Comparison of ocular blood flow by doppler evaluation in middle aged type 2 diabetes patients with and without diabetic macular edema

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Abstract

Introduction: The World Health Organization (WHO) has estimated that the number of people diagnosed with Diabetes is 347 million worldwide. Diabetic macular edema (DME) and Diabetic Retinopathy are the main causes of vision loss in Diabetes mellitus.

Objective: To compare altered ocular blood flow by Doppler evaluation in middle aged type 2 diabetic patients with and without diabetic macular edema.

Materials and Methods: An analytical cross–sectional study was conducted in the out-patient and in-patient department of ophthalmology and the department of radiodiagnosis in a tertiary care hospital including 36 patients in each group (A-with DME & B-without DME). Color doppler was done to evaluate ocular blood flow velocities in internal carotid, ophthalmic and central retinal arteries and central retinal vein.

Results: The majority of diabetes patients in developing countries are middle aged (45–64 years of age). Vascular changes and subsequent ocular hemodynamic changes are critical events in the pathogenesis of diabetic retinopathy. Mean Resistivity Index (RI) and Mean Pulsatility Index (PI) in the ophthalmic artery were found to be significantly high in the DME group. Mean end diastolic velocity (EDV) in the common carotid artery was found to be significantly high in the NO DME group than the DME group. In our study, the mean values of Low Density Lipoprotein (LDL) (mg/dl) , Total cholesterol (mg/dl) , Serum urea (mg/dl), Serum creatinine (mg/dl) was found to be higher (Statistically significant) in the DME group as compared to NO DME group.

Conclusion: Our findings may indicate disturbances of retinal and choroidal circulation in patients with DME. Further studies with larger groups of patients are needed to understand better the role of retrobulbar hemodynamics in the pathogenesis of Diabetic macular edema.

Keywords: Diabetic macular edema, Doppler evaluation, Ocular blood flow.

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. The World Health Organization (WHO) has estimated that the number of people diagnosed with Diabetes is 347 million worldwide (updated November 2014).[(1)] India leads the world with largest number (31.7 million) of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world".[(2)] There are many risks factors of Type 2 Diabetes Mellitus embedded in nature (genetic) as well as nurture (i.e. environmental factors including intrauterine environment) like obesity, physical inactivity, lipid profile abnormalities,[(3)] hypertension,[(4)] dietary habits . Other factors like family history, genetic factors and birth weight also play a role.

The vascular complications of diabetes mellitus are subdivided into microvascular (retinopathy, neuropathy, nephropathy) and macrovascular complications [coronary heart disease (CHD), peripheral arterial disease (PAD), cerebrovascular disease]. The risk of complications increases as a function of the duration and degree of hyperglycemia. A reduction in chronic hyperglycemia prevents or delays its complications. Diabetic retinopathy [DR] is the most common ocular complication in Diabetes Mellitus.[(5)] Worldwide, 93 million people have diabetic retinopathy (DR), including 21 million with diabetic macular Edema (DME); another 300 million people are at risk.[(6)] The reported prevalence of diabetic retinopathy (DR) in diabetics varies substantially between studies, but is probably around 40%. It is more common in type 1 diabetes than in type 2 and sight-threatening disease is present in up to 10%. Diabetic macular edema and Diabetic Retinopathy are the main causes of vision loss in Diabetes mellitus.

Diabetic Retinopathy is the progressive dysfunction of the retinal vasculature caused by chronic hyperglycemia characterized by microaneurysms, retinal hemorrhages, retinal lipid exudates, cotton-wool spots, capillary non-perfusion, macular edema, neovascularization.[(7)] Over time, hypoxia causes increased Vascular Endothelial Growth Factor (VEGF) levels in retinal tissue, leading to formation of new vessels, increased vascular permeability and accumulation of fluid. Theoretically, aldose reductase, (VEGF) and platelet abnormalities are said to play a role in the pathogenesis.

