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CLINICAL STUDY OF RETINOPATHY IN PATIENTS WITH DIABETES MELLITUS TYPE 1 AND TYPE 2 AND ITS ASSOCIATION WITH RISK FACTORS

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Abstract

Aim: To study the relationship between severity of diabetic retinopathy (PDR or NPDR) and systemic complications of diabetes mellitus such as Neuropathy, Nephropathy or Cardiovascular manifestation as hypertension.

Methods and Materials: This prospective observational study of 100 patients suffering from diabetic retinopathy. Such patients were recruited as a part of the study and further examined for any other systemic abnormality as neuropathy, nephropathy or hypertension.

Statistical Analysis: Chi square test, univariate and multivariate logistic regression analysis was performed. P value < 0.05 was taken as significant.

Results: Male: Female ratio of presence of diabetic retinopathy was 2.13: 1. The rate of proliferative diabetic retinopathy (PDR) was 1.47 % in persons who had diabetes for less than 5 years to 7.35 % in persons who had diabetes more than 15 years.

In our study, it was seen that nephropathy was present in 35.71 % cases with PDR as compared to 8.93% of cases with Non proliferative diabetic retinopathy (NPDR).

Conclusion: Our study showed that there is a significant correlation between severity of retinopathy and duration in type 2 Diabetes mellitus patients.

Maximum number of patients with Diabetes mellitus having cardiovascular involvement, had hypertension (68%).In patients suffering from neuropathy as a complication of DM, maximum number of patients had diabetic foot (56%).It was seen that the severity of diabetic retinopathy had some association with presence of nephropathy.

Also it can be postulated that patients with severe NPDR and PDR have high risk of developing nephropathy than patients suffering with mild and moderate NPDR.

Hence it can be recommended that all patients of diabetes mellitus suffering from clinically significant neuropathy, nephropathy or hypertension as a complication of diabetes should always be screened for presence of retinopathy.

Further studies with larger sample size are to be conducted to further look into this association.

Keywords: Diabetic retinopathy, Diabetic nephropathy, diabetic neuropathy, complications

Introduction:

Diabetes mellitus (DM) is a metabolic syndrome with an increasing prevalence and high mortality rate[1] . Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease. In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively[2] . In 2010 China became the world capital of Diabetes with 92.4 million people having Diabetes [3] .According to Wild et al[4] the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India.

Diabetic retinopathy (DR), which is a common complication in diabetes, is characterized by retinal vascular leakage, inflammation and abnormal neovascularization [5,6]

It is considered to be one of the leading causes of vision loss and vision impairment in adults. With the progression of DR, the quality of life of patients decreases, and the financial burden on society increases, both in the DR screening and treatment groups.

DR has been considered to be correlated with many other diabetes-related complications, such as nephropathy, peripheral neuropathy and cardiovascular events, all of which lower the quality of life and produce a high rate of mortality. Therefore, early diagnosis and proper management of DR would be of great significance [. 7]

Worldwide, diabetic retinopathy (DR) is the leading cause of blindness among working age adults . Estimated prevalence remains around 34.6 % (approximately 93 million individuals) and 10.2 % have an advanced stage of the disease . The basic mechanisms by which diabetes mellitus (DM) generates microvascular complications are not fully elucidated[8].

Table 1: Classification of diabetic retinopathy in early treatment of diabetic retinopathy study.

Disease Severity Level	Findings Observable upon Dilated Ophthalmoscopy
Mild nonproliferative retinopathy	At least one microaneurysm, and definition not met for moderate nonproliferative retinopathy, severe nonproliferative retinopathy, early proliferative retinopathy, or high-risk proliferative retinopathy (see below)
Moderate nonproliferative retinopathy	Hemorrhages and/or microaneurysms ≥ standard photograph 2A*; and/or soft exudates, venous beading, or intraretinal microvascular abnormalities definitely present; and definition not met for severe nonproliferative retinopathy, early proliferative retinopathy, or high-risk proliferative retinopathy (see below)
Severe nonproliferative retinopathy	Cotton-wool spots, venous beading, and intraretinal microvascular abnormalities all definitely present in at least two of fields four through seven; or two of the preceding three lesions present in at least two of fields four through seven and hemorrhages and microaneurysms present in these four fields, ≥ standard photo 2A in at least one of them; or intraretinal microvascular abnormalities present in each of fields four through seven and ≥ standard photograph 8A in at least two of them; and definition not met for early proliferative retinopathy or high-risk proliferative retinopathy (see below)
Early proliferative retinopathy (i.e., proliferative retinopathy without Diabetic Retinopathy Study high-risk characteristics) (see Glossary)	New vessels; and definition not met for high-risk proliferative retinopathy (see below)
High-risk proliferative retinopathy (i.e., proliferative retinopathy with Diabetic Retinopathy Study high-risk characteristics) (see Glossary)	New vessels on or within one disc diameter of the optic disc (NVD) ≥ standard photograph 10A* (about one-quarter to one-third disc area), with or without vitreous or preretinal hemorrhage; or vitreous and/or preretinal hemorrhage accompanied by new vessels, either NVD < standard photograph 10A or new vessels elsewhere (NVE) ≥ one-quarter disc area

