Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/37jk5605

A COMPARATIVE STUDY OF DIABETIC MACULOPATHY AMONG NON PROLIFERATIVE AND PROLIFERATIVE DIABETIC RETINOPATHY PATIENTS

Dr. Subbulakshmi. S[1], Dr. Arun Vaidhya. T [2*], Dr. Hamsa. V.S[3]

[1]Assistant Professor, Department of Ophthalmology, Vinayaka missions medical college and hospital, Karaikal, Pondicherry; Vinayaka missions research foundation (deemed to be university), India
[2*]Assistant Professor, Department of Ophthalmology, Vinayaka missions medical college and hospital, Karaikal, Pondicherry; Vinayaka missions research foundation (deemed to be university), India
[3]Assistant Professor, Department of Paediatrics, Shri Sathya Sai medical college and research institute, Chengalpattu, Tamil Nadu; India

[*]**Corresponding Author:** Dr. Arunvaidhya. T
Email: arunvaidhya@gmail.com

ABSTRACT

Background: Diabetic Retinopathy is due to the microangiopathy changes in the retinal precapillary arterioles, capillaries and venules. Diabetic Maculopathy is the leading cause of blindness in Diabetic Retinopathy. Retinal ischemia and edema are the two major intraretinal components of Diabetic Maculopathy. Visual loss is caused by the breakdown of blood retinal barrier, which leads to increase in the extracellular fluid within the retina, resulting in distortion of the retinal architecture. However, Diabetic Retinopathy has an unpredictable evolution and control of this disease is challenging. Hence, with timely detection and treatment, proper follow up and Diabetes Mellitus care, visual loss can be prevented.

This study is done to compare Diabetic Maculopathy among Non-Proliferative and Proliferative Diabetic Retinopathy patients**.** Thus, leading to early treatment and prevention of blindness due to Diabetic Maculopathy.

Objective: Comparison of Diabetic Maculopathy among Non-Proliferative and Proliferative Diabetic Retinopathy in Type 2 diabetic patients.

Methodology: Non-Proliferative and Proliferative Diabetic Retinopathy patients were prospectively enrolled. All the participants in the study were interviewed using a wellstructured proforma. Patient's details including age, sex, type and duration of diabetes, treatment history were recorded. Complete Ocular examination was done including Best corrected visual acuity (BCVA), Anterior segment examination using Slit lamp Retinoscopy, Intraocular pressure measurement using Applanation Tonometer, Amsler Grid, Posterior segment examination includes dilated fundus examination with indirect Ophthalmoscope and Slit lamp biomicroscopy using +90D. Fundus Photography will be taken for documentation using canon fundus camera. Statistical analysis was performed using SPSS software.

Results: This prospective study was conducted in the Department of Ophthalmology at Vinayaka Missions Medical College, Karaikal. On approval by ethical committee, 100 Diabetic Retinopathy

patients were recruited after obtaining informed consent. According to ETDRS Classification patients were recruited in two groups. 50 patients were in non-proliferative and 50 patients were in proliferative Diabetic Retinopathy group. The maximum number of patients belonged to the age group of 51-60 years ie.34 patients (68%) in NPDR Group and 61-70 years ie.21 patients (42%) in PDR group. Females outnumbered males i.e. 26 patients (52%) in NPDR group and 30 patients (60%) in PDR group. The results of the study showed that 21 patients (68%) in NPDR Group had developed Diabetic Maculopathy when compared to PDR Group ie.10 patients (32%) and which was found to be statistically significant. The results of the study also showed that within NPDR group, severe NPDR patients i.e. 10 patients (47%) developed Diabetic Maculopathy when compared to Mild and Moderate NPDR patients.

Conclusion: The results of the study showed that 21 patients (68%) in NPDR Group had developed Diabetic Maculopathy when compared to PDR Group ie.10 patients (32%). The results of the study also showed that within NPDR group, severe NPDR patients i.e. 10 patients (47%) developed Diabetic Maculopathy when compared to Mild and Moderate NPDR patients. Since, the prevalence of Diabetic Maculopathy is increasing nowadays in both NPDR and PDR patients, it is advisable to undergo fundus examinations periodically at regular intervals to detect the Diabetic Maculopathy at the earliest. Early treatment with photocoagulation can stabilize the visual acuity and prevent further visual loss. So, it is recommended that diabetic patients should have regular retinal examinations through a dilated pupil within 3–5 years of diabetes and follow-up yearly.

Keywords: Diabetic Maculopathy, Non-Proliferative Diabetic Retinopathy, Proliferative Diabetic Retinopathy

Introduction

Blindness is one of the most feared complications of Diabetic Retinopathy but also preventable. Diabetic Maculopathy is the common causes of blindness in the world due to Diabetic Retinopathy. It Contributes 4.8% of the 37 million cases of blindness throughout the world. In NIDDM (Type II diabetic mellitus), for the patients with duration of more than 5 years, 40% of those taking insulin and 24% of those not taking insulin have retinopathy. These rates increase with increased duration of diabetes.