The best predictor of diabetic retinopathy is the duration of the disease.[(8)] It is a stronger predictor for proliferative disease than for maculopathy. Raised glycated hemoglobin (HbA1c) is associated with an increased risk of proliferative disease. Improved glycemic control also slowed the progression of early diabetic complications.[(9)] Strict blood pressure control

significantly reduced both macro- and microvascular complications.[10] Impaired renal function is an excellent predictor of the presence of retinopathy.[8]

The classification used is the Early Treatment Diabetic Retinopathy Study (ETDRS – the modified Airlie House classification) internationally.[11]

Diabetic macular edema (DME) remains the most common cause of visual impairment in diabetes.[12] Diabetic Macular Edema can be sub-classified in terms of distribution that is either focal or diffuse. Focal diabetic macular edema results from microaneurysms and/or dilated, leaking capillaries while diffuse DME is thought to result from breakdown of the outer blood retinal barrier (BRB).[13]

Clinically significant DME (CSDME) is defined as retinal thickening within 500µm of the centre of the fovea, hard exudates within 500µm of the fovea associated with retinal thickening, or retinal thickening of 1500µm diameter any part of which lies within 1500µm of the fovea.[14]

Vascular changes and subsequent ocular hemodynamic changes are critical events in the pathogenesis of DR. Color Doppler imaging is a well established technique for assessing ocular blood flow velocities in the retrobulbar vessels.[15] By measuring the frequency shift, blood velocity can be determined.[15] The peak systolic velocity (PSV), end diastolic velocity (EDV) can be measured directly in small orbital vessels and the impedance indices i.e. resistivity index (RI) and the pulsatility index (PI) can be calculated from their values by mathematical formulae.

Orbital blood flow velocities in diabetics were increased in some studies,[16] but decreased in others[17] or unchanged. Numerous clinical studies have demonstrated increase in the Resistivity index (RI) in the retrobulbar vessels with progression of diabetic retinopathy.[17] Increased Resistivity index has also been reported in the ophthalmic and posterior ciliary arteries of DR patients. [18] Few studies have also demonstrated increased pulsatility index with progression of diabetic retinopathy.[11]

Disturbance of retinal hemodynamics is an accepted surrogate marker of early diabetic retinopathy.[14] If any correlation is found between ocular hemodynamics and systemic parameters, it may help in predicting the onset and progression of DR in diabetic patients. As some risk factors like hypertension, hyperlipidemia and glycemic control are modifiable, this may help in controlling the progression of DR in diabetic patients.

Aims and Objectives

To study association if any between altered ocular blood flow and occurrence of diabetic macular edema.

i. To measure the ocular blood flow velocities, resistivity index and pulsatility index in the ophthalmic artery, central retinal artery, central retinal vein and carotid artery using color and spectral doppler analysis in middle aged diabetes patients with(Group-A) and without diabetic macular edema(Group-B) and compare.
ii. To measure the systemic parameters like blood pressure, body mass index, intraocular pressure in middle aged diabetes patients with and without diabetic macular edema and to correlate the systemic parameters with ocular blood flow.

Methodology

i. An analytical Cross – Sectional study was conducted in the out-patient and in-patient department of ophthalmology and the department of radiodiagnosis, North Bengal Medical College and Hospital, Darjeeling from April 2015 to March 2016 (1 year). All patients of diabetes mellitus attending the out-patient and in-patient department of ophthalmology were examined.
ii. The inclusion criteria were diagnosed cases of Type 2 diabetes mellitus of 45-64 years age group. Patient with DME in either eye will be considered as a DME case (Group-A).In case of unilateral DME, that eye will be selected as study eye. In case of bilateral DME, the study eye will be chosen by tossing a coin. Those without DME in either eye, the study eye will be chosen by tossing a coin (Group-B).
iii. The Exclusion Criteria were subjects who have had previous laser photocoagulation in the study eyes or with any disease or anomaly of the study eye which may affect blood flow such as ocular inflammation, trauma, non-diabetic vascular disease, and glaucoma, any ocular surgery in the study eye within last 6 months, any significant media opacity hampering examination of fundus, or with history of a major systemic disease including cardiovascular disease, rheumatoid arthritis. Pregnant and breast feeding women and those subjects who do not give consent were also excluded.

