



Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/12249

DOI URL: <http://dx.doi.org/10.21474/IJAR01/12249>



RESEARCH ARTICLE

FUNDUS FLUORESCIN ANGIOGRAPHY AS A DIAGNOSTIC TOOL IN AGERELATED MACULAR DEGENERATION

M. Lakshmi Sarvani, B.V. Kranthi and S. Mounica Reddy

Department of Ophthalmology, Santhiram Medical College, Nandyal.

Manuscript Info

Manuscript History

Received: 31 October 2020

Final Accepted: 30 November 2020

Published: December 2020

Key words:-

Age Related Macular Degeneration,
Fundus Fluorescein Angiography,
Exudative AMD, Geographic AMD

Abstract

Background: Age related macular degeneration (ARMD) is a leading cause of severe irreversible vision impairment in developed countries. It is a hereditary degenerative condition involving the choriocapillaries, Bruch's retinal pigment epithelium and photoreceptors. Early stage disease is characterized by deposition of drusen under the RPE cells into Bruch's membrane. In late stages disease may progress to either geographic atrophy also known as Dry AMD or neovascular also known as Wet AMD. Loss of vision in dry AMD is due to photoreceptors and atrophy of RPE with loss of choriocapillaries whereas choroidal neovascularization (CNV) is associated with breakthrough of choroidal neovascular vessels through Bruch's membrane and RPE causing hemorrhagic, exudative, or disciform AMD. Although the clinical diagnosis of AMD can be established based on patient's history and fundus examination, Fluorescein Angiography (FA) is the most important ancillary test for classifying the disease in its different subtypes, especially in its wet form. Nowadays, optical coherence tomography (OCT) is being more used than FFA for monitoring the response to treatment, although FA is still very useful in some cases. FA is a powerful imaging modality to identify the presence, location and size of the neovascular complex which is composed of choroidal neovascular lesion and its components. FA is a useful diagnostic method and also an important clinicaresearch tool, displaying lesion morphology data. Many clinical trials of AMD rely on FA characterization for both eligibility and treatment endpoints.

Objectives: To assess the role of fundus fluorescein angiography in age related macular disorders.

To know the varies types of ARMD and its pattern.

To know the progression and response to treatment in ARMD

To find neovascularisation and occult lesions

Study design: Cross sectional study

Methods: This study included 100 patients with macular pathology, who were detected to have

AMD in either eye, who presented themselves to outpatient Department of ophthalmology in SanthiRam medical college and general

Corresponding Author:- M. Lakshmi Sarvani

Address:- Department of Ophthalmology, Santhiram Medical College, Nandyal.

Hoapital,nandyal. A careful detailed history was taken regarding the duration and symptoms of the disease followed by eye examination which included visual acuity, slit lamp examination and macular function test. Detailed fundus examination with 90D indirect and direct ophthalmoscope. Thorough systemic examination was done followed by blood investigations and ECG. Under aseptic precaution blood samples were collected from anterior cubital vein and the following tests were carried out.

1. Complete hemogram
2. Random blood sugar
3. Fasting lipid profile
4. Serum creatinine

And urine routine was done. Medical fitness for the procedure was obtained. Patient was explained the procedure and proper informed consent was taken after which fundus fluorescein angiography was performed.

Results:

Totally 100 patients fulfilling the inclusion criteria were included in the study, with an age range of 50 years and above of both gender. Dry AMD was present in 90 patients (90%) patients and 10 patients (10%) showed wet or exudative AMD.

Interpretation and conclusion:

The fluorescein angiography helped in diagnosis, type of ARMD and its further classification. It also helped in planning treatment and its response at follow up

Copy Right, IJAR, 2020,. All rights reserved.

Introduction:-

The human central retina, “the macula”, is the anatomical structure responsible for fine detailed vision with precise visual acuity, colour differentiation, form sense and stereopsis¹ and when subjected to disease causes irreversible blindness. Macular disorders (MD) were the most frequent constituting 35.6% of all posterior segment diseases. Age related macular degeneration (AMD) constituted 38.6% of all macular disorders; other macular diseases were drug induced maculopathy (3.4%), nonspecific pigmentary maculopathy (43.8%) macular scars and macular holes (18%).²

Most common cause of blindness in developed countries is age related macular degeneration accounting for about 8.7%.^{3–7} particularly in people older than 60 years. Fundus Fluorescein Angiogram (FFA) recognized as a diagnostic tool by Novotony and Alvis the students of Indiana University in 1969 has revolutionized diagnosis and is the most useful and practical investigation which helps in management of numerous retinal disorders including macular lesions as it allows examining the structures beyond the reach of clinical examination.⁸

