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Original Article

Diabetic Maculopathy in Nonproliferative Diabetic Retinopathy in Tertiary Eye Care Hospital in India: A Prospective Nonrandomized Clinical Study

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Abstract

Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder caused by an absolute or relative deficiency of insulin, an anabolic hormone. Insulin is produced in the pancreas by the beta cells of islets of Langerhans. Absence, destruction, or loss of these cells causes an absolute deficiency of insulin, leading to Type 1 diabetes (insulin-dependent DM).

Materials and Methods: In this study, the pattern of presentation of diabetic maculopathy in nonproliferative diabetic retinopathy (NPDR) in diabetics reporting to tertiary eye care hospital during July 2009-November 2010 including the incidence of the different type of maculopathy in NPDR, relationship between serum cholesterol and hard exudates in diabetic maculopathy, effect of laser on visual acuity in treated and untreated patients, role of optical coherence tomography in diabetic maculopathy. This study was conducted by collecting details including age, sex, referring institute, duration of diabetes, blood sugar, and associated systemic complications such as nephropathy, neuropathy, hypertension, hyperlipidemia, and CAHD were noted. Vision in both eyes was tested using Snellen's visual acuity chart.

Results: This study revealed that diabetic maculopathy is the most common cause of visual loss in a patient with diabetic retinopathy and periodic follow-up and examination is necessary to detect the involvement of macula at an earlier stage.

Conclusion: Early treatment with photocoagulation can stabilize the visual acuity and prevent further visual loss.

Key words: Diabetes, Fundus florescent angiography, Maculopathy, Retinopathy

INTRODUCTION

It would be worthwhile to quote Sir. Stewart Dude Elder's words on diabetic retinopathy. "It is one of the major tragedies of ophthalmology in the present generation, always common and rapidly becoming still more common, affecting the young as well as aged, predictable but not preventable and relatively untreatable, chronic and progressive in its course and leading to blindness in a distressing of cases."[1-3]

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Diabetes mellitus (DM) is a major medical problem throughout the world. It causes an array of long-term systemic complications, which have a considerable impact on both the patients and the society because it typically affects individuals in their most productive years. Ophthalmic complications of diabetes include corneal abnormalities, glaucoma, iris neovascularization, cataracts, and neuropathies. However, the most common and potentially most blinding type is retinopathy.[3,4]

DM is a chronic metabolic disorder caused by an absolute or relative deficiency of insulin, an anabolic hormone. Insulin is produced in the pancreas by the beta cells of islets of Langerhans. Absence, destruction, or loss of these cells causes an absolute deficiency of insulin, leading to Type 1 diabetes (insulin-dependent DM [IDDM]). Most children have IDDM and a lifetime dependence on exogenous insulin.[4-8]

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Type 2 diabetes (non-IDDM [NIDDM]) is a heterogeneous disorder. Patients with NIDDM have insulin resistance, and their beta cells lack the ability to overcome this resistance. Although this form of diabetes previously was uncommon in children, 20% or more of new patients with diabetes in childhood and adolescence now have NIDDM, a change associated with increased rates of obesity.[8-12]

With an estimated 35 million people with diabetes, India has the world's largest diabetic population. 20-25% diabetics develop retinopathy. More common in Type 1 (40%) than Type 2 (20%) which comes to around 5.6 million persons out of which 30% require active treatment and 3% of DR could be blind. Risk factors for developing diabetic retinopathy were duration - after 20 years of DM - 99% of Type 1 and 60 of Type 2 have some retinopathy, poor glycemic control systemic hypertension, nephropathy, dyslipidemia, puberty, and pregnancy.[2-4]

Aim

This study is performed with the aim to know the pattern of presentation of diabetic maculopathy in nonproliferative diabetic retinopathy (NPDR) in diabetics reporting to tertiary eye care hospital between July 2009

Table 1: Statistics on age group of patients

Age groups (years)	Number of patients (%)
21-30	3 (6)
31-40	4 (8)
41-50	11 (22)
51-60	16 (32)
61-70	13 (26)
71-80	3 (6)