Classification

The most widely used classification is the **Early Treatment for Diabetic Retinopathy Study Classification (ETDRS)**

NPDR (Non proliferative Diabetic Retinopathy)

It is characterized by presence of retinal hemorrhages, exudates and configurational changes in veins. The severity of retinopathy is further classified as

a. Mild NPDR (At least one microaneurysm)
b. Moderate NPDR (Soft exudates, venous beading & IRMAs (Intraretinal microvascular abnormalities)
c. Severe NPDR (Any one of the following)

i) Hemorrhages and microaneurysms in all 4 quadrants ii) Venous beading in 2 or > quadrant iii) IRMA in atleast 1 quadrant

d. Very Severe NPDR (Any 2 or more of the criteria for Severe NPDR)

PDR (Proliferative Diabetic Retinopathy)

It is composed of NVD (New Vessels on Disc) or NVE (New vessels elsewhere), Vitreous or Pre-Retinal hemorrhages and Fibrous Tissue Proliferation.

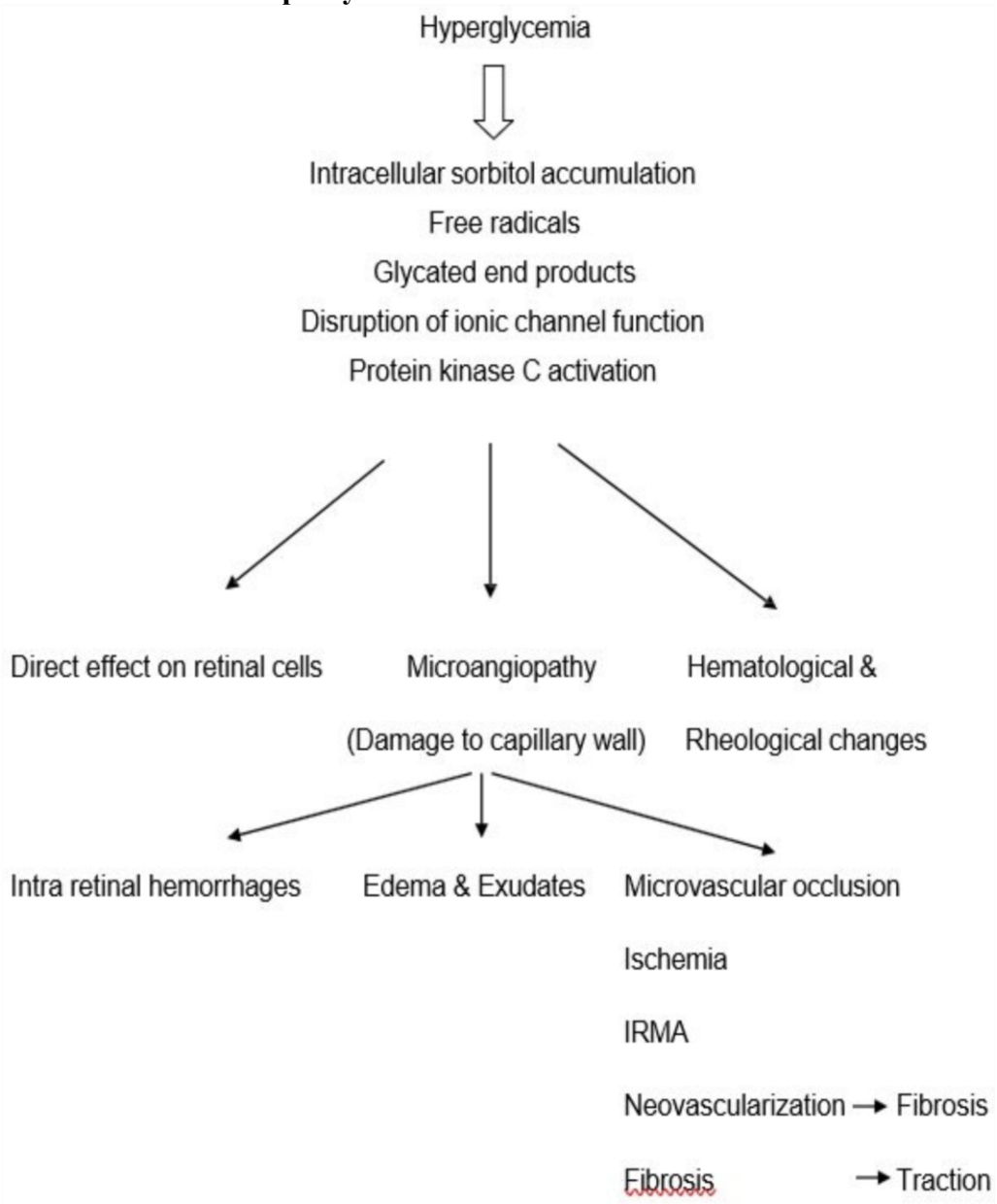
1. Early PDR (New vessels on disc or elsewhere)
2. High risk PDR

i) NVD > 1/3-1/2 Disc area ii) NVD & vitreous or pre-retinal hemorrhages iii) NVE > ½ disc area and vitreous or pre-retinal haemorrhages.
3. Advanced PDR (Extensive vitreous hemorrhages preclude grading and presence of retinal Detachment in the macula)

Classification of Diabetic maculopathy by fundus fluorescein angiography (FFA)
• Exudative Maculopathy/CSME (Focal edema and Diffuse edema), Ischemic maculopathy and mixed maculopathy.