Fluorescein angiography is best to identify wet ARMD and helps to confirm the presence of neovascularization and identifies the characteristics of the lesion including the location and composition of neovascularization, which may be helpful in finding occult cases too, deciding whether treatment is indicated and which therapeutic modality is appropriate and helpful in serving as a baseline exam for

further studies to decide whether the treatment has been effective and the disease regression

Methodology:-

This Study was conducted in the Department of Ophthalmology, Santhi Ram medical college and general Hospital, Nandyal

Study Duration : 6 months (October 2019 to March 2020)

Study Subjects : Patients with suspected macular pathology, Department of Ophthalmology, Santhi Ram medical college and general Hospital, Nandyal

Study Design : Cross-sectional study

Sample Size : 100 patients

Method Of Collection Of Data:

The study was undertaken in patients with suspected macular pathology who attended the OPD during the study period.

A minimum of 100 cases with macular disorders who were diagnosed to have ARMD clinically were selected for the study.

Inclusion criteria:

1. All elderly patients with diminished vision and suspected macular pathology
2. Clear media

Exclusion criteria:

1. Very old uncompliant person.
2. Person's hypersensitivity to fluorescein dye.
3. Diabetic maculopathy
4. Cystoid macular edema
5. Media opacity
6. Subretinal hemorrhage
7. Exudates blocking FA view.

A careful detailed history was taken regarding the duration and symptoms of the disease, smoking history followed by eye examination. Thorough systemic examination was done. Vision testing, anterior segment examination was done followed by slit lamp examination with 90 D and indirect with 20D and macular function tests were done followed by funduscopy, fluorescein angiography. Vision test was done by Snellen chart followed by near vision by Jaegers chart. Colour vision was tested by Ishihara chart and followed by macular function tests listed below.

Macular function tests:

1. Visual acuity
2. Contrast sensitivity

It is the measure of ability of visual system to distinguish an object against its

background

3. Colour vision

4. Two point discrimination test

The patient is asked to see through a cardboard with two holes close to each other with light behind the holes. If patient appreciates two lights indicates good macular function test

5. Maddox rod test

Patient is asked to look through a Maddox rod at a bright light. If the patient sees continuous unbroken and undistorted red line it indicates normal functioning of macula. If the line is broken it indicates disease of macula.

6. Amsler grid test

Patient is asked to close one eye and see amsler chart with the other eye holding at normal reading distance. Patient is asked to look at centre fixing dot in chart and to look for any distortion in the lines, if present indicates macular pathology.

Investigations:

1. complete hemogram
2. urine examination
3. RBS
4. lipid profile
5. Blood urea and serum creatinine and
6. ECG was done.

Medical fitness for performing the procedure was taken. Patient was explained about the procedure and proper written consent was taken. Pupil was dilated using tropicamide and phenylephrine for 20 to 30 min before the procedure. Emergency medicines were kept available if needed. Following the procedure patient was informed regarding urine and skin discolouration.

Zeiss Camera was used throughout the study. The patient was seated comfortably in front of the camera, the antecubital vein was secured and scalp vein was fixed. The patient was asked to place the chin on the headrest and forehead to head bar and was instructed to not to move his head. The patient was asked to fix the gaze with a red fixation target and then the camera was focused to get a good view of fundus. First patient's fundus photograph was taken and then red free photograph was taken using red green filter. Pre injections photographs were taken with exciter and barrier filters. The dye was injected through antecubital vein and serial pictures were taken. All through the procedure patients pulse and general condition was monitored and any reaction was attended to. After the procedure for about 15-20 minutes patient was made to lie down and relax. Patient was then advised to come for follow ups. Based on the FFA findings case was diagnosed to have Dry or wet ARMD and further analyzed.

**Results:-**

Among the 100 ARMD patients studied mean age was 73 years with standard deviation 7.46 and majority were males (79%). Most (56%) of them were smokers among which 55% were males. 52% were between age group 71-80 years. Majority (63%) of the patients had normal vision with their visual acuity <6/12. 86% had normal macular function test and 89% had hyper-flouescence on FFA. Overall 91% had dry ARMD and 9% had wet ARMD. Drusens was the most common finding on

fundoscopy and RPE changes was the second most common finding. No significant association was found between age, gender, history of smoking and type of ARMD with p-value 0.07, 0.8 and 0.46 respectively. Most (68%) of the patients with dry ARMD had visual acuity of range 6/6 to 6/12 and most (77%) of the patients with wet ARMD had visual acuity of <6/60 which is statistically significant with p value <0.001.

