### Original Article

# DIAGNOSIS OF DIABETIC MACULAR EDEMA (DME) BASED ON FUNDUS FLUORESCEIN ANGIOGRAPHY (FFA) FINDINGS:

Qamar Mehboob\*, Zafar Hussain\*\*, Muhammad Arif\*\*\*

\*Assistant Professor, Physiology Department, Independent Medical College, Faisalabad.

\*\*Associate Professor, Physiology KMS Medical College, Sialkot.

\*\*\*\*Assistant Professor, Ophthalmology department, PMC/Allied Hospital, Faisalabad, Pakistan

#### ABSTRACT:

**PURPOSE**: The present study was designed to see the Physiological changes in diabetic macular edema (DME) as assessed by fundus Fluorescein angiography (FFA) and to plan the appropriate treatment regime for the patients after assessing the specific type of diabetic macular edema adopted internationally.

**STUDY DESIGN**: Prospective observational study. The patients were selected by simple random technique.

**MATERIALS AND METHODS**: Total one hundred patients (200 eyes) were selected according to the inclusion and exclusion criteria. They were examined in the outpatient department and diagnosed having as diabetic macular edema with no opacity in refractive media. After checking their visual acuity (VA), FFA was done in the Diagnostic and Research Centre, Department of Ophthalmology, Allied hospital, Faisalabad. Pakistan. The data was collected, arranged and analyzed.

DURATION; Jan 2012 - Jan 2013

**RESULTS**: Out of 200 eyes, on FFA our results showed diffuse maculopathy in 140 eyes (70%), Focal type in 36 eyes (18%) and Ischemic type in 24 eyes (12%).

**CONCLUSION**: The treatment schedule of all types of diabetic macular edema highly differs with each expert other. So, for proper diagnosis and treatment is concerned only clinical examination cannot be relied upon.

KEY WORDS; Diabetic macular edema, FFA, Diffuse, Focal, Ischemic.

#### **INTRODUCTION:**

Diabetic Retinopathy is a well-known complication of diabetes mellitus. Diabetic macular edema is a common complication of diabetic retinopathy and is one of the leading causes of visual acuity loss and blindness worldwide<sup>1</sup>. The prevalence of DME varies with the type, duration and stage of diabetic retinopathy, and found to be 3% in mild non-proliferative retinopathy, 38% in moderate-to-severe non-proliferative retinopathy and 71% with proliferative retinopathy<sup>2</sup>.

Micro aneurysms start to appear after 5 years in 25% of type 1 diabetes cases, affect half of cases at 10 years. After 20 years, it affects nearly all patients. The marked features of PDR appear, as affects almost 40% after 20 years of the disease. A similar pattern is

followed by maculopathy which finally affects 10-20% of the cases. In type II diabetes, the similar changes may be present at diagnosis because subclinical excessive glucose levels may have been present for a prolonged preceding period of disease<sup>3</sup>. Gerald Liew et al reported that diabetic macular ischaemia (DMI) has a definite relation with narrower retinal arterioles in patients with type 2 diabetes<sup>4</sup> .The underlying pathophysiology may have some relation with changes in

Corresponding Author: Dr. Qamar Mehboob Assistant Professor,Physiology Department,Independent Medical College, Faisalabad, Pakistan. Ph: +92313-4458720 E-Mail:qamarmehboob89@yahoo.com levels of oxidative stress and inflammation effecting retinal arteriolar diameter<sup>5</sup> .Retinal vasodilation is said to be impaired in prediabetes and diabetes<sup>6</sup>. It was reported that topical dilating drops have no influence on vessel calibres<sup>7</sup>.The extent of ischemia can also be estimated by using non-invasive haemodynamic measurement techniques<sup>8</sup> or the other way by measuring vascular diameters at different points which are differently affected<sup>9</sup>.

