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Inherited Macular Dystrophies in a Tertiary Care Centre

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ABSTRACT

Background: Inherited macular dystrophies constitute a group of diseases characterized by bilateral central visual loss with symmetrical macular abnormalities usually presenting in the first two decades of life. The aim of this study were to find out the demographic characteristics and disease pattern of inherited retinal dystrophies in subjects attending retina outpatient department in a tertiary care center.

Methods: An observational study among twenty-six participants diagnosed as macular dystrophy visiting a tertiary care centre in Nepal, during January 2018 to June 2018 were included in the study. Detailed history, slit lamp examination, dilated fundus examination, coloured fundus photography, full field electroretinogram, multifocal electroretinogram, automated visual field and colour vision were done.

Results: A total of 52 eyes of 26 subjects were diagnosed with macular dystrophy. The male to female ratio was 1:1. The mean age of presentation was 28.38 years. Most common symptom was blurring of vision seen in 96.15%. The mean visual acuity was 0.67 log mar units in right eye and 0.71 log mar units in the left eye. The most common macular dystrophy was cone dystrophy followed by adult vitelliform macular dystrophy and Stargardts dystrophy.

Conclusions: Cone dystrophy is the most common followed by Stargardt's disease and adult vitelliform macular dystrophy. Most presented in the first two decades of life and the most common presenting symptom was blurring of vision.

Keywords: Adult vitelliform macular dystrophy; best disease; cone dystrophy; macular dystrophy; occult macular dystrophy; stargardt's disease

INTRODUCTION

Inherited macular dystrophies are characterized by bilateral visual loss, symmetrical macular abnormalities, different grades of central visual loss and characteristic macular atrophy.[1] Most manifest within first two decades of life.[2] Rarity, clinical and genetic heterogeneity, unspecific visual complains and mild fundal changes in early stages are challenging features of this disease.[3] Macular dystrophies are confined to macular region during their course of disease and includes Best disease, Cone dystrophy, Stargardt's disease, Adult vitelliform macular dystrophy, Progressive cone dystrophy, North Carolina macular dystrophy and Pattern dystrophy. Certain gene mutations causing hereditary macular dystrophies includeABCA4, ELOVL4, PROML1, VMD2, Peripherin/RDS, TIMP3, XLRS1. No treatment is currently available, however, development of gene therapy offers hope for their treatment in future.[4]The objectives of this study was to find out the demographic characteristics and disease pattern of inherited retinal dystrophies in subjects attending retina outpatient department in tertiary care centre in Nepal.

METHODS

An observational study among twenty-six participants diagnosed as macular dystrophy visiting a tertiary care centre in Nepal, during January 2018 to June 2018 were included in the study. Ethical clearance was

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received from the institutional review committee. We collected a baseline clinical and electrophysiologic characteristics of all patients required for the diagnosis of macular dystrophy. A detailed ophthalmological with systemic history and a comprehensive ophthalmological examination were carried out in all patients. Slit lamp biomicroscopic examination, dilated fundus evaluation and intraocular pressure measurement were carried out in all subjects. Log MAR visual acuity was taken for best corrected visual acuity. Colored fundus photography was done. Full field electroretinogram and multifocal electroretinography incorporating the minimum standards of the International Society for Clinical Electrophysiology of Vision (ISCEV) were performed in all patients .[5,6] Full field electroretinogram included Dark-adapted 0.01 ERG, Dark-adapted 3.0 ERG, Dark-adapted 3.0 oscillatory potentials, Light-adapted 3.0 ERG, Light-adapted 3.0 flicker ERG and Dark adapted 10.0 ERG.[5]The multifocal ERG (mfERG) technique recorded local cone driven 103 responses under light adapted conditions. Visual field assessment was done with Humphrey visual field 10-2 and colour vision was evaluated with Ishihara pseudoisochromatic colour vision chart(38 plates) whenever possible and subjects with very low vision were not subjected to the above mentioned test. All data were entered in Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) Version 20. Descriptive statistics were used to show the demographic characteristics and disease pattern of inherited retinal dystrophies among participants.

RESULTS

A total of 52 eyes of 26 subjects were diagnosed with macular dystrophy. Among them 50% (n=13) were male and 50% % (n= 13) were female. The mean age of presentation was 28.38 years. Baseline characteristics of patients with macular dystrophy is given in Table 1 Family history was positive in four (15.38%) patients. However, none of the subjects gave history of consanguinity in the family. Chi square test did not show any significant association between the duration of disease and visual acuity.

Table 1. Baseline characteristics of patients with macular dystrophy.