Table:- Incidence of Dry and Wet Armd.

	Frequency	Percent
Dry	91	91.0
Wet	9	9.0
Total	100	100.0

The above table shows the incidence of ARMD in patients in this study. Majority of patients included in the study had Dry ARMD (91%) and 9% had wet ARMD

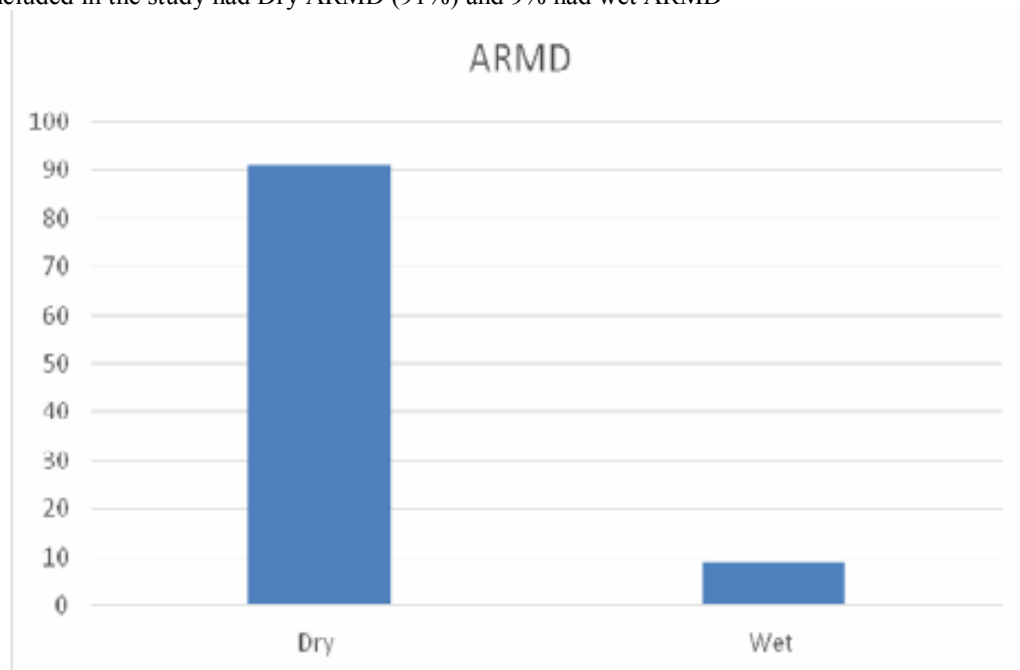


Figure:- Incidence of Dry and Wet ARMD.

Table:- Age distribution of patients studied.

Age in years	Frequency	Percent
<= 60	5	5.0
61 - 70	34	34.0
71 - 80	52	52.0
81 - 90	6	6.0
91+	3	3.0
Total	100	100.0

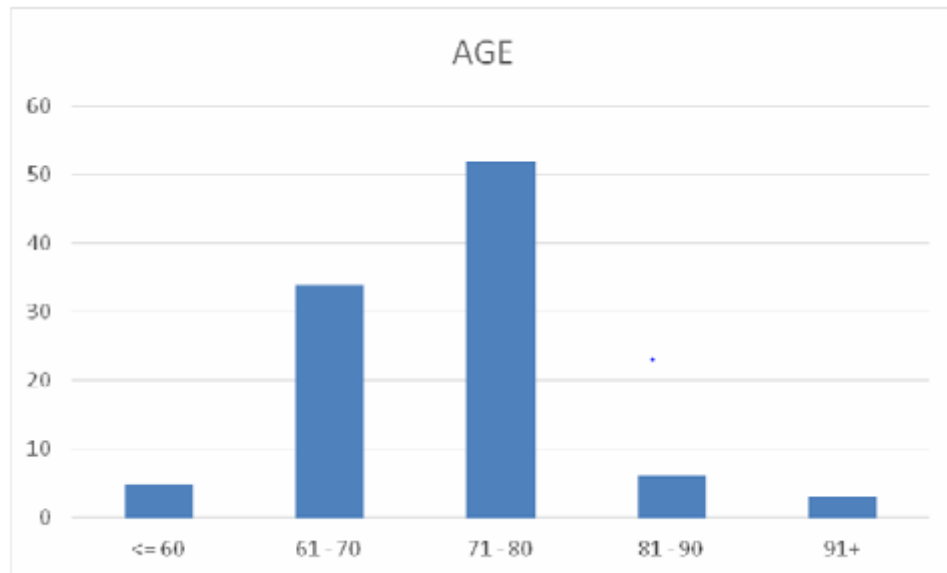
**Figure:-** Age distribution of patients studied.

