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Consanguinity and Ocular Disorders in Pakistani Population: Refractive Errors, Strabismus, and Keratoconus

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ABSTRACT

Background: Previous Consanguineous marriages led to an increased risk of genetic disorders due to the amplification of homozygous alleles. Both genetic and environmental factors contribute to the development of refractive errors and strabismus, while genetic inheritance plays a role in the development of keratoconus. This research aimed to investigate the association between consanguinity and refractive errors, strabismus, and keratoconus. The study also assessed the severity of the problem and made recommendations for prevention. **Methods:** From September 2021 to June 2022, a descriptive cross-sectional study was conducted in a population with refractive errors, strabismus and/or keratoconus in Islamabad. Data were collected from different hospitals using a non-probability sample. Visual acuity testing and refractive testing were performed using standardized methods, while strabismus was assessed using the cover/uncover test, and keratoconus was suspected by signs and symptoms and confirmed with a keratometer. **Results:** Of the 900 patients included in the study, 555 were male and 345 were female. Refractive errors were the most common disorder, observed in 83.6% of patients. Consanguinity was identified in 53% of patients, mostly first cousins. **Conclusion:** The study found a significant association between consanguinity and strabismus and elucidated the multifactorial etiology related to family history, consanguinity, and heredity. Consanguinity and heredity have been identified as critical factors in the development of refractive errors, keratoconus, and strabismus. The results of the study form a basis for educating and advising the population on how to deal with these eye consequences.

Keywords: Consanguinity, Refractive Error, Strabismus, Keratoconus

INTRODUCTION

Consanguinity refers to descent from a common ancestor and includes marriage between people who are related by blood. Such relationships can adversely affect their children's health and reproductive capacity [1]. Consanguinity increases the likelihood that offspring will inherit homozygous alleles, which can lead to a higher incidence of genetic disorders. As a result, affected individuals may have reduced chances of survival and reproduction, ultimately limiting the transmission of these disease-causing genes to future generations and possibly eradicating them from the population [2]. Since treatment options for most genetic disorders are limited, consanguinity is not a recommended choice due to its long-term consequences. Instead, it is cheaper to

opt for non-consanguineous relationships. This can delay the onset of disease by several generations, giving time for advances in medical technology that may offer better solutions [3].

It is worth noting that consanguineous marriages are common in Pakistan, especially among families with lower socioeconomic status [4]. This practice is influenced by the clan-oriented nature of society and the belief that such relationships bring greater stability. Unfortunately, the incidence of autosomal recessive diseases in Pakistan is higher than in more developed countries due to a lack of awareness about the health risks associated with consanguinity [5]. Certain genetic communities within the Pakistani population have been identified with unique inherited diseases caused by regional founder variants [6, 7]. Promoting health education can help reduce this burden and support policymakers in developing strategies and specific genomic databases to correlate disease mutations and uncover clinical phenotypes within ethnic tribes and related regions of Pakistan (8, 9). Blood relationships contribute to an increased development of autosomal recessive diseases [10]. The increased risk of recessive disorders is due to the inheritance of autosomal recessive gene mutations from a common ancestor [11].

In Pakistan, an estimated 4.79 million people suffer from visual impairment caused by refractive errors [2]. Genetic factors significantly influence myopia onset and progression, with a strong association observed between parents' myopia history and occurrence of myopia, particularly high myopia, in children [12]. A gene linkage study identified 25 myopia loci, three of which were on the X chromosome [13]. Another study suggested that consanguinity does not have a statistically significant effect on the type or severity of refractive errors but recommended further investigation with larger samples [14]. Strabismus, a common eye disease, affects approximately 2 to 6% of the global population [15]. In Pakistan, the estimated prevalence of strabismus is 5.4%, with 2.5% of cases occurring in children under 5 years of age [16, 17]. Previous studies have shown that heredity plays a crucial role in the development of comorbid strabismus and that a family history is more common in certain types of strabismus, such as XT and ET [18]. In addition, the risk of developing strabismus is about four times higher when either the siblings or the parents have strabismus [20, 21].

Keratoconus, a condition characterized by thinning and bulging of the cornea, has a documented genetic predisposition, particularly in familial groups and identical twins [22]. Familial keratoconus is predominantly inherited in a dominant autosomal pattern, although an autosomal recessive pattern has also been suggested in populations with high consanguinity [23]. The aim of this research was to examine the relationship between consanguinity and refractive errors, consanguinity and strabismus, and consanguinity and keratoconus. The aim of the study was to assess the seriousness of these problems and to make recommendations for their prevention.

MATERIALS AND METHODS

This study was a descriptive cross-sectional study conducted in different hospitals/clinics in Islamabad from September 2021 to June 2022. The study population consisted of individuals diagnosed with refractive errors, strabismus, and/or keratoconus. The researchers used a non-probability purposive sampling technique to collect data. Data collection instruments included Log Mar's vision chart (Carleton Optical), trial lens box and trial frame (Metallic, China Trial lens box), auto refractometer (TOPCON), retinoscope (HEINE), keratometer (TOPCON), and pen torch (HEINE). A self-structured proforma was used, which included information about diagnosis, family history, and demographics.

The sample size was determined to be 900 subjects (1800 eyes) using the g Raosoft calculator, with a confidence interval of 95% and a margin of error of 5%. The inclusion criteria comprised individuals of all age groups with refractive errors of ≥ 1.00D (hypermetropia, myopia, or astigmatism), any type of manifest deviation, or patients with a minimum of 4D difference between K1 and K2. Individuals with ocular conditions damaged by trauma or external factors, as well as mentally retarded individuals, were excluded from the study.

The data collected were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0.

Data Collection Procedure

The data for this study was collected from multiple eye hospitals and clinics in Islamabad, as the sample size required a large amount of data that couldn't be obtained from a single hospital within the given timeframe. Each patient who met the inclusion criteria was provided with detailed information about the study and obtained both verbal and written consent before participating. A comprehensive medical history was obtained from each subject. The visual acuity of the patients was assessed using the LogMAR vision chart, while refraction measurements were conducted using an automated refractometer and retinoscope. For patients suspected of having keratoconus, corneal curvature was also measured using a keratometer. These measurements were essential for the evaluation and diagnosis of refractive errors, strabismus, and keratoconus in the study subjects.

