



## Proportion of different angiographic patterns / findings in patient referred for Fundus Fluorescence Angiography (FFA)

### A Author's Affiliation

Shaista Usman

Dr. Suhail Sarwar

Correspondence Author:

Shaista Usman  
 Investigative Oculist  
 College of Ophthalmology &  
 Allied Vision Sciences (COAVS)  
 KEMU/ Mayo Hospital Lahore

**Objectives:** To determine the proportionate distribution of different angiographic findings in patients referred for FFA from Jan 2012 to Dec 2012.

**Methodology:** This study was conducted on 1058 patients who underwent FFA in year 2012. Individuals of different age group including male and female with retinal vascular diseases were included. Sample size included all the patients who underwent FFA. Sample design include specially designed MS database for the purpose. Equipment used was fundus camera.

**Results:** Leading cause of retinopathy is diabetes (n=471, 44.5%). Patients having mild Non proliferative diabetic retinopathy (NPDR) were 111, moderate NPDR 137, severe NPDR 109, very severe NPDR 01, high risk proliferative diabetic retinopathy (PDR) 48, low risk PDR 65, multifocal exudative maculopathy 319, diffuse exudative maculopathy 132. Other causes included Central serous chorioido retinopathy (CSCR) 03, Branch Retinal Vein Occlusion (BRVO) 51, Central Retinal Vein Occlusion (CRVO) 11, Pigment Epithelium Window Defect (PEWD) 205, Hypertensive Retinopathy (HR) 03, Choroiditis 12, Choroidal Neovascularization (CNV) 21 and normal 361.

**Conclusion:** There is great need of patients' awareness about angiography for patients of diabetes and hypertension because majority of patients have retinopathy due to uncontrolled/ unknown diabetes and hypertension that can lead to blindness.



## INTRODUCTION

Fluorescein angiography is the technique of using intravenous fluorescein to evaluate ocular blood circulation. Fluorescein angiography is a remarkable *in vivo* technique. The study and diagnosis of retinal, macular and choroidal pathologic lesions have been greatly revolutionized with the advent of fundus fluorescein angiography (FFA) and, with its help, retinopathy can be diagnosed quite early.<sup>1</sup>

It is also of great value in evaluating causes of visual acuity loss in diabetics as well as in the documentation of non perfusion of their peripheral retinas.<sup>2</sup> FFA is and has been employed for diagnosing posterior segment disorders. It can also serve as a guideline tool to evaluate the development and course of the disease during treatment. Most commonly, it is used to study retinal vasculature and any related disorder or any abnormality of the retino-choroidal junction. It is also utilized, albeit less often, for studying choroidal and optic nerve head pathologies.

Sodium fluorescein ( $C_{20}H_{10}O_5Na_2$ ) is an organic water soluble dye. The dye absorbs light in the blue range (particularly between 465 to 490 nm) of the visible spectrum and emits light from 500 to 600 nm with a maximum intensity at 520 to 530 nm (green-yellow). When the exciting beam reaches the fluorescein molecule, the latter gives off light of a different wavelength that can be detected. Approximately 70–80% of the sodium fluorescein binds to plasma proteins; 20–30% does not bind.

Fluorescein angiography using parenteral sodium fluorescein is generally effective and safe in standard clinical practice but occasionally may cause adverse, and sometimes serious, side effects.<sup>3,4</sup>

In humans the retina is perfused by the central retinal artery and the posterior ciliary arteries. Normal retinal vessels are impermeable to fluorescein due to zonula occludentes. Fluorescein dye is injected intravenously and is useful in evaluating the retinal circulation. It demonstrates the rate of flow, leakage from capillaries, staining of tissues, areas of non perfusion and neovascularization. Blood volume can also be determined by staining red cells with fluorescein sodium.<sup>5</sup>

The Blood-Retinal Barrier (BRB) is a situation of restricted permeability which is present between the blood and the retina.<sup>6</sup>

Sodium fluorescein has been proven to be the agent of choice for sensitive detection of leakage of vessels of the retina. Direct comparisons of the diagnostic capability of free and encapsulated sodium fluorescein in blood are now possible.<sup>7</sup>

The time between injection of the dye into the antecubital vein and its first detection in the central retinal artery is called the arm-retina-time which is usually from 7 to 15 seconds, depending upon age of the person (being shorter

in young people and longer in the elderly) the length of the cubital vein, cardiac output and blood pressure of the patient and the speed with which it is injected. The dye appears first in the choroid and, soon after that, in the central retinal artery.