CSME (Clinically Significant Macular Edema)
1. Thickening of the retina < 500 microns from the center of the macula.
2. Hard exudates at or within 500 microns from the center of macula, ifassociated with thickening of the adjacent retina.
3. A zone of retinal thickening, 1 disc area or larger in size, a part of which is within 1 disc diameter from center of macula.

Pathogenesis of Diabetic retinopathy



Pathogenesis of Diabetic maculopathy

The most common cause of impairment of vision in Diabetic Retinopathy is due to macular edema. The deterioration of vision is due to macular edema, presence of hard exudates in the macula and hemorrhages in the macula. The increased vulnerability of macula in particular is due to abundance of Henle`s layer in the macula which are more hydrophilic, relative a vascularity when compared to the rest of the retina, which limits fluid absorption, thin basal lamina which offers little protection against any biochemical effects and exudates are common in the macula because the Outer Plexiform Layer at the macula has large potential interstitial space between cells.

Management

Complete Ocular examination including Best corrected visual acuity (BCVA), Anterior segment examination using Slit lamp Retinoscopy, Intraocular pressure measurement using Applanation Tonometer, Amsler Grid, Posterior segment examination includes dilated fundus examination with indirect Ophthalmoscope and Slit lamp biomicroscopy using +90D should be done. Fundus fluorescein angiography (FFA) and Optical coherence tomography (OCT) is the mandatory investigations needed for confirmation of the diagnosis, documentation of the various lesion, deciding about the management and follow up. Good Glycemic Control is the mainstay of treatment. Depending on the severity of the retinopathy intravitreal injections, pan retinal photocoagulation (PRP) or surgical approaches (Vitrectomy) can be done.

Aim of the study

Comparison of Diabetic Maculopathy among Non-Proliferative and Proliferative Diabetic Retinopathy in Type 2 diabetic patients.

Methodology

Ethics approval: With prior approval from our institutional ethical committee, this study was conducted in the department of ophthalmology at Vinayaka Missions Medical College, Karaikal. Informed consent was taken from all participating patients. Patients were explained in their vernacular language and were informed that they could drop out of the study at any point. An informed written consent was obtained from the patients.

Study population: Study population included 100 patients diagnosed with Diabetic retinopathy (50 Non proliferative and 50 Proliferative Diabetic Retinopathy patients) who attended the Ophthalmology out-patient department at Vinayaka Missions Medical College, Karaikal.

Study design: This study is a prospective, Comparative case study conducted in Vinayaka Mission Medical College, Karaikal.

Inclusion criteria: Patients of both sexes ageing more than 35 years with Non-insulin dependent Diabetes mellitus having Non Proliferative and Proliferative Diabetic Retinopathy were included in the study. According to ETDRS classification 50 patients in Non Proliferative Diabetic Retinopathy group and 50 patients in Proliferative Diabetic Retinopathy.

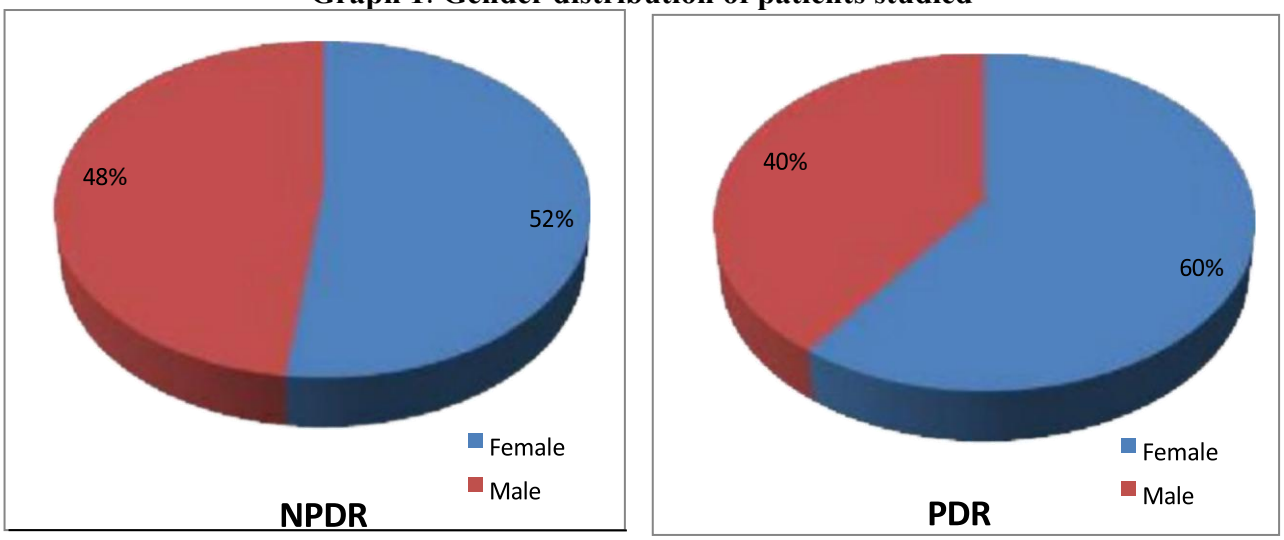
Exclusion criteria: Patients with Hypertensive Retinopathy, hazy media due to dense cataract, Glaucoma, Uveitis, Corneal opacities or irregularities, Ocular infections and any other major medical problems

