

Study by Fundus Fluorescein Angiography as a Diagnostic Tool in Various Retinal and Choroidal Disorders

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Abstract

Objective: To determine the prevalence and pattern of retinochoroidal pathologies at our tertiary eye care centre in western India.

Method: A hospital based retrospective randomized study was done which included 475 patients who attended the Retina clinic during last one year study period. Detailed history was taken from the patients and a thorough ocular and systemic examination was done. All patients were examined by conventional methods of ophthalmoscopy (direct, indirect and slit lamp examination with +90 D lens) followed by a Fundus fluorescein angiography. Patients were advised necessary ocular and systemic treatment.

Results: 475 cases were analyzed and sub-divided into different categories of Age related macular degeneration (ARMD), Diabetic retinopathy, Hypertensive retinopathy, vascular occlusive disorders, central serous chorioretinopathy (CSCR) and other macular disorders, optic nerve related disorders, vasculitis & other inflammatory disorders. Of total 475 cases, 119 cases were of diabetic retinopathy (25.05%), 76 cases of ARMD (16%), 49 cases of vascular occlusions (10.31%), 45 cases of vasculitis & other related inflammatory disorders (9.47%), 31 cases of optic nerve related disorders (6.52%), and 27 cases of CSCR (5.68%) were studied. On statistical analysis, using chi square test FFA proved to be a far superior diagnostic modality than clinical examination (ophthalmoscopy).

Conclusions: FFA has major role in diagnosing various retinal and choroidal pathologies. It is a superior diagnostic modality to confirm the diagnosis and monitoring of the treatment of retinal vascular, macular disorders, and chorioretinal diseases. It provides definitive diagnosis in CSCR and detects exact leakage points. FFA has a limited role in evaluation of macular dystrophies.

Keywords: Retinal and choroidal pathologies, Macular disorders, ARMD, CSCR

I. Introduction

Fundus fluorescein angiography (FFA) does play a crucial role in our understanding of different disease processes affecting the eye. It involves photographic surveillance of the passage of fluorescein through the retinal and choroidal circulations following intravenous injection^[1]. Earliest description of fluorescein angiography was provided by Chao and Flocks in 1958 by measuring retinal circulation time after injecting trypan blue dye^[2]. It was introduced in clinical use in 1961 by Novotny and Alvis who perfect the photographic study of the human retinal circulation^[3]. For over 30 years, fundus photography and fluorescein angiography have been extremely valuable for expanding our knowledge of anatomy, pathology and pathophysiology of the retina and choroid, and have aided the diagnosis, helps in identifying the cause of the pathology and monitoring of the treatment of retinal vascular, macular disorders, and chorioretinal diseases. The current study was undertaken to evaluate the epidemiology regarding prevalence and pattern of retinal and choroidal disorders from cases underwent FFA at our tertiary eye care centre in western India.

