FREQUENCY OF DIABETIC RETINOPATHY IN TYPE 2 DIABETES MELLITUS WITH REFERENCE TO RISK FACTORS IN A TERTIARY CARE HOSPITAL IN SOUTH WESTERN MAHARASHTRA

Ophthalmology

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ABSTRACT

AIM: To estimate the frequency of Diabetic Retinopathy and the possible risk factors associated with Diabetic Retinopathy.

MATERIALS AND METHODS: All patients of diagnosed type 2 Diabetes Mellitus attending Ophthalmology Outpatient Department in Government Medical College and Hospital, Miraj during the study period were included. History was taken and a complete ophthalmic examination was done. Diabetic Retinopathy was graded according to ETDRS classification. Data was analyzed using SPSS 22 version software.

RESULT: A total of 275 patients with diagnosed Diabetes Mellitus were examined. Frequency of diabetic retinopathy in the study was 30.91%. Significant association was found with male gender ($p=0.008$), duration of Diabetes Mellitus more than 10 years ($p<0.001$), positive family history ($p<0.001$), use of insulin ($p<0.001$), raised systolic and diastolic blood pressure ($p<0.001$), fasting and post prandial blood sugar levels ($p<0.001$). Age, smoking status and body mass index were not found to be significant risk factors for the development of diabetic retinopathy.

KEYWORDS

Diabetic retinopathy, Diabetes Mellitus

INTRODUCTION

Diabetes Mellitus currently affects 425 million people worldwide. It is anticipated that the number of people with diabetes will be more than double as a consequence of population aging, increased life expectancy, obesity, reduced physical fitness, urbanization and improved detection¹.

Diabetic Retinopathy is the most common microvascular complication of diabetes and was until recently regarded as the most prevalent cause of visual impairment in the working age population in developed countries².

Patients with Diabetic retinopathy are 25 times more likely to become blind than non diabetics³.

In the Indian subcontinent, only limited data is available on the prevalence of Diabetic Retinopathy in the general population. Studies of various complications in Indian diabetics is therefore of great interest. Hence, this study was undertaken to screen the population with Type 2 Diabetes Mellitus for diabetic retinopathy and to explore risk factors for developing diabetic retinopathy among them.

OBJECTIVES

- To study the frequency of Diabetic Retinopathy among diagnosed Type 2 Diabetes Mellitus patients.
- To study the relation of Diabetic Retinopathy with risk factors such as age, gender, duration of diabetes, blood sugar levels, ongoing pharmacotherapy, family history.

MATERIALS AND METHODS

After receiving approval from our local ethics committee and prior written informed consent a descriptive hospital based cross sectional study was done on patients with diagnosed type 2 Diabetes Mellitus attending the Ophthalmology Outpatient Department at Government Medical College and Hospital, Miraj considering the inclusion and exclusion criteria over a period of 18 months (January 2017 to June 2018).

A detailed history, ocular examination and relevant systemic examination was done.

History included the following general information of the patient, duration since diagnosis of type 2 Diabetes Mellitus, treatment modality for diabetes, family history, smoking habit and ocular history. A detailed ophthalmological examination included recording of visual acuity (best corrected visual acuity), examination of ocular adnexa and extraocular structures, Slit lamp biomicroscopic examination of the anterior segment. Pupils were dilated using mydriatic agents namely combination of 0.8% Tropicamide and 5% Phenylephrine eye drop 3 times at an interval of 10 minutes. Detailed examination of the posterior pole was done using direct ophthalmoscope and slit lamp

biomicroscope with +90D lens. Retinal periphery was examined by indirect ophthalmoscopy using +20D lens. Diabetic retinopathy was classified according to Modified Airlie House classification - Early Treatment Diabetic Retinopathy Study (ETDRS). The worse affected eye of the participant was considered for the purpose of further statistical analysis.

A thorough systemic examination was done with measurement of height, weight and body mass index, systolic and diastolic blood pressure in supine position, fasting plasma glucose and 2 hour post prandial plasma glucose.

Data was analysed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation.

Independent t test was used as test of significance to identify the mean difference between two quantitative variables.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

INCLUSION CRITERIA:

All patients of diagnosed type 2 Diabetes Mellitus attending Ophthalmology Outpatient Department during the study period who are willing to participate in the study.