Table 2: Early onset diabetes mellitus with maculopathy

Duration	Number of patients	Number of patients with maculopathy	% of DME
<5 years	5	0	0
<10 years	1	1	11.1
<20 years	3	3	33.3

Table 3: Incidence of diabetic maculopathy with advancing severity of diabetic retinopathy

Type of NPDR	Number of patients with DME	% of patients with DME
Mild	5	10
Moderate	20	40
Severe	25	50

NPDR: Nonproliferative diabetic retinopathy

Table 4: FFA types

Type	Number of cases		Total	% of DME
Focal	22	22	44	44
Diffuse	18	16	34	34
Ischemic	10	12	22	22

FFA: Fundus fluorescein angiography

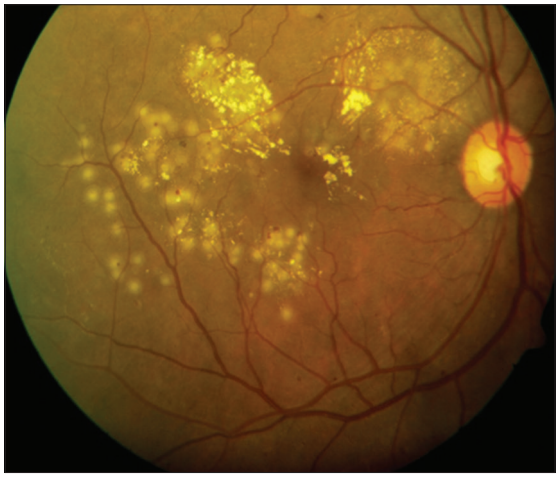

Figure 1: Focal maculopathy with focal laser in inferotemporal to macula

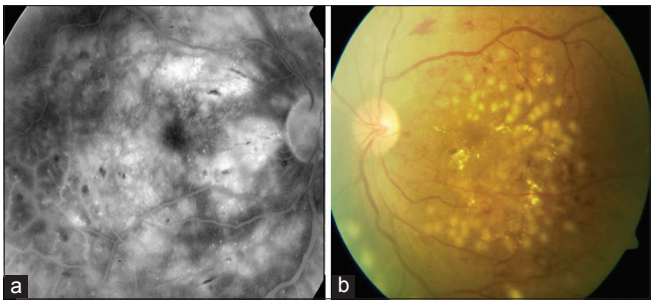

Figure 2: (a) Diffuse macular edema in fundal fluorescein angiography, (b) grid laser in fundus photography

Table 5: Serum lipids versus hard exudates

Total cholesterol			LDL cholesterol			Total/HDL cholesterol		
Level	Number of patients	% of patients	Level	Number of patients	%	Level	Number of patients	%
<148	10	10	<86	10	10	<2.803	5	5
148-165	23	23	86-99	15	15	2.804-3.283	15	15
166-181	12	12	100-114	25	25	3.283-3.777	25	25
182-203	20	20	115-132	20	20	3.777-4.429	26	26
>204	35	35	>133	30	30	>4.429	29	29

LDL: Low-density lipoprotein, HDL: High-density lipoproteins

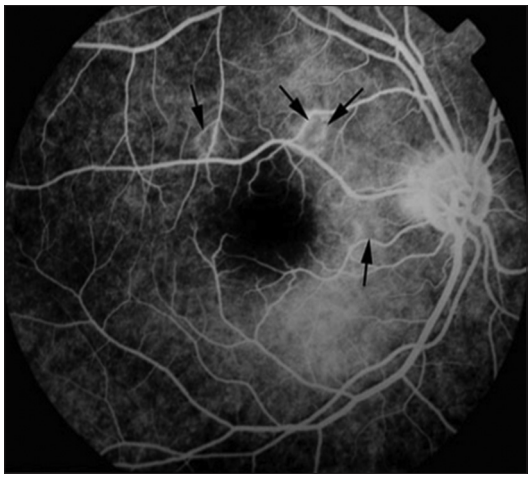

Figure 3: Fundal fluorescein angiography shows ischemic maculopathy in the right eye