Data collection: Patient's details including age, sex was recorded. Complete Ocular examination including Best corrected visual acuity (BCVA), Anterior segment examination using Slitlamp biomicroscopy, Retinoscopy, Intraocular pressure measurement using Applanation Tonometer and Posterior segment examination includes dilated fundus examination with Slitlamp biomicroscopy using +90D, Amsler grid and fundus Photography was taken for documentation using canon fundus camera.

Data management and statistical analysis: Collected data was entered into the Microsoft Excel sheet and the statistical software SPSS version 25 was used to analyze the data. The data were presented in percentages and proportions using tables and charts. Using suitable statistical tests, associations were calculated, and a p-value of <0.05 was considered statistically significant.

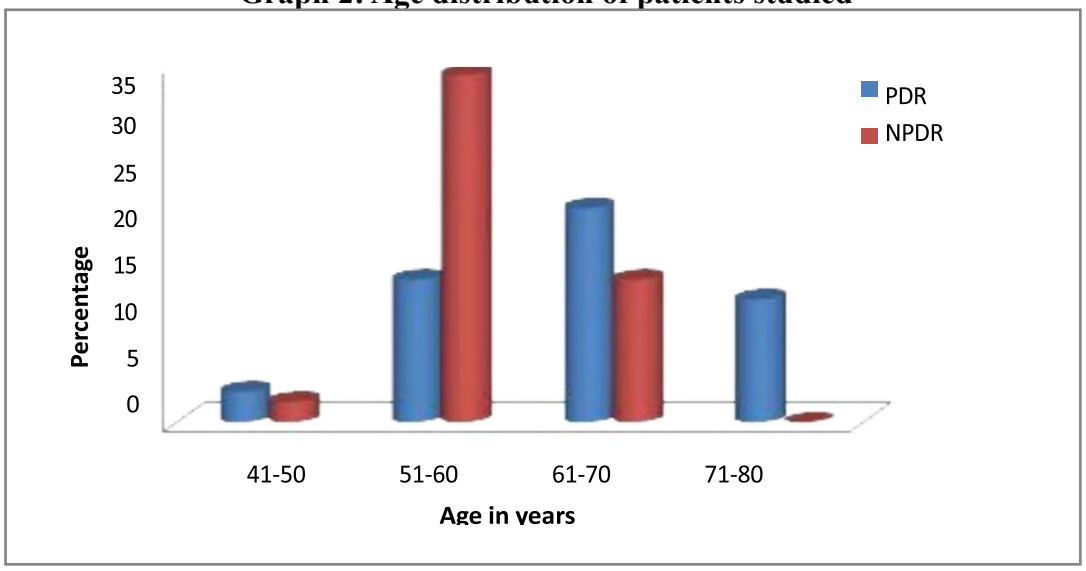
Results

Graph 1: Gender distribution of patients studied



Out of 50 patients in NPDR Group majority i.e. 26 patients (52%) were females and only 24 patients (48%) were males. In PDR Group also majority i.e. 30 patients (60%) were females and only 20 patients (40%) were males.

Graph 2: Age distribution of patients studied



Out of 50 patients studied in NPDR Group, maximum number of patients belonged to age group of 51-60 years i.e. 34 patients (68%), followed by the age group 61- 70years i.e. 14 patients (28%) and Only 2 patients (4%) belonged to the age group of 41-50 years of age.Out of 50 patients studied in PDR Group, maximum number of patients belong to age group of 61-70 years i.e. 21 patients (42%), followed by the age group of 51-60 years, i.e. 14 patients (28%) and 71-80 years of age i.e. 12 patients (24%). Only 3 patients (62%) were in 41-50 years of age group. The P value was found to be less than 0.001.

Table 1: Type of Diabetic Retinopathy (According to ETDRS Classification)

Type of Diabetic Retinopathy	No. of patients	Percentage
PDR	50	50.0
Mild NPDR	19	19.0
Moderate NPDR	16	16.0
Severe NPDR	15	15.0
Total	100	100%

Table 2: Diabetic Retinopathy in relation to Duration of Diabetes

Crosstab							
			DIABETIC RETINOPATHY GROUPS				Total
			PDR	MILD NPDR	MODERATE NPDR	SEVERE NPDR	
Duration (Years)	1-5 Years	Count	0	12	3	0	15
		%	0.0%	63.2%	18.8%	0.0%	15.0%
	6-10 Years	Count	3	7	9	6	25
		%	6.0%	36.8%	56.2%	40.0%	25.0%
	11-15 Years	Count	10	0	4	9	23
		%	20.0%	0.0%	25.0%	60.0%	23.0%
	16-20 Years	Count	23	0	0	0	23
		%	46.0%	0.0%	0.0%	0.0%	23.0%
	Above 20 Years	Count	14	0	0	0	14
		%	28.0%	0.0%	0.0%	0.0%	14.0%
Total		Count	50	19	16	15	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square =105.684* p=0.001