EXCLUSION CRITERIA

- Patients who are non-compliant.
- Pregnant and lactating women.
- Immunocompromised patients.
- Patients with other systemic diseases.

RESULTS

A total of 275 diagnosed patients of type 2 Diabetes Mellitus attending the Ophthalmology Outpatient Department were included in the study. 4.7% were in the age group <50 years, 26.2% were in the age group 51 to 60 years, 51.6% were in the age group 61 to 70 years and 17.5% were in the age group 71 to 80 years. Mean age of the study population was 64.55 ± 8.236 years. 56.4% were males and 43.6% were females. Duration of Diabetes Mellitus was <5 years in 49.8%, 6 to 10 years in 30.2% and >10 years in 20%. In the study 17.5% had family history of Diabetes Mellitus and 11.6% were smokers. Treatment protocol in 13.5% was dietary and lifestyle modifications, in 66.5% was Oral Hypoglycemic agents and in 20% was Insulin. 88.4% were Non-smokers and 11.6% were smokers.

In the study out of 275 subjects, 30.9% had diabetic retinopathy and in 69.1% diabetic retinopathy was absent. 82.35% had Non Proliferative

Diabetic Retinopathy (NPDR) and 17.65% had Proliferative Diabetic Retinopathy (PDR). Among NPDR patients 23.52% had Mild NPDR, 37.65% had Moderate NPDR, 16.47% had Severe NPDR and 4.71% had Very Severe NPDR.

20% of the patients with diabetic retinopathy had Clinically Significant Macular Edema (CSME). Overall among diabetic patients, CSME was present in 6.18%.

Gender, duration of diabetes mellitus, family history and treatment modality were significant risk factors for diabetic retinopathy. Age and smoking status did not affect the presence of diabetic retinopathy significantly. Diabetic retinopathy was commonly seen among males (37.4%), those with longer duration of DM i.e. >10 years (70.9%), those with positive family history (70.8%), those who were on Insulin (61.8%) and among smokers (43.8%). [Table-1]

Table 1: Association between probable risk factors and Diabetic Retinopathy

Parameter		Diabetic Retinopathy present		Diabetic Retinopathy absent		P value
		No. of subjects	Percentage	No. of subjects	Percentage	
Age	<50 years	3	23.1%	10	76.9%	0.811
	51 to 60 years	25	34.7%	47	65.3%	
	61 to 70 years	43	30.3%	99	69.7%	
	> 70 years	14	29.2%	34	70.8%	
Gender	Female	27	22.5%	93	77.5%	0.008*
	Male	58	37.4%	97	62.6%	
Duration of Diabetes	<5 years	21	15.3%	116	84.7%	<0.001*
	6 to 10 years	25	30.1%	58	69.9%	
	>10 years	39	70.9%	16	29.1%	
Family History	No	51	22.5%	176	77.5%	<0.001
	Yes	34	70.8%	14	29.2%	
Treatment	Diet	3	8.1%	34	91.9%	<0.001*
	OHA	48	26.2%	135	73.8%	
Modality	Insulin	34	61.8%	21	38.2%	0.094
	Smoking	71	29.2%	172	70.8%	
	Yes	14	43.8%	18	56.2%	

There was significant difference in duration of diabetes, systolic blood pressure, diastolic blood pressure, fasting blood sugar and post prandial blood sugar between the patients with diabetic retinopathy and those without diabetic retinopathy. [Table-2].

Table 2: Association between quantitative variables and Diabetic Retinopathy

Parameter	Diabetic Retinopathy present		Diabetic Retinopathy absent		P value
	Mean	SD	Mean	SD	
Duration of Diabetes	11.13	6.31	5.23	3.68	<0.001*
Systolic BP	130.52	14.44	123.52	12.03	<0.001*
Diastolic BP	83.95	8.52	77.62	8.66	<0.001*
Body Mass Index	23.24	1.71	22.89	1.54	0.094
Fasting BSL	141.66	47.68	91.33	33.32	<0.001*
Post Prandial BSL	232.42	89.03	181.54	48.32	<0.001*

DISCUSSION

Diabetic Retinopathy is an emerging health problem with involvement of both medical and economic considerations. It is now considered as the commonest cause of new cases of legal blindness among the working age individuals in developing and developed countries.