Gender-wise Distribution of Data

During the period of December 2021 to April 2022, a comprehensive examination was conducted on a total of 900 patients who were presented with one or more of the following ocular disorders: refractive errors, strabismus, and keratoconus. These patients sought treatment at the Eye Outpatient Departments (OPDs) of multiple hospitals in Islamabad. The details of this patient population are presented in Table 1.

Table 1. Gender-wise distribution of the Data.

Gender	Frequency	Percent
Male	555	61.7
Female	345	38.3
Total	900	100.0

Relative Frequencies of Ocular Disorders

The participants in this study were individuals diagnosed with one of three ocular disorders: refractive errors, strabismus, and keratoconus. Among these disorders, the highest frequency of patients was observed in the refractive errors category, followed by strabismus. Keratoconus had the lowest frequency as it is less prevalent compared to the other two disorders. These frequencies are illustrated in Table 2 and Figure 1.

Table 02. Relative Frequencies of the Ocular Disorders

Ocular Disorder	Frequency	Percent
Refractive Error	752	83.6
Strabismus	126	14.0
Keratoconus	22	2.4
Total	900	100.0

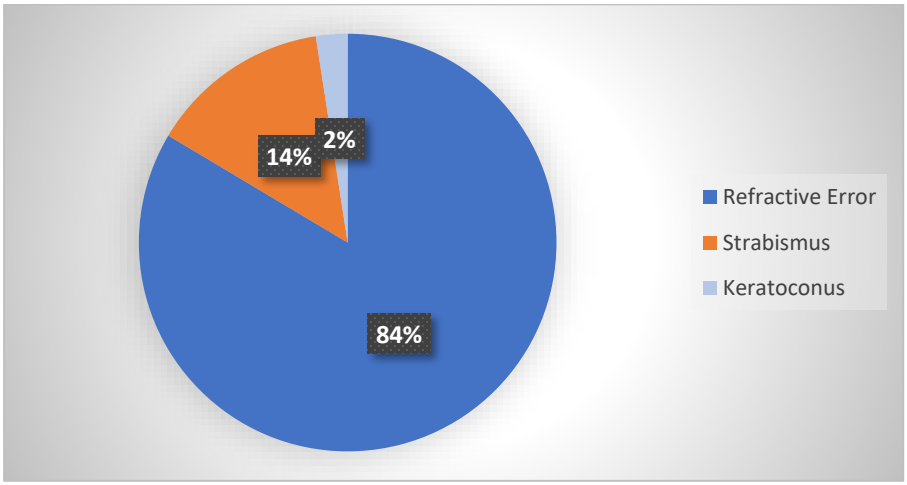

Figure 01. Relative Frequencies of the Ocular Disorders

Gender-wise Distribution of the Ocular Disorders

In the studied population, it was observed that the frequency of refractive errors and strabismus was slightly higher among females compared to males. On the other hand, keratoconus was exclusively found in the male population. These gender-based differences are depicted in Table 3 and Figure 2.

Table 3. Gender-wise Distribution of the Ocular Disorders

Type of Disorder	Male (n = 555)		Female (n = 345)	
	Frequency	Percentage	Frequency	Percentage
Refractive Error	458	82.5	294	85.2
Strabismus	75	13.6	51	14.8
Keratoconus	22	3.9	0	0.0
Total	555	100.0	345	100.0

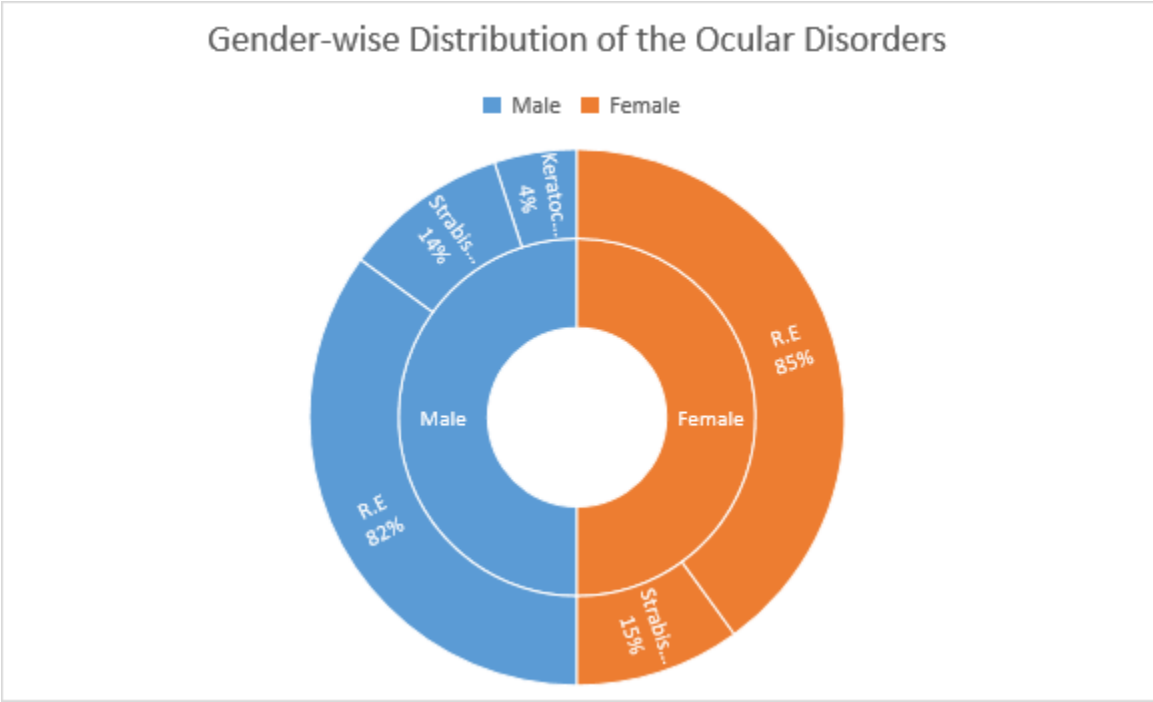

Figure 2. Gender-wise Distribution of the Ocular Disorders

Frequency of Same Disorder in Parents or Grandparents

The frequency of a Parent having the same disorder was higher as compared to the frequency of a Grandparent having the same disorder as shown in Table 4 and Figure 3.