The above table depicts that out of 100 patients, 50 patients (50%) were in PDR group and remaining 50 patients (50%) were in NPDR group. In the duration of diabetes of 1 to 5 years, no one having PDR and15 patients (30%) having NPDR. In the period of 6-10 years 3 patients (6%) having PDR and 22 patients (44%) having NPDR. In the period of 11-15 years, 10 patients (20%) having PDR and 13 patients (26%) having NPDR and with 16-20 years of duration 23 patients (46%) having PDR and above 20 years of duration 14 patients (28%) having PDR. Which was found to be statistically significant i.e. $p<0.05$.

Table 3: Diabetic Maculopathy in relation to duration of diabetes of patients studied

MACULOPATHY	DURATION OF DIABETES											
	1-5 YRS		6-10YRS		11-15 YRS		16-20 YRS		>20 YRS		TOTAL	
WITH MACULOPATHY	patients	percentage	patients	percentage	patients	percentage	patients	percentage	patients	percentage	patients	Percentage
	0	0%	15	60%	8	35%	6	26%	2	14%	31	31%
WITHOUT MACULOPATHY	15	100%	10	40%	15	65%	17	74%	12	86%	69	69%
Total	15	100%	25	100%	23	100%	23	100%	14	100%	100	100%

The chi-square statistic is 15.2067**. The p-value =0 .004.

Out of 31 patients with Diabetic Maculopathy, Majority of 15 patients (60%) developed Diabetic Maculopathy in 6-10 years duration of diabetes, followed by 8 patients (35%) in 11- 15 years of diabetes and 6 patients (26%) in 16-20 years of diabetes. Only 2 patients (14%) developed Diabetic Maculopathy in more than 20 years of duration of diabetes.

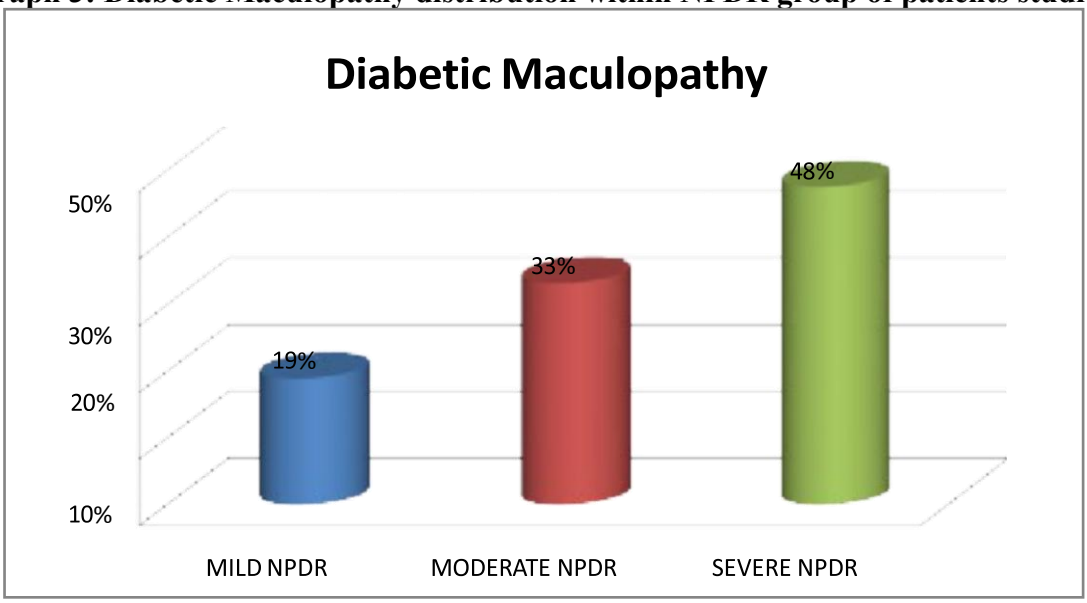
Table 4: Diabetic Maculopathy distribution in two groups of patients studied

DIABETIC MACULOPATHY * group Cross tabulation					
			Group		Total
			PDR	NPDR	
DIABETIC MACULOPATHY	With Maculopathy	Patients	10	21	31
		Percentage	32.26%	67.74%	31.00%
	Without Maculopathy	Patients	40	29	69
		Percentage	57.97%	42.03%	69.00%
Total		Patients	50	50	100
		Percentage	100.00%	100.00%	100.00%

Pearson chi-square = 5.657* p= 0.02

The above table depicts that, out of 100 patients studied 31 patients having Diabetic Maculopathy. Among the 31 Diabetic Maculopathy patients, 21 patients (68%) were in NPDR group and 10patients (32%) in PDR group. Chi square value was 5.657 which was statistically significant $p<0.05$, which shows that NPDR group patients developed Diabetic Maculopathy more than PDR group.