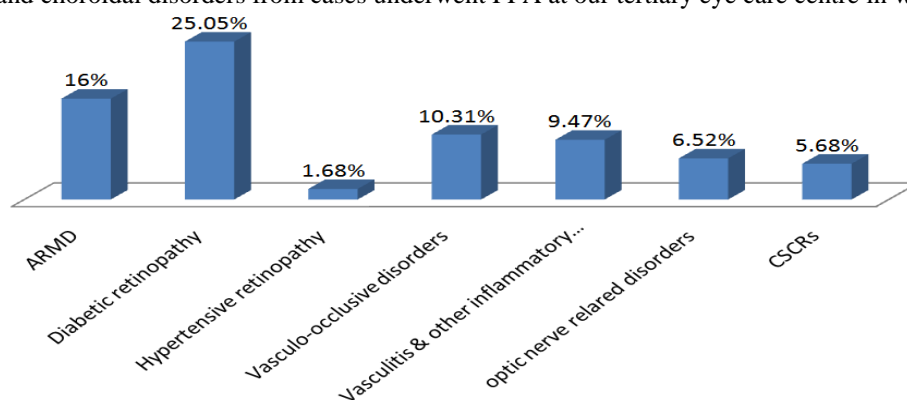


Figure 1: Distribution of cases with different diagnosis studied

II. Material And Methods

This retrospective study was carried out on 475 patients with some retinal and choroidal pathologies, attending the Retina Clinic of our outpatient department of ophthalmology at tertiary eye care centre in western India for fundus fluorescein angiography over a study period in last one year duration .It was carried out after obtaining permission from ethical committee of the Institution and consent from all the patients after explaining condition of the eye, the procedure, purpose and possible side effects of FFA.. Patients with retinal disorders with suspected age related macular degeneration (ARMD), Diabetic retinopathy, Hypertensive retinopathy , vascular occlusive disorders, macular dystrophy and central serous chorioretinopathy (CSCR), vasculitis & other inflammatory disorders optic nerve related disorders were included in the study. Retinal disorders other than the above mentioned, viz., very old, uncompliant patients, pregnant women, and immunocompromised status patients, patients with hypersensitivity to fluorescein dye, renal insufficiency or cardiovascular diseases were excluded. Detailed history was obtained from each patient. Patients were evaluated and investigated by physician to note the presence of any systemic diseases especially to rule out unfitness for the procedure. Patients underwent a detailed clinical examination that included unaided visual acuity and best corrected visual acuity with snellens chart and near vision; pupil size and reactions; anterior segment examination and slit lamp biomicroscopy; measuring intraocular pressure (IOP) using Goldmann applanation tonometer. A thorough, careful and detailed examination of the fundus was done initially by a direct ophthalmoscope and subsequently with an indirect ophthalmoscope and slit lamp examination with +90 D lens giving special attention to macula.



Figure 2a: Clinical picture of wet ARMD

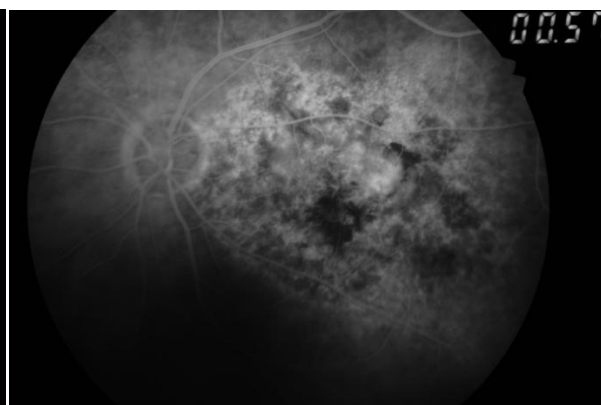


Figure 2b: FFA picture of wet ARMD showing CNVM



Figure 3a: Clinical picture of CSME

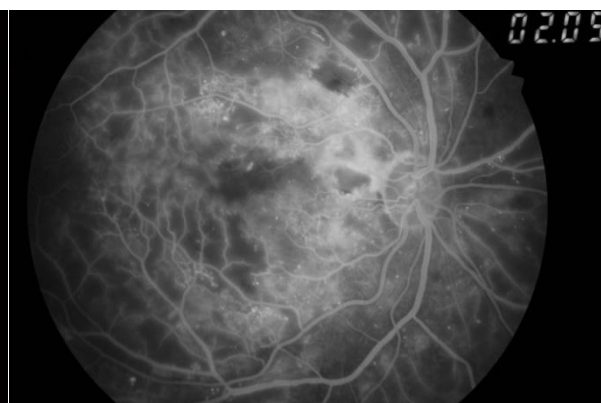


Figure 3b: FFA picture of CSME

III. Inclusion Criteria

The criterias for inclusion in our study were all patients clinically diagnosed to have retinal / choroidal pathology underwent fundus fluorescein angiography of all age group patients. Both the eyes of all bilateral patients and involved eye of unilateral patients were included in the study.