Table 4. Frequency of Parents and Grandparents having the same disorder

Has Same Disorder	Parents		Grandparents	
	Frequency	Percentage	Frequency	Percentage
Yes	250	27.8	104	11.6
No	650	72.2	796	88.4
Total	900	100.0	900	100.0

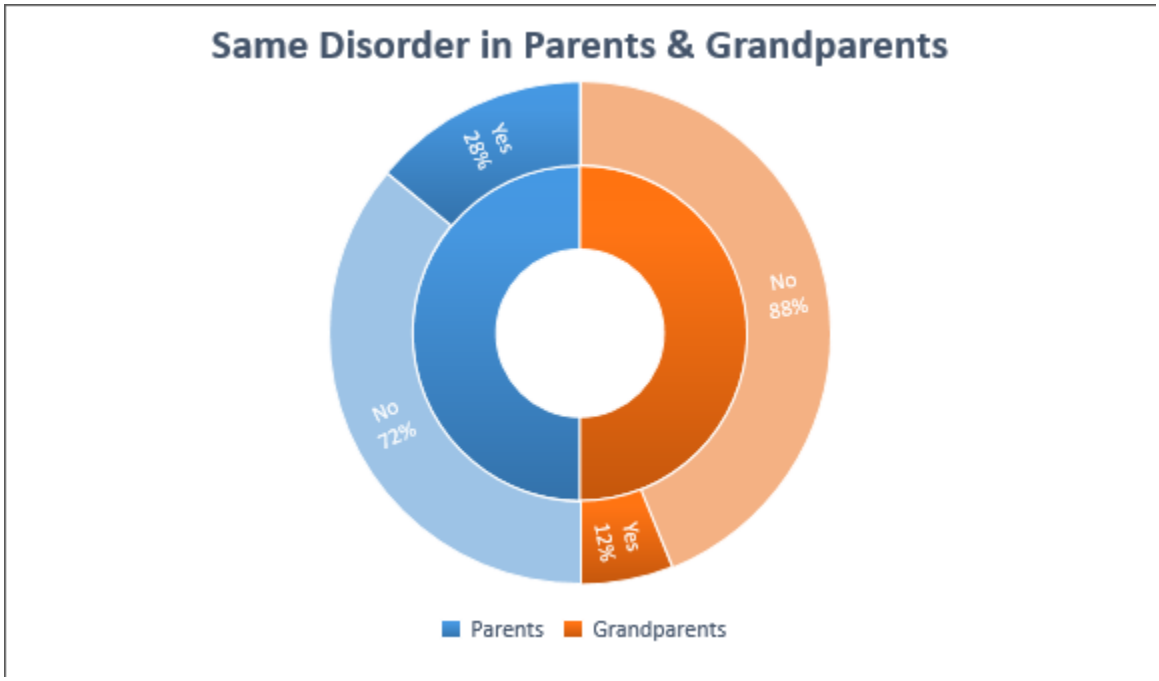

Figure 3. Frequency of Parents and Grandparents having the same disorder

Frequency of Parents' Relatedness

There was a negligible difference observed in the frequencies of parents being "related" and "not related" to the patients. Among the related parents, the most common type of relation found was "first cousins," as depicted in Table 5 and Figure 4.

Table 5. Frequency of Parents' Relation.

Parents' Relation	Frequency	Percentage
Not Related	422	46.9
First Cousin	448	49.8
First Cousin Once Removed	30	3.3
Total	900	100.0

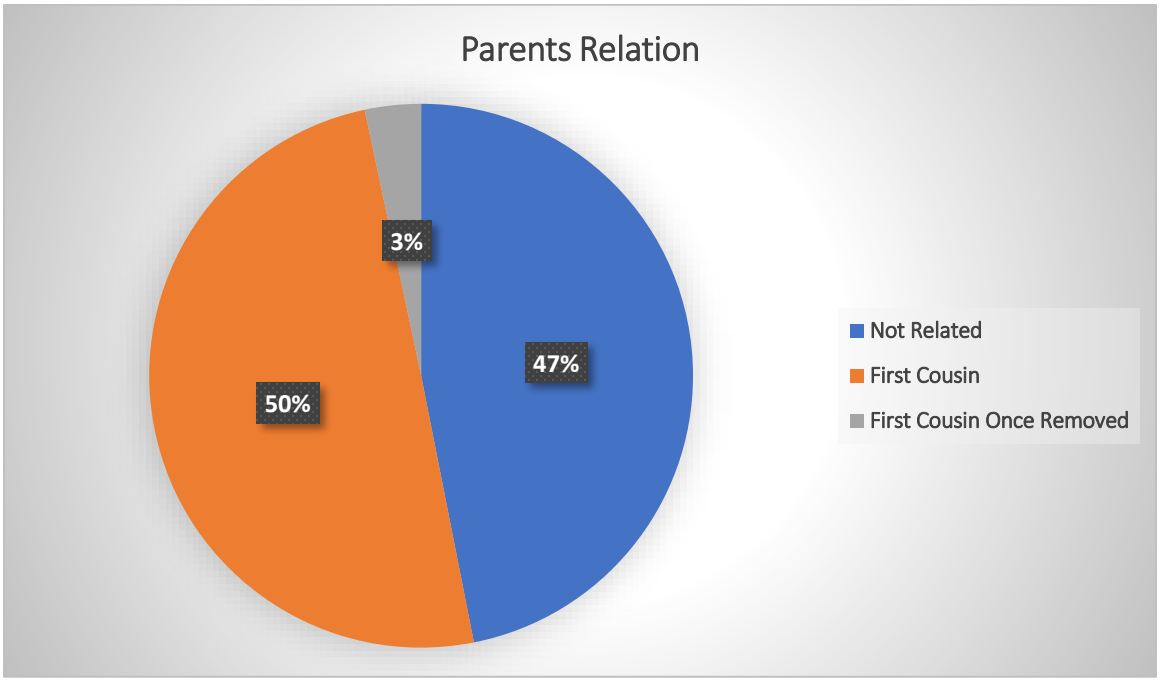

Figure 4. Frequency of Parents' Relation

Frequency of Consanguinity being a Common Practice

For most of the study participants, consanguinity was not commonly practiced in their families as shown in Table 6 and Figure 5.

