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ORIGINAL ARTICLE

CLINICO-EPIDEMIOLOGICAL STUDY AND TREATMENT OUTCOME OF EALES' DISEASE AT A TERTIARY EYE CARE HOSPITAL IN EASTERN INDIA

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ABSTRACT: BACKGROUND: Eales' disease is an idiopathic inflammatory venous occlusion that primarily affects the peripheral retina of adults. Retinal changes include perivascular phlebitis, peripheral non-perfusion, and neovascularization. The present-day modalities of treatment are confined to corticosteroids, anti-VEGF (Vasculo-endothelial growth factor) therapy, and photocoagulation with or without anterior retinal cryoablation, and vitrectomy at various stages of the disease process. **AIM:** This study was conducted to study the age and sex distribution along with the mode of presentation of Eales disease. The natural course, aetiopathogenesis, treatment outcome in the study population was also studied. **MATERIAL AND METHODS:** In this descriptive study, 63 eyes of 37 newly diagnosed cases of Eales disease were enrolled. The demographic profile and clinical parameters of each patient were studied with special reference to place of origin, age and sex, mode of presentation, and treatment outcome. All patients underwent complete systemic and ophthalmologic examinations. Study patients were classified according to the stage of their disease and treated accordingly. **RESULTS:** Young males (21-30 years) were mostly affected and 70% had bilateral presentation. 61% presented with symptoms related to posterior segment disease. Recorded best corrected visual acuity were 6/6-6/12 in 44.5%, 6/12-6/60 in 20% and <6/60 in 36.5%. 2 patients were kept on observation, 17 with medical treatment alone, 10 with photocoagulation alone, 3 with photocoagulation and medical treatment and 5 were taken for vitreo-retinal surgery. Good visual recovery was observed in all subgroups at subsequent follow-up visits. **CONCLUSION:** As noted by this study, Eales disease is a disease mostly in the young. These patients can present with no typical symptom or can be asymptomatic. Staging of the disease at presentation is important and correct treatment options should be given in order to achieve good visual outcomes.

KEYWORDS: Eales disease, Perivascular phlebit's, photocoagulatron, Anterior retinal cryoablation.

INTRODUCTION: In 1880 and 1882, Henry Eales, a British Ophthalmologist, described the clinical picture of recurrent retinal hemorrhage in young adults.[1,2] He believed it to be a vasomotor neurosis, and not retinal vasculitis. Wardsworth described the associated signs of retinal inflammation 5 years later.[3] In later years, a number of early researchers, such as Elliot, Kimura et al, and Keith Lyle and Cross, have documented various clinical and pathological features of this inflammatory retinal condition.[4,5,6,7] Eales' disease had been reported from the United Kingdom, the United States, and Canada in the latter half of the nineteenth and early twentieth century. But for unclear reasons, it is now rare in developed countries and is more

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commonly reported in Indian subcontinent.[8,9,10] it is wondered whether this is associated with environmental cleanliness, general nutrition, and health of individuals.

The reported incidence in India is one in 200-250 ophthalmic patients. Eales' disease predominantly affects healthy young adults, mostly male; in the age group of 20–30 years.[9] most symptoms include that of vitreous hemorrhage, such as small specks, floaters, cobwebs, or sudden decrease in visual acuity. Others have mild reduction of vision associated with retinal vasculitis but without vitreous hemorrhage.[10] the three hallmarks of this disease include retinal phlebitis, peripheral non-perfusion (Fig. 1) and retinal neovascularization.[11] (Fig. 2) the aetiopathogenesis of Eales' disease to date has remained controversial and ill-understood. Tuberculosis, hypersensitivity to tuberculo protein and immune-mediated mechanisms have all been proposed as possible etiological factors.[12,13,14,15] the treatment of Eales' disease is symptomatic. It is aimed at reducing retinal perivasculitis and associated vitritis, reducing the risks of vitreous hemorrhage from new vessels on the retina and/or the optic nerve head by retinal ablation, and surgical removal of non-resolving vitreous hemorrhage and/or vitreous membranes. The present-day modalities of treatment are confined to corticosteroids, anti-VEGF therapy, and photocoagulation with or without anterior retinal cryoablation, and vitrectomy at various stages of the disease process.[16,17,18,19]

There has been a lot of research work till now by renowned Indian ophthalmologists in finding out the etiology and pathophysiology of this dreadful disease of the young. But it is still an undiscovered entity in many parts of the country with variations in incidence, type of presentation etc. in relation to geographical distribution. So there was definitely a need to study the natural course of the disease, stage them and treat them accordingly with all newer modalities, recording their visual outcome and comparing the results with other studies done by different investigators.