Table above, shows the age distribution of patients in this study. Majority of patients included in this study were in age group 71-80 years(52%). 31 (34%) patients were in 61-70, 5 (6%) patients were in 81-90, 4 (5%) patients were in <60%.

Table 5:- Gender distribution of patients studied.

Gender	No. of patients	Percent
Female	21	21.0
Male	79	79.0
Total	100	100.0

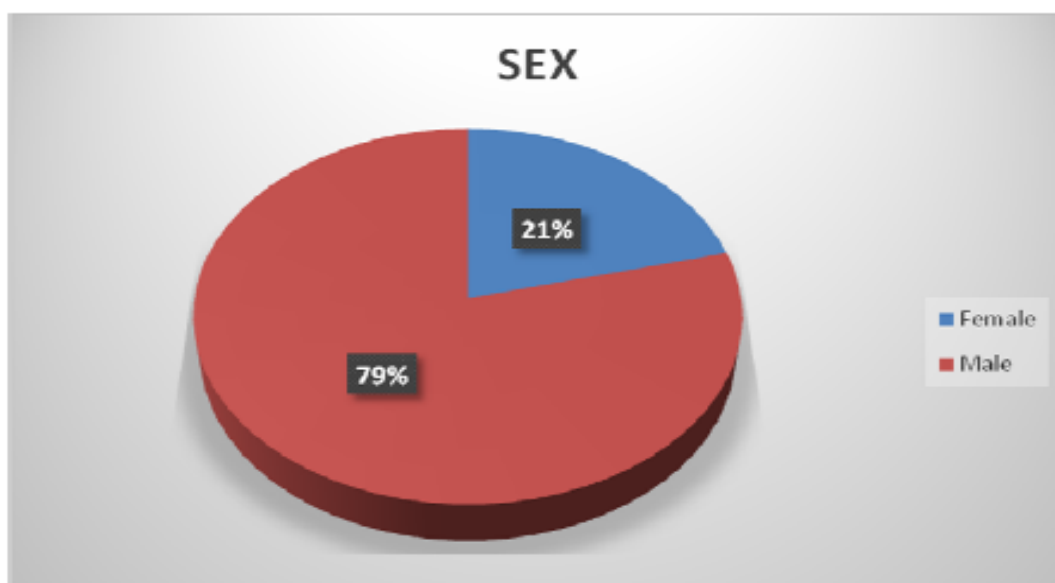


Figure:- Gender distribution of patients studied.

The above table shows the gender distribution of the patients in this study, out of 100 patients 79% were males and 21% were females.

Table:- History Of Smoking

History Of Smoking	No. of patients	Percent
No	44	44.0
Yes	56	56.0
Total	100	100.0

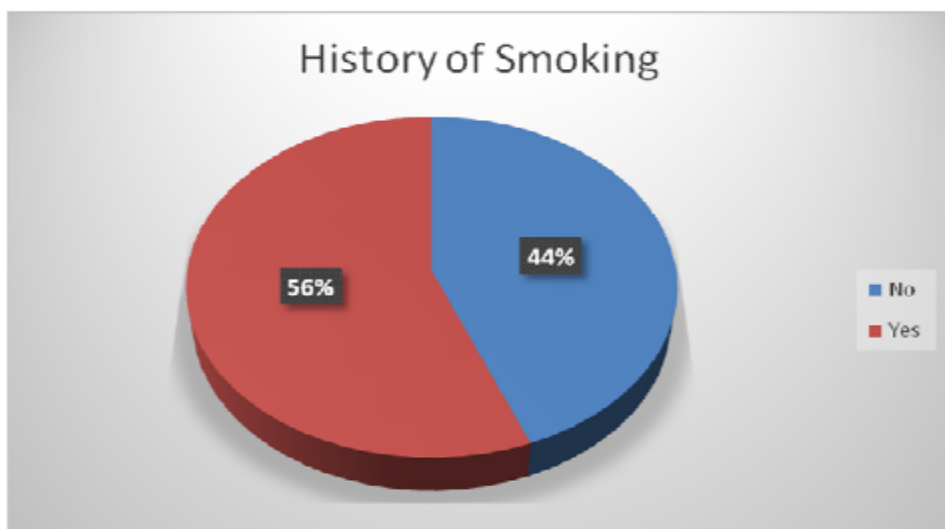


Figure:-History Of Smoking

The above table shows majority of patient 56% in the study had history of smoking

Table:- Macular Function Test.