In the present study, different types of diabetic retinopathy were observed in 85 patients out of the total 275 patients i.e. the frequency of Diabetic Retinopathy in our study was 30.91%.

The results of this study were comparable with other studies. [Table-3, Table-4]

Table 3: Evidence base for Prevalence of Diabetic Retinopathy in India

Study and Authors	Year	Region Type of DM	Total no. of cases	% of DR
Gadkari SS et al ³	2016	Urban and rural, India Type 1 and 2 DM	5130	21.7 %
Raman R et al SN-DREAMS III ⁴	2014	Rural, South India Type 2 DM	13079	10.3%
Namperumalsamy P et al ⁵	2009	Urban and rural Tamil Nadu, India Type 2 DM	25969	10.8%
Raman R et al SN-DREAMS II ⁶	2008	Urban, South India (Chennai) Type 2 DM	5999	18.0%
Rema M et al, CURES ⁷	2005	Urban, South India (Chennai) Type 2 DM	1736	17.6%
Agrawal RP et al ⁸	2000	Urban and rural, Bikaner, India Type 2 DM	4400	28.9%
Dandona L et al ⁹	1999	Urban population Hyderabad Type 2 DM	2532	22.4%
Rema M et al ¹⁰	1996	Urban and rural, South India Type 2 DM	6792	34.1%

Table 4: Evidence base for Prevalence of Diabetic Retinopathy in different populations throughout the world

Study and Authors	Year	Region	Total no. of cases	% of DR
Jin G et al, The Yangxi Eye Study ¹¹	2017	Rural China Type 2 DM	476	8.19%
Wong T et al, The Singapore Malay Eye Study ¹²	2008	Singapore Type 2 DM	757	35.0%
Varma R et al Los Angeles Latino Eye Study ¹³	2004	Los Angeles, USA Type 2 DM	1217	46.9%
Leske MC et al, Barbados Eye Studies ¹⁴	2003	Barbados, West Indies Type 2 DM	306	28.8%
Mitchell P et al, The Blue Mountains Eye Study ¹⁵	1998	Urban area west of Sydney Type 2 DM	252	29.0%
Klein R et al, Beaver Dam Eye Study ¹⁶	1988-90	Beaver Dam, Wisconsin, USA Type 2 DM	410	35.1%
Klein R et al, WESDR ^{17,18}	1980-82	Southern Wisconsin, USA Type 1 and 2 DM	1313	50.3%

In the present study of the total 85 patients with diabetic retinopathy, 70 patients (82.35%) had non proliferative diabetic retinopathy (NPDR), 15 patients (17.65%) had proliferative diabetic retinopathy (PDR). Mild NPDR was present in 20 patients (23.52%), Moderate NPDR was present in 32 (37.65%), Severe NPDR was present in 14 (16.47%) and Very Severe NPDR was present in 4 (4.71%) among the patients with diabetic retinopathy. More number of cases of NPDR compared to PDR were also observed by Rema M et al (1996)¹⁰, Dandona L et al⁹, Agrawal RP et al⁸, Narendran V et al¹⁹, Rema M et al (CURES)⁷.

Clinically significant macular edema (CSME) was seen in 17 patients (20%) among the patients with diabetic retinopathy and in 6.18% patients among all the study subjects which was similar to the findings of Varma et al (LALES)¹³ (6.2%), Broadbent DM et al (Liverpool Eye Disease Study)²⁰ (6.4%), Leske MC et al (Barbados Eye Study)¹⁴ (4.5%).

In the present study, diabetic retinopathy was seen in 23.1% patients <50 years, 34.7% between 51-60 years, 30.3% between 61-70 years and 29.2% in those >70 years. The association was not found to be significant (P=0.811). It did show an increased prevalence in sixth decade compared with the fifth decade of life, in the seventh decade, it levelled off and later it dropped. Similar trends also were observed by Raman R et al (SN-DREAMS II)⁶, Agrawal RP et al⁸, The Beaver Dam Study¹⁶, The Blue Mountain Eye Study¹⁵ and The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)¹⁸.

37.4% males and 22.5% females had diabetic retinopathy. This difference was found to be statistically significant ($P=0.008$). A similar male preponderance in the presence of diabetic retinopathy was found by Rema M et al (CURES)⁷, Raman R et al (SN-DREAMS II)⁶, Namperumalasamy P et al⁵, UKPDS study²¹ and Dandona et al⁹.

