Section: Ophthalmology

Original Research Article

STUDY ON VARIOUS OCULAR CONGENITAL ANOMALIES AND ITS ASSOCIATION WITH CONSANGUINEOUS MARRIAGE

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ABSTRACT

Background: Congenital ocular anomalies contribute to a major portion of childhood blindness. Consanguineous marriages are not uncommon in India. They cause various congenital anomalies in a foetus. They also cause Ocular disorders that cause visual impairment in a significant majority of those affected in their early decades of life. The purpose of the study is to describe the distribution of congenital ocular disorders in patients and its association with consanguinity.

Materials and Methods: This cross-sectional study includes 45 patients - children in the age group of 0- 15yr with various congenital ocular anomalies. History of any significant antenatal events like prevailing chronic disease, infectious diseases during the antepartum period, History of intake of toxic substances or medications (ocular teratogens) were enquired. Thorough clinical history was obtained and comprehensive ocular examination was done in each case.

Results: Out of 45 children the most common ocular congenital anomaly was Retinitis Pigmentosa, with a frequency of 8 cases (17.8%), followed by Congenital ptosis with 7 cases (15.6%) and Congenital cataract with 5 cases (11.1%). Consanguinity was present in 24 cases (53.3%) and absent in 21 cases (46.7%). The p-value for the association between consanguinity and ocular congenital anomalies was 0.016, which is statistically significant at a 5% level of significance. Among the 24 cases with consanguineous parents, 12 cases (50%) had 2nd-degree consanguinity, 11 cases (45.8%) had 3rd-degree consanguinity, and 1 case (4.2%) had 4th-degree consanguinity. For Retinitis Pigmentosa, consanguinity was present in 5 cases (62.5%) and absent in 3 cases (37.5%). The p-value was 0.001, indicating a highly significant association between consanguinity and Retinitis Pigmentosa. For Congenital cataract, consanguinity was present in 4 cases (80%) and absent in 1 case (20%). The p-value was 0.001, indicating a highly significant association between consanguinity and Congenital cataract.

Conclusion: The prevalence of congenital anomalies were mostly high in consanguineous marriages compared to non-consanguineous marriages. 2nd and 3rd degree marriages being the most common. Premarital genetic counselling prevents most of the congenital ocular malformations in the children.

Keywords: Congenital ocular anomalies, Consanguineous marriages, degree of consanguinity.

INTRODUCTION

Congenital eye diseases are an important cause of childhood blindness.[1] It is caused due to defective development of eye tissue during the intrauterine life. It can present in isolation or in combination with other anomalies as a part of a syndrome. Congenital ocular anomalies are the result of

defective development of ocular tissues during the intrauterine life, which can result from adverse genetic effects, environmental factors, any significant antenatal events like prevailing chronic disease, infectious diseases (Toxoplasma, Rubella, Cytomegalovirus, and Herpes) during the antenatal period, teratogens, or chromosomal anomalies in the developing embryo. Maternal malnourishment also attributes to the ocular defects. It is reported that severe vitamin A deficiencies can cause Anophthalmos in a foetus.[2]Lack of awareness of the effect of certain drugs, (both therapeutic and recreational) still results in foetal malformations. A study showed, Among 50 children whose mothers had consumed thalidomide during pregnancy, A significant number of thalidomide children had ocular motility disorders such as Duane's retraction syndrome.[3]Distinct congenital malformations, including several ocular defects, have been well described as fetal anticonvulsant syndrome. This condition was observed in newborns whose mothers were on anticonvulsant therapy. Around 16.7% of total childhood blindness is caused by congenital ocular anomalies like anophthalmos, microphthalmos, and coloboma.[5]

Consanguineous marriages describe unions between couples who share at least one common ancestor. Children born out of consanguineous unions may be at increased risk of acquiring genetic disorders because of the expression of autosomal recessive gene mutations inherited from a common ancestor in a homozygous state.[6]

Consanguinity is prevalent in many Middle Eastern and Arab cultures and societies.[7] Consanguineous marriages are performed in the southern Indian states of Tamil Nadu, Karnataka, and Andhra Pradesh.[8] First-cousin marriages (3rd degree consanguinity) and uncle-niece (1st degree unions consanguinity) are common.[9]

MATERIAL AND METHODS

Design: Hospital based cross sectional study performed in a tertiary health centre of Karnataka.

