Original Article

Consanguinity and ocular disorders in India: Electronic medical records driven big data analytics

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Purpose: To describe the distribution of ocular disorders in patients with a family history of consanguinity presenting to a multi-tier ophthalmology hospital network in India. **Methods:** This cross-sectional hospital-based study included 2,805,267 new patients presenting between August 2010 and April 2021. Patients with a family history of consanguinity were included as cases. The sociodemographic and clinical data were collected using an electronic medical record system. **Results:** Overall, 20,445 (0.73%) new patients were documented to have a family history of consanguinity. The prevalence rates were 4.04% in children (age: <16 years) and 0.21% in adults. The mean age of the patients was 11.87 ± 11.06 years. The majority of the patients were males (56.48%) and students (54.43%) by profession. The majority (93.05%) of the patients were in the 0–30-years age bracket, with over half of them (53.71%) presenting in the first decade of life. A significant number of patients were from higher socioeconomic status (73.48%) and the rural region (47.62%). The most common degree of consanguinity documented was second degree (3.95%). The most common ocular disorders associated with a high proportion of consanguinity were congenital hereditary endothelial dystrophy (CHED) (100%), corneal macular dystrophy (83.78%), xeroderma pigmentosum (80.95%), and ocular albinism (73.59%). A tenth of the patients (9.8%) reported a similar history of ocular disorders among the family members and more commonly among the siblings (70.4%). **Conclusion:** Consanguineous marriages are not uncommon in India. They cause ocular disorders that cause visual impairment in a significant majority of those affected in their early decades of life. Genetic counseling plays a role in prevention.

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Consanguinity refers to the interbreeding in between couples who share a common ancestor. The risk of ocular manifestation increases due to the inheritance of autosomal recessives genes in the event of both parents having a similar abnormal identical gene.[1] The prevalence of consanguineous marriages varies from community to community, constituting 20%–60% of the population of North Africa, Middle East, West Asia, and south India.[2] Sharma *et al*.[3] reported that the prevalence rate of different types of consanguineous marriage is 9.9% in India. Kemmanu *et al*.[4] found that the risk of diseases with potent genetic etiology increases by 2.5% in children having consanguineous parents than in the non-consanguineous marriage. A study conducted by Nirmalan *et al*.[5] in Andhra Pradesh found that 26.7% of all screened subjects had a consanguineous parent. A hospital-based study in south India found that 28.8% of the patients who had a history of consanguinity had ocular genetic disorders. The most common ocular disorders due to consanguineous marriages were retinitis pigmentosa, congenital cataract, oculocutaneous albinism, and retinal dystrophies.[6] Genetic counseling is necessary for preventing or reducing genetic disorders.[7] Most of the studies report that the prevalence of consanguinity is more in rural than in urban areas due to the factors of high illiteracy rate, lack of awareness, and socioeconomic status. There is a need to increase awareness about the consequences of consanguineous marriages and stressing the importance of genetic testing and counselling. There is paucity in the literature on distribution of ocular disorders in patients with a history of consanguinity in India. The purpose of the study is to present the sociodemographic and ocular profile of patients with a history of consanguinity at a large multi-tier ophthalmology network in India by using electronic medical record-driven big data analytics.

Methods

Study Design, Period, and Approval: This cross-sectional observational hospital-based study included all patients presenting between August 2010 and April 2021 to an ophthalmology network spread across four adjacent neighboring states (Telangana, Andhra Pradesh, Odisha, and Karnataka) of India.[8] A standard consent form for electronic data sharing

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was filled by the patient or the parents or guardians of the patient at the time of registration. None of the data that were used for analysis had identifiable parameters of the patient. The study adhered to the Declaration of Helsinki and was approved by the institute's ethics committee. The clinical data of each patient who underwent a comprehensive ophthalmic examination using a standardized template was entered into a browser-based electronic medical records system (eyeSmart EMR) by uniformly trained ophthalmic personnel and supervised by an ophthalmologist.[9]

Cases: A total of 2,805,267 new patients of all ages presented to the tertiary and secondary centers of the network during the study period. The eyeSmart EMR was initially screened for patients with a documented positive or negative history of consanguinity either in the chief complaints, personal history, past history, family history, or plan of treatment in their electronic medical record by trained ophthalmic personnel. A total of 57,775 patient records were extracted using these search criteria, and a total of 20,445 patient records were identified with a positive family history of consanguinity and were labeled as cases for further analysis.

