Original Article

Stages of Diabetic Retinopathy and Its Relationship with Blood Sugar Level and Duration of Diabetes Mellitus

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Background: The worldwide prevalence of Diabetes Mellitus (DM) has risen. Diabetics are 25 times more likely to become blind than non-diabetics due to Diabetic Retinopathy (DR). The DR could either be delayed or treated by diagnosis at an early stage which is possible by regular ophthalmoscopic examination. Hyperglycemia is the major pathogenetic factor for DR and frequency and progression from non-proliferative to proliferative increases with increasing duration of DM. Studies show reduction in the rate of progression of DR from non-proliferative (background to pre-proliferative to proliferative) by good glycaemic control and treatment with laser can be offered if treating physician identifies it at an early stage.
Material and Methods: This descriptive and analytical study was carried out on 250 patients visiting diabetic clinic at Sir Ganga Ram Hospital, Lahore. The aim of this study was to identify the stages of DR and to find effect of BSL and duration of DM on stages of DR.
Subjects and Methods: BSL was measured with glucometer. Ophthalmoscopy was done on dilated pupils and stages were noted as background, pre-proliferative and proliferative DR.
Results: Out of 250 diabetic patients 72 (28.8%) had DR. The stage of DR had advanced with increased BSL and duration of DM.
Conclusion: With increasing duration of DM and poorly controlled BSL, diabetic retinopathy progresses from background to pre-proliferative to proliferative stage. Sight threatening DR can be delayed by good glycaemic control or treated by timely laser therapy which requires identification of stages of DR at an early occasion.
Key Words: Glycaemic control, Diabetic retinopathy, Ophthalmoscopy

Introduction

Diabetes mellitus (DM) is a major medical problem throughout the world. Fundamentally, diabetes is an abnormality of glucose metabolism due to altered insulin production or activity, clinically manifested by elevated levels of blood glucose. DM causes numerous long-term systemic complications that have considerable associated morbidity. Since complications most commonly affect the individuals in their economically productive years, the disease has enormous social and economic impact.

10-15% of diabetic population has insulin dependent diabetes mellitus (IDDM) also called type-1 diabetes usually diagnosed up to age of 30 years. The majority of diabetic patients however have Non-Insulin dependent diabetes mellitus (NIDDM) also called type-2 diabetes usually diagnosed after age of 30.

Diabetic retinopathy is a highly specific vascular complication of both type-1 and type-2 diabetes mellitus (DM). The duration of DM is a significant risk factor for the development of retinopathy. After 20 years of diabetes, nearly all the patients with IDDM, and more than 60% with NIDDM, have some degree of retinopathy.[1,2,3] Diabetics as a group have 25 times the usual risk of blindness. The prevalence of diabetic retinopathy in the general population has dramatically increased over the past 40 years. Improved care for DM allows patients to live longer and accounts for much of this increase in diabetic retinopathy resulting into increased morbidity than mortality.

The advent of pan-retinal photo-coagulation for the treatment of proliferative diabetic retinopathy (PDR) and findings of the diabetic retinopathy study group (DRS), Early treatment diabetic retinopathy study (ETDRS), diabetic retinopathy vitrectomy study (DRVS) and diabetic control and complications trial (DCCT) provide valuable insights into the understanding and management of DR.

Proper treatment can reduce 5-year risk of retinal visual loss.

Despite recent advances, there is still much we do not know about DR. We are unable to prevent its onset, and we have no cure for the condition. Consequently, DR remains a leading cause of new blindness. Blindness usually results from non-resolving vitreous haemorrhage, tractional retinal detachment and

findings of the DRS, ETDRS, DRVS and DCCT in conjunction with annual eye exams, can result in significant saving of sight and reduction of social costs. Presently, however, clinical goals must concentrate on identifying ages at the risk of visual loss and ensuring that appropriate and timely surgery is offered to reduce the risk of visual loss.

Since DR is often asymptomatic when most amenable to treatment, so early detection of DR through regularly scheduled ocular examination is critical.[4,5]

Annual or biennial screening is more efficient way to detect early stages of DR because patients who are repeatedly re-examined will not develop un-treatable or sight threatening retinopathy before being detected by next examination, when they can still be referred for treatment. It does not matter whether this examination is done by ophthalmologist, diabetologist or family practitioner provided examiner has been appropriately trained to recognize the condition.[6]

Despite all, this knowledge, people with diabetes do not have their eyes examined regularly.

