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Prevalence and associated risk factors for diabetic retinopathy at first ophthalmological contact

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ABSTRACT

Background: Type 2 diabetes mellitus (DM) is now considered as a growing global public health concern due to cost associated with diabetic micro and macrovascular complications. Diabetic retinopathy (DR) is one of the leading causes of vision loss. Accurate estimation of prevalence of DR among diabetic patients and associated risk factors are of crucial importance to plan and execute preventive strategies in the community. **Aims and Objectives:** The present cross sectional hospital based observational study was undertaken to determine the prevalence of DR in diabetic patients at their first ophthalmological contact and to evaluate associated risk factors. **Materials and Methods:** In this cross sectional hospital based observational study, all diabetic patients visiting ophthalmology clinic for the first time after being diagnosed as diabetic were enrolled. After recording demographic data and biochemical findings, each patient was investigated for DR and correlated with associated risk factors. **Results:** Of 1699 patients, majority (68.9%) of them had come to ophthalmology clinic with complaint of decreased vision. Only 16.12 % (274) patients had been referred for retinal exam by treating physician. DR was prevalent in 242(16.98%) non-referred and 31(11.31%) referred patients. Mean age and mean duration of diabetes was significantly higher in non-referred patients. Vision threatening DR was also significantly higher in non-referred patients. Prevalence of DR was significantly correlated with age at presentation, duration of diabetes, rural background, uncontrolled diabetes, systolic blood pressure and high BMI. **Conclusion:** Low referral by treating physician and lack of awareness among patient accounts for late presentation of diabetic patients to ophthalmologist. Beyond just developing strategies to promote screening programs for early detection and management of DR, education of the patients,comprehensive planning and coordination between ophthalmologist and physician can go a long way to decrease the economic and social burden of preventable blindness due to diabetic retinopathy.

Key words: Diabetes, Diabetic retinopathy, First presentation, Risk factors

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INTRODUCTION

Diabetes Mellitus (DM) is one of the fastest growing global emergencies which project a serious threat to global health. Since 2000, the estimated prevalence of diabetes in people aged 20–79 years has risen from 151 million (4.6% of the global population at that time) to 463 million (9.3%). Without sufficient action to address the pandemic, it is predicted that 578 million people (10.2% of the projected population) will have diabetes by 2030 and it will jump to a staggering 700 million (10.9%) by 2045.[1]

According to WHO, 31.7 million people were affected by diabetes in India in the year 2000 and it is estimated to rise to 79.4 million by 2030, the largest number in any nation in the world. More than 75% of patients who have DM for more than 20 years will have some degree of retinopathy.[2] A meta analysis revealed that 2.6 million people were

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visually impaired because of diabetic retinopathy and were estimated to rise to 3.2 million in 2020.[3] In a cross sectional study in India, prevalence of Diabetic retinopathy (DR) was 21.7%. It was more in males (p=0.007), those above 40 years (p=0.01) and with duration of diabetes>5 years (p=0.001). [4]

The prevalence of DR at screening level is an indirect measure of performance of healthcare system. Though the strength of DR screening in bringing down the risk of vision loss has been effectively documented, participation for screening has remained consistently low either because of lack of awareness or for the reason that patients may remain asymptomatic until the advanced stage of DR.

The purpose of the present hospital based observational study was to assess the prevalence of severity of diabetic retinopathy at the first contact of diabetic patient with ophthalmologist and explore the risk factors responsible for the development of DR.

MATERIALS AND METHODS

This cross-sectional observational study was conducted on 1699 patients over 2 years who attended the outpatient department of a Regional institute of Ophthalmology in Northern India for the first time after being diagnosed with DM. Patients with hazy media or any other retinal disease were excluded. Socio-demographic variables including age, gender, height, weight, body mass index, smoking status, duration of diabetes, family, education and referral history was taken and analysed. The blood pressure was measured in the right arm of each patient in a sitting position. Complete ophthalmological examination including best corrected visual acuity using Snellen's chart, Intra ocular pressure measurement and detailed slit lamp examination was done before dilating the pupil for retinal examination. HbA1c of each patient was documented. Retinal evaluation was done using indirect ophthalmoscope. SD-OCT using Nidek RS300 with software Navis E × 3000 was done in each patient and fundus photograph was taken for grading of retinopathy. Retinopathy was graded according to International Clinical Disease severity Scale for DR as No Diabetic retinopathy, Non proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) and presence or absence of macular edema.[5]

The retinopathy or maculopathy grade for an individual was defined as the grade of the worst eye or the eye with clear media in the presence of vitreous haemorrhage. For correlation of risk factors with diabetic retinopathy patients were divided into patients with retinopathy and without retinopathy.