The mean duration since diagnosis in our study in patients with diabetic retinopathy was 11.3 ± 6.31 years and in those without retinopathy was 5.23 ± 3.68 years.

Increase in duration of diabetes mellitus was a strong predictor for the development of diabetic retinopathy in the present study ($P<0.001$) and was also reported by Varma R et al¹³, Wong T et al¹² and Jin G et al¹¹. Rema M et al in CURES (2005)⁷ stated that 41.8% patients had diabetic retinopathy after 15 years of diabetes. In addition they have also stated that for every 5 year increase in duration of diabetes, the risk of developing increases by 1.89 times⁷.

Positive family history was found to be a significant risk factor in the present study and similar results were reported by Rema M et al (CURES)⁷.

The present study, diabetic retinopathy was present in 61.8% of the patients on insulin as a treatment modality compared to 26.2% in those on oral hypoglycemic agents and 8.1% in the ones on dietary and lifestyle modifications. This association was found to be statistically significant ($P<0.001$). This was probably because of longer duration of diabetes or poor glycemic control prompting the use of insulin. These results are consistent with various other studies like Klien et al (WESDR)^{17,18}, Broadbent DM et al²⁰, Agrawal RP et al⁸, Leske MC et al (Barbados Eye Study)¹⁴, Raman R et al (SN-DREAMS II and SN-DREAMS III)^{6,4}, Gadkari SS et al³.

Increased systolic and diastolic blood pressure was found to have significant association with presence of diabetic retinopathy in the present study similar to the findings of Raman R et al (SN-DREAMS III)⁴, Raman R et al (SN-DREAMS III)⁶ and UKPDS²¹.

Both fasting and post prandial blood sugar levels were significantly high in patients with diabetic retinopathy ($P<0.001$) in our study. Most of the studies considered glycosylated haemoglobin for the association of glycemic status with presence of diabetic retinopathy instead of blood sugar levels. Rema M et al (CURES)⁷, Agrawal RP et al⁸ and Raman R et al (SN-DREAMS II)⁶ supported the evidence that poor glycemic control is an important risk factor for development and progression of diabetic retinopathy.

Body mass index and smoking status were not found to have statistically significant association with diabetic retinopathy in the present study. Raman R et al (SN-DREAMS II)⁶ also reported that prevalence of diabetic retinopathy in patients who were smokers was more than non-smokers but the association was not statistically significant. Studies conducted by Narendran V et al¹⁹, Jin G et al¹¹ and Mitchell P et al¹⁵ also found no association between BMI and presence of diabetic retinopathy.

CONCLUSION

Diabetic Retinopathy can be considered to be a major health problem in patients with Type 2 Diabetes Mellitus. Clinically Significant Macular Edema which is a major cause of reduced visual acuity in patients with Diabetic Retinopathy and should be detected early in the course of the disease. As the duration of Diabetes Mellitus increases, the chances of developing Diabetic Retinopathy also increase and thus the screening intervals should be reduced with increased duration. Also the higher frequency of retinopathy in the patients requiring insulin is probably due to prolonged exposure to hyperglycemia and possible delay in the initiation of insulin treatment. Thus, targeting these patients during screening is essential. And lastly strict control of blood pressure and blood sugar levels can possibly delay the development and progression of Diabetic Retinopathy.

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REFERENCES

1. International Diabetes Federation. Diabetes Atlas. 8th ed. 2017.
2. Heng LZ, Comyn O, Peto T, Tadros C, Ng E, Sivaprasad S, Hykin PG. Diabetic retinopathy: pathogenesis, clinical grading, management and future developments. *Diabet Med*. 2013 Jun;30(6):640-50.