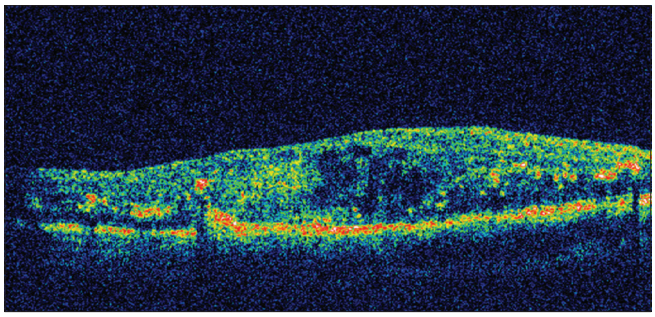

Figure 4: OCT shows spongy macular edema, loss of foveal contour and hard exudates

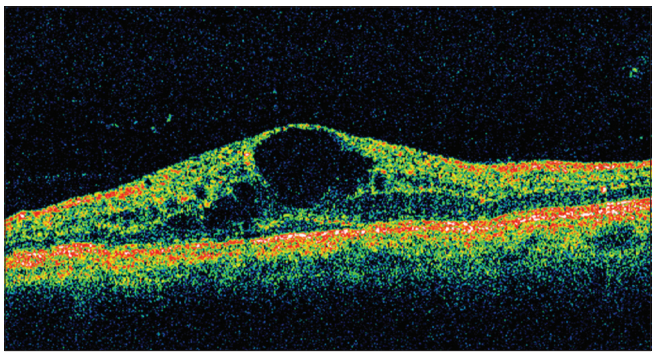

Figure 5: Cystoid macular edema in OCT

Table 6: Visual acuity on presentation to the type of maculopathy

V/A	Focal			Diffuse			Ischemic		
	RE	LE	Total (%)	RE	LE	Total (%)	RE	LE	Total (%)
6/6-6/9	5	6	11 (11)	-	-	(-)	-	-	(-)
6/12-6/18	9	12	21 (21)	2	2	4 (4)	1	1	2 (2)
6/24-6/36	7	4	11 (11)	7	7	14 (14)	4	6	10 (10)
6/60-4/60	2	-	2 (2)	9	8	17 (17)	4	4	8 (8)
<4/60	1	1	2 (2)	1	1	2 (2)	2	2	4 (4)

Table 7: Effect of focal laser on visual acuity in mild-to-moderate NPDR after 2 years

Visual acuity after 2 years	Number of patients	% of visual loss
Improved	4	17.3
Unchanged	17	73.91
Worsened	2	8.6

Table 8: Visual acuity after grid laser after 2 years

V/A after 2 years	Number of patients	% of patients
Improved	3	16.6
Unchanged	11	61.1
Worsened	4	22.2

Table 9: Retinal thickening after 1 year follow-up with OCT

Number of patients		Retinal thickening persistence	% of persistence
Treated	40	14	35
Untreated	10	7	63

and November 2010. Special emphasis was laid on the following aspects.

1. Incidence of the different type of maculopathy in NPDR.
2. Relationship between serum cholesterol and hard exudates in diabetic maculopathy.
3. Effect of laser on visual acuity in treated and untreated patients.
4. Role of optical coherence tomography in diabetic maculopathy.

MATERIALS AND METHODS

The study was conducted from July 2009 to November 2010. 100 eyes of 50 patients who were referred to tertiary eye care hospital, Regional Institute of Government Ophthalmic Hospital, Madras medical college, Chennai, Tamil Nadu, India, were evaluated. Details including age, sex, referring institute, duration of diabetes, and blood sugar and associated systemic complications such as nephropathy, neuropathy, hypertension, hyperlipidemia, and coronary artery diseases were noted. Vision in both eyes was tested using Snellen's visual acuity chart. Other materials used were:

1. Direct ophthalmoscope
2. Indirect ophthalmoscope
3. Slit lamp examination with +90D lens
4. Schiotz and Gold-mann applanation tonometer
5. Gold-mann 3 mirror
6. Topcon fundus camera

7. Laser machine (COHERENT)
8. Fundus fluorescein angiography
9. Blood pressure
10. Urine albumin, sugar
11. Diabetic profile
12. Optical coherence tomography.