Data Retrieval and Processing: The data of 57,775 new patients included in this study were retrieved from the electronic medical record database and segregated in a single Excel sheet. The columns included the data on demographics, clinical history, family history, ocular diagnosis, and plan of treatment and were exported for analysis. The Excel sheet with the required data was then used for analysis using the appropriate statistical software. The ocular disorders with a known genetic pattern of inheritance were classified, and the proportion of patients with a positive or negative family history of consanguinity were segregated. Family history of similar ocular disorders documented in the case history was used for categorization into presence of the disease among a sibling, parent, relative, or grandparent. Genetic counseling was offered to the patients where feasible by an onsite qualified genetic counselor. Standardized definitions were used for occupation, socioeconomic status, and geographic categorization.[10] The states of India were categorized into North, East, West, South, Central, and North-East based on the National Family and Health Surveys.[11] The visual acuity was classified according to the WHO guidelines.[12]

Statistical Analysis: Descriptive statistics using mean ± standard deviation and median with interquartile range (IQR) were used to elucidate the demographic data. Chi-square test (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) was used for univariate analysis to detect significant differences in the distribution of demographics features between patients with a family history of consanguinity and the overall population.

Results

Prevalence: Of the 2,805,267 new patients who presented across the eye care network during the study period, 20,445 patients had a family history of consanguinity, translating into a prevalence rate of 0.73% (95%CI: ± 0.0073%) or 7,288/million population.

Age: The mean age of the patients with a family history of consanguinity was 11.87 ± 11.06 years, while the median age was 10 (IQR: 4–16) years. The overall prevalence was 4.04% (15,401/381,254) in children (≤16 years) and 0.21% (5,044/2,424,013) in adults (>16 years). The frequency distribution of patients was highest between 0 and 10 years of age (53.71%) and 11–20 years of age (28.99%), followed by a gradual decline from 31 to 40 years of age (4.12%) in the subsequent decades thereafter. The decade-wise distribution of the patients is detailed in Fig. 1.

Sex: There were 11,547 (56.48%) male and 8,898 (43.52%) female patients with a family history of consanguinity. The overall prevalence of consanguinity was significantly greater ($P < 0.00001$) in males (0.76%; 11,547/1,511,733) as compared to females (0.69%; 8,898/1,293,534). Among the patients with a history of consanguinity, the mean and median age were 12.32 ± 11.15 and 10 (IQR: 4–17) years for men and 11.28 ± 10.92 and 9 (IQR: 3–16) years for women, respectively. The overall mode was 0 years and was similar for men and women.

Rural-Urban-Metropolitan Distribution: There were 9,735 (47.62%) patients with a family history of consanguinity from rural districts: 8,705 (42.58%) from urban districts and 2,005 (9.81%) from metropolitan regions. The overall prevalence of consanguinity was statistically significant ($P < 0.00001$) in rural community (0.78%; 9,735/1,253,388) as compared to the urban (0.71%; 8,705/1,225,936) or metropolitan community (0.62%; 2,005/325,943).

Geographic Distribution: Of the 20,445 patients, the prevalence of patients with a family history of consanguinity in North India, East India, West India, South India, Central India, and North-East India was 0.91% (52/5,718), 0.12% (752/602,816), 1.49% (1,116/74,741), 0.88% (183,444/2,090,963), 0.79% (166/21,039), and 0.14% (14/9,840), respectively. The state-wise distribution of the patients is detailed in Fig. 2.

Socio-economic Status: There were 5,421 (26.52%) patients with a family history of consanguinity from the lower socioeconomic class: 14,580 (71.31%) from the lower middle class, 357 (1.75%) from the upper-middle class and 87 (0.43%) from the upper class. The overall prevalence of consanguinity was significantly higher ($P < 0.00001$) in the lower socioeconomic strata (0.8%; 5,421/676,294) as compared to higher socioeconomic strata (0.71%; 15,024/2,128,973).

