

ORIGINAL ARTICLE

Study of Fundus Fluorescein Angiography: a Diagnostic Tool in Retinal and Choroidal Pathologies

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Abstract

To evaluate epidemiology of retinal and choroidal diseases and to calculate the Foveal Avascular Zone (FAZ), diameter and its variation with different diseases and analyse its impact on BCVA (Best corrected visual acuity) using Fundus fluorescein Angiography as diagnostic tool. Materials and methods: The study was conducted in 100 cases of retinal and choroidal pathologies undergoing FFA. Out of 100 patients maximum were in the age group 50-60 yrs with Diabetic Retinopathy as maximum incidence. FAZ in within normal eyes were in the range of 0.400mm-0.500mm while it increased in Diabetic retinopathy, BRVO, CRAO and hypertensive retinopathy. Eyes with larger FAZ had lower BCVA.

Key Words

Fluorescein Angiography, FAZ, BCVA, Retinal Diseases, Choroidal Diseases

Introduction

Chao and Flocks (1) provided the earliest description of fluorescein Angiography in 1958. It was introduced in clinical use in 1961 by Novotny and Alvis. (2) 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 choroids and have aided the diagnosis and monitoring of the treatment of retinal vascular, macular diseases, and chorioretinal diseases. Technological advances in digital imaging and computer analysis have further expanded the clinical and research applications of fluorescein angiography. Progression of various disease entities and treatment decisions as well as guidance during laser treatment, often are based on fluorescein angiography. The current study was undertaken to evaluate the epidemiology of retinal and choroidal diseases from cases undergoing fundus fluorescein angiography & the best corrected visual acuity range of the study population as well as to calculate the foveal avascular zone diameter and study its variation with different posterior segment diseases. Further to analyze the impact of foveal avascular zone diameter on best corrected visual acuity and to evaluate the incidence of adverse reactions to intravenous fluorescein angiography.

Material and Methods

This study was conducted in 100 cases of retinal and choroidal pathologies undergoing fundus fluorescein angiography in the Department of Ophthalmology, M.G.M. Medical College and M.Y. Hospital, Indore (M.P.) over a period of two years. The criteria for selection of cases was:

Inclusion Criteria

All patients clinically diagnosed to have retinal / choroidal pathology undergoing fundus fluorescein angiography; All age group patients; Only 'active' cases of choroiditis (definition of active is- leakage on FFA around lesions); Both the eyes of all bilateral patients and involved eye of unilateral patients.; The 'other eye' of unilateral patients, if no posterior segment pathology, no anterior segment pathology and nuclear sclerosis < Grade III as 'within normal limit (WNL)'

Exclusion Criteria

- Patients with gross anterior segment pathology like corneal opacity, or retinal detachment, hazy media or patients with nuclear sclerosis > Grade III in both eyes. Extra exclusion for FAZ calculation were: The diseases causing hyperfluorescence in foveal area creating difficulty in calculating FAZ, e.g. CME, Non-CME, ARMD, CSR, Solar Retinopathy, Stargardts; Diseases causing blocked fluorescence (due to hemorrhage) in foveal area. E.g. CRVO; Fundus fluorescein angiography

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photograph other than 50° field; Fundus fluorescein angiography photographs not clicked at 20 sec

All the patients were examined and their findings were recorded. FAZ was calculated using the software 'Eye-Imaging' that helped in capturing and serving metrics for the various sections selected by a user on a scanned retinal image of fluorescein angiography. It provides user the ability to select a region on the image (here FAZ). The desired region is covered by an N-sided polygon formed as a result of the clicks. N-sided polygon is a proven industry standard in graphical computations of these nature. The metrics that the tool captures for the highlighted section are as follows: *Average width of selected region (FAZ)* in pixels and microns. *Average height of the region (FAZ)* in pixels and microns. *Area of the region (FAZ)* in square pixels.

Results

The study was conducted in 100 cases of retinal and choroidal pathologies undergoing fundus fluorescein angiography. Out of 100 cases, maximum were in age group 50 -60 years. There were no patients below 10 years. 42 diabetic patients included 2 BRVO patients, 3 with hypertensive retinopathy, 3 with CME and 6 with non-CME. Cases of macular edema other than cystoid type were included in group non-cystoid.