Statistical analysis was done using SPSS version 20.0 software (IBMCorp.,Armonk,NY, USA) Chi square test was used for categorical variables whereas *t* test was used for continuous variables. P value of <0.05 was used as the level of significance.

RESULTS

Of 1699 patients, 46% were males. Their average age was 61.4 ± 7.4 years. More than half (66.9%) had rural background. In 53.61% of patients, they had education equal to or below secondary school. Family history of diabetes was present in nearly 35.5% of them. In 73.8% diabetes for more than 5 years and 92.4% of them were taking oral medication (Table 1).

Of 1699 participants, 1171(68.9%) visited hospital for decrease in vision, 254(14.94%) for itching, lacrimation or red eye while only 16.12 % (274) were referred for screening for diabetic retinopathy (Table 2). Of 56 patients who complained of sudden vision loss, 18 (1.26%) had either Central Retinal Vein Occlusion or Branch Retinal Vein Occlusion and 38 (2.66%) had vitreous hemorrhage or tractional retinal detachment. Of patients with gradual drop in vision, 588 (34.6%) patients had refractive error, 527(31%) had varying degree of cataract, 238(14%) had Glaucoma and 273(16%) patients had retinopathy (Table 2).

Mean age and Mean duration of diabetes was significantly less in referred patients (p<0.001). Patients with diabetic retinopathy were significantly more in non-referred patients (16.98% versus 11.31%). One hundred three (7.22%) non referred and 11 (4.01%) referred patients had newly detected DR. Nineteen (1.33%) patients were detected as diabetic during their retinal examination (Table 3).

The prevalence of moderate NPDR was significantly lower (0.72%) in referred patients than in non-referred patients (4.07%). Similarly prevalence of PDR was also lower in referred patients but it was not statistically significant (p=0.102) but vision threatening DR and CSME was seen only in referred patients (p<0.001) Table 4.

Of 273 diabetics 123(15.6%) were males and 150(16.43%) were females. Prevalence of DR increased from 2.52% in patients below 40 years to 18.38% above 60 years of age. It increased substantially from 7.67% to 24.17% in patients with duration of diabetes from <5 years to >10 years. DR was found to be higher in patients coming from rural background (20.8%) as compared to urban (13.5%). Only 10.44 % (63/273) patients with DR had positive family history of diabetes.74.3%patients (203/273) with DR had

Table 1: Socio-demographic characteristics of enrolled subjects

		Number (n)	%	Non referred		Referred patients	
				1425	%	274	%
Gender	Male	786	46.26	666	46.7	120	43.7
	Female	913	53.74	759	50.8	154	56.3
Age (Years)	<40	119	7	94	6.59	25	9.12
	40-60	699	41.14	564	39.57	135	49.27
	>60	881	51.85	767	53.82	114	41.6
Population base	Rural	1121	66.9	991	69.54	130	47.44
	Urban	578	34	434	30.45	144	52.44
Educational status	lower/equal to secondary school	911	53.6	799	56.07	112	40.87
	Higher than Secondary School education	788	46.4	626	43.93	162	59.12
Family history	positive	603	35.5	425	29.8	178	65
	negative	1096	64.5	1000	70.2	96	35
Duration of Diabetes	< 5years	443	26.07	319	22.38	124	45.25
	5-10 years	954	56.1	856	60	98	35.76
	>10 years	302	17.8	250	17.54	52	18.97
Treatment	Oral Hypoglycemic drugs	1570	92.4	1304	91.5	266	97
	Others	129	7.6	121	8.5	8	3

Table 2: Distribution of patients according to their purpose to visit Ophthalmologist

Purpose of visit			No of patients	%
Screening(Referred by physician)			274	16.12
Decreased vision			1171	68.9
a	sudden(56)	Vein Oclusion	18	1.26
		VH/TRD	38	2.66
b	gradual(1115)	Refractive Error	588	34.6
		Cataract	527	31
		Glaucoma	238	14
		Diabetic retinopathy	273	16
Miscellaneous complaints			254	14.94

