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Profile of Fundus Fluorescein Angiography in Patients of Choroidal Neovascular Membrane with Age related macular degeneration at Western Regional Institute of Ophthalmology

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Abstract: *We present a prospective population based study of 100 cases presenting at the retina clinic of Western Regional Institute of Ophthalmology, Ahmedabad during a study period of 1 year. This study describes the pattern of Fundus Fluorescein Angiography (FFA) findings in Patients of Age related macular degeneration (ARMD) and compares it with studies done elsewhere.*
This study also substantiates using FFA as a main modality for diagnosing ARMD in resource poor setting.
Key Words*: Age related macular degeneration, Choroidal neovascularisation, Fundus fluorescein angiography*

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I. Introduction:

Age-related macular degeneration accounts for 8.7% [1-5] of all blindness worldwide and is the most common cause of blindness in developed countries, particularlyin people older than 60 years. Choroidal neovascularization (CNV) is associated with breakthrough of choroidal neovascular vessels through Bruch's membrane and RPE[6]. The earliest frame where leakage starts defines the CNV lesion. Based on the time of appearance of leakage and the intensity of leakage, CNV has been divided into two main categories: classic and occult. 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. Its prevalence is likely to increase as a consequence of exponential population ageing. There have been significant advances in the management of exudative or so-called wet age-related macular degeneration with the introduction of anti-angiogenesis therapy [7], and patients now have effective treatment options that can prevent blindness and, in many cases, restore vision. However, these treatments are expensive and not available to all patients in many countries. Thus, understanding the prevalence, burden, and population impact of AMD is essential for adequate health care planning and provision, which require both precise and contemporary estimates of disease prevalence.

II. Materials And Methods:

Of the 100 subjects recruited in the population-based study in Western India, 100 subjects with macular disorders who were diagnosed to have AMD clinically and gradable images on 30° three-field retinal and FFA photographs were analyzed. AMD was graded based on the Macular Photocoagulation study (MPS)[6]. All subjects underwent a detailed history, physical examination, and a comprehensive ocular examination. A written consent was obtained from all the participating subjects as per the Declaration of Helsinki.

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

Exclusion Criteria:
1. Hypersensitivity to fluorescein dye.
2. Media opacity
3. Diabetic Maculopathy

4. Cystoid Macular Edema

Clinical examination protocol:
A detailed history, including data on demographic, socioeconomic, and ocular history, was obtained and analysed from all patients at the hospital. A detailed questionnaire was administered regarding the medical history, a general
physical examination, smoking, tobacco and alcohol consumption history, and educational and occupational history.

Ophthalmic examination:
All subjects underwent detailed ophthalmic evaluation, which included assessment of visual acuity and refraction using modified Early Treatment Diabetic Retinopathy Study chart (Low Vision Products; LightHouse, New York, NY, USA), anterior segment examination using a Zeiss SL 130 (Carl Zeiss, Jena, Germany) slit-lamp, intraocular pressure measurement using Goldmann applanation tonometer (Zeiss AT 030; Carl Zeiss), and fundus examination using binocular indirect ophthalmoscope with 20D (Keeler Instruments, Broomall, PA, USA). Grading of lens opacities was performed.

Retinal photographs were obtained after pupillary dilatation (Fundus Camera, Carl Zeiss, Jena, Germany) in colour as well as red free filter. Antecubital vein was secured, scalp vein fixed and the dye was injected and series of photos were taken at 15 secs interval, 1st shot being taken at 0 secs.
CNV was graded according to Macular Photocoagulation Study.
Classic CNV [(6)]: fills the dye in a well defined lacy pattern of intense hyperfluorescence during early transit, subsequently leaking into the subretinal space over 1-2 minutes, with late staining of fibrous tissue. Most CNV is subfoveal, extrafoveal being defined as > or = 200 microns from the centre of foveal avascular zone on fluoresceinangiography.
Atypical Classic CNV [(6)]: Variant of classic which differs with leakage that is not as intense as the typical one and the leakage starts in the early-mid phase of the FA. At times, it has a greater component of fibrosis.
Occult CNV [(6)]: CNV whose limits cannot be fully defined in fluorescein angiography. Variants are **Fibrovascular PED** and **late leakage of undeterminedsource (LLUS).**
Fibrovascular PED: Irregular elevation of the RPE with stippled or granular fluorescence.
LLUS: A scarce variant of occult CNV with ill defined demarcated areas of leakage which appears at the level of RPE in the late phase of angiogram.