Progression of retinopathy is affected by the severity and the length of time that hyperglycemia exists<sup>10</sup>. Prevention to the progression of DR may significantly decrease the economic burden related to this complication of diabetes<sup>11</sup>.

#### **DIABETIC RETINOPATHY ASSESSMENT:**

The most important standard for diagnosis is retinal photography of the dilated eye with accompanying ophthalmoscopy, especially when the retinal photographs are of poor view) $^{12}$ . quality (e.g cataract clouding Diagnosis depends on signs and symptoms, examination and investigations. Diabetic status is checked according to Criteria"<sup>13</sup>. Diagnostic "Diabetes Clinical examination includes ophthalmoscopy and slit lamp examination, indicating specific signs. Other specific investigations include Fundus Fluorescein Angiography (FFA) and Optical Coherence Tomography (OCT). In FFA, retinal photographs are taken after injecting Fluorescein dye.

## FUNDUS FLUORESCEIN ANGIOGRAPHY (FFA):

The sodium fluorescein is an orange-red crystalline hydrocarbon with a molecular weight of 376 daltons that diffuses through most of the body fluids. . It is available as 2-3 ml of 25% concentration or 5 ml of 10% concentration in a sterile aqueous solution. It is injected into a peripheral vein and enters the ocular circulation via the ophthalmic artery 8-12 seconds later, depending on the rate of injection and the patient's age and cardiovascular status. The retinal choroidal vessels fill during the transit phase, which ranges from 10 to 15 seconds. Choroidal filling is characterized by a patchy choroidal flush, with the lobules often visible. Because the retinal circulation has a longer anatomical course, these vessels fill after the choroidal circulation<sup>14</sup>. **FFA** is a specific test by which we can evaluate not only the stage of the disease but also guide the treatment with laser photocoagulation<sup>15</sup>. FFA images are clinically very useful in the treatment of macular edema<sup>16</sup>. These images can show a full view of the retinal vessels which cannot be clearly visualized by colour fundus images<sup>17</sup>.

#### **MATERIAL AND METHODS:**

A total number of 100 known diabetic selective patients (200 eyes) with macular edema were included in present study. It was an observational and interventional study. The patients were selected following inclusion and exclusion criteria. Only known diabetics with complaint of decreased vision with diabetic macular edema having vision in both eyes were included while patients with dense opacities in refracting media; cataract, corneal opacity or vitreous hemorrhage, patients with history of hypersensitivity reaction to Inj. Fluorescein., known cases of glaucoma, any macular disease like age related macular degeneration which can alter retinal architecture, patients having only one seeing eye or normal 6/6 visual acuity, were excluded. The study was complicated in collaboration of Ophthalmology Department, Allied Hospital, Faisalabad. The average age of the patients was 50.02±4.21 years. The minimum and maximum ages wee noted as 40 and 64 years respectively. Both male and female patients were studied. Sixty seven were male and thirty three were female patients. The study was conducted for a period of one year. A written consent was taken from every patient. The pupils were dilated with 1% tropicamide (Mydriacyl) eye drops. One drop was instilled three times in each eye with 15 minutes interval. The pupil remains dilated for 4-5 hrs after completion of the test and the patient feels blurring of vision for that duration. All the patients were well informed about these effects.

#### **FUNDUS EXAMINATION:**

Detailed fundus examination was done with the help of slit-lamp biomicroscope along with +78D fundus viewing VOLK lens.

#### PREPARATION FOR FFA:

5ml 10% Inj.Fluorescein i/v was given to the patients before doing FFA. If slight haziness found in refracting media. 3ml of 25% Inj. Fluorescein was used. All the patients were well informed about the purpose and side effects of the dye.

#### **POSITION OF THE PATIENT:**

All the patients were examined in comfortable sitting position with chin placed on chin rest plate and head well coinciding with head belt.