14 BRVO patients included 1 with CME and hypertensive retinopathy, 2 diabetic and 1 with hypertensive retinopathy only. The CRAO patient had hypertensive retinopathy also. Thus, all the 6 hypertensive patients, 4 out of 14 BRVO patients, 4 of the 5 CME patients and 6 out of 8 non-CME patients were associated with one or the other retinopathy.

The category 'others' included 2 patients of retinitis pigmentosa, 2 patients of trauma (one from iron FB, one from hard and blunt object) and 1 patient of Stargardts disease, 1 glaucoma patient and 1 with papillopathy. As few patients had more than one disease, the total number of patients will not be exactly 100 but more in graph. There were 64 males and 36 females and M : F = 1.76 : 1. In our study CRVO, CRAO, sickle cell retinopathy, and solar retinopathy and CSR were found in males only. More often affected group was male except for hypertensive retinopathy and BRVO, where female incidence was dominant. There were 29 patients in age group 50-60 years. All the patients were between 10-80 years. Maximum number of cases of diabetic retinopathy were seen in 50-60 years. BRVO patients were all above 50 years of age. In our study 28 patients were office workers and 34 were housewives. Only 9% patients were agriculture workers. In our study the BCVA ranged from <6/60 - 6/6 (measured on Snellen's visual acuity chart). 42 (51.2%) diabetic retinopathy eyes were in BCVA group 6/36-6/24. 8 out of 14 BRVO eyes (57%) were

having BCVA in 6/60-6/24 range. In active choroiditis patients, 10 out of 15 eyes (66.6%) were having BCVA in range 6/18-6/12. ARMD eyes had BCVA < 6/24. 'WNL eyes' were those with no posterior segment pathology, no gross anterior segment pathology and nuclear sclerosis < Grade III. These were among the 'other eye' of unilateral patients. Total of 142 eyes were evaluated for FAZ diameter using an 'Eye-Imaging' software (total of table will not correspond because of 10 eyes had more than one disease). The other diseases were excluded according to the exclusion criteria for FAZ. There were 26 eyes within normal limits. Eyes with 6/36-6/24 BCVA had mainly FAZ diameter in the range 0.600-0.700 mm. As the table shows, larger the FAZ diameter lower was the BCVA. (Fig.1-3; Table 1-5)

Discussion

Present study demonstrated DR (42%) as the most common presentation followed by BRVO (14%) and ARMD in (9%), active choroiditis (9%). According to WESDR (Wisconsin Epidemiological Study of Diabetic Retinopathy (1984)³, the incidence of DR was 40.3%. Kahn (1974)⁴ also demonstrated DR as a major cause of visual impairment. BRVO (14%) was the second most common presentation. Branch vein occlusion study group, 1983 also stated BRVO to be a common cause of retinal vascular disease. In the present study BRVO was associated with hypertension in 3 patients (21.42%) and diabetes in 2 patients (14.3%). Blankenship and Okun (1973)⁵ reported the incidence of hypertension to be 65% and DM (13%) in BRVO patients. Gutman and Zegarra (1974)⁶ found incidence to be 75% and 2.5% in hypertension and diabetes mellitus respectively. Appiah AP (1989)⁷ found the incidence of hypertension in patients with venous occlusion to be 66.2% and diabetes mellitus to be 19.1%.

ARMD incidence in present study was 8%. In Beaver Dam Study (2007)⁸, the 15-year cumulative incidence was 14.3% for early AMD and 3.1% for late AMD. There was an increased incidence of AMD lesions with age ($P < 0.05$). In our study incidence of CME was 5% and non-CME was 8%. Three CME patients and 6 non-CME patients had concomitant diabetic retinopathy also. One CME patient had BRVO and hypertensive retinopathy. According to Cunha-Vaz J *et al* (9) diabetic retinopathy is the most common of the retinal vascular diseases associated with disruption of the blood retinal barrier and macular edema. In hypertensive retinopathy, hydrostatic and ischemic factors play a role in the disruption of the inner and sometimes outer blood retinal barrier leading to macular edema. In our study, maximum number of patients (29) were in the age group 50-60 years. 50-60 years age group patients showed maximum incidence of DR (21 out of 42 patients, 50%), hypertension (3 out of 6

