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ORIGINAL ARTICLE

Evaluating the Association of Keratocunus with Consanguinity

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ABSTRACT

Objective: Purpose of this study is to determine the frequency of keratoconus with consanguinity.
Study Design: Comparative/cross-sectional study
Place and Duration: This comparative/cross-sectional study was conducted at Shahida Islam Medical and Dental College Lodhran and Jinnah International Hospital, Abbottabad in the period from May, 2022 to October, 2022.
Methods: Total 53 patients of keratoconus were presented in this study. Included patients were aged between 8-32 years. Participants completed a self-administered survey that inquired about demographic information, KC findings, clinical symptoms, and parental marital status. All data was analyzed using SPSS 20.0.
Results: There were 31 (58.5%) females and 22 (41.5%) males in all cases. Mean age of the patients was 19.25±12.92 years. 35 (66.03%) cases had rural residency and 18 (33.97%) cases were had urban residency. 25 (47.2%) cases had poor socio-economic status. Of the patients surveyed, 29 (54.7%) had first-cousin weddings between their parents, 16 (30.2%) had second-cousin marriages, 5 (9.4%) had third-cousin marriages, and 3 (5.7%) had marriages beyond the immediate family. Significant associations between consanguinity and KC were found at the p <0.05 level. Patients with first-degree consanguineous parents were shown to be more likely to have keratoconus and to have more advanced cases of the disease.
Conclusion: Results from this study provide credence to the idea that there is still a significant direct correlation between KC and consanguinity. According to the findings, first-degree parental consanguinity poses a much greater risk of KC development than other types of intermarriage. The progression of KC was shown to be faster in this vulnerable population.
Keywords: Consanguinity, Inheritance,Genetics, Keratoconus

INTRODUCTION

In keratoconus, the cornea bulges outward in a cone shape, causing severe vision impairment. There is a gradual and bilateral pattern to the illness. Reducing visual acuity, picture distortion, and an excessively high sensitivity to light and glare are the primary clinical outcomes. [1] Because of the uneven astigmatism caused by the corneal asymmetry, refractive correction using sphero-cylinder lenses is challenging in this situation. [2,3] Clinical manifestations of the illness often begin around adolescence and continue into the second and third decades of life, however verified progression has been seen in patients as old as 30. There is considerable inter-individual variation in both illness presentation and development (see also [4]). Even within the same patient, keratoconus often affects different eyes, and occurrences of unilateral keratoconus have been documented. [5,6]

The importance of determining the prevalence and incidence of an illness cannot be overstated, as this information can be used to establish and evaluate healthcare policy [7], as well as to better understand the causes of the disease and develop strategies to prevent, monitor, and treat it [8]. When a disease is said to be "prevalent," it means that "a part (percentage or proportion) of a defined population is affected by a particular medical disorder at a given point in time, or over a specified period of time," while a "incidence rate" refers to "the frequency of new occurrences of a medical disorder in the studied population at risk of the medical disorder arising in a given period of time" [8]. Incidence is measured by longitudinal research designs, whereas prevalence is determined through cross-sectional samples [9].

Inconsistencies in clinical terminology and diagnostic standards contribute to wide discrepancies in reported rates of KC prevalence and incidence. Approximately 0.249 percent of the population in Iran is thought to have KC at any given time [10]. Geographical context and data provenance both affect estimates of KC's prevalence. In the United States, for instance, the overall frequency of KC is estimated at around 600 cases per 100,000 people, although the prevalence among hospitalised patients is just 54.5 cases per 100,000. Although KC often presents itself around adolescence, it can show up as late as the fourth decade of life, and its progression differs between groups. New research suggests that more severe clinical subtypes of KC are prevalent in younger patients, implying an inverse relationship between KC severity and age. Breaks in Bowman's layer and a thinned corneal stroma are two of the histological hallmarks of KC; in a keratoconic cornea, all layers (save the endothelium) show evidence of histopathological structural alterations [11, 12]. Contact lens use, eye rubbing, atopic illness, connective tissue diseases, and genetics are also contributors [13, 14]. KC has been linked to a variety of underlying conditions, including Down syndrome, mitral valve prolapse, and Leber's congenital amaurosis, as detailed in a number of studies. While KC might appear out of nowhere, a sizable percentage of individuals have a good family history. Complex genetic and environmental variables [15, 16] contribute to KC's multifaceted pathogenesis. Patients with KC are between 6-23.5% likely to have a family history of the disease [17, 18]. However, studies have shown that CM increases the risk of having a child with a congenital abnormality by as much as 80% [19, 20]. Given the existing state of knowledge and agreement about any links between KC growth and consanguinity, it was necessary to conduct the present investigation. As such, the purpose of the research was to assess how closely KC is linked to being related via blood.

MATERIAL AND METHODS

This comparative/cross-sectional study was conducted at Shahida Islam Medical and Dental College Lodhran and Jinnah International Hospital, Abbottabad in the period from May, 2022 to October, 2022. Non-probability convenience sampling technique was used to collect the data. Detailed socio-demographics of selected people included age, sex, residence, occupational status, were recorded after taking informed written consent. Patients were excluded from the study if they had any systemic or ocular conditions positively or negatively associated with KC, Immunodeficient patient, anti-cancerous drugs users, patients with eye trauma, patients reported with ectasia or pellucid marginal degeneration were not included in this study.