MATERIAL AND METHODS: The present study was conducted for a period of 2 years from September 2008 to September 2010. In this study 63 eyes of 37 newly diagnosed cases of Eales' disease were enrolled. The demographic profile and clinical parameters of each patient were studied with special reference to place of origin, age and sex, mode of presentation, and treatment outcome. All patients underwent detailed history taking, a comprehensive ophthalmic examination including visual acuity, detailed slit lamp examination, Fundus evaluation by Indirect Ophthalmoscope and Fundus Fluorescein angiography. Special investigations like complete bold count, Erythocyte sedimentation rate, Mantoux test, tests to rule out other similar diseases were done. According to the clinical status patient was given observational, medical or surgical therapy. Patient was evaluated on further follow up at 1 month, 3 months, 6 months and 1 year. All the findings were noted till the last visit. The efficacy of therapy was judged by pre and post treatment visual acuity measurements and the recurrence or non-recurrence of vitreous hemorrhage.

RESULTS AND DISCUSSION: In the present study it is evident that out of 0.65% of patients diagnosed as Periphlebitis Retinae only 0.39% was diagnosed as Eales' disease. The number correlates to other studies due to a relatively good number of attendances of patients. The maximum incidence (56.7%) occurred in the age group of 21-30 years followed by the age group

of 31-40 years (24.3%).86% of cases of Eales' disease are male.70.3% of cases of Eales' disease had bilateral involvement.

This bilateralism may be due to the etiology which is systemic in nature. Comparing the demographic profile of patients in other similar studies as showed in Table 1, it is evident that the incidence is higher in Indian population than other countries and the percentage in the present study correlates to other Indian studies.

It is evident from table2 that (61%) of Eales disease presented with floaters and black spots in the field of vision. 36.5% of patients presented with relatively sudden gross loss of vision, 38.5% of patients suffered from defective vision and 2 patients had come for routine eye examination which revealed inactive vasculitis.

Table 3 shows the clinical types of the cases of Eales disease studied in the present series of 37 cases, 86.4% of cases were of peripheral type which corroborates the work of Pahwa et al.[8] who opined that most cases belong to the peripheral type. 8.1% cases were of mixed type and central Eales' disease (Fig. 3) which is uncommon constitutes only 5.5% of cases in this study similar to Gilbert et al.[20]

It is evident from table 4 that 36.5% eyes presented with vitreous hemorrhage constituting the maximum number of cases followed by ischemic changes (32%) and 27% presenting with active perivasculitis, 2 eyes (3%) presented with inactive vasculitis, 1 eye presented with Tractional Retinal Detachment. (Fig. 4)

The Table 5 shows that maximum cases presented with periphlebitis and sheathing (52) (Similar to Das et al,[11] Atmaca et al,[21] Badrinath et al,[22] followed by neovascularization (40) (Similar to Badrinath et al, Atmaca et al, Das et al, Renie et al.[23]) next to it was dilatation and irregular vessels. There were 11 cases of retinitis proliferans, retinal detachment in 3 cases and 24 cases showed pigmentation in the course or at bifurcation of vessels & circumscribed pigmented areas suggestive of healed chorioretinitis.

The Table 6 shows that 81% patients presenting with Periphlebitis retinae showed a positive Mantoux response but about 59.4% patients with Eales' disease showed a positive Mantoux test. Comparing with similar studies from Indian population, the present study shows a higher percentage of patients with confirmed cases of tuberculosis since the patients come from a poor background living in crowded and unhygienic conditions with exposure to Tubercle bacilli.

The management of Eales' disease depends on the severity of the disease. In the present study we followed the below mentioned staging system given by Biswas et al.[24]

Stage 1- stage of inflammation, amenable to medical therapy, followed by Laser photocoagulation if required. Done only after active inflammation has subsided.

Stage 2- stage of ischemia and neovascularization, which requires observation/laser photocoagulation.

Stage 3- stage of proliferation, which requires laser / pars plana vitrectomy and laser.

Stage 4- stage of complications, requires sophisticated surgical management strategies.

I. In the present study, 2 patients (2 eyes) with inactive vasculitis with good visual acuity (6/6) were kept on observation on a 6 monthly basis for 1year.Vision remained to be 6/6 on subsequent follow-ups.

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II. 23 eyes with fresh vitreous hemorrhage (Visual acuity—Hand movements) with no visible fundus (underlying retina found to be attached by ultrasound) were kept on observation, advised for absolute bed rest with head end elevated and followed up at 4 week intervals.