Fig. 1 Distribution of 100 Patients in Various Diagnostic Categories

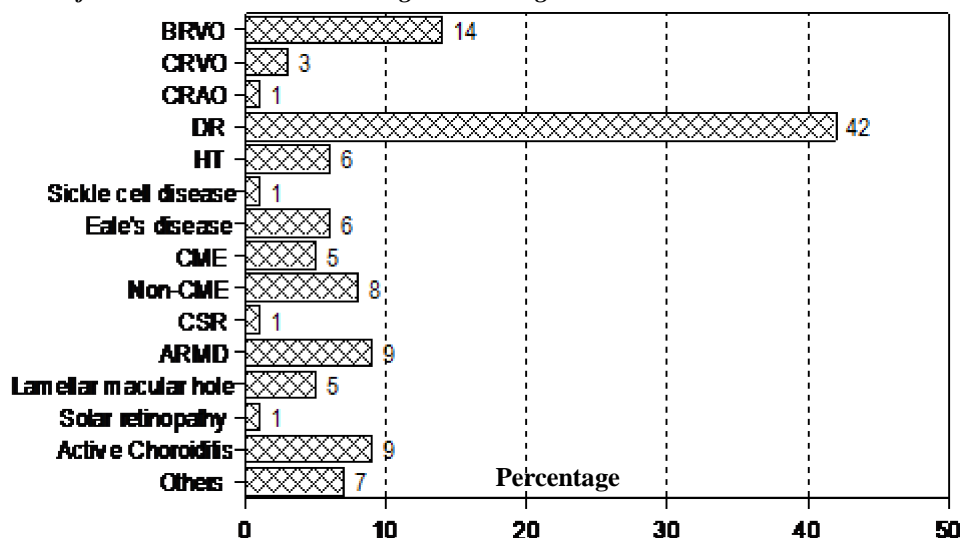


Table 1. Incidence of Retinal and Choroidal Diseases with Respect to Different Age Groups

Disease	0-10 yrs	10-20 yrs	20-30 yrs	30-40 yrs	40-50 yrs	50-60 yrs	60-70 yrs	70-80 yrs
Vascular occlusion								
• BRVO						2	5	7
• CRVO							1	2
• CRAO					1			
Diabetic retinopathy					12	21	9	
Hypertensive retinopathy					1	3	2	
Retinopathy in blood dyscrasias								
• Sickle cell disease				1				
Vascular inflammation								
• Eale's disease		1	4	1				
Macular disease								
• CME			1			2	1	1
• Non-CME				1		4	3	
• CSR					1			
• ARMD						2	7	
• Lamellar Hole			2	3				
• Solar retinopathy		1						
Active choroiditis				1	6	2		
Others		1	1	2	2	1		

patients, 50%), CME and non-CME (4 out of 8 patients, 50%). Kahn HA (4) also reported high incidence of retinopathy (upto 68%) in older diabetics. BRVO and CRVO were common in 70-80 years age group. Hayrey SS and Zimmermann MB (10) found venous occlusion to be common in 6th decade. As originally described by Eale's in 1880 and 1882 our study also showed occurrence of this disease in many young individuals. Most of them were in between age group 20-40 years (5 out of 6 patients, 83.3%). ARMD showed maximum occurrence

in age group 60-70 years (7 out of 9 patients). In the Framingham Eye Study (11), the estimates of 5 year incidence rates were 2.5%, 6.7% and 10.8% for individuals who were 65, 70 and 75 years of age. In our study, one male patient was of central serous chorioretinopathy (CSC) in age group 30-40 years. Gass JDM (12) also reported CSC to be common in age group 30-50 years. More often affected group was male except for hypertensive retinopathy and BRVO. Oparil (13) reported that hypertension is more prevalent in men.