	Number	Percentage
Age group (years)		
11-20	9	34.6
21-30	6	23
31-40	5	19.2
41-50	5	19.2
51-60	1	3.9
Duration (years)		
Less than 1	9	34.6
1 to ≤3	4	15.3
>3 to ≤ 5	2	7.69
≥ 5	11	42.3
Chief complains*		
Diminution of vision	25	96.29
Central scotoma	2	7.40
Photophobia	7	25.92
Metamorphopsia	1	3.7
Colour vision defects(red-green)	1	3.7
Asymtomatic	1	3.7

*Multiple response

The visual acuity ranged from 0.0 to 1.77 log mar units in both the eyes. The mean visual acuity was 0.67 log mar units in right eye and 0.71 units in the left eye. Details of the visual acuity is given in Table 2.

Table 2. Visual acuity in patients with macular dystrophy (n=26).

Visual acuity (log MAR)	Frequency (RE)	Percent (RE)	Frequency (LE)	Percent (LE)
0.0- 0.5	9	34.6	9	34.6
0.6-1	15	57.6	14	53.8
>1	2	7.69	3	11.5

The distribution of causes of macular dystrophy is shown in Table 3 and patient characteristics among different diseases is given in Table 4.

Table 3. Distribution of causes of macular dystrophy (n=26).

Diagnosis	Frequency	Percentage
Cone dystrophy	10	38.6
Stargardts disease	5	19.2
Adult vitelliform macular dystrophy	5	19.2
Occult macular dystrophy	4	15.38
Best disease	2	7.69

Table 4. Patient characteristics among different diseases.

Disease	Mean Age (years)	Males n(%)	Female n(%)	Mean visual acuity (RE) (log mar units)	Mean visual acuity (LE) (log mar units)
Cone dystrophy	18.9	5 (50)	5 (50)	0.82	0.89
Adult vitelliform macular dystrophy	45.4	1 (20)	4(80)	0.3	0.14
Best disease	28	2(100)	0	0.4	0.9
Stargardt's disease	32.6	2 (40)	3 (60)	0.8	0.8
Occult macular dystrophy	26	3 (75)	1 (25)	0.77	0.77

In our study 38.46% (n=10) of the patients were diagnosed with Cone dystrophy. All ten patients had chief complaint of blurring of vision and two complained of photophobia. Temporal disc pallor was present in one patient. Macula looked ophthalmoscopically normal in three patients, seven patients had pigmentary changes in macula and one patient had tapetal retinal reflex in one eye and atrophy in other eye. Automated visual field (10-2) showed central scotoma in 40% (n=4). Four patients had diagnosed siblings with Cone dystrophy and the parents were unaffected. Colour vision was defective in all the patients. Multifocal electroretinogram showed decreased response with loss of central peak response and full field electroretinogram showed an abnormal photopic response Figure 1 shows an abnormal photopic response in full field ERG in a patient with Cone dystrophy.

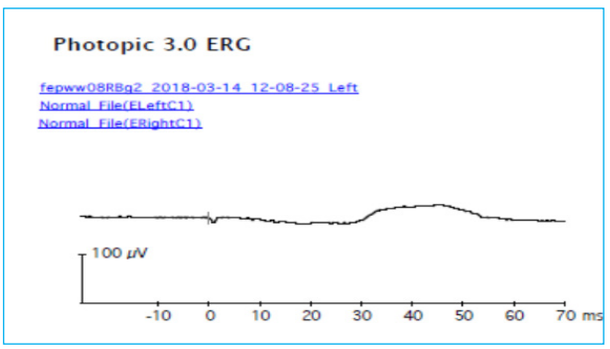

Figure 1. Cone response in full field electroretinogram. Selective abnormalities of photopic component (Photopic 3.0 ERG) in a patient with cone dystrophy.

Five patients (19.2%) presented with adult vitelliform macular dystrophy. Eighty percent presented with blurring of vision. Three had unilateral disease. Three patients underwent full field electroretinogram, and was normal.

Two patients (7.69%) were diagnosed as Best disease. One presented in the vitelloeruptive stage and the other patient presented in the atrophic stage. Electrooculogram in one subject with best disease showed a decreased Arden ratio which was 1.1 in the right eye and 1.4 in the left eye. Figure 2 is a fundus photo of a subject with Best disease.

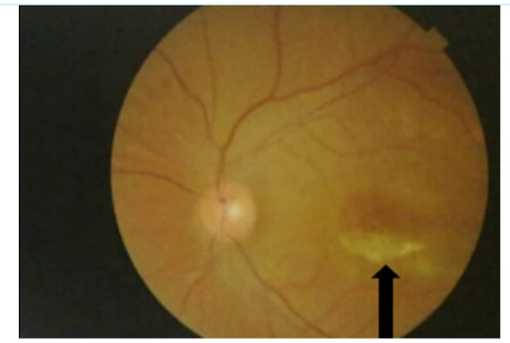

Figure 2. Fundus photo of LE of a patient with Best disease in pseudohypopyon stage where there is yellowish substance seen at the inferior half of the lesion (black arrow).