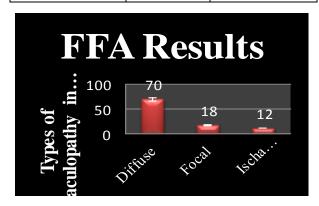
#### FFA:

It was done in a dark room with TOPCON TRC 50DX TOKOYO JAPAN, to see physiological changes. The dye was injected intravenously and multiple fundal pictures were taken at the same time, firstly for right and then left eye. Diabetic maculopathy was graded by use of the Early Treatment Diabetic Retinopathy study (ETDRS) criteria<sup>18</sup>. All the results were collected and arranged according to table-1.

**RESULTS**: Graphical Presentation of FFA Results, data recorded in Table:1.

Table 1: Description about FFA Results of the study group.

Type of maculopathy	No.of eye n=200	Percentage
Diffuse	140	70
Focal	36	18
Ischemic	24	12
Total	200	100



In Diabetic macular edema, due to the disease process, swelling of the retina takes place. The fluid is leaked out from blood vessels within the macula and disturbs the vision. Mainly it is the distributary pattern and the amount of the edematous fluid and vascular changes by which we decide the type of DME. If the fluid is diffusely present, it will be categorized as Diffuse Diabetic Macular Edema (DDME). If the fluid is focally present, it will be categorized as Focal Diabetic Macular Edema. If with edema, we have ischemic changes, we label it as Ischemic maculopathy. On FFA, diffuse leakage of fluorescein dye can be seen in DDME. FFA shows foci of fluorescein dye in Focal Diabetic Macular Edema and ischemic changes neovascularization in Ischemic type. In our study, we found three different FFA patterns. Diffuse maculopathy was seen in 140 (70%) eyes, Focal type in 36 (18%) and Ischemic type in 24 (12%) eyes. Our results showed that diffuse type is the most common in these cases.

#### **DISCUSSION:**

Diabetes mellitus is the condition in which blood glucose level remains persistently high. It is the leading cause of blindness all over the world including the developed countries. It can affect the overall quality of life and one's ability to work. If it is not managed, it can even threaten the life. Mainly diabetic retinopathy is of 2 types non-proliferative and proliferative. These can be differentiated by the presence (proliferative) or absence (nonproliferative) of abnormal new blood vessels<sup>19</sup>. In the past, the management choices were easy, although not always successful: The choice was between observation and laser photocoagulation. Today, management of chronic DME has become one of the biggest day-to-day challenges for the retina specialist. This has happened for good reasons. We understand the disease better, we have better technologies to visualize DME, and we have more treatment options. So it was planned to conduct a study in which assessment of DME should be done through the most advance investigations because treatment plan greatly depend upon proper and comprehensive diagnosis.

In present study DME was assessed by FFA, OCT, visual acuity and blood analysis. We studied 100 known cases (200 eyes) of DME

with an average age of  $51.04 \pm 6.26$  years. The minimum and maximum ages were noted as 42& 63 years respectively.

On FFA our findings suggest three types of DME, Diffuse (70%), Focal (18%) and Ischemic (12%). According to our results, diffuse type is the most common type. Same results are reported by Sarfaraz and his colleagues<sup>20</sup>. Karan<sup>21</sup> described same types of DME. In Priyank's<sup>22</sup> study we find same FFA patterns. His study work also showed that in the clinical diagnosis of diabetic macular ischemia, FFA indicates areas of retina with scanty blood flow through the macular capillaries as relative hypo fluorescent. Our results slightly differ from the results of Kang<sup>23</sup>. He classified fluorescein angiographic leakage in DME into three different types. Type I includes focal leakage which is a welldefined focal area of leakage either from dilated capillaries; or microaneurysms. Type II is the diffuse leakage showing widespread leakage from retinal capillary bed; or the intraretinal microvascular abnormalities. Type diffuse cystoid leakage accumulation of the dye in the cystic spaces of the macula in the late phase of the angiogram.