Occupation: Of the 20,445 patients with a family history of consanguinity, 11,128 (54.43%) were students, 1,374 (6.72%) were professionals, 579 (2.83%) were homemakers, 293 (1.43%) were manual laborers, 250 (1.22%) were agriculture-related, and 21 (0.10%) retired from employment. In 5,431 (26.56%), the occupational category was not applicable, and in 1,369 (6.7%) patients, it was not available. The overall prevalence of consanguinity was significantly higher ($P < 0.00001$) in patients who were students (2.38%, 11,128/467,544) in comparison to other professions.

Ocular Disorders: In the 20,445 patients with a family history of consanguinity, the ocular disorders that had a higher proportion of consanguinity were congenital hereditary endothelial dystrophy (CHED) in 109 (100%) patients, corneal macular dystrophy in 31 (83.78%) patients, xeroderma pigmentosum in 34 (80.95%) patients, ocular albinism in 301 (73.59%) patients, and Leber congenital amaurosis (LCA) in 241 (72.16%) patients. The degree of consanguinity where documented was first degree in 230 (1.12%) patients, second

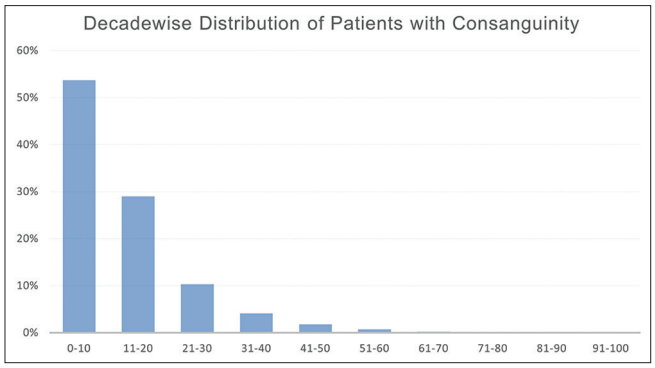

Figure 1: Decade-wise distribution of patients with a family history of consanguinity

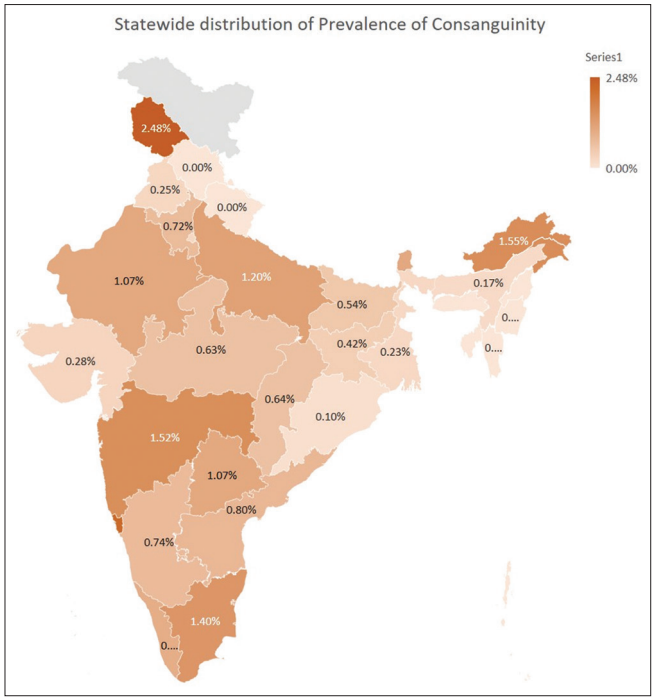

Figure 2: State-wise distribution of patients with a family history of consanguinity

degree in 808 (3.95%) patients, third degree in 675 (3.3%) patients, and not available in 18,732 (91.62%) patients. The detailed list of the distribution of ocular disorders and the proportion of consanguinity in them is described in Table 1.