Predominantly or minimally classical CNV [(6)]: when classic element is greater or less than 50 % of total lesion.

Three dominant measurements procured from FA: total lesion area, total CNV area and leakage area.

Total lesion area is the sum total of CNV area and the areas of each of the non- CNV lesion components. The total CNV area is enumerated by defining the boundaries of the CNV and is measured from the image where the CNV first appears. For classic type, this area is seen in the early phase and for occult, the late phase.

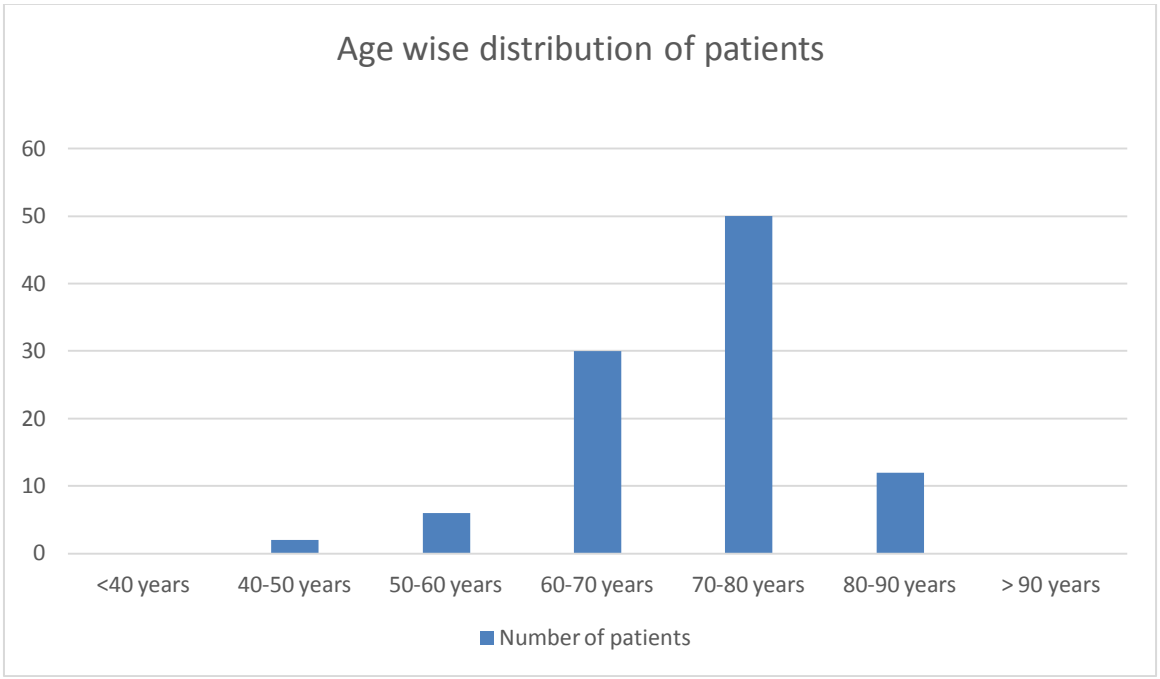
Fluorescein leakage area is the cornerstone of CNV and thus detection of its onset and evaluation of its course across the various phases of angiogram is crucial.