Graph 3: Diabetic Maculopathy distribution within NPDR group of patients studied



Out of 50 patients in NPDR group, 21 patients having Diabetic Maculopathy. Among the 21 Diabetic Maculopathy patients, 10 patients (48%) belong to Severe NPDR group 7 patients (33%) belong to Moderate NPDR group and 4 patients (19%) belong to Mild NPDR group, which shows that in NPDR group, maximum number of patients with Severe NPDR developed Diabetic Maculopathy when compared to Mild and Moderate NPDR group. And p value is found to be significant

Table 5: Visual acuity on presentation in Diabetic Maculopathy patients studied

TYPE OF RETINOPATHY		WITH MACULOPATHY EYE	WITHOUT MACULOPATHY EYE
Mild NPDR	4	6/24 -6/12 (IN ALL 4 EYES)	6/9-6/6 (IN ALL 4 EYES)
Moderate NPDR	7	6/36 – 6/12 (IN ALL 7 EYES)	6/12-6/6 (IN ALL 7 EYES)
Severe NPDR	10	6/60 – 6/24 (IN ALL 1O EYES)	6/18-6/9 (IN ALL 10 EYES)
PDR	10	>6/60 (IN ALL 10 EYES)	6/60-6/24 (IN ALL 10 EYES)

The chi-square statistic is 29.0118. The p-value is < 0.00001.

Out of 4 patients in the Mild NPDR group, Diabetic Maculopathy eye has 6/24-6/12 visual acuity when compared to normal eye i.e. 6/9-6/6.Out of 7 patients in the Moderate NPDR group, Diabetic Maculopathy eye has 6/36-6/12 visual acuity when compared to normal eyei.e.6/126/6.Out of 10 patients in the Severe NPDR group, Diabetic Maculopathy eye has 6/60-6/24 visual acuity when compared to normal eye i.e.6/18-6/9.Out of 10 patients in the PDR group, Diabetic Maculopathy eye has less than 6/60 visual acuity when compared to normal eye i.e.6/60-6/24. Hence, there is a drop of two Snellen lines between normal eye and Diabetic Maculopathy eye in all groups. And also found to be statistically significant.

Table 6: Treatment for T2DM in relation to Diabetic Maculopathy patients studied

Treatment for T2DM	With maculopathy		without maculopathy		Total	
	Patients	Percentage	Patients	Percentage	Patients	Percentage
Insulin	9	29.0%	20	29.0%	76	76.00%
OHAS	22	71.0%	49	71.0%	24	24.00%
Total	31	100.0%	69	100.0%	100	100.00%

Out of 31 patients with Diabetic Maculopathy, majority of 22 patients were on treatment with Oral Hypoglycemic Agents and only 9 patients were on treatment with insulin. Out of 69 patients without Diabetic Maculopathy, majority of 49 patients were on treatment with Oral Hypoglycemic Agents and only 20 patients were on treatment with insulin.

Discussion

Out of 50 patients in NPDR Group majority i.e. 26 patients (52%) were females and only 24 patients (48%) were males. In PDR Group also majority i.e. 30 patients (60%) were females and only 20 patients (40%) were males. Out of 50 patients studied in NPDR Group, maximum number of patients belonged to age group of 51-60 years i.e. 34 patients (68%), followed by the age group 61-70 years, i.e. 14 patients (28%) and Only 2 patients (4%) belonged to the age group of 41-50 years of age. Out of 50 patients studied in PDR Group, maximum number of patients belong to age group of 61-70 years i.e. 21 patients (42%), followed by the age group of 51- 60 years, i.e. 14 patients (28%) and 71-80 years of age i.e. 12 patients (24%). Only 2 Patients (62%) was in 4150 years of age group. The P value was found to be less than 0.001. Among patients with Diabetic Retinopathy of1 to 5 years, no one having PDR and15 patients (30%) having NPDR. In the period of 6-10 years 3 patients (6%) having PDR and 22 patients (44%) having NPDR. In the period of 11-15 years, 10 patients (20%) having PDR and 13 patients (26%) having NPDR and with 16-20 years of duration 23 patients (46%) having PDR and above 20 years of duration 14 patients (28%) having PDR. which was found to be statistically significant i.e. $p<0.05$. Out of 100 patients studied 31 patients having Diabetic Maculopathy. Among the 31 Diabetic Maculopathy patients, 21 patients (68%) were in NPDR group and 10patients (32%) in PDR group. Chi square value was 5.657 which was statistically significant $p<0.05$, which shows that NPDR group patients developed Diabetic Maculopathy more than PDR group. Out of 50 patients in NPDR group, 21 patients having Diabetic Maculopathy. Among the 21Diabetic Maculopathy patients, 10 patients (47%) belong to Severe NPDR group, 7 patients (33%) belong to Moderate NPDR group and 4 patients (19%) belong to Mild NPDR group, which shows that in NPDR group, maximum number of patients with Severe NPDR developed Diabetic Maculopathy when compared to Mild and Moderate NPDR group. And p value is found to be significant. Out of 31 patients with Diabetic Maculopathy, Majority of 15 patients (60%) developed Diabetic Maculopathy in 6-10 years duration of diabetes, followed by 8 patients (35%) in 11-15 years of diabetes and 6 patients (26%) in 16-20 years of diabetes. Only 2 (14%) patients developed Diabetic Maculopathy in more than 20 years of duration of diabetes. Out of 4 patients in the Mild NPDR group, Diabetic Maculopathy eye has 6/24- 6/12 visual acuity when compared to normal eye i.e. 6/9-6/6.Out of 7 patients in the Moderate NPDR group, Diabetic Maculopathy eye has 6/36-6/12 visual acuity when compared to normal eye ie.6/12-6/6.Out of 10 patients in the Severe NPDR group, Diabetic Maculopathy eye has 6/60-6/24 visual acuity when compared to normal eye ie.6/18-6/9.Out of 10 patients in the PDR group, Diabetic Maculopathy eye has less than 6/60 visual acuity when compared to normal eye ie.6/60- 6/24.Hence, there is a drop of two snellen lines between normal eye and Diabetic Maculopathy eye in all groups. And also found to be statistically significant. Out of 31 patients with Diabetic Maculopathy, majority of 22 patients were on treatment with Oral Hypoglycemic Agents and only 9 patients were on treatment with insulin.