Criteria for diagnosis of diabetic macular edema

i. Patients will be diagnosed with DME as per modified Early Treatment Diabetic Retinopathy Study (ETDRS) classification.[11]
ii. DME is a general term defined as retinal thickening within two disc diameters of the foveal center. It can be either focal or diffuse in distribution.[13]

Clinically significant macular edema (CSME) is a form of DME that was precisely defined by the Early Treatment Diabetic Retinopathy Study (ETDRS). CSME exists if any of the following criteria are met:

i. Any retinal thickening within 500 mcm of the foveal center;
ii. Hard exudates within 500 mcm of the foveal center that are associated with adjacent retinal

thickening (which may lie more than 500 mcm from the foveal center);

iii. An area of retinal thickening at least 1 disc area in size, any part of which is located within 1 disc area of the foveal center.

Study Parameters / Variables for objective 1 were retrobulbar blood flow velocities: peak systolic velocity (PSV) and end diastolic velocity (EDV), resistivity index (RI) & pulsatility index (PI) [retrobulbar vessels and the carotid arteries of the left side in every subject using orbital Color Doppler Ultrasonography imaging technique]

And those for objective 2 were best corrected visual acuity (BCV_A), intraocular pressure, body mass index, systolic and diastolic blood pressure , pulse pressure, fasting and post-prandial blood sugar, glycated hemoglobin (HbA1c), total lipid profile – HDL (high density lipoprotein), LDL (low density lipoprotein), VLDL (very low density lipoprotein), serum triglycerides and total cholesterol, serum albumin and globulin, serum urea and creatinine.

Sample size = 36 in each group

Methods

Diabetic macular edema was diagnosed as per the modified ETDRS (Early treatment and diabetic retinopathy study) classification:

Group 1: Diabetics without any diabetic macular edema (No DME group)

Group 2: Diabetics with diabetic macular edema (DME group)

Best corrected visual acuity (BCV_A) was measured for each subject by refraction and converted to LogMAR (Logarithm of Minimum Angle of Resolution) value. A thorough ocular examination was done in each subject to rule out any other disease.

Dilated fundoscopy (with tropicamide-0.5% and phenylephrine-2.5% eye drop) was performed in every subject with a 90 Dioptre Volk lens using slit lamp biomicroscopy. The diagnosis of presence or absence of diabetic retinopathy was done as per modified Early Treatment Diabetic Retinopathy Study (ETDRS) classification.

The following parameters were measured for each subject: BCVA, intraocular pressure was measured by Goldmann Applanation tonometry, systolic and diastolic blood pressures were measured by using aneroid sphygmomanometer. Pulse pressure was calculated for each subject. (Pulse pressure =Systolic BP – Diastolic BP). Body mass index was calculated after measuring height and weight with a ruler and a weighing machine [BMI = (weight in kg) / (height in metre).[2]

Using the values of PSV and EDV, the following parameters were calculated for each vessel:

i. Resistivity index (RI) = (PSV-EDV)/PSV[19]
ii. Pulsatility index (PI) = (PSV-EDV)/V mean

[where V mean = 1/3 (PSV-EDV) + EDV[20]], in all patients].

Statistical Analysis

Collected data was entered in Microsoft Excel worksheet and analysed using the principles of descriptive and inferential statistics. The mean values were calculated for the variables and compared between the two groups using the Student's Unpaired t-test in the IBMM SPSS Statistics Software Version 20. Findings were presented in the forms of tables and charts as well as percentages were calculated.

Results

In No DME group, 17 subjects (47%) females and 19 subjects (52%) were males whereas in DME group, 18 subjects (50%) were females and 18 subjects (50%) males.

Comparison of the means of systemic parameters between the diabetics with no DME group and diabetics with DME group.