Table 2. Incidence of Disease with Respect to Occupation

Disease	Agri. Worker	Labourer	Office worker	House wife	Student	Misc. + retired
Vascular occlusion						
• BRVO	-	-	-	8	-	6
• CRVO	-	-	-	-	-	3
• CRAO	-	-	1	-	-	-
Diabetic retinopathy	-	-	22	14	-	6
Hypertensive retinopathy	-	-	2	3	-	1
Retinopathy in blood dyscrasias						
• Sickle cell disease	-	-	1	-	-	-
Vascular inflammation						
• Eale's disease	1	2	-	-	3	-
Macular disease						
• CME	-	-	3	2	-	-
• Non-CME	-	-	4	4	-	-
• CSR	-	-	1	-	-	-
• ARMD	4	-	-	3	-	2
• Lamellar Hole	2	3	-	-	-	-
• Solar retinopathy	-	-	-	-	1	-
Active choroiditis	1	3	1	4	-	-
Others	1	-	1	2	3	-

Table 3. BCVA with Respect to Different Diagnostic Categories

Disease	6/60	6/60-6/36	6/36-6/24	6/24-6/18	6/18-6/12	6/12-6/9	6/9-6/6
WNL			1		0	1	24
Vascular occlusion							
• BRVO	5	5	3	1			
• CRVO	3						
• CRAO	1						
Diabetic retinopathy	11	9	42	11	3	6	
Hypertensive retinopathy	3	3	1	5			
Retinopathy in blood dyscrasias							
• Sickle cell disease							1
Vascular inflammation							
• Eale's disease					2	7	1
Macular disease							
• CME	6						
• Non-CME	7	4					
• CSR		1					
• ARMD	3	10	3				
• Lamellar Hole			3	2			
• Solar retinopathy			1				
Active choroiditis				1	10	3	1
Others		2			4	0	6

However, sixth report of Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (1997) reported that over age 50, women have a higher prevalence of hypertension than men.

Brown GC and Magargal LE (14) reported that men are more frequently affected with CRVO. In our study 35% cases were unilateral and 65% were bilateral. Few diseases like BRVO, CRVO, CRAO, sickle cell

Table 4. FAZ Diameter in Different Diagnostic Categories

Diagnostic Category		No. of Eyes in Different FAZ Ranges				
		< 0.400 mm	0.400-0.500 mm	0.500-0.600 mm	0.600-0.700 mm	> 0.700 mm
Normal eyes			25	1		
BRVO				8	3	1
CRAO				1		
DR	1		6	11	49	
HT retinopathy				5	6	
Sickle Cell Disease			1			
Eale's Disease			9	1		
Lamellar hole					5	
Active Choroiditis			3	12		
Retinitis Pigmentosa			1	3		

Table 5. Correlation of FAZ Diameter and BCVA

BCVA		No. of Eyes in Different FAZ Ranges				
		< 0.400 mm	0.400-0.500 mm	0.500-0.600 mm	0.600-0.700 mm	> 0.700 mm
< 6/60		1		3	1	1
6/60 – 6/36				6	4	
6/36 – 6/24				3	43	
6/24-6/18				6	10	
6/18-6/12			3	16		
6/12-6/9			15	1	1	
6/9-6/6 (includes 6/6)			27	1		

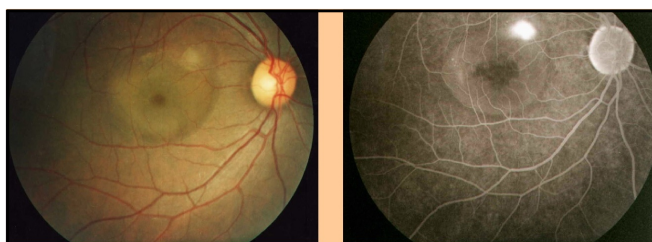


Fig.2 Fundus Photograph of a Case of Central Serous Choroidopathy with Corresponding FA Photograph
retinopathy, solar retinopathy, CSR and lamellar hole were totally unilateral. Hayreh SS and Zimmermann (10) reported venous occlusion to be unilateral in majority. Mainly bilateral presentation was seen in DR (95.2%), ARMD (63%), Active choroiditis (66.6%) and others. Klein ML reported 25.7% bilaterality in central serous choroidopathy. (8) Maximum incidence of retinal and choroidal diseases was in housewives (34%) and office workers (28%), followed by retired persons (14%). Only 9% were agriculture workers. Oparil S (13) reported that hypertension is rare in agrarian societies and in individuals who are physically active. Present study showed higher incidence of ARMD (4 out of 7 patients, 57.1%) in agriculture workers. This finding may because participants exposed to the summer sun for more than 5 hours / day during their teens, in their 30s and at the baseline examination are at a higher risk of developing age related