Family History: The occurrence of the same ocular disorder was documented in the family history in 2005 (9.8%) patients. The ocular disorders that had a higher proportion of family history were xeroderma pigmentosum in 14 (41.18%) patients, congenital ichthyosis in 1 (33.33%) patients, corneal macular dystrophy in 10 (32.26%) patients, vitelliform dystrophy in 2 (28.57%) patients, and aniridia in 7 (23.33%) patients. Overall, a minority of 212 (1.04%) patients attended genetic counseling. The detailed list of the distribution of ocular disorders with a positive family history in patients with consanguinity is described in Table 2.

Presenting Visual Acuity: In the 20,445 patients with a family history of consanguinity, mild or no visual impairment (20/20–20/70) was seen in 8,643 (42.27%) patients, moderate visual impairment (>20/70–20/200) in 2,371 (11.6%) patients, severe visual impairment (>20/200–20/400) in 757 (3.7%) patients, blindness 3 (>20/400–20/1200) in 1,289 (6.3%) patients, blindness 4 (>20/1200 to perception of light) in 583 (2.85%) patients, blindness 5 (no perception of light) in 184 (0.9%) patients, and undetermined or unspecified in 4,172 (20.4%) patients. Fixing and following light was documented in 2,446 (11.96%) patients.

Discussion

This study sought to describe the clinical profile and demographic distribution of ocular disorders in patients with a family history of consanguinity in a large cohort of patients presenting to a multi-tier hospital network in India by using electronic medical records-driven big data analytics. The primary purpose of the study was to determine the relative proportion and demographic profile of the various ocular disorders in patients with a family history of consanguinity documented in the clinical care setup. The overall prevalence of consanguinity was 0.73% of all the patients who presented between 2010 and 2021 (10 + year period). The patients were commonly males and students. The majority presented in the first three decades of life, and the prevalence of consanguinity was higher in the lower socioeconomic strata and in rural communities.

Kemmanu *et al*.[4] determined the association of consanguinity with the occurrence of genetically transmitted ocular disorders by screening 8,553 children (0–15 years) in south India. They found a higher proportion of consanguinity among 34.33% in their cohort, and 75% of the children who were blind and 54.29% of the ocular disorders with a potential genetic etiology were born out of consanguineous marriages. They found a prevalence of 0.41% (95%CI: 0.29–0.57) of ocular diseases (anophthalmos, microphthalmos, pediatric cataract, coloboma, and retinal dystrophy) that could be a product of a consanguineous marriage. Our study also found a similar prevalence of 0.44% (95%CI: ±0.0044%) in our cohort. Most studies in India have shown that early postnatal mortality is higher in the progeny of consanguineous unions due at least in part to the expression of deleterious recessive genes in the offspring. Consanguinity-associated deaths are largely concentrated during the first year of life,[13] and multiple deaths have been reported in specific consanguineous families in proportion to their level of parental genetic relatedness, indicating that these patients are affected quite early in life.[14] In our study, a significant majority of the cohort of patients presented to us in their first three decades of life (93.05%), indicating an early manifestation of the disease due to genetic etiology. The prevalence of patients with consanguinity was highest in the first decade of life (5.14%), followed by the second decade (2.06%). Three-fourth of our patients were children under 16 years of age (75.33%) and had a higher prevalence (4.04%) as compared to adults (0.21%). Our study also saw a higher proportion of the patients who were males (56.48%), which was statistically significant (P =< 0.00001), which may be due to the inheritance pattern of the genetic diseases and increased access to eyecare services as compared to females.