Out of 23 eyes, 19 eyes showed signs of resolution within 3 months of follow-up(most of the cases showed clearing within 4 weeks) and 4 eyes were categorized as non-resolving vitreous hemorrhage(no clearing of fundus within 3 months). Non-resolving cases were kept for pars plana vitrectomy.

Corticosteroids remain the mainstay of therapy in the active perivasculitis stage of Eales disease. There are no definite guidelines for the dosage of oral corticosteroids in the retinal perivasculitis stage of Eales disease. Dosage must be tailored for each patient on the basis of severity of inflammation (Quadrants of retina involved). In the present study, out of 63 eyes, there were 30eyes with active perivasculitis (17 eyes showing active perivasculitis at presentation and rest of the cases showing vasculitis after clearing of vitreous hemorrhage) for which oral prednisolone 1mg/kg of body weight was given. This was tapered to 10mg per week over 6 to 8 weeks. Some patients also required a maintenance dose of oral prednisolone 15 to 20mg per day for 1 to 2 months. In cases of associated macular edema, periocular depot steroid injection was also added. In cases where periphlebitis and macular edema did not resolve even after oral & periocular steroid injections, Intra-vitreal triamcinolone (IVTA) (4mg in 0.1ml) was given.

Anti-tubercular along with oral corticosteroids was prescribed to 9 newly diagnosed cases of tuberculosis. Anti-tubercular treatment regimen included two drugs (Rifampicin 450 mg and Isonazid 300 mg, once daily x 9 months, Ethambutol 15mg/kg/day once daily and pyrazinamide 25mg/kg/day once daily x 2 months).Visual acuity was recorded prior to and after medical treatment at intervals of 1 month, 3 months, 6 months and 1 year.

Table 7 shows that 24 eyes (80%) showed improvement in vision attaining a final visual acuity of ≥6/12 at the end of 1 year.5 eyes (14.7%) attained a final visual acuity of 6/12-6/60 and only 3% eyes did not show a remarkable improvement in vision. IVTA proved to be useful in cases of inflammation which could not be controlled with oral as well as periocular steroids.

In the present study we categorized the eyes according to the fundus findings and applied different techniques of laser:

Type of finding Type of laser done:

1. Retinal neovascularization Elsewhere FOCAL or DIRECT LASER (NVE).
2. Microaneurysm -do-
3. Arterio-venous shunt -do-
4. Capillary non-perfusion areas SECTORAL SCATTER LASER.
5. New vessels proliferating into FEEDER VESSEL PHC vitreous.
6. Neovascularization on Disc (NVD) PAN-RETINAL/ SCATTER LASER.
7. Branch Retinal Vascular Occlusion -do-
8. Central Retinal Vascular Occlusion -do-

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Successful treatment was defined as:

1. Partial or complete regression of new vessels by Fundus fluorescien angiogram (FFA).
2. Decrease in the number of capillary drop-out areas (by FFA).
3. Improvement in Snellen visual acuity by two lines or stabilization of Best Corrected Visual Acuity (BCVA).

Deterioration in treatment was defined as loss of BCVA two lines on Snellen chart.

In the present study 20 eyes had presented at the stage of ischemia and neovascularization (stage II, III) which were subjected to Laser photocoagulation. Also 6 patients whose inflammation had subsided with medical treatment but later vascular proliferation were seen also subjected to laser treatment. Argon green laser wavelength 514nm was used. From the Table 8, 9 it is evident that vision improved in 12.3% eyes, remained stabilized in 77.4% and deteriorated in 10.3% eyes. These numbers match with that of other studies as shown in Table 10.

In the present study a total of 5 patients were subjected to vitreo-retinal surgery with the following indications:

1. Non –resolving vitreous hemorrhage (>3 months) - 3 eyes.
2. Primary tractional retinal detachment – 1 eye.
3. Post-pan retinal photocoagulation retinal detachment—1 eye.

Visual improvement was seen in 4 eyes following early vitrectomy. During the follow-up period 6/60 or better vision was seen in 2 eyes at 3 months, and 1 eye at 6 months and the other at 1 year. There was recurrence of vitreous hemorrhage at 1 year in one patient (1 eye). Much conclusions could not be drawn from this subset of patients as the number of patients enrolled were very few and for the short follow-up period.

CONCLUSION: Eales' disease, with its characteristic clinical features and Fluorescein angiographic findings, is a specific vitreoretinal disease. The disease can mimic several other ocular and systemic diseases presenting as retinal vasculitis or proliferative vascular retinopathy as we saw in our study where few patients showed positive tests for sickle cell disease, syphilis, toxoplasmosis and leukemia. Young males are most commonly affected. The disease is most commonly bilateral although may present unilaterally. Ultimately the disease becomes bilateral within 2-5 years. Since its original description, many investigators have considered an association with tuberculosis (Hypersensitivity to tuberculoprotein) to be the prime cause of this disease as also the same is revealed by the present study.