The following are six phases of a normal fluorescein angiogram:

1. Choroidal filling 8 – 15 seconds after injection
2. Retinal arterial filling 1 – 2 seconds after choroidal filling
3. Venous lamellar filling 2 – 3 seconds after arterial filling
4. Full venous circulation < 11 seconds after arterial filling
5. Recirculation 30 – 150 seconds after injection
6. Late phase 10 – 30 minutes after injection

To analyze an angiogram, it is important to look at

- (i) Phase of the angiogram (the when) i.e. whether it is choroidal/ arterial/ arteriovenous/ capillary/ venous/ late.
- (ii) the site of the lesion (the where) i.e. nasal/ temporal/ superior/ inferior/ the level in the retina/choroid/pigment epithelium or.
- (iii) the nature of the lesion (the what) i.e. normal vessel/ abnormal (leaking) vessel (hyperfluorescence) or blocking defect (hypofluorescence).

On angiography aneurysms become more clearly defined and numerous and their relationship to capillary bed is evident. They fill relatively slowly because of the sluggish blood flow and appear as hyper fluorescent dot. Some of the aneurysms may lose their sharply defined margins in the late phases of angiograms due to mild leakage of dye.

The fluorescein angiographic hallmark of retinal hemorrhage is hypofluorescence with obstruction of the underlying anatomical layer.

In arterial phase of angiography, the hard exudates appear as hypofluorescent ring due to fluorescein blockage and in late venous phase may appear as mild hyperfluorescent due to some diffusion of dye into the exudates.

### Capillary non-perfusion:

Angiographic hypofluorescence after the arterial phase.

Intra-retinal microvascular abnormalities:

Arterial phase will be normal. Venous phase will be hyperfluorescent with slowly increasing fluorescence.

Neovascularization:

Angiographic patterns of hyperfluorescence are observed due to leakage of vessels.

### Hypertensive retinopathy:

On fluorescein angiography, cotton wool spots show an area of central hypofluorescence with a margin of dilated





capillaries. In the late phase, the dye may diffuse into the central patch. In the presence of macular star no leakage of dye is usually seen.

#### Diabetic retinopathy:

The grading of diabetic retinopathy from fundus photographs may have a potential advantage over conventional classifications of diabetic retinopathy.<sup>8</sup>

According to ETDRS there is substantial statistical agreement between severity of fluorescein leakage and cystoid spaces, and moderate for capillary loss, capillary dilatation, narrowing of arteriolar side branches, staining of arteriolar walls, and source of fluorescein leakage (microaneurysms versus diffusely leaking capillaries).<sup>9</sup>

According to these features, diabetic retinopathy can be defined as mild, moderate and severe non proliferative retinopathy low risk and high risk proliferative retinopathy.

#### Retinal vein occlusion:

Delayed arterio-venous transit time in the involved area, areas of capillary non-perfusion, blocked fluorescence, dilatation and tortuosity of involved vessels, collaterals, retinal disc neovascularization and macular edema and ischemia.

#### Retinal arterial occlusion:

Non-filling or delayed filling of involved vessels and hypofluorescence of involved region, staining of sclerotic vessels.

In the previous studies it has been shown that fundus fluorescein angiography has been used for various diagnostic tools of retinal vasculature abnormalities.

The techniques used nowadays in retinal angiography such as utilization of a fundus camera using an exciter and a barrier filter, and electronic flash to sequentially record the retinal blood flow on film following a injection of sodium fluorescein were pioneered by H.R. Novotny and D.L. Alvis in 1961.

Changes in the vascular endothelium and retinal pigment epithelium result in abnormalities of retinal vasculature that causes increased permeability or disruption of the inner and outer BRB, respectively.

In clinical ophthalmology, for the diagnosis of breakdown of the BRB, vascular retinopathies and pigment epitheliopathies can be diagnosed by fluorescein angiography. These pathologies are present in Diabetic and hypertensive retinopathies, retinal vein obstruction, retinal & choroidal neovascularization, blood diseases, trauma or surgery to the eye, temporary arterial obstruction, perivasculitis, Behcet's and Coats' diseases, certain retinal tumours, choroidal ischaemia, detachment of the pigment

epithelium, retinal detachment, central serous choroidopathy, multifocal inner choroiditis and acute placoid pigment epitheliopathy.<sup>10</sup>