Conclusion

Diabetic Maculopathy is the most common cause of visual loss in a patient with Diabetic Retinopathy. Visual loss is caused by the breakdown of blood retinal barrier, which leads to increase in the extracellular fluid within the retina, resulting in distortion of the retinal architecture.

The results of the study showed that 21 patients (68%) in NPDR Group had developed Diabetic Maculopathy when compared to PDR Group ie.10 patients (32%) and which was found to be statistically significant. The results of the study also showed that within NPDR group, Severe NPDR patients i.e. 10 patients (47%) developed Diabetic Maculopathy when compared to Mild and Moderate NPDR patients and which was found to be statistically significant. The results of the study showed

that 22 patients (71%) on Oral Hypoglycemic Agents had developed Diabetic Maculopathy. Since, the prevalence of Diabetic Maculopathy is increasing nowadays in both NPDR and PDR patients, it is advisable to undergo fundus examinations periodically at regular intervals to detect the Diabetic Maculopathy at the earliest. Early treatment with photocoagulation can stabilize the visual acuity and prevent further visual loss.

Conflict of interest: None

Source of funding: None

References

1. Raman R, Gupta A, Krishna S, Kulothungan V, Sharma T. Prevalence and risk factors for diabetic microvascular complications in newly diagnosed type II diabetes mellitus. Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS, report 27) J Diabetes Complications. 2012; 26(2):123–8. doi: 10.1016/j.jdiacomp.2012.02.001. [PubMed] [Cross Ref]
2. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. Lancet. 2010; 376(9735):124–36. doi: 10.1016/S0140-6736(09)62124-3. [PubMed] [Cross Ref]
3. Bourne RR, Stevens GA, White RA, Smith JL, Flaxman SR, Price H, et al.Causes of vision loss worldwide, 1990–2010: a systematic analysis. Lancet GlobHealth. 2013;1(6):e339–49. doi: 10.1016/S2214-109X(13)70113-X. [PubMed] [Cross Ref]
4. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al.Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care.2012;35(3):556–64. doi: 10.2337/dc11-1909. [PMC free article] [PubMed] [Cross Ref]
5. Lightman S, Towler HM. Diabetic retinopathy. Clin Cornerstone. 2003; 5(2):12–21. doi: 10.1016/S1098-3597(03)90015-9. [PubMed] [Cross Ref]
6. Mottl AK, Pajewski N, Fonseca V, Ismail-Beigi F, Chew E, Ambrosius WT, et al.The degree of retinopathy is equally predictive for renal and macrovascular outcomes in the ACCORD Trial. J Diabetes Complications. 2014; 28(6):874–9. doi:10.1016/j.jdiacomp.2014.07.001. [PMC free article] [PubMed] [Cross Ref]
7. Thomas RL, Dunstan FD, Luzio SD, Chowdhury SR, North RV, Hale SL, et al.Prevalence of Diabetic Retinopathy within a national Diabetic Retinopathy screening service. Br J Ophthalmol. 2015; 99(1):64–8. doi: 10.1136/bjophthalmol-2013-304017. [PubMed] [Cross Ref]
8. Pedro RA, Ramon SA, Marc BB, Juan FB, Isabel MM. Prevalence and relationship between Diabetic Retinopathy and nephropathy, and its risk factors in the North-East of Spain, a population-based study. Ophthalmic Epidemiol. 2010; 17(4):251–65. doi: 10.3109/09286586.2010.498661. [PubMed] [Cross Ref]
9. Bertelsen G, Peto T, Lindekleiv H, Schirmer H, Solbu MD, Toft I, et al. Tromso eye study: prevalence and risk factors of diabetic retinopathy. Acta Ophthalmol. 2013; 91(8):716–21. doi: 10.1111/j.1755-3768.2012.02542.x. [PubMed] [Cross Ref]
10. Knudsen LL, Lervang HH, Lundbye-Christensen S, Gorst-Rasmussen A. The north Jutland CountyDiabetic Retinopathy study: population characteristics. Br J Ophthalmol. 2006; 90(11):1404–9. doi: 10.1136/bjo.2006.093393. [PMC free article] [PubMed] [Cross Ref]
11. Dedov I, Maslova O, Suntsov Y, Bolotskaia L, Milenkaia T, Besmertnaia L.Prevalence of Diabetic Retinopathy and cataract in adult patients with type 1 and type2diabetesin Russia. Rev Diabet Stud. 2009;6(2):124–9. doi:9.10.1900/RDS.2009.6.124. [PMC free article] [PubMed] [Cross Ref]
12. Roy MS, Klein R, O'Colmain BJ, Klein BE, Moss SE, Kempen JH. The prevalence of Diabetic Retinopathy among adult type 1 diabetic persons in the United States. Arch Ophthalmol. 2004; 122(4):546–51. doi: 10.1001/archopht.122.4.546. [PubMed] [Cross Ref]