Table 3: The characteristics of participants in the two study groups

Total patients 1699	Non Referred patients 1425	Referred patients 274	p value
Mean Age	65.3 ± 12.1	54.4 ± 5.2	<0.001
Mean duration of diabetes	8.5 ± 3.2 years	5.5 ± 1.2 years	<0.001
Patients with DR 273(16%)	242(16.98%)	31(11.31%)	0.019
Newly detected DR 114(6.7%)	103(7.22%)	11(4.01%)	0.0517
Newly detected Diabetes	19(1.33%)	0(0%)	0.0550

HbA1c >7, 69.59% patients (190/273) had systolic blood pressure >150, 56.04 % (153/273) had BMI >25 (Table 5).

DISCUSSION

Diabetics are presenting late to the ophthalmologist. As a result DR is emerging as a leading cause of blindness. Of 1699 enrolled patients, 83.87% diabetics had come to seek ophthalmic care following some ocular complaint while only 274 patients(16.12%)were referred for fundus examination. 1352(95%) of non-referred patients were unaware of significance of routine retinal screening. Similarly another study revealed that 82.6% diabetics came for some other ocular complaints and only 17.4% patients were referred for screening for DR.[6]

A USA based study also reported that in diabetic patients who were being monitored for the last 10 years, only 64% of them had their retina examined.[7]

A study reported prevalence of DR in rural India as 10.3%. Out of 865 participants in that population based study only three patients were known to have DR and the rest were newly detected on eye examination.[8] A retrospective study highlighted that 63% of participants were unaware that diabetes affects retina and 68% of them were unaware if DR can be prevented or treated.73% of these patients were not recommended by their diabetes care providers for retinal examination and 92% of them had undergone their first fundus examination.[9]

A study on inpatient diabetics, fundus examination was done for the first time in 44.4% of the cases and nearly half (46%) of the cases were not aware of existing DR.[10]

Sixty eight point nine percentages of the cases had come following decreased vision due to cataract (62.9%)

Table 4: Distribution of patients according to their severity of Retinopathy

Stage of Retinopathy	Non Referred patients 1425		Referred patients 274		p value Chi Sq
	N	Prevalence	N	Prevalence	
No Retnopathy	1183	83	243	88.68	0.0193
Retinopathy present	242	16.98	31	11.31	0.0193
Mild NPDR	110	7.71	20	7.29	0.81
Moderate NPDR	58	4.07	2	0.72	0.0059
Severe NPDR	13	0.91	3	1.09	0.777
PDR	61	4.28	6	2.18	0.102
CSME	122	8.56	0	0	<0.001
VTDR*	124	8.7	0	0	<0.001

*NPDR= non proliferative diabetic retinopathy. PDR=proliferative diabetic retinopathy. CSME= clinically significant macular edema. * Severe NPDR, PDR, CSME*

Table 5: Prevalence of Diabetic retinopathy according to Demographic and systemic risk factors

		Diabetic Patients			
		Total n=1699	With retinopathy 273(%)	Without retinopathy 1426	P value
Gender	Male	786	123 (15.6)	663 (84.35)	0.66
	Female	913	150(16.43)	763(83.57)	
Age (years)	<40	119	3(2.52)	116(97.48)	<0.001
	40-60.	699	108(15.45)	591(84.55)	
	>60.	881	162(18.38)	719(81.62)	
Duration of diabetes (years)	< 5years	443	34(7.67)	409(92.3)	<0.001
	5-10 years	954	166(17.47)	788(82.54)	
	>10 years	302	73(24.17)	229(75.82)	
Population base	Urban	1121	152(13.5)	969(86.44)	<0.001
	Rural	578	121(20.9)	457(79.06)	
Educational status	Lower/equal to Secondary school education	911	155 (17.01%)	756 (82.98%)	0.253
	Higher than Secondary School education	788	118 (14.98)	670 (85.02)	
Family history	positive	603	63 (10.44)	540 (89.55%)	<0.001
	negative	1096	210 (19.16)	886 (80.83%)	
HbA1c	<7	743	70(9.42)	673(90.57)	<0.001
	>7	956	203(21.2)	753 (78.77)	
Systolic Hypertension	>150	1046(61.57)	190(18.16)	856(81.83)	0.003
	<150	653(38.43)	83 (12.71)	570(87.28)	
BMI	<25	840	120(14.29)	720(85.71)	0.048
	>25	859	153(17.81)	706(82.19)	

refractive disorder (56.6%) vein occlusion (1.26%), or vitreous hemorrhage (2.66%) Similarly in another study 44.1% of the diabetics presented for decreased vision, out of which 37.8% had cataract and 2.2% had conjunctival, corneal or eyelid disease.

