WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 8, Issue 6, 1086-1094. Research Article ISSN 2277– 7105

# IRREVERSIBLE BLINDNESS CAUSING HEREDITARY DISEASES

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Article Received on
13 March 2019,
Revised on 03 April 2019,
Accepted on 24 April 2019,
DOI: 10.20959/wjpr20196-14879

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## ABSTRACT

Vision is one of the important sense of human body. There is wide range of eye diseases which may be caused due to many reasons like environmental, hormonal imbalance and genetic factors responsible for some eye diseases. Retinoblastoma, Retinitis Pigmentosa etc. are well known hereditary diseases. Inheritance of many vision disorders and their heterogeneous nature poses a challenge to genetic testing of patients for mutations. In present study some other eye diseases like glaucoma, diabetic retinopathy subjects were selected for knowing their co relation with cytogenetic as well as their hereditary pattern of occurrence in selected subjects & their colour vision is also studied.

**KEYWORDS:** Diabetic Retinopathy, Retinoblastoma, Retinitis Pigmentosa, Amblyopia, Age Related Macular Degeneration, Iridocyclitis.

## INTRODUCTION

Human eye is very sensitive organ of body it has different parts. In internal structure which may be affected and this causes vision loss.[1],[2] Both the mendelian and complex inherited ocular disorders are important causes of blindness in the India. The load of genetic diseases varies widely between different population depending on its structure, reproductive practices and other factors.[4], [10] The burden of genetic diseases is enormous in view of the large size of the population. This is further increased due to the high number of consanguineous marriages in certain communities. Consanguinity is directly linked to a higher risk of autosomal recessive monogenic disorders.[13] It is also probably related to increased frequency of congenital anomalies and a higher prevalence of late onset complex medical diseases involving vision disorders.

In ophthalmology there are vast group of diseases responsible for irreversible blindness in humans. Any structural or numerical change in the diploid number of 46 chromosomes of human may result in physical and developmental problems. A number of chromosomal abnormalities are known to be associated with a specific syndrome.[7] Group includes diseases like Glaucoma, DR, Congenital cataract, Coloboma, Hyper myopia, RP, colour blindness, hyper metropia, Age related macular degeneration, amblyopia and Iridocyclitis were studied. Hereditary pattern and cytogenetic studies are also performed for revealing their connection with chromosomal aberration.[5]

## MATERIAL AND METHODS

1000 subjects were frequently attended on ophthalmology clinic famous as "Aankhon ka aspatal". Further 240 subjects were selected. Subjects who had done eye surgery, any laser treatment or any other infection causes vision impairment not included in present study. Patient data name, age, address, declaration for supporting present study work were documented. Further other investigation charts were fulfilled according research protocol. Ethical approval for present work was taken from ethical committee of Barkatullah university Bhopal.

### Vision analysis test

Vision affected test or clinical vision test was done by Standard Snellen Vision testing chart. This test clarifies subject vision. Subject distance, intermediate, near and peripheral vision loss studied by vision analysis chart.[6],[11]

### Ishihara plate test

Colour blindness tests were performed in the population of Bhopal by using Ishihara Plates, which consist of a series of pictures of coloured spots. A figure is embedded in the picture as number of spots in a slightly different colour and can be seen with normal colour vision, but not with a particular colour defect.[12] The full set of tests has a variety of figure / background colour combination, and enable diagnosis of which particular visual defects is present. Alternative colour vision tests were developed using only symbols for young children or illiterate people, who have not yet learned to use numerals. Relevant information of the respondent was collected in scheduled structured proforma for proper identification.

**Pedigree analysis**

Complete family history of the incidence of the disorder is analysed to determine the pattern of inheritance of the condition. The mode of inheritance and age of onset of progression of disease was calculated and noted by pedigree construction. Pedigree was constructed after discussing about their family history. For the record of family information standard pedigree symbols of genetics were used.

**Blood sample collection**

After clarifying all these parameters only 50 subjects were selected for cytogenetic analysis. Blood sample was collected from selected ones after his/ her informed consent as per the ethical norms 2 ml of heparinized blood sample was withdrawn from subject with a disposable syringe.