Total 53 patients of keratoconus were recruited in this study after detail examination. Included patients were aged between 8-32 years. Participants completed a self-administered survey after giving an explanation about the research project to the KC diagnosed patients that inquired about demographic information, KC findings, clinical symptoms, and parental marital status. Frequencies and percentages were utilized to describe the data, and the chi-square test was performed to determine whether or not there was a connection between KC and consanguinity. If the probability value was less than 0.05, it was judged to be significant. The entire data was analyzed by using SPSS 20.0version.

RESULTS

There were 31 (58.5%) females and 22 (41.5%) males in all cases. Mean age of the patients was 19.25±12.92 years. 35 (66.03%) cases had rural residency and 18 (33.97%) cases were had urban residency. 25 (47.2%) cases had poor socio-economic status while the rest 28 (52.8%) had better socio-economic status. No prevalence was observed on the basis of sex, residential state and socio-economic status. (Table 1)

Table 1: Demographic characteristics of the KC diagnosed patient

Variables	Frequency (n=53)	Percentage%
Age (mean)	19.25±12.92 years	
Sex		
Male	22	41.5
Female	31	58.5
Residence		
Rural	35	66.03
Urban	18	33.97
Socio-economic status		
Poor	25	47.2
Better	28	52.8

In our study, of the patients surveyed it was found that 29 (54.7%) had first-cousin weddings between their parents, 16 (30.2%) had second-cousin marriages, 5 (9.4%) had third-cousin marriages, and 3 (5.7%) had marriages beyond the immediate family. Significant associations between consanguinity and KC were found at the p <0.05 level. Patients with first-degree consanguineous parents were shown to be more likely to have keratoconus and to have more advanced cases of the disease. (Table 2)

Table 2: Parents consanguinity of the KC developed patients

Variables	Frequency (n=53)	Percentage%	p-value
Consanguinity degree			
First-cousin marriages	29	54.7	<0.05
Second-cousin marriages	16	30.2	
Third-cousin marriages	5	9.4	
Out of family	3	5.7	
Total	53	100	

DISCUSSION

Prevalence estimates range from as low as 0.0003% in Russia to as high as 5.3% among male Arab students in Israel. [21,22] There was a big research done in the Netherlands that revealed a frequency of 1:375 (0.27%)[23], and more recently a rather high incidence (1.2%) was observed in an Australian community using scheimpflug imaging. [24] Possible explanations for this discrepancy include racial and cultural diversity, endogamy, advances in diagnosis, and the absence of uniform cutoffs. [25] It is generally acknowledged that environmental, biomechanical, genetic, and metabolic abnormalities are likely to all play a role in the pathophysiology of this illness, which has no clear main cause. [26] Keratoconus is mostly diagnosed using corneal pachymetry, tomography, and topography. [27]

In our study, There were 31 (58.5%) females and 22 (41.5%) males in all cases. Mean age of the patients was 19.25±12.92 years. 35 (66.03%) cases had rural residency and 18 (33.97%) cases were had urban residency. 25 (47.2%) cases had poor socio-economic status while the rest 28 (52.8%) had better socio-economic status. No prevalence was observed on the basis of sex, residential state and socio-economic status. Heredity plays an important role in keratoconus (KC). Consanguineous marriage (CM) can affect the transmission of recessively inherited conditions. This study aimed to determine the frequency of keratoconus with consanguinity. Results of this study showed that the prevalence of Keratoconus is higher 54.7% in the children of first-cousin married parents than the second and third-cousin married parents as they showed 30.2% and 9.4% and it was very low 5.7% in the children of parents who married beyond the immediate family. This study's findings are consistent with those of a previous one [28] that found a significant association between KC and first-cousin marriages but not with second- or third-cousin marriages, while this study found a significant association between KC and total parental consanguinity (first-, second-, and third-cousin marriages). Offspring of consanguineous marriage had a fivefold chance of having KC, according to a prevalence research conducted by Shneor et al. in Haifa (2014), which surveyed 314 college students. However, only parental first cousin consanguinity was shown to be relevant. [28] Another compelling piece of evidence supporting genetics comes from examinations of identical twins. In a study of 18 sets of twins conducted in the United Kingdom, Tuft et al. found that KC was more concordant among monozygotic than dizygotic twins. [29] However, the current study did not include any twins among its patients. Patients who acquired KC were also shown to be the children of cousins in research by Thomas [30], Jochen Graw [31], and Duke Elder and Leigh [32].

In this study, patients with high frequency of first degree parental consanguinity were observed, that can be the customary practices of the contemporary regions. This showed similarity with a study of Gordan-Shaag [33]. Some other studies also discussed the prevalence of KC found in India, [34] Lebanon, [35] Saudi Arabia [36] and Israel [37], have high persistence of KC as compared to others, theyexplainedthattraditionofconsanguinityand environmental factors are behind this peak. A comparative studyconductedinYorkshire,Englandfoundthatthe Pakistani who came from a consanguineous family have KC susceptibility of 1 in 400 as compare to 1 in 30,000 whites [33].

CONCLUSION

Results from this study provide credence to the idea that there is still a significant direct correlation between KC and consanguinity. According to the findings, first-degree parental consanguinity possessed a much greater risk of KC development than other types of intermarriage. The progression of KC was shown to be faster in this vulnerable population.

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