Table 6. Frequency of Consanguinity being a Common Practice

Consanguinity Commonly Practiced	Frequency	Percentage
Yes	266	29.6
No	634	70.4
Total	900	100.0

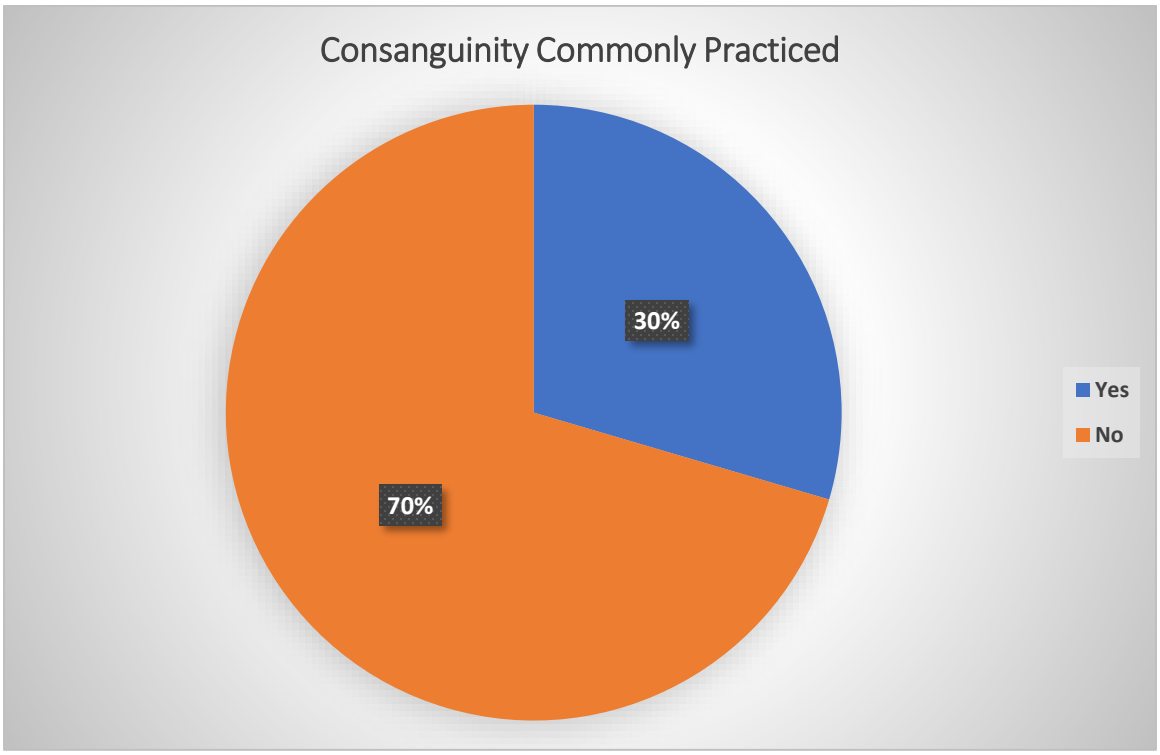

Figure 05. Frequency of Consanguinity being a Common Practice

Frequency of Different Types of Refractive Errors

Within the category of refractive errors, myopia was identified as the most prevalent type, followed by astigmatism. Hypermetropia was observed to be the least common type of refractive error, as indicated in Table 7 and Figure 6.

Table 07. Frequency of Different Types of Refractive Errors.

Type of Refractive Error	Frequency	Percentage
Myopia	364	48.4
Hypermetropia	124	16.5
Astigmatism	263	35.1
Total	751	100.0

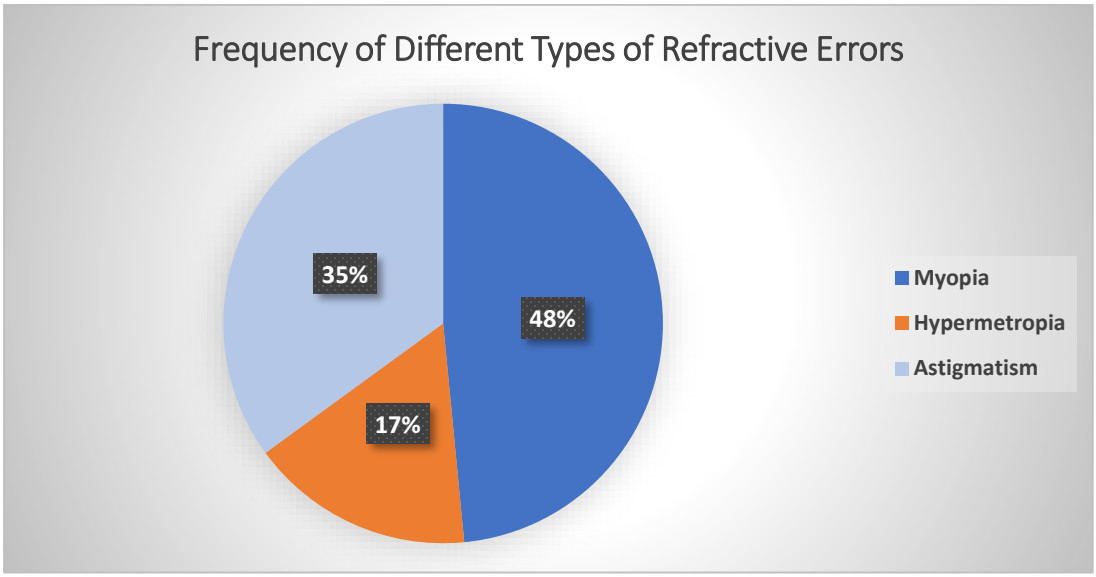

Figure 06. Frequency of Different Types of Refractive Errors

Association of Refractive Errors with Consanguinity

The association of Consanguinity with the Refractive Errors using the Chi-Square test was not found significant ($p<0.5$) as shown in Table 8 and Figure 7.

Table 8. Association of Refractive Errors with Consanguinity.