In their research work, Se W et al 24 found that focal leakage was more than diffuse leakage. We get almost same results in our study. A report forwarded by Nizan Kowska et al<sup>25</sup> the incidence of diabetic maculopathy was 81.6%. These results are comparable with our study work. In their research Suresha et al<sup>26</sup> reported that out of 17 cases of Diabetic maculopathy, 5 cases were of CSME (29.4%), 3 cases were focal maculopathy (17.6%), 4 cases were diffuse maculopathy (23.52%) and 5 cases were found to be of ischemic maculopathy (29.4%) by FFA. These results are comparable with our study. In another report forwarded by Ahmadou<sup>27</sup> incidence for diabetic maculopathy was found to be 14.5% (59/407) of all participants, and 36% (59/164) of patients with DR. The present study has bloom out the correlation between the findings of the two important clinical examinations for clinically significant diabetic macular edema. Our study results showed focal leakage on FFA, closely correlated with a smooth foveal thickening on pronounced in subretinal space or the outer layers of retina. Findings of both OCT and FFA imply that diabetic macular edema is a disease of broad

spectrum and its treatment should be decided according to the subtypes of macular edema. The interpretation of clinically significant diabetic macular edema based on OCT and FFA findings would help to select an appropriate treatment plan for the diverse manifestations of diabetic macular edema.

#### **CONCLUSION:**

Greater emphasis must be placed preventing complications, which will require better understanding mechanisms by which diabetes affects the retina and an improved means of detecting retinopathy. So that a comprehensive treatment plan can be designed to treat these cases individually according to the international standards. Only medical treatment is not sufficient. Surgical treatment should also be advised, where it is required. It is a great fact that better and accurate the diagnosis, the exact will be the treatment plan. So diagnostic measures should be sophisticated for effective treatment regimen.

#### **REFERENCES:**

- 1. Karim R, Tang B (2010); Use of antivascular endothelial growth factor for diabetic macular edema. Clin Ophthalmot; 4:493-517.
- Rosenblatt B, Benson W (2003); Kanski"s Clinical Ophthalmology: A systematic approach. Kanski JU, editor. London: Butterworth and Heinemann.
- Younis N, Broadbent DM, Vora JP et al (2003); Incidence of sight-threatening retinopathy in patients with tpe 2 diabetes in the Liverpool Diabetic Eye Study: a cohort study, Lancet, Jan 18, 361(9353): 195-200.
- Gerald Liew, Dawn A. Sim et al (2015); Diabetic macular ischaemia is associated with narrower retinal arterioles in patients with type 2 diabetes. Acta Ophthalmologica, 93, 1, e45– e51, February, DOI: 10.1111/aos.1251
- Daien V, Carriere I, Kawasaki R, Cristol JP, Villain M, Fesler P, Ritchie K & Delcourt C (2013): Retinal vascular caliber is associated with cardiovascular biomarkers of oxidative stress and inflammation: the POLA study. PLoS One 8: e71089.
- 6. Lott ME, Slocomb JE, Shivkumar V, Smith B, Quillen D, Gabbay RA, Gardner TW & Bettermann K (2013): Impaired