Procedure

Patients referred or detected as having diabetic retinopathy were taken into study. This included IDDM and NIDDM patients. History relevant to time of onset of DM, duration, family history, drug schedule, and dietary habits was taken. Associated systemic factors such as hypertension, ischemic heart disease, and renal disease were recorded.

Proliferative diabetic retinopathy, retinopathy without maculopathy, associated eye problems such as glaucoma, uveitis, central retinal vein occlusion, and hypertensive retinopathy were exclusions of this study.

Complete ocular examination was done:

i. Best corrected visual acuity
ii. Intraocular pressure
iii. Anterior segment examination
iv. Amsler grid in selected patients
v. OCT in selected patients
vi. Visual fields
vii. Fundus examination - pupil was dilated with 1% tropicamide eye drops, fundus examination was done with a direct ophthalmoscope, indirect ophthalmoscope, slit lamp with +90D lens and Gold-mann 3 mirror.
viii. Fundus photograph was taken with Topcon fundus camera
ix. Fundus fluorescein angiography was done in cases with 3 ml of 20% sodium fluorescein injection IV in dorsal vein of hand with the patient seated in front of fundus camera.

Importance was given to:

a. Leaking microaneurysms and its distribution
b. Focal leak from vessels
c. Diffuse leak
d. Ischemia and capillary non perfusion zones.

Criteria for Photocoagulation

a. Focal leak at peri and parafoveal area signifying macular edema. Direct treatment of leaking microaneurysms, were carried out with 200 u spot size of Argon laser for 0.05-0.1 s to produce mild-to-moderate intensity burns.
b. Diffuse leak and cystoid leak were treated with 50-200 u spot burns for 0.05-0.1 s in a grid pattern.
c. Ischemic maculopathy associated with ischemia elsewhere in fundus were given scatter photocoagulation.

Patients were followed fortnightly for 2 months and then at monthly intervals. Visual acuity and fundus examination made and documented.[12-20]

RESULTS

Out of 100 eyes, 21 patients were below 50 years and 29 patients were above 50 years.

Among early onset type, 33.3% had macular edema in patients with duration of 20 years, and 11.1% had macular edema in the duration of 10 years. Among late onset type of diabetes, and those on oral hypoglycemic agents with duration of 20 years 22.2% had macular edema and in those with duration of 10 years, 11.1% had macular edema. Among the late onset type of diabetes and those on insulin with duration of 20 years 38.4% had macular edema, and those with duration of 10 years 15.3% had macular edema. 50% of patients with severe NPDR had macular edema as compared to 40% with moderate NPDR and 10% with mild NPDR. In fundus fluorescein angiography (FFA), 44% had focal type, 34% had diffuse type, and 22% had ischemic type. When total cholesterol >204 mg/dl 35% of the patients had hard exudates compared to 10% when the levels were <148 mg/dl. When low-density lipoprotein (LDL) cholesterol >133 mg/dl 30% had hard exudate as compared to 10% when levels were <86 mg/dl. When total cholesterol/high-density lipoproteins (HDL) cholesterol >4.429, hard exudates were present in 29% and when levels <2.803, 5% had hard exudates. Among untreated patients, 30% had moderate visual loss, and 10% had severe visual loss. Among laser treated patients, 25% had moderate visual loss, and 2.5% had severe visual loss. Following focal photocoagulation vision improved in 17.3%, worsened in 8.6% and unchanged in 77%. Following grid laser vision improved in 16.6%, worsened in 22.2%, unchanged in 61.1%. 31% patients had 6/24-6/36 visual acuity on presentation, and 8% had <4/60. Patients with diffuse maculopathy had visual acuity in the range of 6/60-4/60 on presentation. Ischemic maculopathy patients had visual acuity of 6/24 or less on presentation. Most of the patients with a focal type of lesion had good visual acuity initially among treated patients retinal thickening persisted in 35% and 63% of untreated patients with OCT followed for 1 year (Tables 1-9 and Figures 1-5).