IV. Exclusion Criteria

Patients with gross anterior segment pathology like corneal opacity, hazy media or patients with nuclear sclerosis more than grade III in both eyes, or retinal detachment, and patients allergic to florescein dye were excluded from the study

Patients with retinal disorders with suspected AMD, Diabetic maculopathy, vascular occlusive disorders, other macular pathologies and CSCR were included in the study. Retinal disorders other than the above mentioned, viz., very old, uncompliant patients, pregnant women, and immunocompromised status patients, patients with hypersensitivity to fluorescein dye, renal insufficiency or cardiovascular diseases were excluded. Using a preformed proforma, detailed history was obtained from each patient. Patients underwent a detailed clinical examination that included unaided visual acuity and best corrected visual acuity with Snellens chart and near vision; pupil size and reactions; anterior segment examination and slit lamp biomicroscopy; measuring IOP using Goldmann applanation tonometer. A thorough, careful and detailed examination of the fundus was done initially by a direct ophthalmoscope and subsequently with an indirect ophthalmoscope and slit lamp examination with +90 D lens giving special attention to macula.

Procedure: Patient’s pupils were dilated with a combination of 5% phenylephrine and 1% tropicamide 30 minutes prior to the procedure. An intradermal test dose of the dye was given 10 minutes prior to the procedure. A 21 gauge scalp vein set was put in the antecubital vein. Patient was seated in front of the fundus camera and the dye was injected. Procedure was conducted under supervision of standby anaesthetist. Using a Topcon fundus camera Colour fundus photographs, Monochromatic fundus photographs (red free) were taken prior to performing FFA. 3ml of 25% fluorescein dye was injected in the antecubital vein. Pictures were taken after 10sec at an interval of 1.5-2sec approx. 6 photographs were taken in succession. Patient was monitored for one hour after procedure. On analysis of findings, patient was advised general and specific ocular treatment according to the disease. Statistical analysis using chi square test was created with FFA confirmed and FFA altered diagnosis and declared $p < 0.05$ as statistically significant. With the above mentioned background this study was conducted to assess and evaluate the role of fluorescein angiography as an important tool in diagnosis of retinal and choroidal disorders.



Figure 4a: Clinical picture of CSCR

Figure 4b: FFA picture of CSCR showing smoke stake type leakage

V. Results

475 cases were analyzed and sub-divided into different categories of AMD, Diabetic retinopathy, Hypertensive retinopathy, vascular occlusive disorders, other macular disorders and CSCR, optic nerve related disorders, vasculitis & other type inflammatory disorders and others (Table 1). Of the 475 cases 119 cases of diabetic retinopathy (25.05%), 76 cases of AMD (16%), 49 cases of vascular occlusions (10.31%), 45 cases of vasculitis & other inflammatory disorders (9.47%), 31 cases of optic nerve related disorders (6.52%), and 27 cases of CSCR (5.68%) were studied.(Figure 1)

Table 1: Distribution of 475 cases in various Diagnostic Categories (n=475)

Disease	0-10 yrs	11-20 yrs	21-30 yrs	31-40 yrs	41-50 yrs	51-60 yrs	61-70 yrs	71-80 yrs	81 yrs & above
Vascular Occlusion									
BRVO	0	0	3	3	4	4	5	3	1
CRVO	0	0	0	2	2	3	4	1	1
CRAO	1	0	0	0	0	5	0	1	0
BRAO	0	0	0	0	0	1	0	0	0
Other type occlusions	0	0	0	0	1	2	2	0	0
Diabetic Retinopathy	0	0	0	6	20	47	33	11	2
Hypertensive Retinopathy	0	0	0	0	4	1	1	1	1
Macular Diseases									
Dry ARMD	0	0	0	3	2	5	10	11	7
Wet ARMD	0	0	0	0	3	6	14	13	2
Cystoid Macular Edema	0	2	0	4	1	2	3	1	0
CSCR	0	1	3	13	8	1	1	0	0
Macular scar	0	0	0	0	2	7	5	4	3
Macular hole	0	2	1	0	2	2	3	0	0
Other degenerative maculopathies	0	2	0	3	0	0	1	2	2
Optic nerve related disorders	0	9	4	7	3	3	3	2	0
Vasculitis	0	1	5	3	1	0	0	0	0
Other Inflammatory diseases									
Active Choroiditis	0	7	9	4	2	0	0	0	0
CMV Retinitis	0	0	0	5	0	1	0	0	0
HIV Related Retinopathy	0	0	0	2	1	0	0	0	0
Chorioretinitis	0	2	1	0	0	1	0	0	0
Others	0	8	10	7	10	11	10	5	5