On retinal examination DR was prevalent in 273(16%) patients. It was significantly higher in non-referred (16.98%) patients as compared to referred patients (11.31%).

Our study was distinctive in delineating the prevalence of DR in homogenous group of diabetic patients whose retinal exam was done for the first time after they were diagnosed as diabetic irrespective of their duration of diabetes.

Average duration of diabetes in patients was 7.5 ± 4.5 years. It was significantly lesser in referred (5.5 ± 1.2years) than non-referred patients (8.5 ± 3.2 years) (p<0.001). One hundred three (7.22%) non-referred and 11(4.01%) referred patients were newly diagnosed diabetics (duration < 1 year) with diabetic retinopathy. Nineteen (1.33%) non-referred patients were detected as being diabetic during their ophthalmological checkup.

Mean duration of diabetes in patients during their first ophthalmological examination in another similar study was 8.3 years. They also found duration to be significantly lesser in referred patients (p=0.013).[6]

The prevalence of DR detected on first retinal exam indicates that DR had remained undiagnosed for long duration. Our results were lower than the prevalence (34.06%) reported in the All India Ophthalmological Society study in our region.[4] This may probably be because we excluded those diabetic patients who had already got retinal exam done and additionally we included patients who were newly detected as diabetics.

Our results were also lower (24.6%) than the observations reported in another similar study.[6] The difference could

be due to different region and genetic predisposition. Cross-sectional analysis of inpatient diabetics in USA estimated prevalence of previously undiagnosed DR as 25%.[11] Similarly Thapa et al., observed that 38.26% of the inpatient diabetics had DR and nearly half (46.6%) them were not aware of DR. [10] The higher prevalence of undiagnosed DR in inpatients could be because of associated co- morbidities. Unattended DR can progress from mild NPDR to vision threatening diabetic retinopathy (VTDR). Moss et al., revealed that in patients diagnosed with diabetes for more than 14 years, 8% with PDR would lose their vision in one eye and 10% of these patients who had high risk characteristics would lose vision in both eyes.[7] A systematic meta-analysis reported global prevalence of 34.6% for any DR, 6.96% for PDR, 6.81% for Diabetic Macular Edema and 10.2% for vision threatening DR.[11] The estimated prevalence of DR in the inpatient population was 44%, out of which 19% had sight threatening DR[11] where as in our study NPDR was detected in 12.7%, PDR in 4.28% and CSME in 8.56% in non-referred patients and 9.12%, 2.18% and 0% NPDR, PDR and CSME respectively in referred patients. It was significantly lower in the later group emphasizing the significance of early screening. The high prevalence of vision threatening DR (8.7%) at first retinal exam project is a matter of serious social and economic concern. Delayed diagnosis results not only in increase in cost of management but also may end up with irreversible visual impairment to the extent of blindness. The prevalence of VTDR was found to be similar to other studies in developing and developed countries. [6,10,12]

Contrary to our results, prevalence rates of VTDR (2.5%), diabetic macular edema (2.8%), and CSME (0.9%)in China and Nepal (CSME 5.78% and PDR 2.52%)were significantly lower on their first retinal exam.[13,14] Lower prevalence in these studies could be attributed to their inherent ethnic difference in their susceptibility to DR or other environmental factors.

The Singapore epidemiology of eye disease study also revealed that prevalence of DR of any grade in Chinese population (26.2%) was lower than in Indians (30.7%).[15] The major risk factors for DR in our study were the age at presentation, longer duration of diabetes, higher levels of glycosylated haemoglobin, higher systolic blood pressure and lower BMI. It was consistent with the findings in previous studies. [6,9,13,14]

We found a strong and significant relation between the presence of DR with increasing age. It increased from 2.52% in patients below 40 years to 15.45% and 18.38% between 40 – 60 years and >60 years of age group respectively. It was similar to the observations by Shan K et al.[9,16] The findings of our study was in accordance with other studies and didn't find significant gender difference in the development of DR, [13,17-19] but it was in contrast to other studies which documented males are more affected with DR than females, [9,14,16] while studies from Sweden and Japan observed it to be more in female patients. [20,21] However no clear evidence has been established for gender as a possible determinant of DR in any of the study.