Most common presenting symptom includes floaters, black spots in the field of vision followed by mild diminution of vision and sudden gross loss of vision. The disease has got a definite tendency to affect the peripheral veins Interestingly a single case in our study was found to be of central variety where periphlebitis lesions such as tortuousity of veins, exudates, hemorrhage and sheathings situated close to the disc whose margin is also blurred. Most common stage of presentation includes a fresh episode of vitreous hemorrhage or resolving hemorrhage (where patients complain of floaters etc.).

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Although its aetiopathogenesis remains unclear, the management options are quite well established. Systemic corticosteroids have been found to be beneficial in the active perivasculitis stage. IVTA also shows good results where inflammation cannot be controlled with oral/periocular corticosteroids. Photocoagulation is the mainstay of therapy in proliferative stage of the disease. Laser photocoagulation leads to resolution of retinal neovascularization due to its anti-VEGF effect. In cases of gross capillary non-perfusion photocoagulation is suggested.

For NVE and NVD, sectoral scatter photocoagulation and pan retinal photocoagulation, respectively is suggested. Vitrectomy alone or combined with other vitreoretinal surgical procedures is often required. Vitrectomy for non-resolving vitreous hemorrhage done at 3-6 months has better visual outcome than done after 6 months.

Sl. No.	NAME OF STUDY AND GEOGRAPHICAL LOCATION	YEAR	NO. OF EYES AND PATIENTS	INCIDENCE	AGE	SEX	BILATERALITY
1.	J.Biswas et al S.N Chennai, INDIA	2008	222/160		30.50+/-9.47 yrs	Male-89%	59%
2.	Dipankar Das et al North East India	2007	156/100	1 in 65	25yrs (15-55)	Male >female	56%
3.	M. Ishaq et al Rawalpindi, Pakistan	2002	99		28+/-12 yrs	Male>female	NA
4.	Nagpal et al INDIA	1998	1214/800	1 in 57	26.9 yrs	Male>female	>50%
5.	Das et al INDIA	1994		1 in 200-250		Male >female	70-80%
6.	Gadkari SS et al	1992			76%(11-30 yrs)	Male>female	
7.	Namperumalsamy et al	1986			20-30 yrs	Male -70%	70-85%
8.	PRESENT STUDY	2008-09	63/37	1 in 256 (0.39%)	24.8 yrs (15-55)	Male -86%	83.3%

Table 1

Symptoms	No. of eyes	Percentage
Sudden gross loss of vision	23	36.5%
Floaters, Black spots in the field of vision	38	61%
Mild Diminution of vision	24	38.5%
Asymptomatic	2	3%

Table 2

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Types		No. of cases	Percentage
1.	Central	2	5.5
2.	Peripheral	32	86.4
3.	Mixed (both central and peripheral)	3	8.1
Total		**37**	**100**

Table 3

Stage		No. of eyes	Percentage
I.	Stage of Inflammation	17	27
II.	Stage of Ischaemia	20	32
III.	Stage of vitreous hemorrhage & Proliferation	23	36.5
IV.	Stage of Complication	1	1.5
Stage of inactive vasculitis		2	3
Total		**63**	**100**

Table 4

Findings	No. of eyes
Periphlebitis and Sheathing	52
Retinal haemorrhage	12
Retinal edema	12
Dilatation and irregularities of caliber of vessels	26
Neovascularization	40
Proliferation of fibrous bands in the plane of retina into vitreous	11
Vitreous opacities	13
Completely hazy vitreous due to haemorrhage	23
Pigmentation in course or at bifurcation of vessels & circumscribed pigmented areas suggestive of healed chorioretinitis	24
Retinal detachment	1
Disc edema	2
Optic atrophy	2

Table 5

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Cases with tuberculosis	No of cases	Percentage
1. No of cases already diagnosed to be tubercular (Cases receiving antitubercular treatment).	10	27%
2. No of cases diagnosed to have tuberculous focus After examination and investigations.	9	24%
3. Non-tuberculous.	18	49%

Table 6

Sl. No	Treatment modalities	No. of eyes	BCVA at last follow-up of 1 yr.		
			≥6/12	6/12-6/60	<6/60
1.	Oral steroids alone	17	15	2	-
2.	Oral+periocular steroids	4	3	1	-
3.	Intravitreal triamcinolone(in resistant cases of subgroup 2)	4	3	1	-
4.	Oral steroids+ATT	5	3	1	1
	Total	**30**	**24**	**5**	**1**