On analysis of 76 cases of Age related macular degeneration, 89.47% cases were aged above 50 years and both kind of presentation Wet ARMD (Figure 2a & 2b) and Dry ARMD was common in this age group. (Table 2)

Table 2: Incidence of Age Related Macular Degeneration (ARMD)

Age	Wet ARMD	Dry ARMD
<50yrs	3	5
>50yrs	35	33
Total no. of patients	38	38

Table 3: Role of FFA in ARMD

Disease	No of cases	Percentage
ARMD	76	100
FFA Confirmed	52	68.42
FFA Altered	24	31.57

$\chi^2 = 10.316$ p=0.00131882, statistically significant

FFA confirmed the diagnosis in 68.42% of AMD cases, altered the diagnosis in 31.57% cases (Table 3). On analysis of 38 cases of wet AMD (10%), 50% cases of PED were diagnosed by clinical examination and 50% by FFA. All cases of CNVM (100%) were diagnosed by FFA (Table 3).

Diabetic Retinopathy was most common in all studied patients (25.05%). Presentation was more prevalent in population aged above 50 years. In various presentation of Diabetic Retinopathy, Non proliferative diabetic retinopathy (NPDR) was more common (47.05%). NPDR with CSME (Figure 3a & 3b) and PDR alone were present in 22.68 % and 21.84% cases respectively. 8.4% cases presented with PDR with CSME (Table 4)

Table 4: Incidence of Diabetic Retinopathy (n=119)

Age	NPDR alone	NPDR with CSME	PDR alone	PDR with CSME
<30yrs	0	0	0	0
30-50yrs	11	3	7	5
>50yrs	45	24	19	5
Total	56	27	26	10
Percentage	47.05%	22.68%	21.84%	8.4%

Table 5 : Role of FFA in Diabetic Maculopathy

Disease	Number of cases	Percentage
Diabetic maculopathy	37	100
FFA confirmed diagnosis	9	24.32
FFA altered diagnosis	28	75.67

$\chi^2 = 9.757$, p= 0.00178641, statistically significant

In this study, out of 37 cases of diabetic maculopathy, FFA has confirmed type of diabetic maculopathy only in 9 cases compared to clinical examination alone and has altered diagnosis in 28 cases (Table 5).

In analysis of Vasocclusive disorders, Branch Retinal Vein Occlusion was more prevalent and it was present in 40.35% cases . Presentation was more common in population aged above 50 years. Next to this was Central Retinal Vein Occlusion, present in 22.80% cases. Hypertensive Retinopathy and Central Retinal Artery occlusion were present in 14.03% and 12.28% respectively among cases of Vasocclusive disorders (Table 6).

Table 6: Incidence of vasocclusive disorders (n= 57)

Age	BRVO	CRVO	CRAO	BRAO	Hemiretinal Vein occlusion	Tributary vein occlusion	Hypertensive retinopathy
<30yrs	3	0	1	0	0	0	0
30-50yrs	7	4	0	0	1	0	4
>50yrs	13	9	6	1	1	3	4
Total (%)	23 (40.35%)	13 (22.80%)	7 (12.28%)	1 (1.75%)	2 (3.50%)	3 (5.26%)	8 (14.03%)

Table 7: Role of FFA in vasocclusive disorders

Disease	Number of cases	Percentage
Vasocclusive disorder	49	100
FFA confirmed diagnosis	40	81.63
FFA altered diagnosis	9	18.36

$\chi^2 = 19.612$, p= 0.00000949, statistically significant

On analyzing vascular occlusions, FFA has confirmed diagnosis in 40 cases (81.63%) and has altered its diagnosis in 9 (18.36%) cases (Table 7).

Macular pathologies other than ARMD and Diabetic Maculopathy includes Macular hole, Macular Scar, Cystoid macular edema and other degenerative macular changes. Macular hole and other degenerative maculopathies did not show affection to any age group. Macular Scar was common in aged above 50 years and Cystoid macular edema was common in middle aged less than 50 years (Table 8).