Mean duration of Type 2 Diabetes mellitus was found to be 8.89 years (SD= 4.79) in DME group whereas it was 5.46 years (SD= 3.80) in NO DME group. The results were significant (**p-value = 0.001** by student's unpaired t-test)

Mean duration of Hypertension was found to be 3.96 years (SD= 6.34) in DME group whereas it was 1.39 years (SD= 2.54) in No DME group. The results were significant. (**p-value = 0.027** by student's unpaired t-test)Mean Intraocular pressure was found to be 16.44 mmHg (SD= 2.25) in DME group whereas it was 15.89 mmHg (SD= 2.53) in No DME group. (p-value = 0.328 by student's unpaired t-test)Mean Pulse pressure was found to be 53.11 mmHg (SD= 9.67) in DME group whereas it was 49.44 mmHg (SD= 12.09) in No DME group. (p-value = 0.160 by student's unpaired t-test)Mean Body Mass Index (kg/m^2) was found to be 24.64 kg/m^2 (SD= 2.57) in DME group whereas it was 23.70 kg/m^2 (SD= 2.75) in No DME group. (p-value = 0.138 by student's unpaired t-test)

Mean Fasting Blood Sugar (FBS) (mg/dl) was found to be 170.0 mg/dl (SD= 69.52) in DME group whereas it was 153.25 mg/dl (SD= 63.37) in No DME group. (p-value = 0.289 by student's unpaired t-test)

Mean Post Prandial Blood Sugar (PPBS) (mg/dl) was found to be 246.99 mg/dl (SD= 90.26) in DME group whereas it was 237.11 mg/dl (SD= 81.33) in No DME group. (p-value = .627 by student's unpaired t-test)

Mean Glycated Hemoglobin (HbA1c) (%) was found to be 8.10 % (SD= 1.54) in DME group whereas it was 8.08 % (SD= 1.57) in No DME group. (p-value = 0.958 by student's unpaired t-test)

Mean High Density Lipoprotein (HDL) (mg/dl) was found to be 45.76 mg/dl (SD= 14.72) in DME group whereas it was 45.10 mg/dl (SD= 8.77) in No DME group. (p-value = 0.819 by student's unpaired t-test)

Mean Low Density Lipoprotein (LDL) (mg/dl) was found to be 118.91 mg/dl (SD= 37.36) in DME group whereas it was 100.07 mg/dl (SD= 40.33) in No DME group. (**p-value = 0.043** by student's unpaired t-test)

Mean Very Low Density Lipoprotein (VLDL) (mg/dl) was found to be 32.31 mg/dl (SD= 12.95) in DME group whereas it was 28.81 mg/dl (SD= 6.33) in No DME group. (p-value = 0.149 by student's unpaired t-test)

Mean Serum Triglycerides (mg/dl) was found to be 165.68 mg/dl (SD= 64.19) in DME group whereas it was 154.48 mg/dl (SD= 33.41) in No DME group. (p-value = 0.357 by student's unpaired t-test)

Mean Serum Total Cholesterol (mg/dl) was found to be 192.95 mg/dl (SD= 44.35) in DME group whereas it was 167.64 mg/dl (SD= 37.44) in No DME group. (p-value = 0.011 by student's unpaired t-test)

Mean Serum Urea (mg/dl) was found to be 31.57 mg/dl (SD= 8.43) in DME group whereas it was 27.63 mg/dl (SD= 7.42) in No DME group. (p-value = 0.039 by student's unpaired t-test)

Mean Serum Creatinine (mg/dl) was found to be 1.09 mg/dl (SD= 0.32) in DME group whereas it was 0.95 mg/dl (SD= 0.20) in No DME group. (p-value = 0.025 by student's unpaired t-test)

Mean Serum Albumin (gm/dl) was found to be 3.95 gm/dl (SD= 0.58) in DME group whereas it was 3.82 gm/dl (SD= 0.63) in No DME group. (p-value = 0.365 by student's unpaired t-test)

Mean Serum Globulin (gm/dl) was found to be 3.10 gm/dl (SD= 0.66) in DME group whereas it was 3.35 gm/dl (SD= 0.60) in No DME group. (p-value = 0.102 by student's unpaired t-test)

Mean Serum Total Protein (gm/dl) was found to be 7.05 gm/dl (SD= 0.82) in DME group whereas it was 7.16 gm/dl (SD= 0.62) in No DME group. (p-value = 0.496 by student's unpaired t-test)