This study showed an increasing prevalence of DR with longer durations since the diagnosis of diabetes. The prevalence was 7.67% in patients with less than 5 years of diabetic age and highest (24.17%) in patients with duration of diabetes >10 years.These results were consistent with results reported globally.[6,13,14,16,18,19] Logistic regression analysis in a study from India reported that for every 5 year increase in duration of diabetes, the risk for DR increased by 1.89 fold.[16] Shah K also revealed strong association with duration of diabetes by reporting that diabetes for more than 5 years was associated with DR in more than half of their patients however another study found that within the first 10 years of diabetes duration, the prevalence of DR is low and infrequent and most patients have NPDR which can be reversible.[9,22] We found that patients having a good glycemic control (HbA1c<7) had lower prevalence of DR (12.1%) as compared to those having poor control (HbA1c>7). It was consistent with findings in previous studies. [13,14,18,19] Logistic regression analysis in a study reported that a 2% increase in HbA1c resulted in a 1.7 fold increase in risk for DR.[16] On the contrary a study observed that there was no significant association of retinopathy with single high level of HbA1c. Recent study also concluded that though more cases were reported with poor glycemic control but it was not statistically significant.[23] Of the total patients, 61.15% had systemic hypertension. Higher systolic blood pressure was observed as independent risk factor for development of DR in patients with diabetes. High blood sugar level is believed to disrupt autonomic regulatory mechanism of the retinal capillaries and make capillary endothelium vulnerable to damage from higher blood pressure resulting in ischemia and eventually retinopathy. Similar observations have been made in other studies,[9,13,14,18,19] while a study from Saudi Arabia did not find systolic hypertension to be significantly associated with DR on univariate or multiple logistic regression analysis.[17] Consistent with studies we observed positive correlation of higher BMI with increased risk of DR, [13,14] while other studies did not find obesity as a significant risk factor for DR. [17,19] Contrary to these observations, some studies revealed that individuals with low BMI are more prone to DR.[16,24]

We observed DR in significantly high numbers in patients with no family history of diabetes. It was

contrary to the observations by CURES which supported genetic susceptibility. It could probably be explained that because of no family history of DR, they were ignorant about the importance of routine eye checkup and they presented late when they had already developed DR. Moreover we did not check more than one patient from the same family to confirm with the results of CURES.[17]

The prevalence of retinopathy was higher in those who were less educated. In contrast in China it was reported that diabetic subjects with higher education had higher prevalence of DR. Under reporting of under educated diabetic patients could be the reason of their lower prevalence.[21]

A valuable message transpired from this study was that in the era of pandemic of diabetes, diabetic patients are not getting their retina examined at the outset. They are presenting to ophthalmologists when DR has already progressed to stage where even aggressive treatment might only prevent blindness and fail to restore normal visual acuity. Moreover the cost of managing DR would put enormous economic burden on the society. Therefore effective management of DR would be preventing the development rather than treating DR.

Limitations of the study

The limitation of this study is that it is a single centre based study and the sample size is small but being a tertiary care hospital, demographic profile of the patients represent the population of this region. The strength of our study is that diagnosis and grading of retinopathy was based on retinal photography and OCT imaging.

CONCLUSION

This prospective study reported significantly low referral by physicians treating diabetes and high unawareness for DR in patients. Prevalence of DR is strongly correlated with duration and control of diabetes. Early detection and aggressive management is required to reduce blindness in diabetic patients. Our study confirms that in addition to the effective screening of diabetic retinopathy at the diagnosis, public needs to be educated and made aware of DR, the risk factors responsible for it's progression to vision threatening complications. Beyond screening and education of the patients comprehensive planning and coordination between ophthalmologist and treating physician can go a long way to decrease the economic and social burden of preventable blindness on the society due to diabetic retinopathy.

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PK- Concept and design the study, interpreted the results, reviewed the literature, revision of manuscript, coordination; **BS-**Concept and design, manuscript preparation, reviewed the literature, statistically analysed and interpreted results; **JS-** Interpreted the results, reviewed the literature, revision of manuscript; **PG-** interpreted the results and statistically analysed, reviewed the literature, revision of manuscript.

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