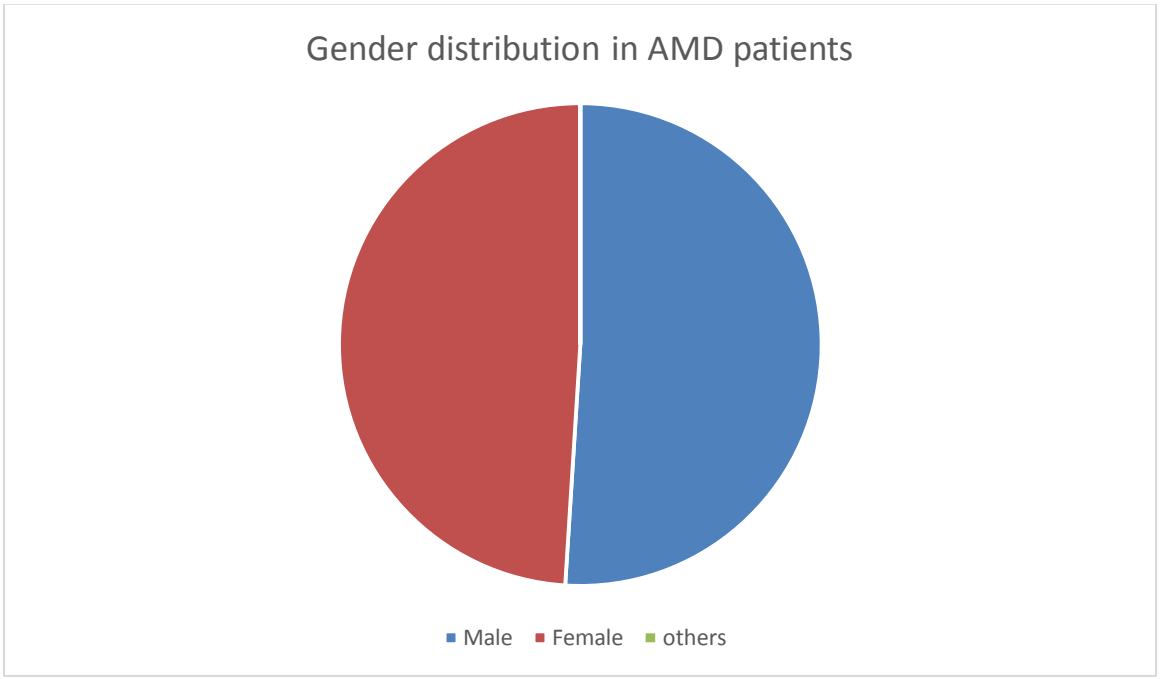
Total area of leakage is measured from the late frames of the angiogram.