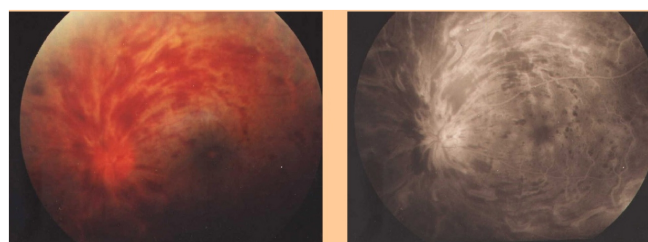


Fig.3 Fundus Photograph of a Case of CRVO with Corresponding FA Photograph

maculopathy by 10 years than those exposed to sun for less than 2 hours / day during the same period. WHO in 1985 reported that NIDDM appears to be linked with sedentary life style, overnutrition and obesity, so correction of these may reduce the risk of diabetes mellitus and their complications. In the present study most of the patients of DR (42%) were in the visual acuity group 6/36 - 6/24. 20% of the patients had visual acuity < 6/36. This contradicts the findings of western literature where at presentation visual acuity is less severely compromised due to early detection of diabetic retinopathy and slow progression of disease due to good metabolic control. Here, late detection and late presentation to ophthalmologists are the probable causes. 57% of BRVO patients in our study had BCVA in range of 6/60 - 6/24.

Nussenblatt RB, Kaufmann SC *et al* (15) reported that present visual acuity in CME usually ranges from

20/25 to 20/80, but may be as poor as 20/400. In our study 'eye imaging' software was used to calculate FAZ diameter. We manually delineated FAZ, while a study by Yalin Zheng *et al* (16) automated segmentation technique was used to calculate FAZ. Later on Shin KU, Kim S *et al* (17) studied noninvasive detection of FAZ using confocal red free imaging in Diabetic retinopathy.

The maximum horizontal diameter of FAZ in the normal eyes was found to be 0.400-0.500 mm. Bresnick GH, Condit R (18) measured FAZ in the normal eyes and gave values ranging from 0.160 to 0.730 mm. Our study has come out with interesting results with regard to FAZ diameter. Capillary perfusion in macular region was decreased (as shown by enlargement of FAZ) in Diabetic Retinopathy and Hypertensive Retinopathy, BRVO, CRAO, Retinitis Pigmentosa, lamellar hole, and even active choroiditis. FAZ diameter increase in DR corresponds with the study of Conrath J, *et al* (19).

Capillary closure is well established angiographic and histopathological sign of Diabetic retinopathy (18). Surprisingly our study has revealed increase in FAZ in active choroiditis patients. Explanation for this might be some role of chemical / neural mediators between retinal and choroidal circulation during inflammation of choroid (requires further research). In our study with FAZ diameter range 0.400-0.500, maximum eyes had BCVA in range 6/9-6/6 (60%). BCVA decreased with increase in FAZ diameter. This finding is similar to the reports of Arend O, *et al*. (20). Few authors in their study of BRVO patients reported that extent of capillary non-perfusion in macular area seemed to have an important bearing on visual acuity and found that patients with intact perifoveal capillary arcade have a better visual prognosis than those with broken arcade.

Conclusion

In our study Diabetic retinopathy had the maximum incidence and males were the more often affected group except for hypertensive retinopathy and BRVO. Disease incidence was maximum in housewives and office workers and less in agriculture workers. Diabetic retinopathy eyes showed BCVA mainly in the range of 6/36-6/24. Eyes of BRVO patients had BCVA mainly < 6/24. Eyes of CRVO, ARMD, CME and non-CME had BCVA < 6/60.

Maximum 'Within normal limits' eyes had horizontal foveal avascular zone diameter in the range of 0.400-0.500 mm (25 eyes). FAZ diameter was increased in diseases like diabetic retinopathy, BRVO, CRAO, hypertensive retinopathy, lamellar macular hole, retinitis pigmentosa and active choroiditis. Eyes with larger maximum horizontal foveal avascular zone diameter had lower visual acuity.

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