Studies have shown that the prevalence of consanguineous marriages is highest in poor rural communities, which are

Table 1: Overview of ocular disorders with possible genetic etiology in patients with a family history of consanguinity

Ocular Diseases	Male	%	Female	%	Age	SD	Bilateral	%	Unilateral	%	Present*	%	Absent#	%
Congenital Hereditary Endothelial Dystrophy (CHED)	56	51.38%	53	48.62%	9.19	8.87	109	100.00%	0	0.00%	109	100%	0	0.00%
Corneal Macular Dystrophy	19	61.29%	12	38.71%	23.84	9.91	31	100.00%	0	0.00%	31	83.78%	6	16.22%
Xeroderma Pigmentosum	18	52.94%	16	47.06%	15.26	8.99	34	100.00%	0	0.00%	34	80.95%	8	19.05%
Ocular/Oculocutaneous Albinism	168	55.81%	133	44.19%	11.66	9.71	299	99.34%	2	0.66%	301	73.59%	108	26.41%
Leber Congenital Amaurosis	128	53.11%	113	46.89%	8.69	8.57	241	100.00%	0	0.00%	241	72.16%	93	27.84%
Retinitis Pigmentosa	1247	60.89%	801	39.11%	22.94	12.94	2029	99.07%	19	0.93%	2048	69.42%	902	30.58%
Gyrate Atrophy	6	30.00%	14	70.00%	19.70	11.95	18	90.00%	2	10.00%	20	66.67%	10	33.33%
Cone-Rod Dystrophy	184	60.53%	120	39.47%	14.48	9.59	304	100.00%	0	0.00%	304	66.52%	153	33.48%
Nanopthalmos	19	65.52%	10	34.48%	21.03	15.66	26	89.66%	3	10.34%	29	65.91%	15	34.09%
Congenital Stationary Night Blindness	18	78.26%	5	21.74%	12.70	9.10	23	100.00%	0	0.00%	23	65.71%	12	34.29%
Stargardt's Disease	138	62.73%	82	37.27%	17.55	9.29	220	100.00%	0	0.00%	220	63.22%	128	36.78%
Macular Dystrophy Retina	76	58.02%	55	41.98%	17.44	9.91	131	100.00%	0	0.00%	131	62.68%	78	37.32%
Cornea Plana	7	35.00%	13	65.00%	10.60	11.38	17	85.00%	3	15.00%	20	62.50%	12	37.50%
Nystagmus	623	55.13%	507	44.87%	11.87	10.02	1130	100.00%	0	0.00%	1130	57.86%	823	42.14%
Congenital Retinoschisis	27	90.00%	3	10.00%	14.03	7.86	28	93.33%	2	6.67%	30	55.56%	24	44.44%
Megalocornea	16	48.48%	17	51.52%	5.97	7.13	25	75.76%	8	24.24%	33	54.10%	28	45.90%
Familial Exudative Vitreo-retinopathy	78	56.93%	59	43.07%	4.58	6.21	131	95.62%	6	4.38%	137	50.93%	132	49.07%
Optic Nerve Pit	0	0.00%	4	100.00%	18.25	12.37	0	0.00%	4	100.00%	4	50.00%	4	50.00%