12. Kempen JH, O'Colmain BJ, Leske MC, Haffner SM, Klein R, Moss SE, et al.The prevalence of Diabetic Retinopathy among adults in the United States. Arch Ophthalmol. 2004; 122(4):552–63. doi: 10.1001/archopht.122.4.552. [PubMed] [Cross Ref]
13. Zhang X, Saaddine JB, Chou CF, Cotch MF, Cheng YJ, Geiss LS, et al.Prevalence of Diabetic Retinopathy in the United States, 2005–2008. JAMA. 2010; 304(6):649–56. doi: 10.1001/jama.2010.1111. [PMC free article] [PubMed] [CrossRef]
14. Raman R, Rani PK, Reddi Rachepalle S, Gnanamoorthy P, UthraS, Kumaramanic kavel G, et al. Prevalence of Diabetic Retinopathy in India: SankaraNethralaya Diabetic Retinopathy epidemiology and molecular genetics study report 2. Ophthalmology. 2009; 116(2):311–8. doi: 10.1016/j.ophtha.2008.09.010. [PubMed] [Cross Ref]
15. Liu L, Wu X, Liu L, Geng J, Yuan Z, Shan Z, et al. Prevalence of Diabetic Retinopathy in mainland China: a meta-analysis. PLoS One. 2012; 7(9):e45264. doi:10.1371/journal.pone. 0045264. [PMC free article] [PubMed] [Cross Ref]
16. Huang OS, Tay WT, Ong PG, Sabanayagam C, Cheng CY, Tan GS, et al.Prevalence and determinants of undiagnosed Diabetic Retinopathy and visionthreatening retinopathy in a multi-ethnic Asian cohort: the Singapore Epidemiology of Eye Diseases (SEED) study. Br J Ophthalmol. 2015. [PubMed]
17. Zheng Y, Lamoureux EL, Lavanya R, Wu R, Ikram MK, Wang JJ, et al. Prevalence and risk factors of Diabetic Retinopathy in migrant Indians in an urbanized society in Asia: the Singapore Indian eye study. Ophthalmology. 2012; 119(10):2119–9.24. doi: 10.1016/j.ophtha.2012.04.027. [PubMed] [Cross Ref]
18. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of Diabetic Retinopathy in urban India: the Chennai Urban Rural Epidemiology Study (CURES) eye study, I. Invest Ophthalmol Vis Sci. 2005;46(7):2328–33. doi: 10.1167/iovs.05-0019. [PubMed] [Cross Ref]
19. Al Ghamdi AH, Rabiu M, Hajar S, Yorston D, Kuper H, Polack S. Rapid assessment of avoidable blindness and Diabetic Retinopathy in Taif, Saudi Arabia. Br J Ophthalmol. 2012; 96(9):1168–72. doi: 10.1136/bjophthalmol-2012-301874. [PubMed] [Cross Ref]
20. Papakonstantinou E, Tsinopoulos I, Dimitrakos S, Dehghan MH, Katibeh M,Ahmadieh H, et al. Prevalence and risk factors for Diabetic Retinopathy in the 40 to80 year-old population in Yazd, Iran: the Yazd Eye Study. J Diabetes. 2015; 7(1):139–41. doi: 10.1111/1753-0407.12205. [PubMed] [Cross Ref]
21. Wang FH, Liang YB, Zhang F, Wang JJ, Wei WB, Tao QS, et al. Prevalence of Diabetic Retinopathy in rural China: the Handan Eye Study. Ophthalmology. 2009; 116(3):461–7.doi:10.1016/j.ophtha .2008.10.003. [PubMed] [Cross Ref]
22. Kung K, Chow KM, Hui EM, Leung M, Leung SY, Szeto CC, et al. Prevalence of complications among Chinese diabetic patients in urban primary care clinics: a crosssectional study. BMC Fam Pract. 2014; 15:8. doi: 10.1186/1471-2296-15-8. [PMC free article] [PubMed] [Cross Ref]
23. Tong L, Vernon SA, Kiel W, Sung V, Orr GM. Association of macular involvement withproliferative retinopathy in type 2 diabetes. Diabet Med. 2001; 18(5):388–94. doi:10.1046/j.1464- 5491.2001.00483.x. [PubMed] [Cross Ref]