**Cytogenetic analysis**

Blood samples were aseptically transferred into a sterile culture bottle with RPMI 1640 medium with fetal bovine serum and phytohaemaglitinin. The cultures were incubated in incubator after washing of sample slides prepared. All the slides were observed under 10x objective of motic Olympus BX60 (phase contrast) microscope to locate the metaphases in them and for the observation of minutes' chromosomal aberrations 100x (oil immersion) objective was used well spread metaphases were analysed per sample and the chromosomal aberrations were recorded in a standard format and classified according to the international nomenclature (ISCN 1995) for the study.

**RESULTS**

240 selected subjects belong to different religions. Highest frequency of Hindu 54.7% and lower Sikh 0.83% religion subjects were found. Other group of religion include Parsi, Jain, Bodh etc. Male frequency was more than female.

**Table: 1: Distribution of subjects on the basis of religion and sex.**

| S. No. | Religion | Total investigate subjects | No. of selected subjects | % | Males | Females |
|---|---|---|---|---|---|---|
| 01. | Hindu | 410 | 130 | 54.7 | 60 | 70 |
| 02. | Muslim | 250 | 71 | 29.58 | 57 | 14 |
| 03. | Sikh | 50 | 02 | 00.83 | 02 | 00 |
| 04. | Christian | 80 | 09 | 03.75 | 04 | 05 |
| 05. | Others | 210 | 28 | 11.67 | 15 | 13 |
| 06. | Total | 1000 | 240 | 100.00 | 138 | 102 |

Vision disorderaffect every age group which is represented in table 2. Affected subject belong to group newly born to 70 years old. Highest frequency 61-70 years' age group was noted in present study.

**Table: 2: Age and Sex Wise Distribution of Selected Subjects.**

| S. No. | Age | Investigated subjects | Selected subjects | % | Selected Males | Selected Females |
|---|---|---|---|---|---|---|
| 01. | Congenital | 10 | 03 | 01.2 | 03 | 00 |
| 02. | Under 18 | 80 | 24 | 11.25 | 11 | 13 |
| 03. | 19-30 | 100 | 20 | 8.33 | 14 | 09 |
| 04. | 31-50 | 150 | 67 | 27.92 | 40 | 23 |
| 05. | 51-60 | 310 | 77 | 31.06 | 38 | 39 |
| 06. | 61-70 | 350 | 49 | 20.42 | 33 | 17 |
| 07. | Total | 1000 | 240 | 100 | 138 | 102 |

Study revealed that glaucoma affected subjects are found to be higher than other genetic disorders. Diabetic retinopathy was second leading cause of irreversible vision loss in this work. Amblyopia and Iridiocyclitis were noted and least causing factors for irreversible vision loss diseases. It is found that subjects age between 51-60 years are severe affected by different disease than any other age group. They have too much difficulty with their vision.

**Table: 3: No. of Subjects Suffering According To Vision Disorder Diseases.**

| S. No. | Disease | Total | % | Male | Female |
|---|---|---|---|---|---|
| 01. | Glaucoma | 95 | 39.58 | 55 | 40 |
| 02. | Diabetic Retinopathy | 55 | 22.92 | 35 | 20 |
| 03. | Congenital Cataract | 20 | 8.33 | 11 | 09 |
| 04. | Coloboma | 15 | 6.25 | 10 | 5 |
| 05. | Hyper Myopia | 11 | 4.58 | 4 | 7 |
| 06. | Retinitis Pigmentosa | 12 | 5.00 | 5 | 7 |
| 07. | Colour Blindness | 10 | 4.17 | 7 | 3 |
| 08. | Hyper Metropia | 07 | 2.92 | 4 | 3 |
| 09. | Age Related Macular Degeneration | 06 | 2.50 | 2 | 4 |
| 10. | Amblyopia | 05 | 2.08 | 3 | 2 |
| 11. | Iridocyclitis | 04 | 1.67 | 2 | 2 |
| 12. | Total | 240 | 100 | 138 | 102 |

This test (V-ADL) was performed for knowing subject vision. They were thoroughly investigated and the results were noted in present table qutionarie. According to medical dictionary terminology distance vision means 20 feet clear vision. We found all affected one had problem with their distance vision they were not able to find things clear far to them.