Table 8: Incidence of macular pathologies other than ARMD and Diabetic Maculopathy (n=54)

Age	Macular Hole	Macular Scar	CME	Other Degenerative Maculopathies
<50yrs	5	2	7	5
>50yrs	5	19	6	5
Total	10	21	13	10

Table 9: Role of FFA in Macular Pathologies

Diseases	No of cases	Percentage
Macular pathologies	54	100
FFA confirmed diagnosis	54	100
FFA altered	0	0

In the analysis of macular pathologies other than ARMD and Diabetic maculopathy, FFA has confirmed diagnosis in all cases (Table 9). Out of 54 cases of macular pathologies studied, 13 were found to be CME (24.07%), 21 were Macular scar (38.89%), 10 were Macular hole (25%) and 10 were other maculopathies (25%).

Of all inflammatory chorioretinal disorders Chorioiditis (48.88%) and Vasculitis(22.22%) was more common especially in young population aged less than 30 years. CMV Retinitis and HIV Related retinopathy was more prevalent in middle aged population between 30 to 50 year of age (Table 10).

Table 10: Incidence of inflammatory chorioretinal disorders (n=45)

Age	Vasculitis	CMV retinitis	HIV related retinopathy	Chorioiditis	Chorioretinitis
<30yrs	6	0	0	16	3
30- 50yrs	4	5	3	6	0
>50yrs	0	1	0	0	1
Total	10 (22.22%)	6 (13.33%)	3 (6.66%)	22(48.88%)	4 (8.88%)

Table 11: Role of FFA in inflammatory chorioretinal disorders

Disease	No of caese	Percentage
Inflammatory chorioretinal disorders	45	100
FFA confirmed diagnosis	33	73.33
FFA altered	12	26.67

$X^2 = 9.8$, $p = 0.00174512$, statistically significant

On analyzing inflammatory chorioretinal disorders, FFA has confirmed diagnosis in 33 (73.33%) cases and has altered its diagnosis in 12 (26.67%) cases (Table 11).

In the analysis of Optic nerve related disorders Optic neuritis was more common (58%) and affected young to middle age population upto 50 years of age. Optic atrophy (29.03%) was common in middle to old aged above 30 years. Pappiloeidema was prevalent in young age group less than 30 years (Table 12).

Table 12: Incidence of optic nerve disorders (n= 31)

Age	Pappilloedema	Optic neuritis	Optic atrophy	AION
<30yrs	2	9	2	0
30- 50 yrs	0	5	4	1
>50yrs	0	4	3	1
Total (%)	2 (6.45%)	18 (58.06%)	9 (29.03%)	2 (6.45%)

Table 13: Role of FFA in Optic nerve related disorders.

Diseases	No of cases	Percentage
Optic nerve disorder	31	100
FFA confirmed diagnosis	20	64.51
FFA altered	11	35.48

$X^2 = 2.613$, $p = 0.10599108$, statistically not significant

On analyzing optic nerve related disorders, FFA has confirmed diagnosis in 20 cases (64.51%) and has altered its diagnosis in 11 (35.48%) cases (Table 13).

Out of all cases of Central Serous Chorioretinopathy (Figure 4a & 4b), 77.77% cases were of middle age group between 30 to 50 years of age (Table no 14).

Table 14 : Incidence of Central Serous Retinopathy (n=27)

Age	CSR
<30yrs	4
30-50yrs	21
>50yrs	2
Total	27

On analysis of FFA appearance in CSCR 50% showed inkblot appearance and 50% showed smoke stack appearance (Table 15).