Adapted with permission from the Early Treatment Diabetic Retinopathy Study Research Group. Early Treatment Diabetic Retinopathy Study design and baseline patient characteristics: ETDRS report number 7. Ophthalmology 1991;98:742.

* Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs--an extension of the modified Airlie House classification: ETDRS report number 10. Ophthalmology 1991;98:786-806.

Diabetic nephropathy is a dreaded complication of diabetes. It contributes to serious morbidity and mortality. As it progresses to end stage renal disease it imposes enormous medical, economic and social costs on both the patient and the health care system.
Diabetic neuropathy is a common cause of morbidity and death among patients with diabetes, generating a huge economic burden.
This study has been done to evaluate the association of hypertension, neuropathy and nephropathy and severity of retinopathy in diabetic patients.

MATERIAL AND METHODS:

This Prospective observational study was conducted at the outpatient Department of Ophthalmology of a Medical college and Tertiary Health care centre in North Maharashtra

STUDY POPULATION: The study was conducted on 100 patients of Diabetic retinopathy who were either seen in our OPD or admitted in the hospital.

SELECTION OF PATIENTS: All patients diagnosed as diabetic by blood sugar level (fasting) and (Post

prandial) or known case of Diabetes Mellitus and/or now presented with any systemic complication of Diabetes.

Materials and Method:

A detailed clinical history of each patient was taken. Information regarding the age of onset, duration of the disease, whether associated with any other systemic illness, whether taking treatment regularly or irregularly and history of any ocular complaint was noted.

Complete ophthalmic examination:

- Ocular examination was done by torch light.
- Visual acuity for distance was examined on Snellen's chart.
- Near vision was examined by Jaeger's chart.
- Slit lamp biomicroscopy was done to study the anterior segment and anterior vitreous.
- Fundus examination was done by direct ophthalmoscopy and Indirect ophthalmoscopy.

This study was approved by the Local Institutional Review board and Ethics Committee. Informed consent was taken from all the patients.

Data was collected using a questionnaire especially developed for this research and included: presence or absence of DR, demographic data (gender and age), glycemic (BSL , fasting and post prandial, DM profile (diabetes duration, type of DM and insulin use) and comorbidities (hypertension, dyslipidemia, and diabetic nephropathy). Clinical findings confirmed by direct and indirect ophthalmoscopy

Regarding comorbidities, diagnosis was entirely based on clinical charts, considering previous clinical history and laboratory tests. Hypertension was set as blood pressure ≥140/90 mmHg (in distinct measures during the outpatient care) or use of antihypertensive therapy ; diabetic nephropathy set as blood urea nitrogen…>20mg/dL and serum creatinine > 1.3mg/dL or history of renal dialysis or previous diagnosis of disease. Diabetic neuropathy was assessed if there was any history of tingling and numbness or presence of foot ulcers or past amputations, history of frozen shoulder or any nerve palsy.

Patients with no diabetic changes seen in retina or lens opacities and those in which the pupil dilation could not be performed were excluded (pregnant, uncontrolled hypertension and suspected of narrow-angle glaucoma). All information collected was finally analyzed for the study variables.

Statistical Analysis

Chi square test, univariate and multivariate logistic regression analysis was performed. P value < 0.05 was taken as significant.

Results:

Out of 100 patients studied, diabetic retinopathy was predominantly seen in 68 males while only 32 females were affected. The male: female ratio was 2.13:1.