4 no difficulty, 3 less difficulty, 2 more difficulties, 1 no vision.

| **Table: 4: Distance** | **4** | **3** | **2** | **1** |
|---|---|---|---|---|
| Read street Signs? | 04 | 73 | 118 | 45 |
| Recognize seasonal changes? | 32 | 98 | 65 | 45 |
| Walk alone outside your neighbourhood? | 04 | 73 | 118 | 45 |
| Adjust to dark coming from light? | 02 | 128 | 65 | 45 |
| Adjust to light coming from dark? | 02 | 128 | 65 | 45 |

Intermediate vision refers to focal points that are approximately 16 inches away from eyes. Most of the affected subjects fell in category 2 that means they had more difficulty with distance vision.

| **Table: 5: Intermediate** | **4** | **3** | **2** | **1** |
|---|---|---|---|---|
| Watching television? | 32 | 98 | 65 | 45 |
| Distinguish objects in the room? | 30 | 47 | 118 | 45 |
| Notice steps and use them? | 32 | 77 | 86 | 45 |
| Handle food on your plate? | 35 | 60 | 100 | 45 |
| Pour yourself a drink? | 32 | 45 | 118 | 45 |
| Cut your finger nails? | 04 | 32 | 159 | 45 |

Near vision refers vision near 2 feet from eye distance. Results show that most of the subject came under category 2 means they are near to total vision loss. They were not able to read any document. They can identify money by their analytical nature.

| **Table: 6: Near** | **4** | **3** | **2** | **1** |
|---|---|---|---|---|
| Read news-paper headline? | 00 | 04 | 191 | 45 |
| Write and sign documents? | 00 | 04 | 191 | 45 |
| Can you identify money? | 10 | 35 | 150 | 45 |

Peripheral vision or indirect vision clarified side vision of subject. In present study we found only 2 out of 240 had little bit difficulty with peripheral vision 150 came under category 2 and only 45 had total vision loss.

| **Table: 7: Peripheral** | **4** | **3** | **2** | **1** |
|---|---|---|---|---|
| Notice stationary or moving targets with side vision? | 2 | 43 | 150 | 45 |
| Locate a target from among other targets crowding the field? | 00 | 45 | 150 | 45 |

Those diseases also affect colour vision. 45 subjects were total blind so they were not included in present table. This test was performed on remained 195 subjects 122 had normal colour vision 25 had partial colour blind means they were confused with red and green. 48 were not able to identify any colour they define each picture colourless. Males were found more colour blind than female.

**Table: 8: Distribution of subjects on the basis of sex for Ishihara test.**

| Subjects | Total Studied subjects | Normal subjects | Partial Colour Blind | Total colour blind |
|---|---|---|---|---|
| Total | 195 | 122 | 25 | 48 |
| Male | 127 | 77 | 17 | 33 |
| Female | 68 | 45 | 08 | 15 |

By Analysing Pedigree as explained by subjects about their family history of disease progression explained that about 154 subjects of all mention diseases have autosomal dominant progression of disease, 69 autosomal recessives only 17 had X- linked hereditary pattern. All disease hereditary pattern clarified their hereditary connection. Highest frequency of autosomal dominant disease was noted X-linked manner was less in studied population.