Five patients (19.2%) presented with Stargardt's disease. Eighty percent presented with blurring of vision. Ophthalmoscopically, two patients had flecks in macula, two showed atrophy and one had beaten bronze appearance. Colour vision was defective in four patients. Three patients had a normal record where as one patient showed a decreased cone response in full field electroretinogram. Automated visual fields in two patients showed central scotoma.

Four patients (15.38%) were diagnosed with occult macular dystrophy. All complained of blurring of vision and had a normal full field electroretinogram with the loss of foveal peak in multifocal electroretinogram.

DISCUSSION

Heriditary macular dystrophies are heterogeneous group of diseases generally presenting in the first two decades of life, affecting the retinal pigment epithelium, photoreceptors and choriocapillaries and characterized by bilateral visual loss and symmetrical abnormalities and atrophy in the macula.[2,7] They can be divided into autosomal dominant, autosomal recessive and X linked inheritance. Diagnosis is done on the basis of visual

acuity , visual field , colour vision, ophthalmoscopic examination, electroretinogram, electrooculogram, fluorescein angiogram, optical coherence tomography and genetic testing.[1]

Progressive cone dystrophies develop in first few decades of life.[8] There is loss of cone function causing bilateral loss of central vision, hemaralopia , colour vision defects, central scotoma, nystagmus and photophobia. Electrophysiological test shows abnormal cone function.[9,10] In our study all the patients with cone dystrophy had colour vision defect but however none of them were aware of colour vision defect, similar to the study by Jacobson DM et al .[8] The symptoms of the disease in our study started from age group as early as 6 years of age till 20 years of age which was a bit different from the age group in a study conducted in a family in Pakistan which was 3-14 years of age.[10]

Best's vitelliform dystrophy (BVD) , a autosomal dominant disease usually presenting in childhood[1,11,12]is characterized by sub RPE and subretinal deposits of yellowish material resembling a egg yolk, abnormal electrooculogram and normal electroretinogram.[13,14] In a study by Fishman et al, there was a significant difference in the vision of 2 eyes of the patients being 2 lines or greater in majority of them and older patient having worse visual acuity and patients younger than 40 years majority had visual acuity of 20/40 or better.[13] In our study too both our patients were less than 40 years and one had visual acuity better than 20/40.

Stargardt's disease is characterized by marked diminution of central vision in the first or second decade of life[15] along with accumulation of lipofusin like substance (yellow white flecks) in retinal pigment epithelium and reduced foveal cone ERG.[16] In a study done by Kenneth G. et al,[15] the commonest presenting symptom was decrease in visual acuity and presented within second to fourth decade of life which matched with the findings of our study where 4 out of 5 patients had presented with decrease in vision and presented between first to fifth decade of life. Colour vision defects (red green defects) were seen in patients with decreased visual acuity and patients with normal colour vision had better visual acuity, the results of which was similar to those in a study done by Vandenbroucke et al.[17]

Occult macular dystrophy is characterized by progressive decline in vision, normal fundus, normal fluorescein angiography, normal full field electroretinogram and abnormal focal macular cone retinogram.[18] A study by Ahn et al discussed the imaging modalities in occult macular dystrophy where the mean age of presentation was 33.5 years where as in our study it was 26 years.[19]

Adult vitelliform macular dystrophy usually develops between fourth and sixth decade of life and is characterized with subretinal deposition of yellowish material in the macula.[20,21] Patients usually presents in the later age group of 30-50 years,[22] the mean age in our study being 45.4 years (41-55 years) . The common symptoms of patients is gradual progressive decrease in vision, metamorphopsia, photophobia, central visual field defects and the disease is very commonly bilateral and symmetrical. Asymmetrical disease is a rare occurrence however in our study 3 out of 5 patients had unilateral disease.

Genetic counselling is important in management of macular dystrophy. No definitive treatment has been identified. Gene therapy and stem cell therapy are being studied. Due to limitation of treatment, low vision aids have a major role in providing visual rehabilitation in these patients. In our study, patients with low vision and who benefited with low vision aids were provided with low vision aids. They were informed about the genetic basis of disease and the need of genetic testing, however we were unable to provide the service due to unavailability of the services. Therefore, macular dystrophies are seen in a substantial proportion of patients presenting with visual loss in younger age group and various multimodal imaging methods and electrophysiological test help us in diagnosing the disease early.

CONCLUSIONS

The most common type of macular dystrophy was cone dystrophy followed by Stargardt's disease and Adult vitelliform macular dystrophy. Most presented in the first two decades of life and the most common presenting symptom was blurring of vision.

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