Clearly, much more needs to be done to examine and treat those with diabetes to prevent unnecessary vision loss and blindness from DR.

The present study was undertaken to estimate the grade of retinopathy, glycaemic control and to assess the level of awareness of patients about DR, its prevention or treatment which will enable them to come for regular screening which is essential to prevent or treat blindness or visual handicap by DR.

Material and Methods

In this study the variables observed were blood sugar levels, duration of diabetes mellitus and presence of diabetic retinopathy. These variables were measured by using following methods.

A proper history was taken from patients who came with the history of DM. Once one became sure of the diabetic status, both pupils were dilated to allow indirect ophthalmoscopy. After full dilatation of pupils both the fundi were thoroughly examined to evaluate severity of disease and stage of DR. The stages of diabetic retinopathy were noted as background, pre-proliferative and proliferative retinopathy.

Capillary blood glucose measurement was carried out with a glucometer.

Exclusion Criteria:

1. Age < 13 years.
2. Hypertension alone.
3. Retinopathy due to other causes.

Inclusion Criteria:

1. Age> 13 years
2. Fulfilling criteria for DM as recommended by American Diabetic Association (ADA) revised in 1997 which is:

a. Symptoms of diabetes plus casual plasma glucose 200 mg/dl. (Casual is defined as any time of the day without regard to time of last meal)

b. Fasting plasma glucose (FPG)
   FPG < 110 = Normal Fasting Glucose.
   FPG 110 and < 126 = impaired fasting glucose.
   FPG 126 = diabetes

c. Oral glucose tolerance test (OGTT)
   Two hours post load glucose < 140 = Normal glucose tolerance.
   Two hours post load glucose > 140 and < 200 = impaired glucose tolerance.
   Two hours post load glucose > 200 = diabetes.

Data Analysis:

Descriptive statistics were calculated and data was analyzed by using SPSS-12. The age, duration of diabetes mellitus and blood sugar level were presented as ± SD (standard deviation). P value <0.05 was taken as significant.

Results

Among the 250 diabetic patients 72 (28.8%) had diabetic retinopathy. Different stages of DR were identified and results showed that among 72 patients with diabetic retinopathy 41(56%) had background, 22 (30.55%) had pre-proliferative and 9 (12.5%) had proliferative DR.

Association of stages of diabetic retinopathy with the blood sugar level and duration of diabetic mellitus was checked.

BSL was divided into the three categories 120, 121-200 and > 200 mg/dl. Among 250 patients 26 patients had BSL 120 mg/dl out which 1 (3.85%) had DR. 149 patients had BSL of 121-200 mg/dl out of which 29 (19.12%) had DR while those having BSL of > 200 mg/dl 42 (56%) had DR with p-value of 0.00 which is significant statistically (**Table-5**). The number of patients having diabetic retinopathy according to stages were calculated in each category of BSL. Among 72 patients with DR, only 1(1.4%) patients had BSL 120 mg/dl and it was background DR. Those having BSL 121-200 mg/dl 29 (40.28%) patients had DR; out these 20 (68.77%) had background, 7 (24.14%) had pre-proliferative while 2(6.9%) had proliferative DR.

Those with BSL > 200 mg/dl 42 (58.3%) had diabetic retinopathy out of which 20 (47.62%) had background, 15 (35.71%) had pre-proliferative and 7 (16.7%) had proliferative DR. It appears from the results that diabetic retinopathy has association with blood sugar level and rate of DR increases with the increasing blood sugar level with p-value of 0.018 which is significant **(Table-1).**

The duration of diabetes mellitus was divided into four categories. According to duration, out of 250 diabetics 137 had duration of <10 years and out of these 3 (2.19%) had DR. 51 had duration of 10-15 years and 14 (26.92%) had DR. 23 diabetics had duration of 16-20 years out of which 17 (77.27%) had DR, while those with the duration of > 20 years, out of 39 diabetics 38(97.4%) had DR with p-value of 0.00 which is significant statistically **(Table-2).**