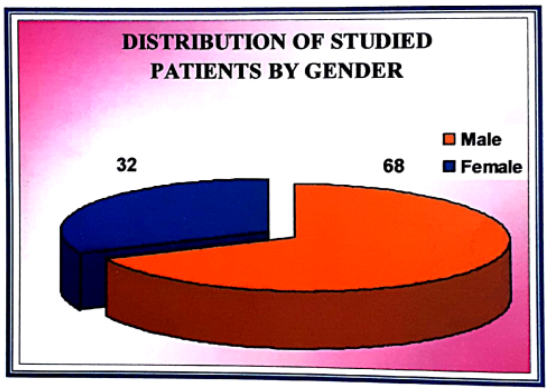


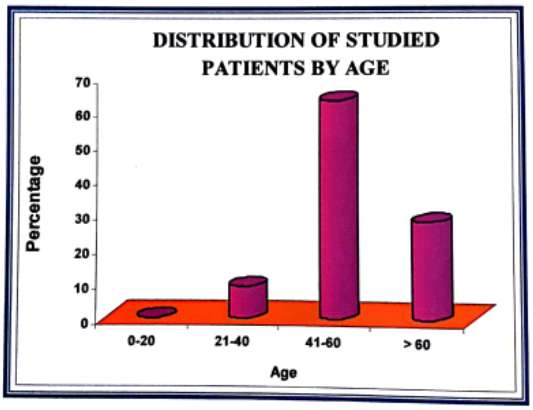
Table 2: Prevalence of diabetic retinopathy (grades) in the diabetic population of diabetic patients.

	Mild NPDR (%)	Mod NPDR (%)	Severe NPDR (%)	PDR (%)
NIDDM	49	8	6	5
IDDM	16	8	4	4

Table 3: Distribution of studied patients by age

DISTRIBUTION OF STUDIED PATIENTS BY AGE

AGE	NO. OF PATIENTS	PERCENTAGE
0-20	0	0
21-40	9	9
41-60	63	63
> 60	28	28
TOTAL	100	100



Most of the cases were in the age group of 41-60 years. 32 patients (32%) studied were of type 1 Diabetes Mellitus and 68(68%) studied were of type 2 Diabetes Mellitus. Incidence of diabetic retinopathy was increased from 2% when the age of onset was 11-20 years to 63% when the age of onset was 41-60 years.

Table 4: Relationship between risk factors and severity of diabetic retinopathy.

RISK FACTORS	NPDR N=91	PDR N=9	P VALUES	SIGNIFICANCE
Age of onset in type 1 DM	**28**	**4**	**>0.999**	**NOT SIGNIFICANT**
Age of onset in type 2DM	**63**	**5**	**0.91**	**NOT SIGNIFICANT**
Duration of DM in type1 DM	**28**	**4**	**0.198**	**NOT SIGNIFICANT**
Duration of DM in type 2 DM	**63**	**5**	**0.00019**	**SIGNIFICANT**
Maculopathy in DM type 1	**11**	**1**	**>0.99**	**NOT SIGNIFICANT**
Maculopathy in DM type 2	**33**	**3**	**0.891**	**NOT SIGNIFICANT**

Table 5: Duration of Diabetes and risk factors

Duration	Nephropathy	Neuropathy	Cardiovascular disease	Total
Upto 10 yrs	5	5	38	48
>10 yrs	5	4	13	22
Total	10	9	51	70

There was no statically significant relationship between duration of Diabetes and various risk factors.

Table 6: Severity of Diabetes Mellitus and Complications of Diabetes

Complication	Mild ,Moderate, Severe & Very Severe NPDR	PDR	Total	Z test statistic	P value
Nephropathy	5 (8.93%)	5 (35.71%)	10	-2.56	0.01
Neuropathy	8 (14.29%)	1 (7.14%)	9	0.40	0.69
Cardiovascular disease	43 (76.79%)	8 (57.14%)	51	1.48	0.14
Total	56	14	70		

p value = 0.01 < 0.05 significant for Nephropathy (Z test of two proportions is applied)
The difference of proportions is significant for nephropathy patients and proportion is more in patients having proliferative diabetic retinopathy and nephropathy

Table 7: Chi square test of trends in proportions of complications within duration of diabetes

Severity of Diabetic Retinopathy	Nephropathy	No Nephropathy	Total	Proportion of Nephropathy within stages	Chi-square for slope (linear trend)	P value
Mild	**0**	**25**	**25**	0.00	7.1359	0.0076
Moderate ,	**3**	**10**	**13**	0.23		
Severe & Very Severe	**2**	**16**	**18**	0.11		
PDR	**5**	**9**	**14**	0.36		
Total	**10**	**60**	**70**	0.14		

P value<0.05 shows linear trends in proportion of nephropathy within stages

Discussion:

In our study the ratio of male: female was 2.31:1. Varghese et al[9] conducted a study in which the male: female ratio was 1.6:1.