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	4.553a	2	.103
Likelihood Ratio	4.304	2	.116
Linear-by-Linear Association	.323	1	.570
N of Valid Cases	900		

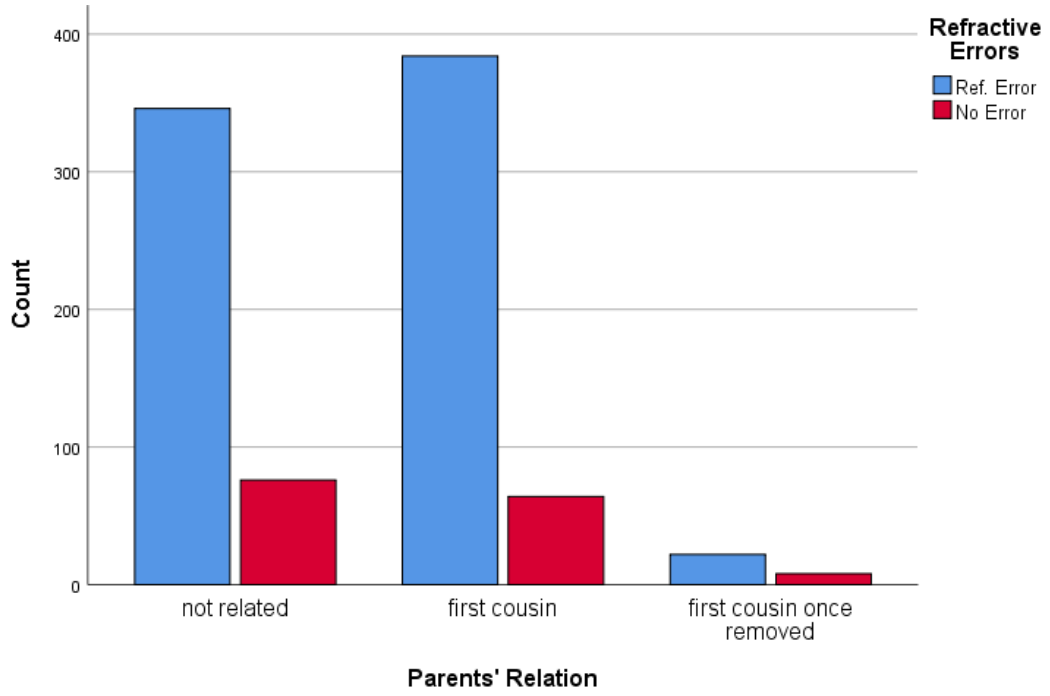

Figure 7. Association of Refractive Errors with Consanguinity

Frequency of Different Types of Strabismus

Among the patients diagnosed with strabismus, esotropia was identified as the most prevalent type of manifest deviation, followed by exotropia, alternate deviation, and hypertropia. However, no individuals with hypotropia were found among the study participants, as illustrated in Table 9 and Figure 8.

Table 9. Frequency of Different Types of Strabismus

Type of Strabismus	Frequency	Percentage
Esotropia	60	47.6
Exotropia	43	34.2
Hypertropia	2	1.6
Hypotropia	0	0.0
Alternate	21	16.6
Total	126	100.0

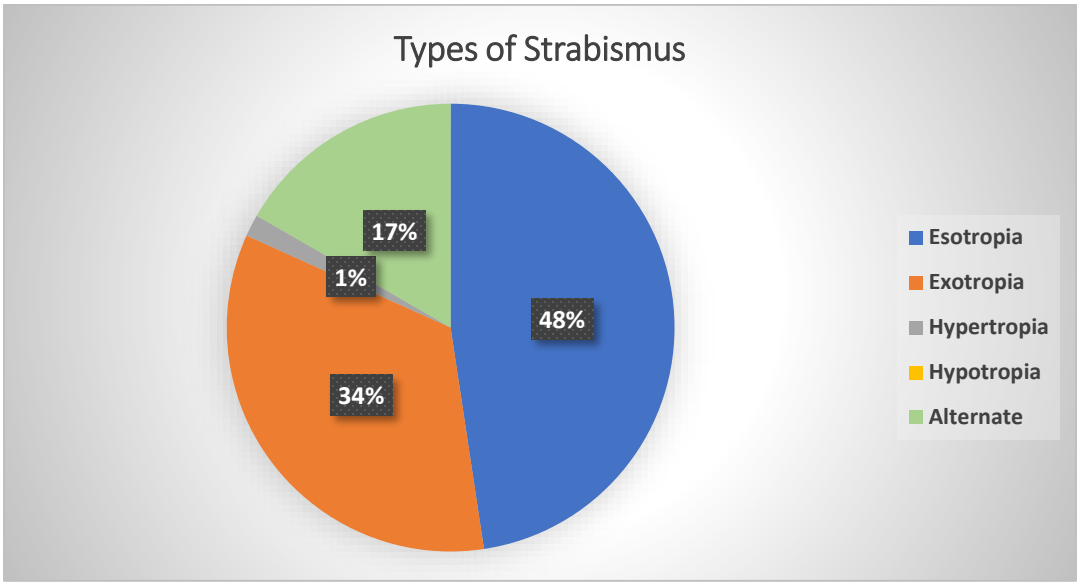

Figure 8. Frequency of Different Types of Strabismus

Association of Strabismus with Consanguinity

The association of Consanguinity with the Strabismus using the Chi-Square test was found significant ($p<0.05$) as shown in Table 10 and Figure 9.

Table 10. Association of Strabismus with Consanguinity.

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	6.283a	2	.043
Likelihood Ratio	6.066	2	.048
Linear-by-Linear Association	1.105	1	.293
N of Valid Cases	900		

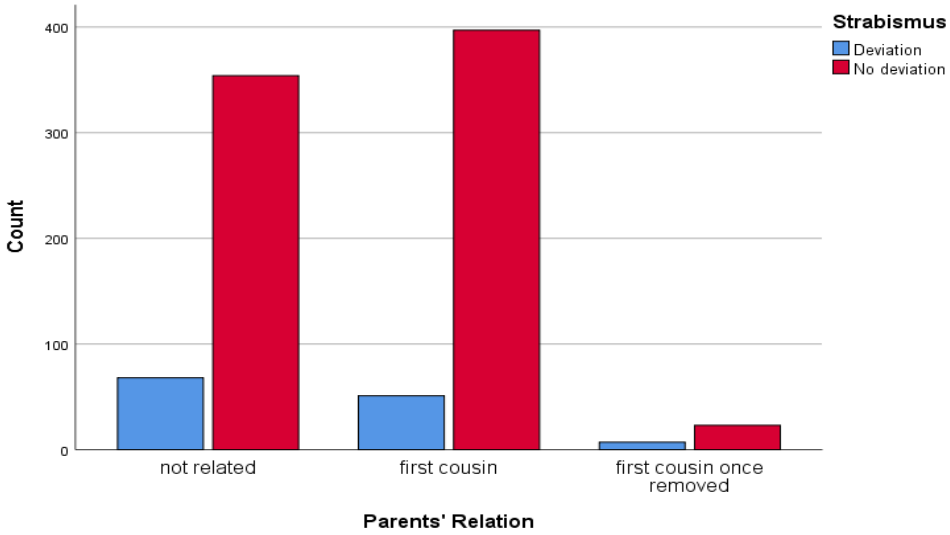

Figure 09. Association of Strabismus with Consanguinity

Frequency of Different Stages of Keratoconus

Among the persons having Keratoconus, the most common severity level was Stage 2, followed by Stage 3, Stage 1, and only 1 person having Stage 4 Keratoconus was found among the study participants as shown in Table 11 and Figure 10.