Ectodermal Dysplasia	1	100.00%	0	0.00%	29.00	NA	1	100.00%	0	0.00%	1	50.00%	1	50.00%
Congenital/Developmental Cataract	598	55.01%	489	44.99%	10.21	11.06	763	70.19%	324	29.81%	1087	48.44%	1157	51.56%
Sclerocornea	34	47.89%	37	52.11%	5.96	7.72	51	71.83%	20	28.17%	71	48.63%	75	51.37%
Keratoconus	143	61.64%	89	38.36%	16.13	5.78	207	89.22%	25	10.78%	232	46.87%	263	53.13%
Microphthalmos	160	54.42%	134	45.58%	9.42	10.16	162	55.10%	132	44.90%	294	45.51%	352	54.49%
Optic Atrophy	318	60.46%	208	39.54%	13.62	10.46	457	86.88%	69	13.12%	526	45.38%	633	54.62%
Vitelliform Dystrophy	4	57.14%	3	42.86%	18.71	18.95	6	85.71%	1	14.29%	7	43.75%	9	56.25%
Microcornea	99	50.51%	97	49.49%	13.31	11.94	129	65.82%	67	34.18%	196	43.65%	253	56.35%
Congenital Ichthyosis	2	66.67%	1	33.33%	2.67	3.79	3	100.00%	0	0.00%	3	42.86%	4	57.14%
Coloboma	205	52.43%	186	47.57%	13.83	10.21	217	55.50%	174	44.50%	391	40.43%	576	59.57%
Congenital Glaucoma	112	52.09%	103	47.91%	3.58	5.71	178	82.79%	37	17.21%	215	39.89%	324	60.11%
Axenfeld Reiger Syndrome	11	50.00%	11	50.00%	9.64	10.92	19	86.36%	3	13.64%	22	37.93%	36	62.07%
Anophthalmos	18	43.90%	23	56.10%	6.05	9.95	23	56.10%	18	43.90%	41	37.27%	69	62.73%
Squint	843	50.15%	838	49.85%	9.65	8.24	1306	77.69%	375	22.31%	1681	36.62%	2909	63.38%
Peter's Anomaly	25	53.19%	22	46.81%	5.79	8.46	26	55.32%	21	44.68%	47	34.56%	89	65.44%
Optic Nerve Hypoplasia	12	57.14%	9	42.86%	11.05	12.76	12	57.14%	9	42.86%	21	33.33%	42	66.67%
Congenital Ptosis	158	54.67%	131	45.33%	7.23	7.00	91	31.49%	198	68.51%	289	32.11%	611	67.89%
Achromatopsia	8	88.89%	1	11.11%	23.33	8.34	9	100.00%	0	0.00%	9	27.27%	24	72.73%
Aniridia	12	40.00%	18	60.00%	10.53	10.69	27	90.00%	3	10.00%	30	26.79%	82	73.21%
Congenital Nasolacrimal Duct Obstruction	361	50.07%	360	49.93%	1.57	2.42	201	27.88%	520	72.12%	721	21.89%	2572	78.11%
Retinoblastoma	77	55.40%	62	44.60%	3.04	2.77	51	36.69%	88	63.31%	139	21.00%	523	79.00%
Retinopathy of Prematurity	520	53.12%	459	46.88%	0.34	1.24	976	99.69%	3	0.31%	979	19.45%	4055	80.55%