DISCUSSION

In our study, the predominant age group affected is the 51-60 years range 32% followed by 61-70 years range 26% and 41-50 years range 22%.

In our study, 54% cases are aged between 41 and 60. This correlates with the Wisconsin Epidemiological study of

diabetic retinopathy (Klein *et al.* Arch. 1986) revealed diabetic retinopathy more prevalent in the middle aged and elderly population affecting people aged 45-64 years.

Among early onset type, 33.3% had macular edema in patients with duration of 20 years, and 11.1% had macular edema in the duration of 10 years.

Among late onset type of diabetes, and those on oral hypoglycemic agents with duration of 20 years 22.2% had macular edema and in those with duration of 10 years, 11.1% had macular edema.

Among the late onset type of diabetes and those on insulin with duration of 20 years 38.4% had macular edema, and those with duration of 10 years 15.3% had macular edema. 50% of patients with severe NPDR had macular edema as compared to 40% with moderate NPDR and 10% with mild NPDR. This correlates with Wisconsin Epidemiological study of diabetic retinopathy which shows macular edema more prevalent in severe NPDR when compared to others.

In FFA, 44% had a focal type, 34% had diffuse type, and 22% had ischemic type. It correlates with ETDRS study which showed nearly same incidence of different type of maculopathy.

When total cholesterol >204 mg/dl 35% of the patients had hard exudates compared to 10% when the levels were <148 mg/dl. When LDL cholesterol >133 mg/dl 30% had hard exudate as compared to 10% when levels were <86 mg/dl. When total cholesterol/HDL cholesterol >4.429, hard exudates were present in 29% and when levels <2.803, 5% had hard exudates. This correlates with ADA 2005 study of medical care in DM: Diabetic care 2006;29.[21,22]

Among untreated patients, 30% had moderate visual loss, and 10% had severe visual loss. Among laser treated patients, 25% had moderate visual loss, and 2.5% had severe visual loss. This correlates with the ETDRS conclusions that laser treatment is effective in preventing visual acuity loss. Following focal photocoagulation vision improved in 17.3%, worsened in 8.6% and unchanged in 77%. This correlates with ETDRS conclusions that focal laser is effective in preventing worsening of visual acuity after 2 years. Following grid, laser vision improved in 16.6%, worsened in 22.2%, and unchanged in 61.1%. This correlates with ETDRS conclusions that grid laser is effective in preventing worsening of visual acuity after 2 years.

Among treated patients, retinal thickening persisted in 35%, and 63% of untreated patients with OCT followed for 1 year. 31% patients had 6/24-6/36 visual acuity on presentation, and 8% had <4/60. Hence, the majority of our patients were presenting in the range of 6/24-6/36 which correlated with a study by Becker *et al.* Patients with diffuse maculopathy had visual acuity in the range of 6/60-4/60 on presentation. Ischemic maculopathy patients had visual acuity of 6/24 or less on presentation. Most of the patients with a focal type of lesion had good visual acuity initially.[23,24]

CONCLUSION

1. Incidence of diabetic maculopathy common after 50 years with diabetes of longer duration.
2. Disease affects both eyes although asymmetrically.
3. Amsler grid is a useful diagnostic aid provided the intelligence of patient is good.
4. FFA is an important diagnostic tool in classifying the type of maculopathy.
5. Focal lesions are more common than other two types.
6. Focal type improves with focal photocoagulation; diffuse type shows some improvement with grid laser and ischemic lesions has worst prognosis as compared to others.
7. OCT is an important diagnostic tool to detect early maculopathy.
8. Diabetic maculopathy is the most common cause of visual loss in a patient with diabetic retinopathy. Periodic follow-up and examination are necessary to detect the involvement of macula at an earlier stage. Early treatment with photocoagulation can stabilize the visual acuity and prevent further visual loss.

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