Inclusion Criteria: Children with ocular congenital anomalies in the age group of 0-15yrs.

Exclusion Criteria: Children with ocular anomalies due to birth trauma.

Children with developmental ocular anomalies.

Data Collection: The study adhered to the basic tenets of the Declaration of Helsinki. Institutional ethical committee clearance was obtained before the start of the study. This is a cross sectional study conducted in a medical college and hospital in south India. Informed consent was obtained from each patient (parent accompanying the child) before enrolling in the study. Thorough clinical history was obtained and comprehensive ocular examination was done in each case. Data was collected by interviewing the mother or adult accompanying the child. History of any significant antenatal events like prevailing chronic disease, infectious diseases (Toxoplasma, Rubella Cytomegalovirus and Herpes) during the antepartum period, History of Intake of toxic substances or medications (ocular teratogens) was enquired.Ex - Foetal alcohol syndrome causes microphthalmia, short palpebral fissures. Cocaine causes optic nerve abnormalities, delayed visual maturation. History of radiation exposure, etc. was obtained. History of any birth trauma, History of consanguinity in the family, similar ocular anomalies in the siblings and family and History of any chronic childhood infections were obtained.

We have classified degrees of consanguinity according to the NHS National Genetics and Genomics Education Centre through their website (www.geneticseduction.nhs.uk).[10]

First degree:Marriage with Parent, Child, or Sibling., Half of the genes in a person are inherited.

Second degree:Marriage with Aunt/Uncle, Nephew/ Niece, Grandparent/ Grandchildren. Shares one-quarter proportion of genes.

Third degree: Marriage with First Cousins. one-eighth proportion of genes are shared.