*Family history of consanguinity - Present #Family history of consanguinity - Absent

Table 2: Overview of family history of similar ocular disorders in patients with a history of consanguinity

Ocular Disorders	Family History	%	Sibling	%	Parent	%	Relative	%	Grandparent	%	Consanguinity Cases
Xeroderma Pigmentosum	14	41.18%	10	71.43%	2	14.29%	2	14.29%	0	0.00%	34
Congenital Ichthyosis	1	33.33%	1	100.00%	0	0.00%	0	0.00%	0	0.00%	3
Corneal Macular Dystrophy	10	32.26%	7	70.00%	5	50.00%	2	20.00%	0	0.00%	31
Vitelliform Dystrophy	2	28.57%	2	100.00%	0	0.00%	0	0.00%	0	0.00%	7
Aniridia	7	23.33%	4	57.14%	6	85.71%	0	0.00%	0	0.00%	30
Gyrate Atrophy	4	20.00%	3	75.00%	1	25.00%	1	25.00%	0	0.00%	20
Retinitis Pigmentosa	406	19.82%	303	74.63%	48	11.82%	48	11.82%	35	8.62%	2048
Ocular/Oculocutaneous Albinism	48	15.95%	34	70.83%	6	12.50%	10	20.83%	3	6.25%	301
Congenital Hereditary Endothelial Dystrophy (CHED)	17	15.60%	13	76.47%	2	11.76%	1	5.88%	1	5.88%	109
Leber Congenital Amaurosis	36	14.94%	30	83.33%	3	8.33%	3	8.33%	1	2.78%	241
Axenfeld Reiger Syndrome	3	13.64%	1	33.33%	0	0.00%	2	66.67%	0	0.00%	22
Cone-Rod Dystrophy	41	13.49%	28	68.29%	8	19.51%	5	12.20%	5	12.20%	304
Stargardt's Disease	28	12.73%	23	82.14%	2	7.14%	3	10.71%	3	10.71%	220
Familial Exudative Vitreo-retinopathy	15	10.95%	13	86.67%	1	6.67%	1	6.67%	0	0.00%	137
Nanopthalmos	3	10.34%	3	100.00%	0	0.00%	0	0.00%	0	0.00%	29
Retinoschisis	3	10.00%	2	66.67%	1	33.33%	0	0.00%	0	0.00%	30
Anophthalmos	4	9.76%	3	75.00%	0	0.00%	1	25.00%	0	0.00%	41
Optic Nerve Hypoplasia	2	9.52%	2	100.00%	0	0.00%	0	0.00%	0	0.00%	21
Congenital Stationary Night Blindness	2	8.70%	1	50.00%	1	50.00%	0	0.00%	0	0.00%	23
Nystagmus	95	8.41%	62	65.26%	14	14.74%	12	12.63%	10	10.53%	1130
Congenital/Developmental Cataract	86	7.91%	72	83.72%	19	22.09%	7	8.14%	1	1.16%	1087
Squint	130	7.73%	51	39.23%	44	33.85%	26	20.00%	34	26.15%	1681
Macular Dystrophy Retina	9	6.87%	8	88.89%	1	11.11%	1	11.11%	0	0.00%	131
Microphthalmos	20	6.80%	12	60.00%	4	20.00%	4	20.00%	2	10.00%	294
Coloboma	24	6.14%	10	41.67%	9	37.50%	5	20.83%	1	4.17%	391
Megalocornea	2	6.06%	2	100.00%	0	0.00%	0	0.00%	0	0.00%	33
Sclerocornea	4	5.63%	4	100.00%	0	0.00%	0	0.00%	0	0.00%	71
Microcornea	11	5.61%	4	36.36%	4	36.36%	3	27.27%	0	0.00%	196
Congenital Glaucoma	10	4.65%	8	80.00%	1	10.00%	1	10.00%	0	0.00%	215
Retinoblastoma	6	4.32%	4	66.67%	1	16.67%	1	16.67%	0	0.00%	139
Keratoconus	10	4.31%	10	100.00%	0	0.00%	1	10.00%	0	0.00%	232
Optic Atrophy	22	4.18%	19	86.36%	2	9.09%	2	9.09%	0	0.00%	526
Congenital Ptosis	8	2.77%	4	50.00%	3	37.50%	0	0.00%	1	12.50%	289
Peter's Anomaly	1	2.13%	1	100.00%	0	0.00%	0	0.00%	0	0.00%	47
Retinopathy of Prematurity	12	1.23%	12	100.00%	0	0.00%	0	0.00%	0	0.00%	979
Congenital Nasolacrimal Duct Obstruction	4	0.55%	3	75.00%	1	25.00%	0	0.00%	0	0.00%	721
Achromatopsia	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	9
Optic Nerve Pit	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	4
Cornea Plana	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	20
Ectodermal Dysplasia	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	1

characterized by low levels of maternal education, short birth intervals, early age at marriage and first birth, and longer reproductive spans.[13,15,16] Rao *et al*.[17] had reported that nearly 50% of the marriages in rural areas and 30% in urban areas were consanguineous in India. They also reported a higher rate of 50% among illiterates as per the husband's education. In our study, we found a higher prevalence of consanguinity in patients presenting from rural communities (0.78%) as compared to urban (0.71%) and found a higher prevalence in the lower socioeconomic strata (0.80%).

Kalam *et al*.[11] analyzed data from the 81,781 and 85,851 ever-married women during the National Family and Health Surveys (NFHS) survey periods 1992–1993 (NFHS-1) and 2015–2016 (NFHS-4) in India and found that those living in the southern region had 9.55 times more likelihood in the prevalence of consanguineous marriages as compared to the northern region after controlling for all other confounding variables. The northern region of India (154%) showed a significant increase in consanguineous marriage, whereas eastern (31%), central (2.3%), northeastern (40%), and southern (8%) regions showed a significant decline. In our study, we found a higher prevalence of patients with a family history of consanguinity in western India (1.49%) followed by northern India (0.91%) and southern India (0.88%).