In the current study, mild diabetic retinopathy was seen in 65%, moderate retinopathy was seen in 16% ,severe retinopathy was seen in 10% and proliferative di abetic retinopathy was seen in 9% of patients. In our study the percentage of patients having non proliferative diabetic retinopathy was high as compared to other studies may be because we have included the patients who had some grade of retinopathy as our subjects. The percentage of

patients having proliferative diabetic retinopathy matches with other studies[10]

The most common age group affected by diabetic retinopathy was 41- 60 years, comprising 63% of the total cases. According to Duke Elder[11], Diabetes mellitus occurs in people in the 5 th and 6 th decades of life, 50% of cases appear between the ages of 40 and 50 years and only 5 % in the first decade and 3% in the eight decade.

In type 1 diabetes patients with diabetic retinopathy(32%) maximum incidence of retinopathy occurred between duration of 11- 20 years(84%) out of which mild NPDR was found to be maximum (48%). In type 2 diabetic patients with diabetic retinopathy (68%), all grades of non-proliferative retinopathy were present since the diagnosis. Maximum incidence was of mild NPDR (72%)

Ossama A.W EL Haddad et al[12] in their study found that the risk of diabetic retinopathy after 10 years of onset of diabetes was increased 8.7 fold compared with patients with duration of diabetes less than or equal to 10 years and risk would increase with the same amplitude for approximately every 5 years of duration afterwards. Lalit Dandona et al[13] in his study found that 87.5% of those with duration of diabetes since diagnosis >= 15 years had diabetic retinopathy compared with 18.9% of those with duration< =15 years.

In our study, the prevalence of diabetic retinopathy was 16.6 % in persons who had diabetes for less than five years and 83.33 % in persons who had diabetes for 15 or more years . In our study the relation between duration of diabetes mellitus and severity of diabetic retinopathy was statistically significant.(p <0.00019)

In The Wisconsin Epidemiologic Study of Diabetic Retinopathy done by Ronald Klein et al the prevalence of diabetic retinopathy varied from 28.8% in persons who had diabetes for less than five years to 77.8% in persons who had diabetes for 15 or more years and it was statistically significant[14]

In our study, the rate of proliferative diabetic retinopathy was 1.47 % in persons who had diabetes for less than 5 years to 7.35 % in persons who had diabetes more than 15 years.

The rate of proliferative diabetic retinopathy varied from 2.0% in persons who had diabetes for less than five years to 15.5% in persons who had diabetes for 15 or more years. [14]

Thus it can be said that development of diabetic retinopathy prevalence is positively associated with duration of diabetes and the severity of retinopathy increased with the duration of diabetes in type 2 diabetes patients.

In our study, we had 9 patients who had clinical features suggestive of diabetic neuropathy. Diabetic foot was found in 5 patients (56%), tingling and numbness in extremities was found in 2 patients (22%). Frozen shouder was seen in 1 patient (11%) and 3 rd nerve palsy was seen in 1 patient(11%).Osuntokun[15] in 1969, studied 758 Nigerian diabetic patients and found that 19 patients had neuropathy and retinopathy and concluded that neuropathy when associated with diabetic retinopathy predisposes to gangrene.

In our study, it was seen that nephropathy was present in 35.71 % cases with PDR as compared to 8.93% of cases with NPDR. The association of nephropathy in patients of proliferative diabetic retinopathy is significant (p< 0.05). Study by El- Asrar Am et al [16] showed similar results.

Study by Won June Lee et al [17] shows that patients with both PDR and NPDR were more likely to have diabetic nephropathy than patients without PDR.

Maximum number of patients with Diabetes mellitus having cardiovascular disease had hypertension(68%) but association of cardiovascular disease with severity of diabetic retinopathy was not significant.

In neuropathy, maximum number of patients had diabetic foot (56%), but association of neuropathy with severity of retinopathy was not significant.

Conclusion:

Our study showed that there is a significant correlation between severity of retinopathy and duration in type 2 Diabetes mellitus patients.

Maximum number of patients with Diabetes mellitus having cardiovascular involvement, had hypertension (68%).

In patients suffering from neuropathy as a complication of DM, maximum number of patients had diabetic foot (56%).

It was seen that the severity of diabetic retinopathy had some association with presence of nephropathy

Also it can be postulated that patients with severe NPDR and PDR have high risk of developing nephropathy than patients suffering with mild and moderate NPDR.

Hence it can be recommended that all patients of diabetes mellitus suffering from clinically significant neuropathy, nephropathy or hypertension as a complication of diabetes should always be screened for presence of retinopathy. Further studies with larger sample size are to be conducted to further look into this association.

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