Table 7

Visual acuity	Pre treatment	Post treatment
<1 m CF	1(4.5%)	1(4.6%)
1-5 m CF	2(8.6%)	1(3.9%)
6/12-6/60	6(23.4%)	8(29.4%)
6/6-6/9	16(63.5%)	16(62.1%)

Table 8

Visual acuity	No. of eyes	%
Improved	3	12.3%
Maintained	20	77.4%
Worsened	3	10.3%

Table 9

Sl. No	Name of study	Improvement in vision	Stabilization	Deterioration
1.	Spitznas et al(1975)	13%	70% in one series,91% in another series	17%
2.	Meyer-Schwickerath et al	10%	87%	3%
3.	Atmaica et al	11%	75%	14%

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4.	Das et al	20%	80%	-
5	Agarwal et al	-	100%	-
6.	**Present study**	**12.3%**	**77.4%**	**10.3%**

Table 10

Figure 1: Color fundus photograph showing obliterated blood vessels as white lines (arrows) surrounded by retinal hemorrhages and corresponding Fluorescein angiogram showing areas of capillary non-perfusion (Arrowhead) distal to obliterated vessels.

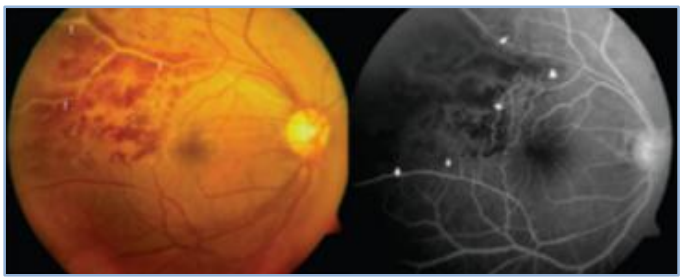

Fig. 1

Figure 2: Color fundus photograph showing tufts of new vessels away from the optic disc.

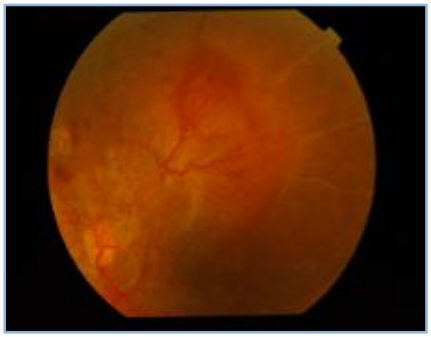

Fig. 2

Figure 3: Central Eales disease in right eye showing massive areas of retinal hemorrhages and periphlebitis at posterior pole, corresponding Fluorescein angiogram showing gross staining of vessels and cystoids macular edema.

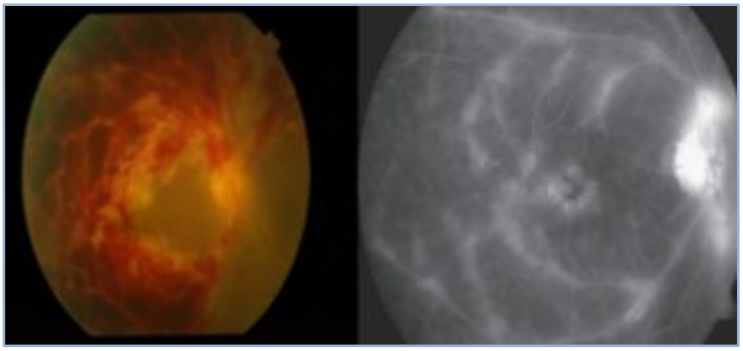

Fig. 3

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Figure 4: Color fundus photograph of right eye showing tractional retinal detachment and associated vitreous hemorrhage.

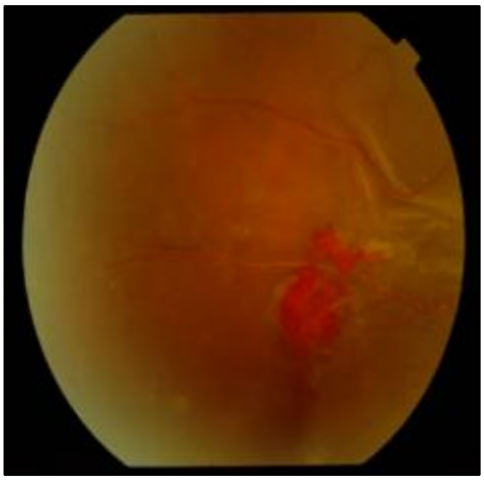

Fig. 4

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