Studies have shown that blindness caused by early-onset retinal dystrophies,[6,18] primary congenital glaucoma,[19] anophthalmos, and microphthalmos[18,20] have been shown to be present at increased prevalence in consanguineous progeny. A study from an ocular genetics practice in south India has reported a consanguinity rate of 28.8% among 2,335 families.[6] The common ocular disorders profiled by them were retinitis pigmentosa (63.9%), Stargardt's disease (4.9%), Ushers syndrome (1.9%), and Oguchi disease (1.3%). In our study, we found a higher proportion of consanguinity among patients diagnosed with congenital hereditary endothelial dystrophy (CHED) (100%), corneal macular dystrophy (83.78%), xeroderma pigmentosum (80.95%), and ocular albinism (73.59%) among others. Certain forms of congenital hereditary endothelial dystrophy with progressive sensorineural deafness (Harboyan syndrome) have reported that more than 50% of the cases were associated with parental consanguinity.[21] Studies have also shown that 91% of CHED and 42% of corneal macular dystrophy requiring keratoplasty in Saudi Arabia were the result of consanguineous marriages.[22] The history of consanguinity in patients with Xeroderma pigmentosum is documented in varying degrees of up to 92.8% from various regions of the world.[23,24] A study on patients with oculocutaneous albinism found a high percentage of consanguineous marriages (73.33%), which is very similar to what we found in our current study (73.59%).[25] Our current study also noted a higher proportion of family history in patients diagnosed with xeroderma pigmentosum (41.18%), congenital ichthyosis in (33.33%), corneal macular dystrophy (32.26%), vitelliform dystrophy (28.57%), and aniridia (23.33%).

Genetic counseling is critical and must be performed in a sensitive, caring, and sensible manner. The consanguineous couples must be referred well before conception, especially when there is a family history of possible autosomal recessive conditions. They should be made to understand that nobody chooses to deliberately pass an illness to their offspring and no one is to be blamed. The limited range of basic carrier tests also limits the potential of premarital screening in these couples. They must be empowered to make intelligent decisions.[26] In our study, a minority of patients (1.04%) attended genetic counseling. This is because of the services being available only at the center of excellence in the network. There is a need for more genetic counselors to be made available for screening and advice for parents and their future offspring at risk.

The strength of the study is the inclusion of a large cohort of patients and the use of a standard protocol across the network of eliciting personal history, family history, and the clinical diagnosis made by a trained ophthalmologist. The insights from this study also add to the paucity of literature on the distribution of ocular disorders in patients with a family history of consanguinity in India. However, there are certain limitations owing to its dependance on including a patient into this cohort only if the history of consanguinity was asked and documented by the caregiver. The order of consanguinity was also not documented in a significant number of patients and this gives us the opportunity to modify the history forms in the electronic medical records for a more structured capturing of the information about consanguinity prospectively.

The current study brings to light the burden of ocular disorders in patients with a family history of consanguinity. It clearly shows the affliction of the diseases in the younger population and the prevalence of similar ocular diseases among siblings due to the genetic nature of the inheritance pattern. There is a need for all the stakeholders involved, including the healthcare providers, government agencies, and the society at large, to highlight the dangers of consanguineous marriages to prevent both the loss of life and vision in the affected individuals. While these practices are rooted in age-old traditions, surveys show a declining trend in India, which is a welcome sign. The focus on literacy, use of public campaigns, provision of educational materials, and genetic counseling services will go a long way in increasing the awareness among the general public, thereby contributing to a change in the mindset of the people towards consanguineous marriages.

Conclusion

In conclusion, this study aimed to describe the epidemiology and clinical presentation of ocular disorders in patients with a family history of consanguinity in 2.8 million new patients presenting to a multi-tier ophthalmology hospital network in India. The findings show that patients with a family history of consanguinity are more commonly males. It is more prevalent in the lower socioeconomic strata and the rural geography. Consanguineous marriages are not uncommon in India. They cause ocular disorders that cause visual impairment in a significant majority of those affected in their early decades of life. Genetic counseling has a role to play in increasing awareness about the potential consequences of consanguinity.

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Conflicts of interest

There are no conflicts of interest.

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