Figure 1: 8yr old boy with bilateral congenital ptosis

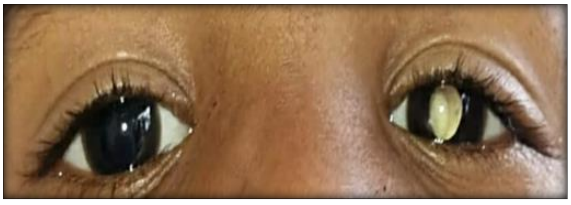

Figure 2: 3yr old boy with unilateral retinoblastoma

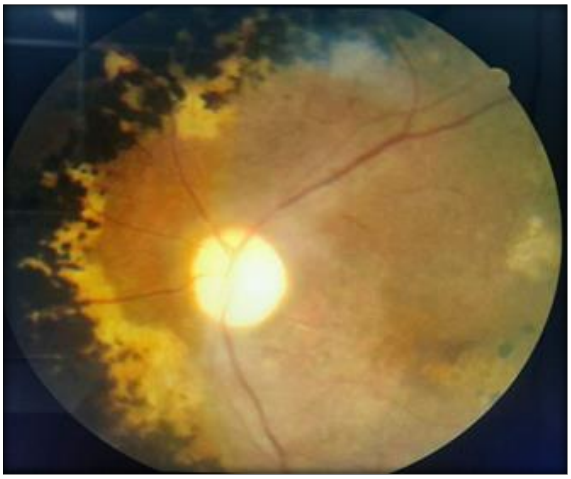

Figure 3: Retinitis Pigmentosa

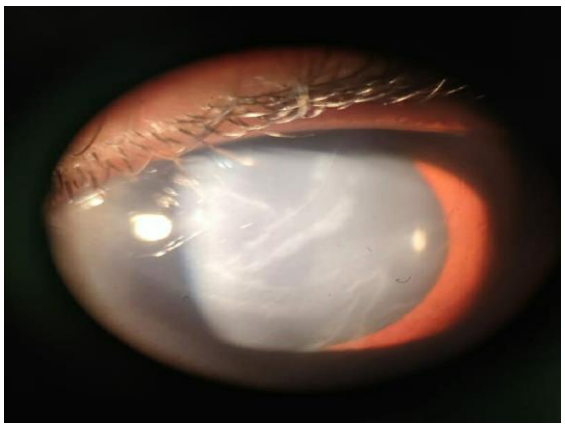

Fig 4: Haab's striae in congenital glaucoma

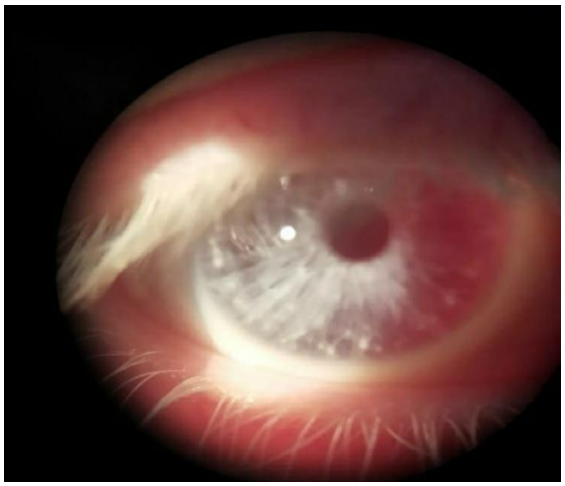

Fig 5: Ocular albinism

Statistical Analysis: The data were analyzed using descriptive statistics, Fisher's exact test, and Chi-square test. Frequencies and percentages were used to summarize the distribution of variables. Fisher's exact test was used to evaluate the association between consanguinity and ocular congenital anomalies, gender and the distribution of anomalies, and consanguinity and the three most common anomalies. The Chi-square test was used to assess the distribution of anomalies across age groups and the association between age group and consanguinity. The level of statistical significance was set at 0.05

RESULTS

Table 1: Frequency distribution of various ocular congenital anomalies

The most common ocular congenital anomaly in the study was Retinitis Pigmentosa, with a frequency of 8 cases (17.8%), followed by Congenital ptosis with 7 cases (15.6%) and Congenital cataract with 5 cases (11.1%). Microcornea was observed in 4 cases (8.9%), while Retinal coloboma, Iris coloboma, and Congenital NLDO each had 3 cases (6.7%). Retinochoroidal coloboma, Macular dystrophy, Blepharophimosis syndrome, and Retinoblastoma each had 2 cases (4.4%). The least common anomalies were Ocular albinism, Anophthalmos, Nystagmus with cataract, Stargardt disease, Atypical retinitis pigmentosa, Congenital glaucoma, and Congenital lid anomaly, each with 1 case (2.2%). The total number of cases in the study was 45.

Table 2: Age distribution of patients with ocular congenital anomalies

The majority of patients with ocular congenital anomalies were in the age group of 5-10 years, with 16 cases (35.6%). The 1-5 years age group had 11 cases (24.4%), followed by the 0-1 year age group with 10 cases (22.2%). The least number of cases were in the 10-15 years age group, with 8 cases (17.8%). The total number of cases was 45.

Table 3: Gender distribution of patients with ocular congenital anomalies

There was a slight male preponderance in the study, with 26 cases (57.8%) being male and 19 cases (42.2%) being female. The total number of cases was 45.

Table 4: Association between consanguinity and ocular congenital anomalies

Consanguinity was present in 24 cases (53.3%) and absent in 21 cases (46.7%). The p-value for the association between consanguinity and ocular congenital anomalies was 0.016, which is statistically significant at a 5% level of significance. This suggests that there is a significant association between consanguinity and the presence of ocular congenital anomalies.

Table 5: Degree of consanguinity among patients with ocular congenital anomalies

Among the 24 cases with consanguineous parents, 12 cases (50%) had 2nd-degree consanguinity, 11 cases (45.8%) had 3rd-degree consanguinity, and 1 case (4.2%) had 4th-degree consanguinity.

