence of keratoconus.

Study Design: Comparative/cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Ophthalmology, CMH, Kharian. June 2022 to March 2023.

Methods: This study included a total of 71 participants who were diagnosed with keratoconus. Following the collection of informed written consent from enrolled cases, complete demographic information was gathered. Patients included in the study ranged in age from 6 to 35 years. Participants filled out a questionnaire that they self-administered and answered questions regarding their demographic information, KC results, clinical symptoms, and the marital status of their parents. Using SPSS24.0, all data was analyzed.

Results: In our study patients mean age was 17.6±13.70 years and had mean BMI 20.13±5.19kg/m^2. Majority of the patients were males and 42 cases had rural residency. 43(60.6%) were married to a first cousin, 19(26.8%) were married to a second cousin, 3(4.2%) were married to a third cousin, and 6(8.4%) were married to someone outside their immediate family. At the 5% significance level, we found that consanguinity was correlated with KC. It was found that the prevalence of keratoconus and the severity of the condition were both higher in patients with first-degree consanguineous parents.

Conclusion: The findings of this study lend support to the theory that KC is strongly correlated with direct kinship. The results indicate that the risk of developing KC is much higher in cases of first-degree parental consanguinity compared to other types of inter marriage. KC was shown to advance more rapidly in this at-risk group.

Key Words: Inheritance, Genetics, Consanguinity, Keratoconus

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INTRODUCTION

Keratoconus is a corneal ectatic disorder characterized by impaired vision and a cone-shaped protrusion of the cornea. It usually worsens over time and impacts equally on both sides of the body.The most noticeable clinical signs include impaired vision and an abnormally high sensitivity to light and glare [1]. Refractive correction with sphero-cylindrical spectacle lenses can be difficult for people with irregular astigmatism due to corneal asymmetry.[2] Clinical manifestation often occurs during the teen years and continues throughout early adulthood, though progression has been observed in those well into their 30s.

Department of Ophthalmology, CKMC / CMH, Kharian.

Correspondence: Dr. Abdul Rafe, Assistant Professor of Ophthalmology, CMH Kharian.
Contact No: 03335424726
Email: mabdulrafe@yahoo.com

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The symptoms and course of an illness can vary widely from patient to patient. Unilateral keratoconus, in which the condition affects just one eye in the same patient, has been reported.[3]

Its precise origin is unknown, although prolonged stress is thought to be a contributing factor for those who are genetically susceptible.It has been associated to systemic diseases such Down syndrome, Leber congenital amaurosis, and connective tissue anomalies, as well as to chronic eye rubbing, the use of rigid gas-permeable contact lenses, and atopy [4, 5]. Although environmental variables do play a role in disease development, genetics seem to be the primary cause [6-8] percent of cases have a positive family history established).[5] KC strikes people of all sexes and all walks of life everywhere. Depending on where you live and whatever country you're in, the KC incidence rate might range from between 4,000 to 6,000 cases per 100,000 people year. Central India had a 2.3% rate, whereas the rate in Iran was 0.24 percent and in Russia it was 0.0003 percent [6]. In Pakistan, KC is more common and has a greater frequency than in the West, and many cases may be traced back to genetics rather than the local environment. Russia and the United States, which have colder climates than countries in the Middle East and Asia, have a lower prevalence of KC[7].

KC has been associated with a number of medical conditions, including Down syndrome, mitral valve prolapse, and Leber congenital amaurosis. Nonetheless, a significant proportion of KC patients have a good family history. Multiple environmental and genetic factors interact to cause KC. There is a genetic component to KC in 6-23.5% of patients[8]. Consanguineous marriage (CM) is the leading cause of fetal abnormalities [9] throughout Asia.