Mean end diastolic velocity (EDV) in the common carotid artery was found to be significantly high in the No DME group (24.16cm/sec ; SD=6.11) than the DME group (21.25 cm/sec ; SD=6.11). [p-value = 0.026 as per student's unpaired t-test]

The ICA vessel velocities and indices were not found to be significantly higher in the DME group compared to the NO DME group.Mean RI in the ophthalmic artery was found to be significantly high in the DME group (0.74; SD =0.11) than the No DME group (0.66; SD =0.13). [p -value = 0.002 as per student's unpaired t-test]Mean PI in the ophthalmic artery was found to be significantly high in the DME group (1.55; SD =0.48) than the No DME group (1.22; SD =0.39). [p -value = 0.002 as per student's unpaired t-test]

The CRA vessel velocities and indices were not found to be significantly higher in the DME group compared to the NO DME group.

The Diastolic Flow (DF) in the Central Retinal Vein (CRV) was not found to be significantly different in the DME group compared to the NO DME group.

Discussion

The majority of diabetes patients in the developing countries are middle aged (45–64 years of age).The number of people with diabetes is increasing in middle age due to urbanization, and increasing prevalence of obesity and physical inactivity. The middle aged patients with diabetes usually have much worse blood sugar control compared with late onset diabetes patients.[21]

In our present study, there was no statistical difference between the two groups – Diabetics with No Diabetic Macular edema (No DME) and Diabetic Macular edema (DME) – with respect to age and gender.

Mean RI in the ophthalmic artery was found to be significantly high in the DME group (0.74; SD =0.11) than the No DME group (0.66; SD =0.13). [p -value = 0.002].Mean PI in the ophthalmic artery was found to be significantly high in the DME group (1.55; SD =0.48) than the No DME group (1.22; SD =0.39). [p -value = 0.002]

Xu W et al reported that PSV and EDV decreased progressively and RI increased gradually in ophthalmic artery in diabetics with and without retinopathy as compared to healthy controls.[22] Dimitrova G et al.[23] MacKinnon JR et al,[24] Basturk T et al[25] and Tamaki Y et al[26] reported an increase in the resistivity index of the ophthalmic artery in diabetics with retinopathy as compared to diabetics without retinopathy. No significant statistical differences were found between the Mean Peak systolic velocity (PSV), end diastolic velocity (EDV), resistivity index and the pulsatility index of the central retinal artery between the two groups. Mehdizadeh M et al reported that resistivity index of the central retinal artery was higher and peak systolic velocity lesser in cases of severe macular edema as compared to less severe grades of macular edema in diabetics with retinopathy.[27] Basturk T et al reported a significant statistical increase in mean resistivity index of central retinal artery in type 2 diabetic patients with retinopathy as compared to without retinopathy.[25]

No statistical significance was found between the Mean End diastolic velocity/flow (EDV/EDF) in the central vein in the two groups in our present study. Dimitrova G et al reported that the patients who developed DR progression showed significantly increased central retinal vein peak systolic velocity (PSV), end diastolic velocity (EDV), and resistivity index (RI) at the final measurement as compared to the initial measurement.[23] Fujioka S et al reported that the higher peak systolic velocity (PSV) in the central retinal vein (CRV) than in the central retinal artery (CRA) was significantly correlated with the severity of non-proliferative DR, especially in the presence of cystoid macular edema.[28] Mean end diastolic velocity (EDV) in the common carotid artery was found to be significantly

high in the NO DME group (24.16cm/sec; SD=6.11) than the DME group (21.25 cm/sec; SD=6.11). [p-value = 0.026]

In our study there was no statistical difference in the Mean peak systolic velocity (PSV) resistivity and pulsatilty index of the common carotid artery between the two groups. No statistically significant difference was found in the velocities and indices of the Internal Carotid artery (ICA) in the two groups. Mehdizadeh M et al reported that the mean peak systolic velocity (PSV) of the internal carotid artery (ICA) was less in eyes with proliferative DR as compared to eyes with non-proliferative DR.[27]

In our study, the mean values of Low Density Lipoprotein (LDL) (mg/dl) , Total cholesterol (mg/dl) , Serum urea (mg/dl), Serum creatinine (mg/dl) was found to be higher (Statistically significant) in the DME group as compared to No DME group.