Table 6: Frequency of similar complaints in the family among patients with ocular congenital anomalies

Similar complaints in the family were present in 7 cases (15.6%) and absent in 38 cases (84.4%). The total number of cases was 45.

Table 7: Distribution of ocular congenital anomalies by age group

Retinitis Pigmentosa was most common in the 10-15 years age group (50%), while Congenital cataract was most common in the 0-1 year age group (40%). Congenital ptosis was equally distributed in the 1-5 years and 5-10 years age groups (18.2% and 18.8%, respectively). Congenital NLDO was only observed in the 0-1 year age group (30%). The distribution of other anomalies varied across age groups.

Table 8: Distribution of ocular congenital anomalies by gender

The distribution of ocular congenital anomalies was not significantly different between males and females. The p-values for the association between gender and each anomaly were greater than 0.05, indicating no statistically significant association.

Table 9: Distribution of consanguinity by age group

The highest percentage of consanguinity was observed in the 0-1 year age group (70%), followed by the 5-10 years age group (56.3%). The lowest percentage was in the 10-15 years age group (37.5%). However, the p-value for the association between age group and consanguinity was 0.4531, which is not statistically significant at a 5% level of significance.

Table 10: Association between consanguinity and the three most common ocular congenital anomalies

For Retinitis Pigmentosa, consanguinity was present in 5 cases (62.5%) and absent in 3 cases (37.5%). The p-value was 0.001, indicating a highly significant association between consanguinity and Retinitis Pigmentosa.

For Congenital ptosis, consanguinity was present in 4 cases (57.1%) and absent in 3 cases (42.9%). The p-value was 0.037, suggesting a significant association between consanguinity and Congenital ptosis at a 5% level of significance.

For Congenital cataract, consanguinity was present in 4 cases (80%) and absent in 1 case (20%). The p-value was 0.001, indicating a highly significant association between consanguinity and Congenital cataract.

Summary

The study analyzed 45 cases of ocular congenital anomalies, with Retinitis Pigmentosa, Congenital ptosis, and Congenital cataract being the most common. The majority of patients were in the 5-10 years age group, and there was a slight male preponderance. Consanguinity was present in 53.3% of cases, with a significant association between consanguinity and ocular congenital anomalies (p=0.016). The most common degree of consanguinity was 2nd-degree (50%). Similar complaints in the family were present in 15.6% of cases. The distribution of anomalies varied across age groups, but no significant association was found between gender and the distribution of anomalies. Consanguinity was highly significantly associated with Retinitis Pigmentosa, Congenital ptosis, and Congenital cataract (p≤0.037).

Table 1: Frequency distribution of various ocular congenital anomalies

Ocular Congenital Anomaly	Frequency (n)	Percentage (%)
Retinitis Pigmentosa	8	17.8
Congenital ptosis	7	15.6
Congenital cataract	5	11.1
Microcornea	4	8.9
Retinal coloboma	3	6.7
Iris coloboma	3	6.7
Congenital NLDO	3	6.7
Retinochoroidalcoloboma	2	4.4
Macular dystrophy	2	4.4
Blepharophimosis syndrome	2	4.4
Retinoblastoma	2	4.4
Ocular albinism	1	2.2
Anophthalmos	1	2.2
Nystagmus with cataract	1	2.2
Stargardt disease	1	2.2
Atypical retinitis pigmentosa	1	2.2
Congenital glaucoma	1	2.2
Congenital lid anomaly	1	2.2
Total	45	100

Table 2: Age distribution of patients with ocular congenital anomalies

Age Group	Frequency (n)	Percentage (%)
0-1 year	10	22.2
1-5 years	11	24.4
5-10 years	16	35.6
10-15 years	8	17.8
Total	45	100

Table 3: Gender distribution of patients with ocular congenital anomalies

Gender	Frequency (n)	Percentage (%)
Male	26	57.8
Female	19	42.2
Total	45	100

Table 4: Association between consanguinity and ocular congenital anomalies

Consanguinity	Ocular Congenital Anomalies			p-value
	Present	Absent	Total	
Present	24 (53.3%)	0 (0%)	24 (53.3%)	0.016
Absent	21 (46.7%)	0 (0%)	21 (46.7%)	
Total	45 (100%)	0 (0%)	45 (100%)	