KC is most common throughout adolescence, but it can last well into adulthood, even for some people. Few people succeed after entering their forties [3, 4]. While warmer nations like India, Lebanon, Iran, and Australia have a higher frequency of KC than colder countries like Russia and Denmark [10,11], the prevalence of KC varies widely around the globe. The annual incidence of KC ranges from 50 to 230 cases per 100,000 individuals. A recent Danish study [11] found that the rate at which KC is spreading throughout the population has increased by a factor of two to three since 2003. Patients who had a close relative with KC, rubbed their eyes frequently, or had a father who was a first cousin were more likely to acquire KC themselves [12,13].

Given the existing state of knowledge and consensus regarding any potential links between KC expansion and consanguinity, the current investigation was necessary. The purpose of this research was to evaluate the degree to which KC is linked to close family ties.

METHODS

This comparative/cross-sectional study was conducted at Department of Ophthalmology, CMH, Kharian. The data was gathered using a non-probabilistic convenience sampling method. Subjects' age, sex, place of residence, and employment status were collected together with other socio-demographic details after obtaining informed written consent. Patients with a history of immunodeficiency, those taking anti-cancer drugs, those who had recently experienced eye trauma, and those who were previously reported to have ectasia or pellucid marginal degeneration were not included in the study.

Following extensive screening, 71 patients with keratoconus were included in the study. Patients' ages ranged from 6 to 35 in this study. Patients with a KC diagnosis were given a brief summary of the study before completing a self-administered survey concerning their demographics, KC findings, clinical symptoms, and the marital status of their parents. Data were presented using frequencies and percentages, and the chi-square test was run to see if there was a correlation between KC and consanguinity. Significant results were considered to have a probability value of less than 0.05. SPSS 24.0 was used for all data analysis.

RESULTS

Majority of the patients 48 were males and 23 cases were females.(figure 1)

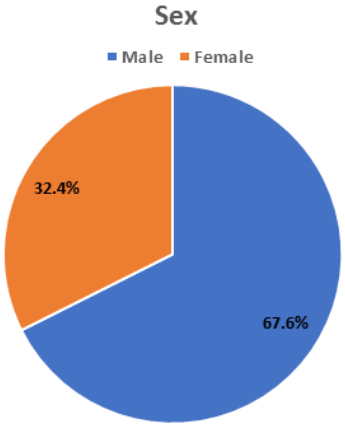

Figure 1: Gender distribution of enrolled cases

In our study patients mean age was 17.6±13.70 years and had mean BMI 20.13±5.19 kg/m^2.(Table 1)

Table-1: Age and body mass index of the enrolled cases

Variables	Mean	Std.
Age (years)	17.6	13.70
BMI (kg/m^2)	20.13	5.19

We found that 43(60.6%) were married to a first cousin, 19(26.8%) were married to a second cousin,3(4.2%) were married to a third cousin, and 6(8.4%) were married to someone outside their immediate family.(figure 2)

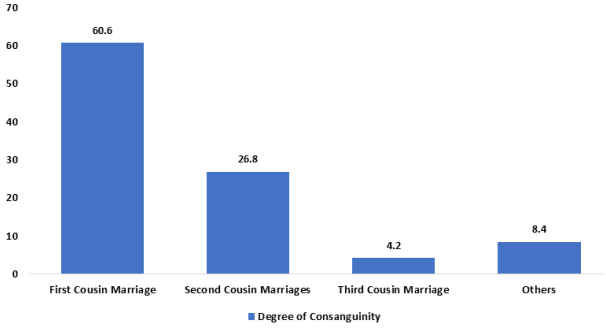

Figure-2: Patients with KC ancestry often have first-degree relatives

At the 5% significance level, we found that consanguinity was correlated with KC. It was found that the prevalence of keratoconus and the severity of the condition were both higher in patients with first-degree consanguineous parents.

DISCUSSION

Finding the root causes of KC in Pakistan was the driving force behind this study. Statistical analysis revealed a link between male gender, eye-rubbing, sun exposure, a family history of KC, and allergic reactions.

Rubbing of the eyes was the most common and hence most significant symptom.