Generalized changes in circulation can be found in arterial hypertension, diabetes mellitus, and arteriosclerosis. But often, the dysfunction is at the local microcirculation level e.g. in central retinal vein occlusion, acute retinal artery occlusion, and ischemic eye disease. The retina is one of the only places where the microcirculation can be investigated non-invasively. The central retinal artery branching divides the retinal circulation into four independent non-communicating quadrants. The time of the arteriovenous passage (AVP) can therefore serve as a good indicator of retinal microcirculation. This parameter was measured before and after treatment using video fluorescence angiography in many patients of retinopathy revealing the abnormalities of the microcirculation.<sup>11</sup>

#### Methodology:

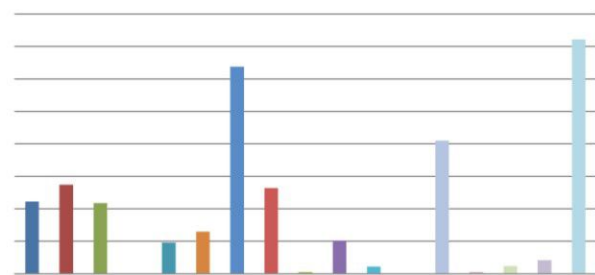
Individuals of different age group including male and female with retinal vascular diseases were included while patients with all types of other ocular diseases were excluded. Duration of study was one year. Sample includes all the patients who underwent FFA. Equipment used was Fundus camera. Data was analyzed using SPSS software.

#### Results

##### Graph 1:

This graph shows distribution of different retinal diseases undergoing FFA.

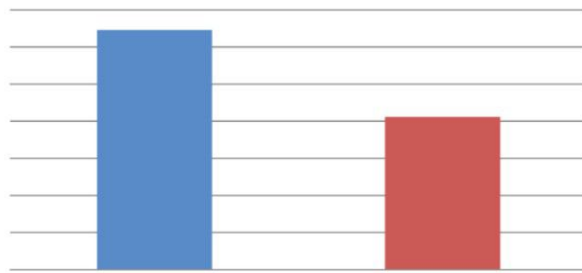
According to this patients having simple diabetic retinopathy are 471 comprising mild NPDR 111, moderate NPDR 137, severe NPDR 109, very severe NPDR 01, high risk PDR 48, and low risk PDR 65, while multifocal exudative maculopathy are 319 and diffuse exudative maculopathy 132. Other pathologies include CSCR 03, BRVO 51, CRVO 11, CRAO 0, PEWD 205, HR 03, Choroiditis 12, CNV's 21. Normal FFA was seen in 361 patients.



Diseases Distribution Graph

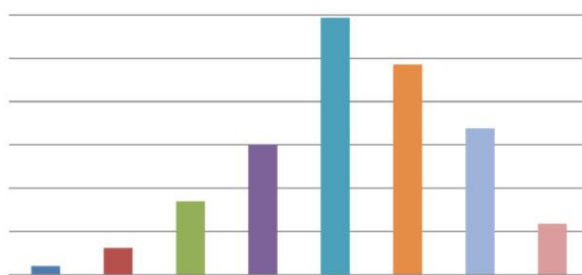
**Graph 2:** This graph shows a preponderance of male as compared to females





**Gender Distribution Graph**

**Graph 3:** This graph shows distribution of different age groups. Almost half of the patients are from fifth and sixth decades



**Age Distribution Graph**

#### Discussion:

In this study, 1058 patients having different retinal vascular diseases had undergone FFA out of which 646 were males and 412 were female ranging age 0 to 70 years as discussed in graphs.

Most of the patients belong to age group 41 to 50 years of age (297). Majority of patients have diabetic retinopathy (471 patients). In Pakistani population uncontrolled and unknown diabetes are main causes of increased number of diabetic retinopathy as shown in data. Second major disease is branch retinal vein occlusion (BRVO). Data shows 51 patients. Leading cause is hypertension which is uncontrolled and even unknown.

Data shows 361 normal findings which show 34% patients have no need of FFA. So indications for FFA should be carefully evaluated before referral in context to potential (even life threatening) side effects.

#### Conclusion:

There is great need of patients awareness about diabetes and hypertension because majority of patients have uncontrolled and unknown diabetes and hypertension. Pre test evaluation is necessary in patients referred for FFA in context to potential side effects of fluorescein dye injection and patients who do not have any evident retinal pathology.

#### Recommendations:

Campaigns should be organized for people awareness about diabetic control and routine check-ups including diabetic retinopathy screening so that diabetic retinopathy complications leading to vision loss can be avoided.

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