Table 15: Distribution of appearance of FFA in CSCR

DISEASE	Ink blot appearance	Smoke stack appearance
FFA appearance in CSCR	25	2

Table 16: Presentation of Other diseases (n=66)

Age	PED	Epiretinal Membrane	Vitreous Haemorrhage	Retinal Detachment	Retinitis Pigmentosa	Normal Study
<30yrs	1	1	2	2	2	10
30-50yrs	3	1	1	1	1	10
>50yrs	6	2	2	0	1	20
Total	10	4	5	3	4	40

Of the total 475 cases, 66 (Patients with other diseases category) were could not be evaluated by statistical analysis (Table 16)

Table 17: Efficacy of FFA diagnosis in relation to Clinical evaluation of macular disorders in patients studied (n=292)

Role of FFA	Number of patients (n=50)	%
FFA Confirmed(A)	208	71.23
FFA altered (B)	84	28.77
Total	292	100
X ² value	52.64	p<0.001
Inference	FFA altered diagnosis significant with P<0.001	

For total sample size (n = 292), between group A & B according to chi square test p< 0.001, is Significant. (Table 17)

On careful analysis

- 71.23% of cases detected positive by ophthalmoscopy were confirmed positive by FFA.
- On the contrary, a 28.77% of cases diagnosed by ophthalmoscopy were altered in their diagnosis by FFA indicating low negative predictive value.
- A very high percentage of cases although diagnosed positive by ophthalmoscopy are categorized into subtypes by FFA.

Table 18: Efficacy of FFA diagnosis in relation to Clinical evaluation of All retinal and choroidal disorders in patients studied (n=409)

Role of FFA	Number of patients	%
FFA Confirmed(A)	325	71.23
FFA altered (B)	84	28.77
Total	409	100
X ² value	32.23	p<0.001
Inference	FFA altered diagnosis significant with P<0.001	

Of the total 475 cases, 66 Patients (with other diseases category) were could not be evaluated by statistical analysis (Table 16). So, for the remaining sample size (n = 409 cases), the analysis between group A & B is found as significant statistically (p<0.001) according to chi square test. (Table 18)

In this present study, FFA has proved to be a far superior diagnostic modality as compared to clinical ophthalmoscopy. This shows that, Clinical Ophthalmoscopy has a high positive predictive value but a low negative predictive value. Hence, FFA is a superior diagnostic tool and is a necessity for evaluating clinically doubtful fundus (Retinal) disorders.

VI. Discussion

Present study demonstrated Diabetic Retinopathy (25.05%) as the most common presentation followed by Age Related Macular Degeneration in (16%), Vasocclusive disorders (10.31 %) and vasculitis & other related inflammatory disorders (9.47%)(Table 1). According to WESDR (Wisconsin Epidemiological Study of Diabetic Retinopathy (1984), the incidence of DR was 40.3%^[4]. Kahn (1974) also demonstrated DR as a major cause of visual impairment^[5]. In this study out of 76 cases of ARMD, 50 % were found to be of dry type and 50 % were of wet type. 80% of dry ARMD cases were diagnosed by clinical ophthalmoscopy and confirmed by FFA. FFA confirmed diagnosis in 76% of wet ARMD cases and altered diagnosis in 24 % cases of wet ARMD. Talks J et al^[6] in their retrospective study showed that 81% cases of wet ARMD could be diagnosed only by FFA. Our study shows FFA confirmed diagnosis in 68.42% cases of ARMD and altered diagnosis in 31.57% cases of ARMD and played an important tool in diagnosing wet ARMD. In present study, 100% cases of choroidal neovascular membrane (CNVM) and 50% cases of pigmentary epithelial defect (PED) could be diagnosed by FFA (Table 2). 92.52% CNVM cases diagnosed were found to be subfoveal type. Talks J et al in their cross sectional study performed FFA on 111 patients and had provided following diagnoses: predominantly classic CNVM (19.8%), serous pigment epithelial detachment (7%), disciform scar (8.1%), occult CNVM (40.5%), dry ARMD (13.5%)^[6].