Table 11. Frequency of Different Stages of Keratoconus.

Stages of Keratoconus	Frequency	Percentage
Stage 1	2	9.1
Stage 2	13	59.2
Stage 3	6	27.2
Stage 4	1	4.5
Total	22	100.0

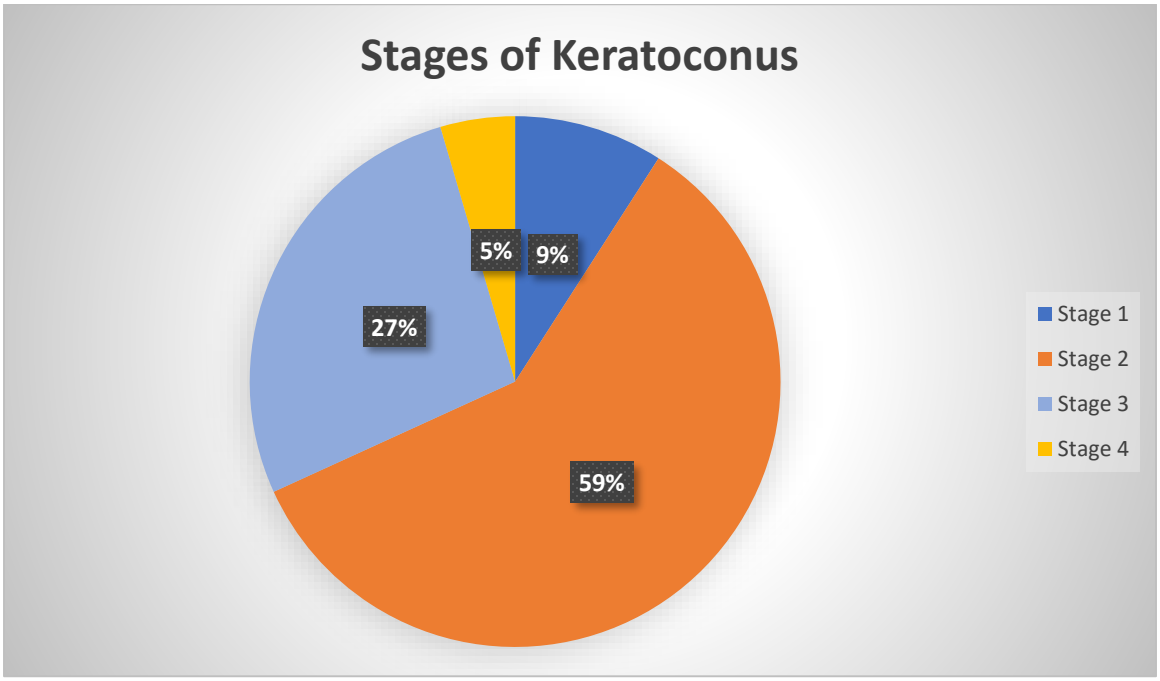

Figure 10. Frequency of Different Stages of Keratoconus

Association of Keratoconus with Consanguinity

The association of Consanguinity with Keratoconus using the Chi-Square test was not found significant ($p<0.5$) as shown in Table 12 and Figure 11.

Table 12. Association of Keratoconus with Consanguinity.

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	1.025a	2	.599
Likelihood Ratio	1.037	2	.595
Linear-by-Linear Association	.993	1	.319
N of Valid Cases	900		

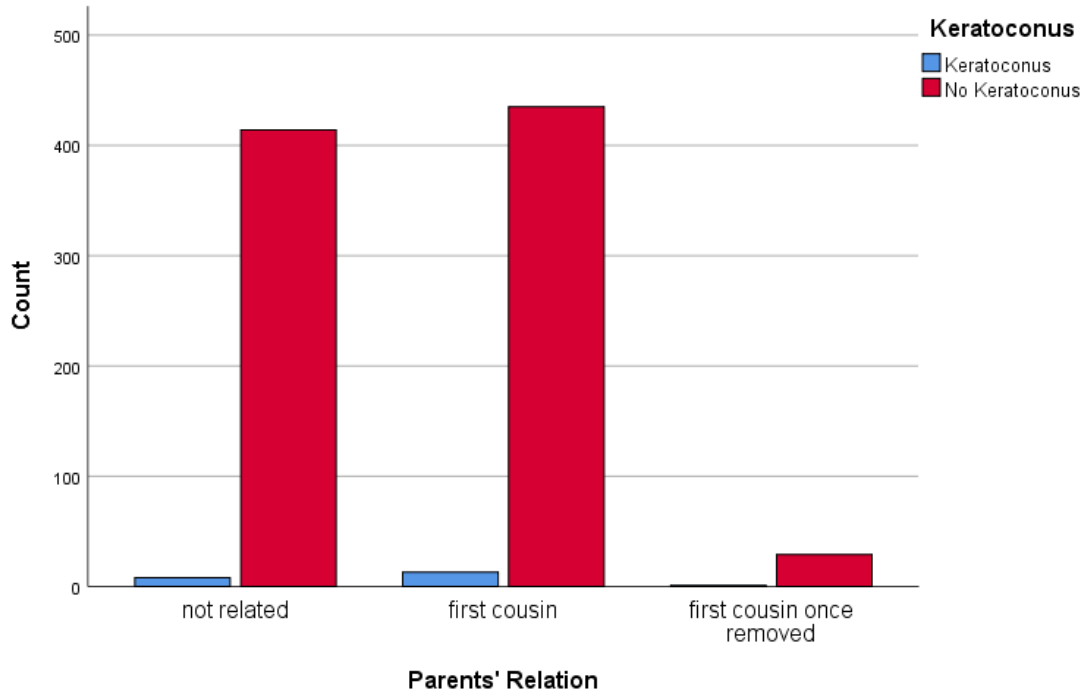

Figure 11. Association of keratoconus with consanguinity.