Table 5: Degree of consanguinity among patients with ocular congenital anomalies

Degree of Consanguinity	Frequency (n)	Percentage (%)
2nd degree	12	50.0
3rd degree	11	45.8
4th degree	1	4.2
Total	24	100

Table 6: Frequency of similar complaints in the family among patients with ocular congenital anomalies

Similar Complaints in Family	Frequency (n)	Percentage (%)
Present	7	15.6
Absent	38	84.4
Total	45	100

Table 7: Distribution of ocular congenital anomalies by age group

Ocular Congenital Anomaly	0-1 year	1-5 years	5-10 years	10-15 years	Total
Retinitis Pigmentosa	0 (0%)	1 (9.1%)	3 (18.8%)	4 (50%)	8 (17.8%)
Congenital ptosis	0 (0%)	2 (18.2%)	3 (18.8%)	2 (25%)	7 (15.6%)
Congenital cataract	4 (40%)	0 (0%)	1 (6.3%)	0 (0%)	5 (11.1%)
Microcornea	0 (0%)	1 (9.1%)	2 (12.5%)	1 (12.5%)	4 (8.9%)
Retinal coloboma	0 (0%)	1 (9.1%)	2 (12.5%)	0 (0%)	3 (6.7%)
Iris coloboma	0 (0%)	1 (9.1%)	1 (6.3%)	1 (12.5%)	3 (6.7%)
Congenital NLDO	3 (30%)	0 (0%)	0 (0%)	0 (0%)	3 (6.7%)
Retinochoroidalcoloboma	0 (0%)	1 (9.1%)	1 (6.3%)	0 (0%)	2 (4.4%)
Macular dystrophy	0 (0%)	1 (9.1%)	1 (6.3%)	0 (0%)	2 (4.4%)
Blepharophimosis syndrome	0 (0%)	1 (9.1%)	1 (6.3%)	0 (0%)	2 (4.4%)
Retinoblastoma	1 (10%)	1 (9.1%)	0 (0%)	0 (0%)	2 (4.4%)
Other anomalies	2 (20%)	1 (9.1%)	1 (6.3%)	0 (0%)	4 (8.9%)
Total	10 (100%)	11 (100%)	16 (100%)	8 (100%)	45 (100%)

Table 8: Distribution of ocular congenital anomalies by gender

Ocular Congenital Anomaly	Male	Female	Total	p-value
Retinitis Pigmentosa	5 (19.2%)	3 (15.8%)	8 (17.8%)	1.0000
Congenital ptosis	5 (19.2%)	2 (10.5%)	7 (15.6%)	0.6851
Congenital cataract	3 (11.5%)	2 (10.5%)	5 (11.1%)	1.0000
Microcornea	3 (11.5%)	1 (5.3%)	4 (8.9%)	0.6269
Retinal coloboma	2 (7.7%)	1 (5.3%)	3 (6.7%)	1.0000
Iris coloboma	1 (3.8%)	2 (10.5%)	3 (6.7%)	0.5641
Congenital NLDO	1 (3.8%)	2 (10.5%)	3 (6.7%)	0.5641
Retinochoroidalcoloboma	1 (3.8%)	1 (5.3%)	2 (4.4%)	1.0000
Macular dystrophy	1 (3.8%)	1 (5.3%)	2 (4.4%)	1.0000
Blepharophimosis syndrome	1 (3.8%)	1 (5.3%)	2 (4.4%)	1.0000
Retinoblastoma	1 (3.8%)	1 (5.3%)	2 (4.4%)	1.0000
Other anomalies	2 (7.7%)	2 (10.5%)	4 (8.9%)	1.0000
Total	26 (100%)	19 (100%)	45 (100%)	