3. National society to prevent blindness. In: Visual problems in the US data analysis definition, data sources, detailed data tables, analysis, interpretation. New York: National society to prevent blindness 1980:1-46.
4. Gadkari SS, Maskati QB, Nayak BK. Prevalence of diabetic retinopathy in India: The All India Ophthalmological Society Diabetic Retinopathy Eye Screening Study 2014. *Indian J Ophthalmol* 2016;64:38-44.
5. Raman R, Ganesan S, Pal SS, et al. Prevalence and risk factors for diabetic retinopathy in rural India. Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study III (SN-DREAMS III), report no 2. *BMJ Open Diabetes Research and Care* 2014;2:000005. doi:10.1136/bmjdr-2013-000005
6. Namperumalsamy P, Kim R, Vignesh TP, Nithya N, Royes J, Gijo T, et al. Prevalence and risk factors for diabetic retinopathy: a population-based assessment from Theni District, south India. *Postgrad Med J*. 2009 Dec;85(1010):643-8.
7. Raman R, Rani PK, Reddi Rachepalle S, Gnanamoorthy P, Uthra S, Kumaramanickavel G, et al. Prevalence of Diabetic Retinopathy in India. Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study Report 2. *Ophthalmology [Internet]*. 2009;116(2):311-8.
8. Rema M, Premkumar S, Anitha B, et al. Prevalence of diabetic retinopathy in Urban India: the Chennai urban rural epidemiology study (CURES) eye study, I. *Invest Ophthalmol Vis Sci*. 2005;46:2328-2333.
9. Agrawal RP, Ranka M, Beniwal R, Gothwal SR, Jain GC, Kochar DK et al. Prevalence of diabetic retinopathy in type 2 diabetes in relation to risk factors: Hospital based study. *Int J Diab Dev Countries*. 2003;23:16-19.
10. Dandona L, Dandona R, Naduvilath TJ, et al Population based assessment of diabetic retinopathy in an urban population in southern India *British Journal of Ophthalmology* 1999;83:937-940.
11. Rema M., Ponnaiya M., Mohan V. Prevalence of retinopathy in non insulin dependent diabetes mellitus at a diabetes centre in Southern India. *Diab Res Clin Pract* 1996; 34; 29-36.
12. Jin G, Xiao W, Ding X, et al. Prevalence of and risk factors for diabetic retinopathy in a rural Chinese population: the Yangxi Eye Study. *Invest Ophthalmol Vis Sci*. 2018;59:5067-5073. <https://doi.org/10.1167/iov.18-24280>.
13. Tien Y Wong, Ning Cheung, Wan Ting Tay, Jie Jin Wang, Tin Aung, Seang Mei Saw et al. Prevalence and Risk Factors for Diabetic Retinopathy: The Singapore Malay Eye Study. *Ophthalmology*. November 2008; 115(11):1869-75.
14. Varma R, Torres M, Pena F, Klein R, Azen S. Prevalence of diabetic retinopathy in adult Latinos: The Los Angeles Latino Eye Study. *Ophthalmology*. July 2004;111(7): 1298-1306.
15. Leske MC, Wu SY, Hennis A, Nemesure B, Hyman L, Schachat A; Barbados Eye Studies Group. Incidence of diabetic retinopathy in the Barbados Eye Studies. *Ophthalmology*. 2003 May;110(5):941-7.
16. Mitchell P, Smith W, Wang JJ, Attebo K. Prevalence of diabetic retinopathy in an older community. The Blue Mountains Eye Study. *Ophthalmology*. 1998 Mar;105(3):406-11.
17. Klein R, Klein BE, Moss SE, Linton KL. The Beaver Dam Eye Study. Retinopathy in adults with newly discovered and previously diagnosed diabetes mellitus. *Ophthalmology*. 1992 Jan;99(1):58-62.e
18. Klein R, Klein BEK, Moss SE, et al. The Wisconsin epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol*. 1984;102:520-526.
19. Klein R, Klein BEK, Moss SE, et al. The Wisconsin epidemiologic study of diabetic retinopathy. III. Prevalence and risk of retinopathy when age at diagnosis is 30 or more years. *Arch Ophthalmol*. 1984;102:527-532.
20. Narendran V, John RK, Raghuram A, Ravindran RD, Nirmalan PK, Thulasiraj RD. Diabetic retinopathy among self reported diabetics in southern India: a population based assessment. 2002;(4):1014-8.
21. Broadbent DM, Scott JA, Vora JP, Harding SP. Prevalence of diabetic eye disease in an inner city population : the Liverpool Diabetic Eye Study. 1999;160-5.
22. UK Prospective diabetes study (UKPDS) group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type-2 diabetes (UKPDS 33). *Lancet* 1998;352:837-53.