Statistically significant positive correlation was seen between the serum LDL (mg/dl) levels and Resistivity index (RI) and Pulsatility Index (PI) of ophthalmic artery (OA) in the DME group. Peak Systolic Velocity (PSV) and End Diastolic Velocity (EDV) of Central Retinal Artery (CRA) was found to be significantly negatively correlated to $HbA1_c$ levels in blood in the DME group.

No statistically significant correlation could be seen between the blood flow parameters of the Central retinal vein (CRV) with glycated hemoglobin (HBA1c), systolic and diastolic blood pressure, pulse pressure, low density lipoprotein (LDL) and total cholesterol in the DME group No statistically significant correlation could be seen between the blood flow parameters of the Ophthalmic artery (OA), Central retinal Artery (CRA) and Central retinal vein (CRV) with glycated hemoglobin (HBA1c), systolic and diastolic blood pressure, pulse pressure, low density lipoprotein (LDL) and total cholesterol in the No DME group.

A Prospective study with a larger sample size and proper randomisation would have yielded more significant results. Presence of comorbidities like hypertension and hyperlipidemia in some patients affects the various parameters differently. Varied drug intake history of the patients was present. To elucidate the complex links of orbital blood flow velocity with DR is a challenge for future research.

Summary and Conclusion

In this cross sectional observational study, using color dopler imaging technique, mean RI and mean PI in the ophthalmic artery was found to be significantly high in the DME group. There was no statistical difference in mean peak systolic velocity (PSV) and end diastolic velocity (EDV) of the ophthalmic artery between the two groups. No significant statistical differences were found between the Mean Peak systolic velocity (PSV), end diastolic velocity (EDV), resistivity index and the pulsatility index of the central retinal artery between the two groups. No significant statistical differences were found between the Mean End diastolic velocity/flow (EDV/EDF) in the central vein was between the two groups.

Mean end diastolic velocity (EDV) in the common carotid artery was found to be significantly high in the NO DME group than the DME group. All the other parameters in the common carotid and internal carotid artery showed no statistically significant differences between the two groups.

The systemic parameters were measured in both the groups and compared by appropriate statistical test.

In our study, the mean values of Low Density Lipoprotein (LDL) (mg/dl), Total cholesterol (mg/dl), Serum urea (mg/dl), Serum creatinine (mg/dl) was found to be higher (Statistically significant) in the DME group as compared to NO DME group.

In conclusion, our findings may indicate disturbances of retinal and choroidal circulation in patients with DME.Further studies with larger groups of patients are needed to understand better the role of retrobulbar hemodynamics in the pathogenesis of Diabetic macular edema.

Table 1: Distribution of DME according to age

	DME	No DME
45-49 years	5	15
50-54 years	15	10
55-59 years	9	3
60-64 years	7	8
GRAND TOTAL	36	36

Table 2: Distribution of the diabetic patients according to status of retinopathy

		Group	
		DME	**No DME**
Retinopathy Level	Mild Npdr	3	16
	Moderate NPDR	20	18
	PDR	2	0
	Severe NPDR	11	2
Total		36	36

Comparison of the means of ocular and carotid blood flow velocities and indices of study eye between the diabetics with NO DME and diabetics with DME

Table 3: Common Carotid Artery (CCA)

Group Statistics				p-value
	Group	Mean	Std. Deviation	
PSV (CCA) cm/sec	DME	83.41	17.79	.641
	No DME	85.61	21.90	
EDV (CCA) cm/sec	DME	21.25	4.64	.026
	No DME	24.16	6.11	
RI (CCA)	DME	0.74	0.07	.113
	No DME	0.71	0.05	
PI (CCA)	DME	1.47	0.26	.065
	No DME	1.37	0.20	