	Frequency	Percent
Normal	86	86.0
Positive Scotoma	4	4.0
Metamorphopsia	10	10.0
Total	100	100.0

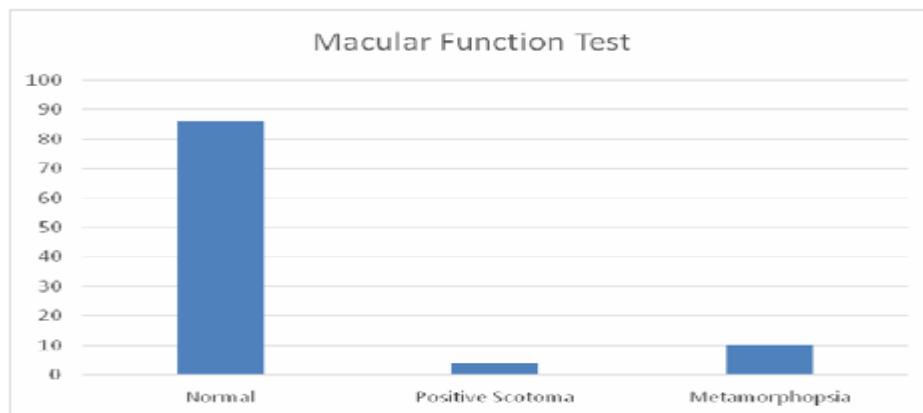


Figure:-Macular Function Test

The above table shows 86% had normal macular function test, 4% had positive scotoma and 10% had metamorphopsia.

Table:-Fundoscopy Of Left Eye.

	Frequency	Percent	Cumulative Percent
Drusens	61	61.0	61.0
RPE changes	32	32.0	93.0
Subretinal fluid/hemorrhage	5	5.0	98.0
Subretinal fibrosis	2	2.0	100.0
Total	100	100.0	

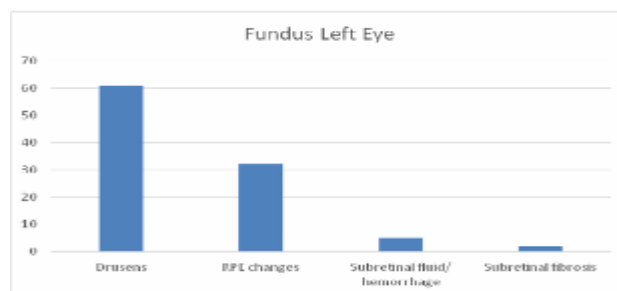


Figure:-Fundoscopy Of Left Eye

The above table shows more common findings are drusens (61%), and second most common RPE changes (32%).

Table:-Visual Acuity RE.

	Frequency	Percent	Valid Percent	Cumulative Percent
6/6-6/12	63	63.0	63.0	63.0
6/18-6/24	27	27.0	27.0	90.0
Valid 6/36-6/60	3	3.0	3.0	93.0
>6/60	7	7.0	7.0	100.0
Total	100	100.0	100.0	