**Table: 9: Inheritance pattern of disease.**

| S. No. | Types | Total | % | Autosomal Dominant | Autosomal Recessive | X- link Manner |
|---|---|---|---|---|---|---|
| 1. | Glaucoma | 95 | 39.58 | 60 | 35 | - |
| 2. | Diabetic retinopathy | 55 | 22.91 | 52 | 03 | - |
| 3. | Congenital cataract | 20 | 08.33 | 15 | 03 | 02 |
| 4. | Coloboma | 15 | 06.25 | 05 | 08 | 02 |
| 5. | Hyper myopia | 11 | 04.58 | 02 | 07 | 02 |
| 6. | Retinitis Pigmentosa | 12 | 05.00 | 09 | 02 | 01 |
| 7. | Colour blindness | 10 | 04.16 | 01 | 00 | 09 |
| 8. | Hyper Metropia | 07 | 02.91 | 03 | 03 | 01 |
| 9. | Age related macular degeneration | 06 | 02.5 | 05 | 01 | 06 |
| 10. | Amblyopia | 05 | 02.08 | 02 | 03 | 00 |
| 11. | Iridocyclitis | 04 | 01.66 | 00 | 04 | 04 |
| | Total | 240 | 100 | 154 | 69 | 17 |

Chromosomal aberration responsible for only hereditary vision loss disease were noted affected one did not had any physical or mental affect problem other than vision disorder. No numerical abnormalities were noted in any affected subject. Any syndromic case was also not found. 9 out of 50 were revealed chromosomal aberration only for vision abnormality.

**Table: 10: Types of chromosomal aberration observed individual disorders.**

| S. No. | Vision | Acrocentric Association | Chromatid Break | Acentric Fragment | Terminal Deletion | Chromosomal gap |
|---|---|---|---|---|---|---|
| 01. | Glaucoma | 1 | 1 | 0 | 0 | 0 |
| 02. | Iridocytin | 1 | 0 | 0 | 0 | 0 |
| 03. | Cong. Cataract | 0 | 1 | 0 | 0 | 0 |
| 04. | Amblyopia | 0 | 0 | 0 | 0 | 0 |
| 05. | Retinitis Pigmentosa | 0 | 0 | 0 | 1 | 0 |
| 06. | Amblyopia with Hyper Metropia | 0 | 0 | 0 | 0 | 1 |
| 07. | Coloboma | 0 | 0 | 0 | 0 | 1 |
| 08. | Myopia with Glaucoma | 0 | 0 | 0 | 0 | 1 |

## DISCUSSION

Inheritance of many vision disorders and their heterogeneous nature passes a challenge to genetic testing of patients for mutations.[6] Present study attempted to highlight the genetic basis of various vision disorders that showed familial aggregation Hereditary vision disorders are heterogeneous group of disorder consisting of phenotypes with both mendelian and complex inheritance. Many vision disorders with complex inheritance pattern demonstrated chromosomal basis.[12],[14]

Subjects with age related cataract were not selected for the present study and only congenital cataracts were documented. Babies of congenital cataract had dense white opacity in pupil due to cataract by birth.[3],[8] A total of 15 had unilateral cataract whereas, five had bilateral cataract. All of them did not have normal vision but after surgery their vision was cured.

In present study, Glaucoma was observed to be leading cause of irreversible blindness after cataract as noted by Sharon (2004) and Quigley (1996). Younger subjects in series demonstrated 6/6 partial vision loss whereas, the old age subjects demonstrated complete vision loss. Distribution of age of glaucoma subjects ranged from 35 to 70 years. Glaucoma subjects with myopic eyes were also observed having 4/60 vision. Retinitis Pigmentosa subjects with hyper myopia and hyper metropia respectively were also found in present study. It was noted that they were not able to do any work without their glasses as their near as well as far vision was not clear. Distribution of age of these subjects ranged between 12 to 52 years.

5(2.08%) subjects who were suffered from Amblyopia with poor vision were selected for present study. Their vision could not be cured than 6/18 by any treatment (Prem, 1983; Donahue, 2005). There were 4 (1.66%) and 6 (2.5%) subjects with Iridocyclitis and ARMD respectively.

Present study attempted to highlight the genetic basis of various vision disorders that showed familial aggregation. Moreover, further exhaustive investigation is required in background of the vast ethnic diversity of Indian population, high inbreeding in some ethnic groups and reports emphasizing the cytogenetic involvement in various vision disorders.

**ACKNOWLEDGEMENT**

I am thankful to Dr. V. K. Nichlanni and his team from "Aankhon ka aspatal" Bhopal for his cooperation and support in studies. Also thankful to patients and their family members for cooperating in research.

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