DISCUSSION

Ocular vascular and inflammatory diseases are recognized as major causes of irreversible blindness worldwide, imposing a significant socioeconomic burden. These disorders disproportionately affect men, women, and those in close family relationships, thereby affecting a vital and productive segment of society [24]. To address this situation, a descriptive cross-sectional study was conducted in different hospitals in Islamabad, Pakistan, with the aim of analyzing the sequelae of eye diseases, including refractive errors, strabismus, and keratoconus, observed in consanguineous offspring. The study population consisted of 900 patients who attended the outpatient departments (OPDs) of different hospitals and were selected using a non-probability sampling technique. Analysis of the data revealed a higher proportion of male patients (61.7%) compared to female patients (38.3%) [25]. Based on the relative frequency of eye diseases, refractive errors were the most common, followed by strabismus and keratoconus. Because of the different definition of refractive error and the relatively lower prevalence of strabismus and keratoconus, direct comparisons with previous studies have been difficult. The high frequency of refractive errors suggests that these disorders are common in Asian populations. Gender analysis showed a higher incidence of refractive errors and strabismus in women compared to men [26]. Similar results were observed for strabismus, indicating the influence of gender on its development. However, keratoconus has only been observed in men. Although both sexes can be affected by keratoconus, genetic variations specific to the studied population and geographic area may contribute to this eye disease being more common in males than in females [27].

As far as the hereditary aspect is concerned, the frequency of eye diseases was higher among the parents than among the grandparents who had the same diseases. This suggests a possible connection between heredity and the occurrence of these disorders. The genetic differences between parents and grandparents can mean that eye diseases occur differently within different generations. However, it is important to note that inheritance of the condition is not guaranteed in unaffected offspring, as explained in the literature review of this study [28]. Although the probability of occurrence is there, current research indicates that it is more common in the parental population. In addition, the study looked at the frequency of consanguineous relationships between parents and found that first cousins had the highest frequency. This finding suggests an indirect hereditary link between grandparents, parents, and first cousins. The inheritance of recessive gene mutations and the increased risk associated with consanguinity contribute to the expression of genetic disorders. It is worth noting that the present study focused on a population with limited consanguinity practices, leading to the conclusion that consanguinity may not be a significant risk factor for the high incidence of eye disease [29].

Refractive errors, which lead to blindness, are a significant public health concern worldwide. In the present research study, myopia was found to be the most prevalent refractive error in the population studied. In contrast, hypermetropia and astigmatism showed lower frequencies. The possible association between refractive errors and consanguineous links was examined using the chi-square test and yielded insignificant results ($p<0.5$). However, a previous study published in the Journal of Ophthalmology Pakistan in 2016 concluded that consanguinity is significantly associated with certain types of refractive errors, namely myopia and myopic astigmatism [30]. To address these issues, effective strategies such as eye screening programs should be implemented in eye care facilities. In the population affected by strabismus, esotropia and exotropia were more common than hypertropia and hypotropia. The study identified a significant association between consanguinity and strabismus ($p<0.5$) and underscores the importance of conducting strabismus screening before consanguineous marriages to prevent future sequelae. Previous research has shown that a positive family history plays a significant role in the increased prevalence and risk of strabismus. In terms of inheritance patterns, the study revealed that recessive forms have a significant impact on the occurrence of concomitant strabismus. In addition, there is a significantly increased risk of strabismus in first-degree relatives of those affected [31].

The current study also examined keratoconus, which is divided into different stages based on central radius, corneal transparency, corneal thickness, and visual acuity. Stage 2, characterized by astigmatism, proved to be the most common degree of severity. Examination of the association between consanguinity and keratoconus yielded insignificant results ($p<0.5$) and shed light on the true role of consanguinity in the etiology of keratoconus. However, a 2013 study published in the Journal of the American Academy of Optometry found that children of consanguineous parents are at a four-fold increased risk of keratoconus compared to children of unrelated parents after accounting for other identified factors associated with the disease [32].

In summary, the present research study examined the multifactorial etiology of refractive errors, keratoconus, and strabismus, focusing on factors such as family history, consanguinity, and heredity. Blood relationships and hereditary factors proved to be decisive for the development of these eye diseases. The study results provide a basis for educating and counseling at-risk populations and addressing the need to overcome such eye consequences.

CONCLUSIONS

The aim of this study was to investigate the association between consanguinity and refractive errors, strabismus and keratoconus in different public and private hospitals in Islamabad. Patients of all ages diagnosed with any of the three conditions were randomly selected to participate in the study. The results showed that refractive errors were the most common among the three diseases. Keratoconus was observed exclusively in males, while the frequency of the other disorders was similar in males and females. More than 50% of the subjects were related by blood. Among the refractive errors, myopia was the most common form. Esotropia was found to be the predominant subtype in patients with strabismus, and stage 2 was the most common stage of keratoconus. The study found a significant association between strabismus and consanguinity, while no significant association was found between the parental relationship and the other two conditions. In addition, the study highlighted that keratoconus is particularly common among visually impaired individuals in Asian populations, particularly in northern Pakistan, where consanguinity has been identified as the predominant risk factor.

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CONFLICT OF INTEREST

The authors have no conflict of interest which can negatively affect the current study.

AUTHOR CONTRIBUTION

All the authors equally contributed to be declared as an author in the current study.