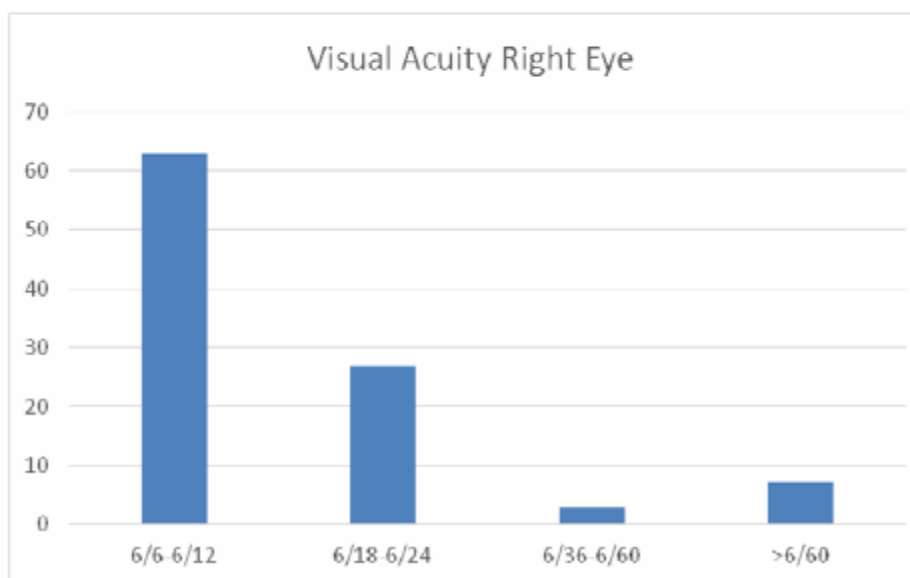


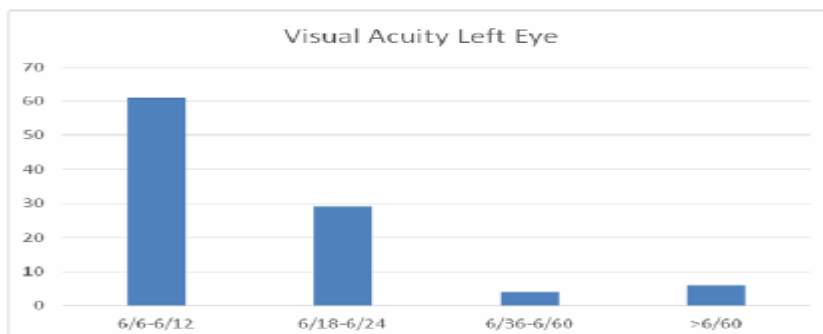
Figure:-Visual Acuity RE

The above table shows best corrected visual acuity in ARMD patients.

Majority of patients with early ARMD have vision varying between 6/6-6/12 and wet ARMD patients had vision <6/60. Most (68%) of the patients with dry ARMD right eye had visual acuity of range 6/6 to 6/12 and most (77%) of the patients with wet ARMD right eye had visual acuity of >6/60 which is statistically significant with p value <0.001.

Table:-Visual Acuity LE.

	Frequency	Percent
6/6-6/12	61	61.0
6/18-6/24	29	29.0
Valid 6/36-6/60	4	4.0
>6/60	6	6.0
Total	100	100.0

**Figure:-**Visual Acuity LE

Most (66%) of the patients with dry ARMD left eye had visual acuity of range 6/6 to 6/12 and most (75%) of the patients with wet ARMD left eye had visual acuity of >6/60 which is statistically significant with p value <0.001

Table:-FFA RE.

	Frequency	Percent	Cumulative Percent
Hyperfluorescence	89	89.0	89.0
Late leakage	10	10.0	99.0
Window defect	1	1.0	100.0
Total	100	100.0	

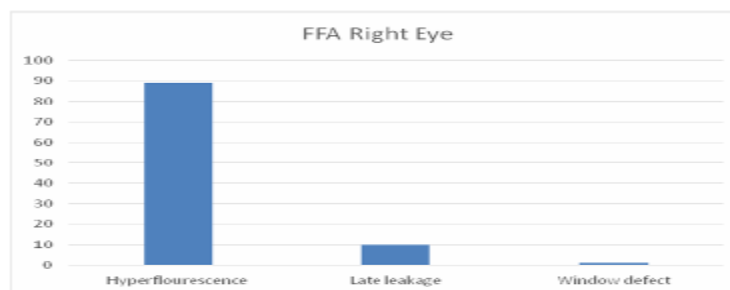
**Figure:-**FFA RE

Table:-FFA LE.

	Frequency	Percent	Cumulative Percent
Hyperfluorescence	89	89.0	89.0
Late leakage	9	9.0	98.0
Window defect	1	1.0	99.0
Normal	1	1.0	100.0
Total	100	100.0	