- retinal vasodilator responses in prediabetes and type 2 diabetes. Acta Ophthalmol **91**: e462–e469.
- 7. Vandewalle E, Abegao PL, Olafsdottir I (2013): Phenylephrine OB & Stalmans 5% added to tropicamide 0.5% eye drops influence retinal does not oxygen saturation values retinal vessel or diameter in glaucoma patients. Acta Ophthalmol **91**: 733–737.
- 8. Pemp B, Cherecheanu AP, Garhofer G & Schmetterer L (2013): Calculation of central retinal artery diameters from non-invasive ocular haemodynamic measurements in type 1 diabetes patients. Acta Ophthalmol **91**: e348–e352.
- 9. Torring MS, Aalkjaer C & Bek T (2014): Constriction of porcine retinal arterioles induced by endothelin-1 and the thromboxane analogue U46619 in vitro decreases with increasing vascular branching level. Acta Ophthalmol **92**: 232–237.Direct Link:
- 10. Bhavsar AR et al (2012); Diabetic Retinopathy, Medscape, Jun.
- 11. Heintz, A.B. Wirehn, B.B. Peebo, U. Rosenqvist, L. a. Levin (2010), Prevalence and healthcare costs of diabetic retinopathy: a population based reregister study in Sweden, Diabetologia, 53, 10, 2147-2154.
- 12. Ockrim z, Yorston d (2010); managing diabetic retinopathy, BMJ, 2010, Oct,25,341: c5400. Doi: 10.1136BMJ.c5400.
- 13. Vijan S (2010) Type II diabetes, Annals of internal medicine, Mar 2, 152(5).
- 14. Carl Regillo, Nancy Holekamp, Mark W.Johnson et al (2012): Cataract surgery in Patients with Diabetes, Retina and Vitreous Section 12, Basic and Clinical Science Course (2011-2012), 131.
- 15. Sankaranethralaya (2014); Fundus fluorescein angiography (FFA) www.sankaranethralaya.org/patient-care-eye-q.html, Sept, 20.
- Swapna T R, Chandan Chakraborty (2014); Diabetic Maculopathy Detection Using Fundus Fluorescein Angiogram Images - A Review, Iwcps,3, 15, Dec. http://www.ijret.org
- Mihaela Florescu, Adriana Stanila.
  (2013).The role of Fluorescein Angiography in Diagnosis and treatment of Diabetic Retinopathy. ACTA Medica

- Transilvanica.pp.275-277.http://www.amtsibiu.ro/Arhiva/2013/ Nr3-en/Florescu.
- 18. Kanski (1990); Diabetic Retinopathy; Clinical Ophthalmology, 2<sup>nd</sup> ed, 302-18.
- 19. <u>Brad H. Feldman.</u>, <u>Dale Fajardo</u>, <u>Dylan Griffiths</u>, <u>Jennifer I</u> et al (2015); Diabetic Retinopathy EyeWiki, Genentech, February 19.
- 20. Srfraz Hussain Syed, |Muhammad Arif, Faisal Saleem (2009); Incidence of angiographic Patterns of Diabetic Maculopathy, APMC:3(2):148-51.
- 21. Karan A K (2011); Diabetic retinopathy, lan 30.
- 22. Priyank Garg, Samarth Agarwal, Arindan Chakravarti et al (2011); diabetic maculopathy, e journal of ophthalmology, www.eophtha.com
- 23. Kang SW, Park SC, Cho HY et al (2007); Triple therapy of vitrectomy, intravitreal triamcinolone, and macular laser photocoagulation for intractable diabetic macular edema, Am J Ophthalmol, 144:878-85.
- 24. Se W, Choul Yond Park, don Ham (2014); the Correlation Between Fluorescein angikgraphic and Optical Coherence tomographic Features in Clinically Significant Diabetic Macular Edemaan J Ophthalmol. 137: 313-322.
- 25. Nizan kowska MH(1995); Incidence and treatment outcome for diabetic retinopathy. Klin Oczna; 97:282-5.
- 26. Suresha Anepla Rajappa, Deepthi Molleti, Nandini C, Donepudi Gayatri Devi and Kudache Janhavi Abhay SA Rajappa Role of fundus fluorescein (2014);angiography in macular disorders International Journal of Biomedical Research, Ι JBR, 05 (10)www.ssjournals.com
- Jingi**,** Jean 27. Ahmadou M Jacques N Noubiap, Augustin Ellong et al (2014); Epidemiology and treatment outcomes of diabetic retinopathy in а diabetic Cameroon, population from BMCOphthalmology , 14:19 doi:10.1186/1471 -2415-14-19

Submitted for publication: 26-02-2014

Accepted for publication: 30-12-2014

\_\_\_\_\_\_\_