Table 4: Internal carotid artery (ICA)

Group Statistics				p value
Group		Mean	Std. Deviation	
PSV (ICA) cm/sec	DME	84.47	47.10	.604
	No DME	80.04	19.52	
EDV (ICA) cm/sec	DME	30.59	16.38	.922
	No DME	30.28	10.04	
RI (ICA)	DME	0.63	0.09	.566
	No DME	0.61	0.11	
PI (ICA)	DME	1.10	0.25	.764
	No DME	1.08	0.34	

Table 5: Ophthalmic artery (OA)

Group Statistics				p value
Group		Mean	Std. Deviation	
PSV (OA) cm/sec	DME	52.32	23.37	.925
	No DME	51.85	18.22	
EDV (OA) cm/sec	DME	14.28	8.31	.154
	No DME	16.89	6.98	
RI (OA)	DME	0.74	0.11	**.002**
	No DME	0.66	0.13	
PI (OA)	DME	1.55	0.48	**.002**
	No DME	1.22	0.39	

Table 6: Central retinal artery (CRA)

Group Statistics				p value
Group		Mean	Std. Deviation	
PSV (CRA) cm/sec	DME	34.17	11.46	.96
	No DME	34.31	10.83	
EDV (CRA) cm/sec	DME	12.85	4.41	.15
	No DME	14.33	4.25	
RI (CRA)	DME	0.60	0.12	.26
	No DME	0.57	0.10	
PI (CRA)	DME	1.06	0.41	.20
	No DME	0.95	0.27	

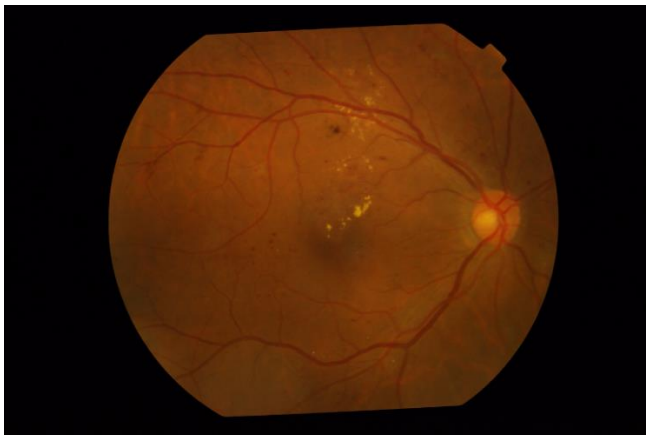

Fig. 1: Diabetic retinopathy with DME

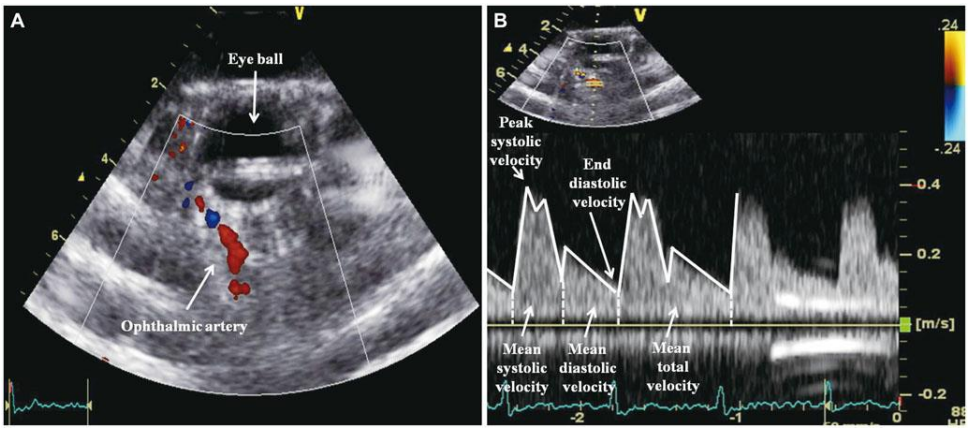

Fig. 2: Ophthalmic artery and its spectral pattern on color doppler ultrasound

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