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REFERENCES

1. Steinmetz JD, Bourne RR, Briant PS, Flaxman SR, Taylor HR, Jonas JB, Abdoli AA, Abrha WA, Abualhasan A, Abu-Gharbieh EG, Adal TG. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. The Lancet Global Health. 2021 Feb 1;9(2):e144-60.
2. Hassan B, Ahmed R, Li B, Noor A, Hassan ZU. A comprehensive study capturing vision loss burden in Pakistan [1990-2025): Findings from the Global Burden of Disease (GBD) 2017 study. PloS one. 2019 May 3;14(5):e0216492.
3. Jadoon MZ, Dineen B, Bourne RR, Shah SP, Khan MA, Johnson GJ, Gilbert CE, Khan MD. Prevalence of blindness and visual impairment in Pakistan: the Pakistan National Blindness and Visual Impairment Survey. Investigative ophthalmology & visual science. 2006 Nov 1;47(11):4749-55.
4. Hussain R. The effect of religious, cultural and social identity on population genetic structure among Muslims in Pakistan. Annals of Human Biology. 2005 Mar 1;32(2):145-53.
5. Bittles AH, Small NA. Consanguinity, genetics and definitions of kinship in the UK Pakistani population. Journal of Biosocial Science. 2016 Nov;48(6):844-54.
6. Merten M. Keeping it in the family: consanguineous marriage and genetic disorders, from Islamabad to Bradford. BMJ: British Medical Journal (Online). 2019 Apr 29;365.
7. Riaz M, Tiller J, Ajmal M, Azam M, Qamar R, Lacaze P. Implementation of public health genomics in Pakistan. European Journal of Human Genetics. 2019 Oct;27(10):1485-92..
8. Khan S, Lin S, Harlalka GV, Ullah A, Shah K, Khalid S, Mehmood S, Hassan MJ, Ahmad W, Self JE, Crosby AH. BBS5 and INPP5E mutations associated with ciliopathy disorders in families from Pakistan. Annals of Human Genetics. 2019 Nov;83(6):477-82..
9. Qasim I, Ahmad B, Khan MA, Khan N, Muhammad N, Basit S, Khan S. Pakistan genetic mutation database (PGMD); a centralized Pakistani mutome data source. European journal of medical genetics. 2018 Apr 1;61(4):204-8.
10. Oniya O, Neves K, Ahmed B, Konje JC. A review of the reproductive consequences of consanguinity. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2019 Jan 1;232:87-96.
11. Bhinder MA, Sadia H, Mahmood N, Qasim M, Hussain Z, Rashid MM, Zahoor MY, Bhatti R, Shehzad W, Waryah AM, Jahan S. Consanguinity: A blessing or menace at population level?. Annals of human genetics. 2019 Jul;83(4):214-9.
12. Ghaderi S, Hashemi H, Jafarzadehpur E, Yekta A, Ostadimoghaddam H, Mirzajani A, Khabazkhoob M. The prevalence and causes of visual impairment in seven-year-old children. Clinical and Experimental Optometry. 2018 May 1;101(3):380-5.
13. Modell B, Darr A. Genetic counselling and customary consanguineous marriage. Nature Reviews Genetics. 2002 Mar;3(3):225-9.
14. Tadmouri GO, Nair P, Obeid T, Al Ali MT, Al Khaja N, Hamamy HA. Consanguinity and reproductive health among Arabs. Reproductive health. 2009 Dec;6(1):1-9.
15. Hamamy H, Bittles AH. Genetic clinics in Arab communities: meeting individual, family and community needs. Public Health Genomics. 2009;12(1):30-40.
16. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. Bmj. 2006 Oct 19;333(7573):831-4.
17. Hussain R. Community perceptions of reasons for preference for consanguineous marriages in Pakistan. J Biosoc Sci 1999;31(4):449–61
18. Caca I, Cingu AK, Sahin A, Ari S, Dursun ME, Dag U, Balsak S, Alakus F, Yavuz A, Palanci Y. Amblyopia and refractive errors among school-aged children with low socioeconomic status in southeastern Turkey. Journal of Pediatric Ophthalmology & Strabismus. 2013 Jan 1;50(1):37-43.

19. Azam M, Iqbal S, Jamshed M, Nadeem HA. Association of different refractive error in parental cousin marriages. Ophthalmology Pakistan. 2016 Jul 1;6(03):19-22.
20. Cai XB, Shen SR, Chen DF, Zhang Q, Jin ZB. An overview of myopia genetics. Experimental eye research. 2019 Nov 1;188:107778.
21. Alsaqr AM. Relationship between Consanguineous Marriages and Incidence and Severity of Refractive Errors: A Cross-sectional Study. International Journal of Ophthalmology & Visual Science. 2019 Nov 5;4(4):81.
22. Hegmann JP, Mash AJ, Spivey BE. Genetic analysis of human visual parameters in populations with varying incidences of strabismus. American journal of human genetics. 1974 Sep;26(5):549.
23. Mash AJ, Hegmann JP, Spivey BE. Genetic analysis of cover test measures and AC/A ratio in human populations with varying incidences of strabismus. British Journal of Ophthalmology. 1975 Jul 1;59(7):380-4.
24. Crawford AZ, Zhang J, Gokul A, McGhee CN, Ormonde SE. The enigma of environmental factors in keratoconus. The Asia-Pacific Journal of Ophthalmology. 2020 Nov 1;9(6):549-56.
25. McGhee CN, Kim BZ, Wilson PJ. Contemporary treatment paradigms in keratoconus. Cornea. 2015 Oct 1;34:S16-23.
26. Edwards M, McGhee CN, Dean S. The genetics of keratoconus. Clinical & experimental ophthalmology. 2001 Dec;29(6):345-51.
27. Behndig A, Karlsson K, Johansson BO, Brännström T, Marklund SL. Superoxide dismutase isoenzymes in the normal and diseased human cornea. Investigative ophthalmology & visual science. 2001 Sep 1;42(10):2293-6.
28. Karimian F, Aramesh S, Rabei HM, Javadi MA, Rafati N. Topographic evaluation of relatives of patients with keratoconus. Cornea. 2008 Sep 1;27(8):874-8.
29. Weed KH, MacEwen CJ, McGhee CN. The variable expression of keratoconus within monozygotic twins: Dundee University Scottish Keratoconus Study (DUSKS). Contact Lens and Anterior Eye. 2006 Jul 1;29(3):123-6.
30. Schmitt-Bernard CF, Schneider CD, Blanc D, Arnaud B. Keratographic analysis of a family with keratoconus in identical twins. Journal of Cataract & Refractive Surgery. 2000 Dec 1;26(12):1830-2.
31. Hughes AE, Dash DP, Jackson AJ, Frazer DG, Silvestri G. Familial keratoconus with cataract: linkage to the long arm of chromosome 15 and exclusion of candidate genes. Investigative ophthalmology & visual science. 2003 Dec 1;44(12):5063-6.
32. Štabuc-Šilih M, Stražišar M, Glavač MR, Hawlina M, Glavač D. Genetics and clinical characteristics of keratoconus. Acta Dermatoven APA. 2010;19(2).