Of the 119 cases of Diabetic Retinopathy, 47 % cases were found to be NPDR type, 22.68 % were of NPDR with CSME, 21.84% were found to be PDR type and 8.4 % were of PDR with CSME. On analysis of 37 cases of Diabetic maculopathy, 11 cases were of CSME (32%), 7 cases were focal maculopathy (18.9%), 9 cases were diffuse maculopathy (24.32%) and 10 cases were found to be of ischemic maculopathy (27.02%). FFA confirmed diagnosis in 24.32 % of Diabetic Maculopathy (9 cases) and altered diagnosis in 75.67 % (28) cases. 70% cases of NPDR were diagnosed by clinical ophthalmoscopy and confirmed by FFA. Wykes et al^[7] showed in their study that FFA confirmed diagnosis in only 40% cases of diabetic maculopathy. Syed et al^[8] in their interventional study on diabetic retinopathy found following angiographic patterns of diabetic maculopathy by FFA: diffuse maculopathy-59.24%, focal maculopathy - 17.69%, ischemic maculopathy-11.55%^[8]. We found that all cases of ischaemic maculopathy were diagnosed by FFA with areas of capillary non-perfusion which are not easily recognised by ophthalmoscopy . FFA has confirmed type of diabetic maculopathy only in 24.32% (9) cases which was diagnosed ophthalmoscopically and has altered diagnosis in 74.67% (28) cases that played important role in categorizing type of diabetic maculopathy and helped in further management and predicting prognosis (Table 5).

In our study Branch Retinal Vein Occlusion (BRVO) was more prevalent and it was present in 40.35% cases (Table 6). Branch vein occlusion study group 1983 also stated BRVO to be a common cause of retinal vascular disease. FFA showed vascular occlusions associated with macular ischemia in 18.36 % cases and confirmed presence of macular edema in all cases. Wykes et al^[7] showed in their study that FFA showed vascular occlusions associated with macular ischemia in 15% cases and that with macular edema in 84% cases. SS Hayreh^[9] in his landmark study in 1994 concluded that "In FFA, the extent of capillary non-perfusion is a reliable criterion to differentiate the two types of CRVO".

Macular pathologies other than ARMD and Diabetic Maculopathy form 11.36% of retinochoroidal disorders.(table 8) All were diagnosed clinically and confirmed by FFA. Wykes et al^[7] showed in their study that FFA confirmed 100% cases of hereditary macular degeneration which was diagnosed by clinical examination. Our study is consistent with the above mentioned study.

In present study 27 cases of Central Serous Chorioretinopathy (CSCR) which were diagnosed by clinical examination, and confirmed by FFA. Of the 25 (92.59%) cases with inkblot type of leakage pattern, single leak point was seen in 20 (80%) cases and multiple leak point in 5 (20%) cases. Whereas smoke stack appearance was seen in 2(7.4%)cases (Table 15). Siddiqui et al^[10] in their hospital based study on CSCR showed that ink blot appearance was seen in 67.64% and smoke stack appearance was seen in 30.35%.

In this study out of 45 cases of all inflammatory chorioretinal disorders 48.89 % were found to be of choroiditis, 22.22 % of vasculitis, 13.33% of CMV retinitis, 8.88 % of chorioretinitis and 6 % were of HIV related retinitis. FFA confirmed diagnosis in 73.33% of cases and altered diagnosis in 24 % cases of inflammatory chorioretinal disorders (Table 10 &11).

FFA showed out of 31 cases of Optic nerve disorders 58.04 % were found to be of optic neuritis type, 29.03 % of optic atrophy and 6.43 % of Papilloedema and AION. FFA confirmed diagnosis in 64.51% of cases and altered diagnosis in 35.48 % cases of inflammatory chorioretinal disorders.(table 12&13)

On applying statistically analysis of comparison between ophthalmoscopic examination and FFA, was found to be significant. Thus,proving FFA to be a superior diagnostic modality. In our study FFA altered the diagnosis in 28.77% of cases and categorized the lesion into specific entities. FFA proved to be a superior modality of diagnosis and categorization of lesions in macular disorders.

VII. Conclusion

After analyzing the above all data we conclude that FFA helps in early diagnosis and treatment of macular disorders as well as retinochoroidal disorders and played a vital role in management of wet ARMD. Most of dry ARMD cases were diagnosed by clinical examination (ophthalmoscopy) and confirmed by FFA. FFA is also very useful to categorise the diabetic maculopathy and other macular pathologies into specific entities and to differentiate ischaemic or non-ischaemic type of lesions in vasoocclusive disorders.

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