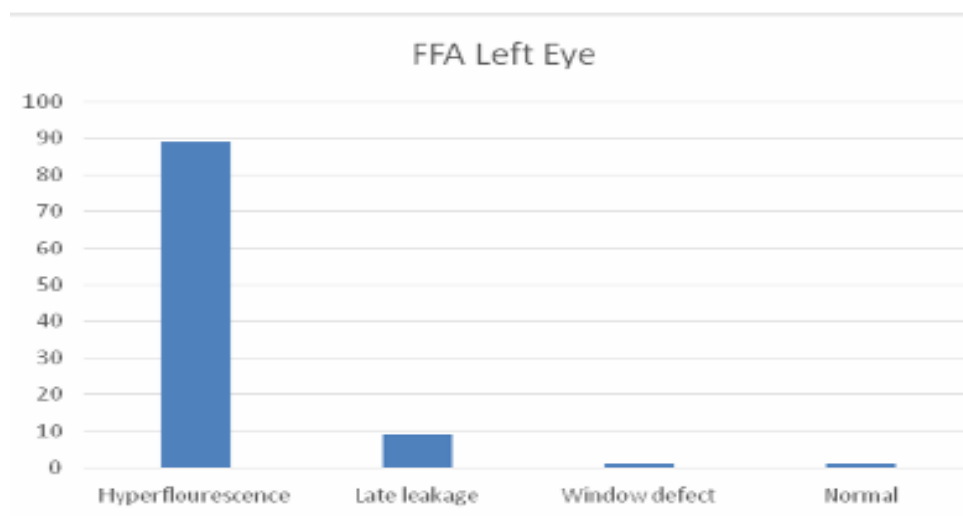
**Figure:-FFA RE**

Table 11 & 12 shows hyperfluorescence is the most common FFA finding (89%) followed by late leakage (9%).

Table:- Association of risk factors with type of ARMD.

Risk factors	ARMD			Chi square	df	p value
	Dry (%)	Wet (%)	Total (%)			
Age						
≤ 60	4	1	5	1.576	4	0.813
61 – 70	31	3	34			
71 – 80	48	4	52			
81 – 90	5	1	6			
91+	3	0	3			
Total(%)	91	9	100			
Gender						
Female	17	4	21	3.277	1	0.07
Male	74	5	79			
Total	91	9	100			
Smoking						
Present	39	5	44	0.536	1	0.46
Absent	52	4	56			
Total	91	9	100			
Visual acuity						
6/6-6/12	62	1	63	79.84	3	<0.001*
6/18-6/24	27	0	27			
6/36-6/60	2	1	3			
>6/60	0	7	7			
Total	91	9	100			

*: Indicates significance.

Discussion:-

In our study, 100 cases of clinically diagnosed ARMD were confirmed by FFA. FA helped in categorizing the ARMD in Dry or Wet ARMD as well as in cases with CNVM – occult or classic varieties and as per location of CNV – as extrafoveal, juxtafoveal, and subfoveal lesions. Age incidence for ARMD: In Framingham study they stated there was a 17-fold increased risk of ARMD comparing the oldest to the youngest age group. The Beaver Dam Eye Study has reported an overall prevalence of 1.6 percent ARMD with 1.2 percent prevalence of exudative disease and 0.6 percent of geographic atrophy.⁷⁹ The five year incidence of early AMD was 3.9% between 43 to 54 yrs of age and 22.8

percent in patients beyond 75 years of age. Similarly higher incidence has been found in the age group of 71-80 yrs in our study. Several studies have shown no overall difference in the frequency of AMD between men and women. Though our studies shows more male preponderance as a similar study done in Japan. Smoking has shown a strong positive association between both wet and dry ARMD. Smoking is a well established risk factor for the development of AMD. Smoking doubles the risk of AMD, and there appears to be a dose response whereby increasing odds are associated with an increased number of pack-years smoked.

In cases with Dry ARMD, FA showed hard and soft drusen as irregular discrete hyperfluorescence due to window defect, there was increased number of

drusen evident on the angiogram as compared to clinical appearance. In our study one case had vision loss out of proportion to clinical findings, FA revealed more extensive areas of RPE atrophy involving the macula which explained the cause of vision loss. In Wet ARMD cases, FA helped in categorizing as classic and occult variety. FA showed presence of subretinal vascular network based on the time of appearance of leakage and the intensity of leakage were categorized as Classic CNVM when early phase showed well demarcated areas with lacy pattern hyperfluorescence and intense late leakage. On other hand, occult CNV showed ill defined area of irregular elevation with stippled hyperfluorescence in mid phase and less intense leakage in the late phase.

Chisholm IH et al stated that "The position and extent of the subretinal neovascular membrane can be demonstrated by FA, as even a through clinical examination will not give enough information about the site and nature of the disturbance especially early asymptomatic small subretinal membrane.

Verma L et al. in their study on CNVM at RP centre, AIIMS stated that "FA as the most useful and practical approach of tracing the macular lesions with FA findings conclusive in most of the cases. Both fluorescein angiographic character and location of the CNV influence in the treatment modality and the outcome.

Though Amsler grid has not been shown to be very sensitive at detecting neovascular ARMD. In our study we found metamorphopsia in all cases of Wet ARMD.