Table 9: Distribution of consanguinity by age group

Age Group	Consanguinity Present	Consanguinity Absent	Total	p-value
0-1 year	7 (70%)	3 (30%)	10 (100%)	0.4531
1-5 years	5 (45.5%)	6 (54.5%)	11 (100%)	
5-10 years	9 (56.3%)	7 (43.8%)	16 (100%)	
10-15 years	3 (37.5%)	5 (62.5%)	8 (100%)	
Total	24 (53.3%)	21 (46.7%)	45 (100%)	

Table 10: Association between consanguinity and the three most common ocular congenital anomalies

Ocular Congenital Anomaly	Consanguinity Present	Consanguinity Absent	Total	p-value
Retinitis Pigmentosa	5 (62.5%)	3 (37.5%)	8 (100%)	0.001
Congenital ptosis	4 (57.1%)	3 (42.9%)	7 (100%)	0.037
Congenital cataract	4 (80%)	1 (20%)	5 (100%)	0.001

DISCUSSION

Consanguinity is widely practiced in India. Consanguineous marriages have been described as an important factor contributing to increased congenital malformations.[11] Ocular Congenital malformations are one of the major causes of childhood blindness.

In our study most common ocular congenital anomaly was Retinitis Pigmentosa, with a frequency of 8 cases (17.8%), followed by Congenital ptosis with 7 cases (15.6%) and Congenital cataract with 5 cases (11.1%). Microcornea was observed in 4 cases (8.9%), while Retinal coloboma, Iris coloboma, and Congenital NLDO each had 3 cases (6.7%). Consanguinity was present in 24 cases (53.3%) and absent in 21 cases (46.7%). Among the 24 cases

with consanguineous parents, 12 cases (50%) had 2nd-degree consanguinity, 11 cases (45.8%) had 3rd-degree consanguinity indicating 2nd and 3rd degree consanguineous marriage are the most common and widely practiced in the study population. For Retinitis Pigmentosa, consanguinity was present in 5 cases (62.5%) and absent in 3 cases (37.5%). For Congenital cataract, consanguinity was present in 4 cases (80%) and absent in 1 case (20%).

In a study conducted by G. Kumaramanickavel; B. Joseph; A. Vidhya; T. Arokiasamy; N. Shridhara Shetty 28.8% of the patients tested for ophthalmic genetic disorders reported a family history of consanguinity. In the patient group as a whole, the most common form of consanguineous union was between first cousins (n = 367), followed by uncle/niece marriage (n = 177), equivalent to a mean coefficient of inbreeding $\alpha = 0.0202$. Among the consanguineous families, 430 of 673 (63.9%) had retinitis pigmentosa, 167 of these cases were autosomal recessive and 199 were isolated cases.[12]

In VasudhaKemmanu,Pavagada Pediatric Eye Disease Study 2 The prevalence of ocular morbidity was 6.54% and blindness was 0.09%. The percentage of consanguineously married couples in the screened population was 34.33%. Among the blind children, 75% were blind with a disease with potential genetic etiology. Out of that, 66.67% were born out of consanguineous marriage (uncle-niece). Among the children with diseases and with a potential genetic etiology, 54.29% of the children were born out of consanguineous union. Most of these children (71.43%) were born out of uncle-niece marriages.[6]

In Heber Anandan, Lional Raj study, Consanguineous marriage among affected patients was significantly higher in our study group [59%] and represented as 41%, 32%, and 27% in the first cousins, one and a half cousins, and second cousins, respectively. Four types of eye diseases such as squint, glaucoma, cataract, and retinitis pigmentosa were prominently found.[13]

In the present study, Pediatric ocular diseases such as congenital cataract, Ptosis and retinitis pigmentosa, were recorded. Consanguineous marriages are associated with an increased risk for congenital malformations with some increased risk of blindness.

CONCLUSION

Consanguineous marriages are practiced in most parts of India. The offsprings are at risk of having various congenital anomalies due to sharing of a common harmful gene and both the parents passing it on to the child (Autosomal recessive inheritance). For a primary prevention, genetic counseling before marriage must be conducted, not only for consanguineous couples but also for any couples that may have a family history of genetic disorders.

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