Our findings confirmed that female gender is an independent risk factor for KC occurrences. This contradicts other studies [14,15] that indicated KC to be more frequent in males. Previous studies have shown that corneal epithelial cells and keratocytes contain androgen, oestrogen, and progesterone receptors [16], which may indicate a connection between sex hormone variation and the microbiological structural functioning of the cornea. Evidence also suggests that an increased concentration of oestrogen may contribute to the development of KC by compromising the cornea's morphological structure [16]. Therefore, the quantity of sex hormones at a given moment and stage in one's life, in addition to the interaction with other environmental factors, may increase or decrease the prevalence of KC in a particular individual or group of either gender. Women, and especially those with higher oestrogen levels, may be at a higher risk for KC because of this. There could be serious consequences if this risk is added to those from other genes and the environment.

We found that 43(60.6%) were married to a first cousin, 19(26.8%) were married to a second cousin,3(4.2%) were married to a third cousin, and 6(8.4%) were married to someone outside their immediate family. These were comparable to the previous researches.[17,18] Between 6 and 8 percent of KC cases have a known positive family history or indications of familial transmission. In contrast to our previous report of a rate of 13% for family history in the United States Collaborative Longitudinal Evaluation of Keratoconus study, researchers in Israel, where the prevalence of KC is high, found a rate of 21.74% for family history. Some genes, such as VSX1, SOD1, COL4A3, and COL4A4, have been suggested to play a role in the development of KC. Few studies have examined the link between consanguineous marriage and the development of KC. By demonstrating a strong correlation between KC or parental first-cousin consanguinity, author provided further evidence that consanguinity and genetics may play a key role in the onset and progression of KC. The findings of both groups are consistent with one another. Recessive kinds of genetic ailments, such as those affecting the eyes, may be more common in a CM environment because of the increased possibility of diverse mutations in a homoallelic situation [19]. Although Akrami et al[21] have noted a rising trend in CM in Tehran, Iran, the disease is more prevalent in Asia and Africa[20]. Consanguineous couples often wonder if their offspring will be affected by their union. It is important for family doctors to understand the various pathologic pathways related with consanguinity. As a result, the screening processes need to be modified to ensure sure consanguineous fathers and their offspring are properly evaluated.

Several potential mechanisms have been proposed to explain why eye-rubbing is linked to the development of KC. Kallinikos and Efron postulated that chronic eye rubbing caused epithelial stress, which in turn enhanced the release of interleukin (IL)-8 and other degenerative enzymes, which in turn facilitated the loss of the corneal fibroblasts, leading to diminished biomechanical stability and ectasia [22]. Additionally, the stromal keratocytes can be traumatised by the variations in intraocular pressure caused by eye rubbing. Rabinowitz found that 83% of 218 KC patients who were tested rubbed their eyes positively [23]. Eye rubbing was the most significant predictor of KC in this study (p0.001), with six subjects (50%) reporting positive eye rubbing.

Our findings corroborate the theory that KC has multiple causes, but that genetics play a major role (via both family history and paternal consanguinity). A positive family history of KC and parental consanguinity were each related with a 25-fold and 3-fold greater risk of KC, while eye rubbing was associated with a more than 4-fold increased risk. These findings provide more evidence that the condition has a complicated genetic and environmental basis and can serve as a foundation for public education and counselling for affected families. In terms of foreknowledge, the correlation with paternal consanguinity is noteworthy. For children who have a positive family history of keratoconus, the authors urge early and thorough management of the habit of rubbing the eyes. It is also discouraged that members of affected households marry within the same family.

CONCLUSION

The findings of this study lend support to the theory that KC is strongly correlated with direct kinship. The results indicate that the risk of developing KC is much higher in cases of first-degree parental consanguinity compared to other types of inter marriage. KC was shown to advance more rapidly in this at-risk group.

Author's Contribution:

Concept & Design of Study:	Abdul Rafe
Drafting:	Mohammed Tariq Munawar, Zaheer ud Din Babar
Data Analysis:	Kainaat Talat
Revisiting Critically:	Abdul Rafe, Mohammed Tariq Munawar
Final Approval of version:	Abdul Rafe

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