In our study, Dry ARMD patients presented with visual acuity ranging from 6/9 to 6/36 and all wet AMD patients had visual acuity less than 6/60 indicating more visual loss in exudative type. There are several case-control studies showing correlation between hyperopia and AMD, but our study did not show any correlation.

With the advent of optical coherence tomography (OCT) and anti- VEGF drugs, the role of FFA for clinical care has changed. However, FA continues to play important part in assessment of ARMD. FA revealed geographic atrophy and early CNV, which was missed with clinical examination. Especially in Wet ARMD FA has played a major role in describing the lesion morphology and also helpful in assessing response to treatment and activity of disease.

Limitation of our study is FFA is an invasive procedure with more time consuming and with side effects unlike OCT which is a non-invasive procedure which is quick and with no side effects and can be repeated many times with no patient discomfort.

Conclusion:-

The Fluorescein Angiography certainly complements the accuracy of the diagnosis by showing the exact site of pathology, type of ARMD and its further classification. It also acts as a guide in treatment planning and as a prognostic indicator of ARMD.

Bibliography:-

1. Sachdeva RP. Functional anatomy of macula and diagnostic procedures for macular function in clear media. Indian J Ophthalmol 1983;31:105-7.
2. Onakpoya OH, Olateju SO, Ajayi IA. Retinal diseases in a tertiary hospital : The need for establishment of a vitreo-retinal care unit. J National Med Assoc 2008 Nov.;100(11):1286-87. <http://JNMA@nmanet.org>.
3. Klein R, Klein BE, Cruickshanks KJ. The prevalence of age-related maculopathy by geographic region and ethnicity. Prog Retin Eye Res 1999; 18: 371–89.
4. Mitchell P, Smith W, Attebo K, Wang JJ. Prevalence of age-related maculopathy in Australia. The Blue Mountains Eye Study. Ophthalmology 1995; 102: 1450–60.
5. Klaver CC, Assink JJ, van Leeuwen R, et al. Incidence and progression rates of age-related maculopathy: the Rotterdam Study. Invest Ophthalmol Vis Sci 2001; 42: 2237–41.
6. Kawasaki R, Yasuda M, Song SJ, et al. The prevalence of age-related macular degeneration in Asians: a systematic review and meta-analysis. Ophthalmology 2010; 117: 921–27.

14. Wong TY, Chakravarthy U, Klein R, et al. The natural history and prognosis of neovascular
15. age-related macular degeneration: a systematic review of the literature and meta-analysis.
16. Ophthalmology 2008; 115: 116–26.
17. Hem. K. Tevari, Lalit Verma, P.venkesh. Evolution of fluorescein Angiography. Fluroscein
18. angiography – A user’s manual.2nd Ed Noida: New Delhi. 3-5
19. Yanoff, M and Duker SJ Ophthalmology 3rd edition London.Mosby:2004:660
20. Saine PJ. Landmarks in the historical development of fluoresceinangiography . J ophthalmic
21. Photogr. 1993 Apr; 15(1):17-23.
22. Von Helmholtz HH. Description of an ophthalmoscope for examining the retina of the living
23. human eye. AMA Arch Ophthalmol. 1951; 46(5):565-583
24. Keeler CR. A Brief history of Ophthalmoscope. Optometryin Practice. 2003; 4(2):137-145
25. Van Cader TC. History of Ophthalmic photography. J Ophthalmic Photogr. 1978: 17-19
26. . Baeyer A. [Ueber eine neue Klasse von Farbstoffen] Ber. Dtsch. Chem. Ges. 1871;4:555-
27. 559
28. Chao P, Flocks M. The retinal circulation time. Am J Ophthalmol. 1958 Jul; 46:8-10.
29. Blachauski PA.Twenty five years of fluorescein angiography. Arch ophthalmology.1985
30. 103(9): 1301-2
31. Verma L, Das T, Binder S, Heriot W J, Kirchhof B , Venkatesh P etal. New approaches in
32. the management of choroidal neovascular membrane in age –related macular degeneration.
33. Indian J Ophthalmol.2000; 48:263
34. 18. Department of Ophthalmology, University Hospital of Wales, Heath Park, Cardiff. British
35. Journal of Ophthalmology 08/1991; 75(7):398-400.
36. 19. Barbazetto I , Burdan A, Bressler NM, Bressler SB et al. Photodynamic therapy of subfoveal
37. choroidal neovascularization with verteporfin: fluorescein angiographic guidelines for
38. evaluation and treatment--TAP and VIP report No. 2. Arch Ophthalmol. 2003;121(9):1253-
39. 68.