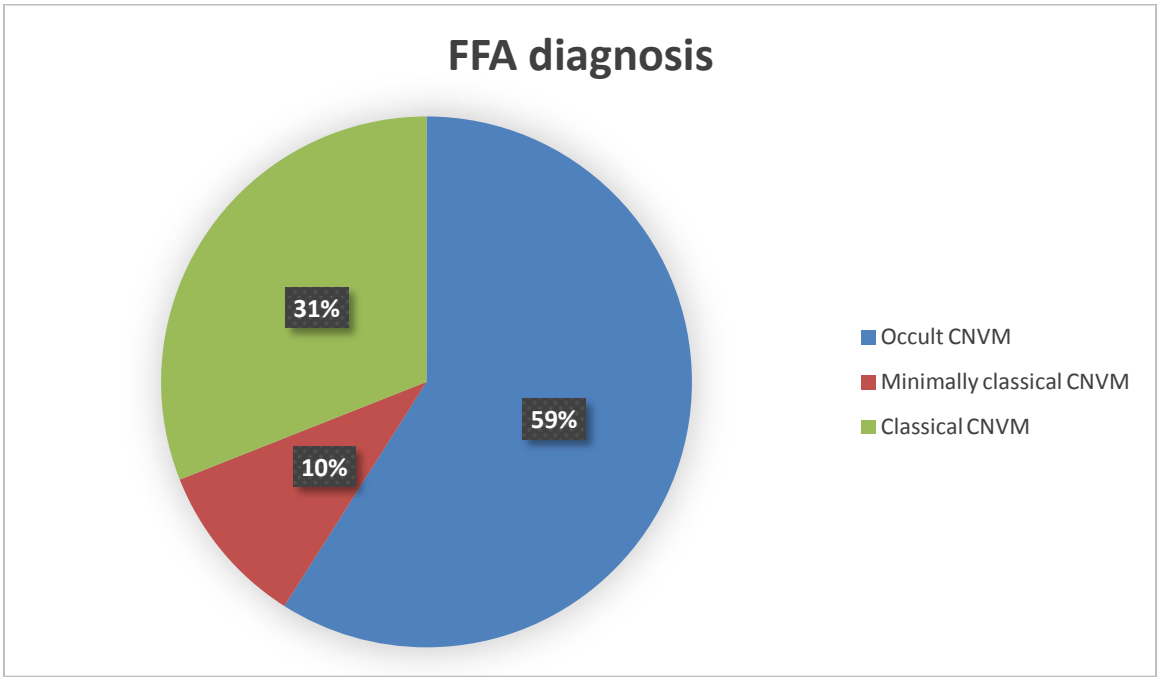
III. Observation:

Among the 100 patients who presented to us with Wet AMD, there were 59 males and 41 females. Mean age of presentation was 74 years with 62 % being above 70 years , 30% being between 60 to 70 years and 8 % being less than 60 years .Out of all 100 patients , 77 patients had visual acuity of <6/60. On
FFA, late leakage (seen in Occult CNVM) was the most common finding seen in 59 patients , 10 patients had features of minimally classical CNV while 31 patients had features suggestive of Classic CNV .

IV. Results:


Age wise distribution of patients
60
50
40
30
20
10
0
<40 years
40-50 years
50-60 years
60-70 years
70-80 years
80-90 years
> 90 years
Number of patients


Gender distribution in AMD patients
Male
Female
others



V. Discussion:

In our study, 100 cases of clinically diagnosed Wet AMD were confirmed by FFA. Three population-based studies-the Beaver Dam Eye Study[8] (USA), the Blue Mountain Eye Study[9] (Australia), and the Rotterdam Study[10] (The Netherlands)-have addressed the prevalence of late AMD in the respective populations. Utilising a similar standard protocol of objective grading using colour fundus photographs, the prevalence of AMD was 1.7% (1.2% exudative; 0.5% geographic atrophy) in the Beaver Dam study, 1.4% in the Blue Mountain study, and 1.2% in the Rotterdam Eye study. The prevalence of AMD in the south Indian population over 70 years is estimated to be 1.1%.[11] Apart from advancing age, the probable risk factors include gender (women are more at risk), cigarette smoking, hypertension, and dyslipedimia.[12] In most studies Caucasians have been found to be more at risk. A prevalence of 1% or less is reported in many population-based studies involving black races.[13-15] The racial difference in late AMD has been attributed to the possible protective effect of melanin pigments. It is probable that melanin acts as a free radical scavenger, protecting the outer layers of the retina and the inner layers of the choroid from degenerative changes.[16]

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.

Smoking has shown a positive association in Wet AMD especially in males and there appears a dose response whereby increasing odds are associated with an increased number of packed years smoked.

Chisholm IH et al [17] 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. [18] in their study area of irregular elevation with stippled hyperfluorescence in mid-late phase. It will be useful to explore the chronological relationship between peripheral changes and the onset and evolution of macular disease through long-term prospective studies combining ultrawide-field autofluorescence and FA. If peripheral perfusion abnormalities precede central fundal changes, and are picked up early, this may provide an opportunity for preventative treatment to preserve central vision.

VI. 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.

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