Number of patients at various stages of DR according to duration of diabetes mellitus were calculated and results showed those having duration of diabetes mellitus less than 10 years 3 (4.16%) patients had DR out of which 2 (66.67%) had background and 1(33.33%) had pre-proliferative DR. Those having the duration of diabetes from 10-15 years 14 (19.44%) had DR out of which 13 (92.9%) had background and 1(7.14%) had pre-proliferative DR. Those patients having the duration of 16-20 years 17 (23.61%) patients had DR out of which 12 (70.6%) had background and 5 (29.4%) had pre-proliferative DR. Among the patients having the duration of diabetes mellitus more than 20 years 38 (52.7%) were found to have DR out of which 14 (36.84%) had background, 15 (39.5%) had pre-proliferative and 9 (23.7%) had proliferative DR. From these results it appears that duration of diabetes mellitus is associated with diabetic retinopathy and rate of DR has increased as the duration has increased with its progression from background to pre-proliferative to proliferative DR with the p-value of 0.006 significant statistically.

Means for various variables including age, BSL and duration of diabetes mellitus were calculated. Mean BSL for background DR calculated was 206.85± 38.07 mg/dl, for pre-proliferative 233.95±53.09 mg/dl and for proliferative DR was 222.22±51.83 mg/dl showing with the increase in average BSL, the stage of DR has advanced from background to pre-proliferative to proliferative DR.

Mean duration of diabetes mellitus for background DR was 16.71±5.62 years, for pre-proliferative 22.41±7.07 and for proliferative was 33.22±8.12 years. It appear that mean duration of diabetes mellitus has increased for various stages of DR from background to pre-proliferative, proliferative DR. Mean age of patients with background DR was 54.71±9.53 years, for pre-prolifterative 55.27±9.01 and for proliferative 70.22±9.96years **(Table-3).**

Discussion

Diabetic retinopathy in its earliest stages usually causes no symptoms. Visual acuity may be excellent at the time of diagnosis and a patient may deny the presence of retinopathy. If retinal disease progresses, visual acuity may be compromised by macular edema,

Table-1: Stages of diabetic retinopathy according to blood sugar level n = 72.

Stage of DR	Blood Sugar Level (mg/dl)			
	≤120 n=1	121-200 n=29	> 200 n=42	Total
Background DR	1 (100%)	20 (68.9%)	20 (47.62%)	41 (56.94%)
Pre-proliferative DR	0 (0%)	7 (24.14%)	15 (35.71%)	22 (30.56%)
Proliferative DR	0 (0%)	2 (6.9%)	7 (16.7%)	9 (12.5%)
Total	1 (1.4%)	29 (40.28%)	42 (58.3%)	72 (100%)

Key: DR = Diabetic retinopathy, ≤ Less than and equal to > More than Chi-square =0.335 df = 4, P-value = 0.018

Table-2: Stages of diabetic retinopathy according to duration of diabetes mellitus n = 72.

Stage of DR	Duration of Diabetes Mellitus in Years				
	< 10 n=3	10-15 n=14	16-20 n=17	> 20 n=38	Total
Background DR	2 (66.67%)	13(92.9%)	12 (70.6%)	14 (36.84%)	41 (56.94%)
Pre-proliferative DR	1(33.33%)	01(7.14%)	05 (29.4%)	15 (39.5%)	22 (30.56%)
Proliferative DR	0 (0%)	0 (0%)	0 (0%)	09 (23.7%)	09 (12.5%)
Total	3(4.16%)	14(19.44%)	17 (23.61%)	38 (52.7%)	72 (100%)

Key: DR = Diabetic retinopathy, Chi-square = 18.041, df = 6, P-value= 0.006

Table-3: Distribution of factors among various stages of DR n=72

Variables	Stage of DR	n	Mean	S.D
BSL (mg/dl)	Patients with background DR	11	206.85	38.07
	Patients with Pre-proliferative DR	22	233.95	53.09
	Patients with proliferative DR	09	222.22	51.83
Duration of DM (Years)	Patients with background DR	41	26.71	05.62
	Patients with pre-proliferative DR	22	22.41	07.7
	Patients with proliferative DR	09	33.22	08.12
Age (Years)	Patients with background DR	41	54.71	09.53
	Patients with pre-proliferative DR	22	55.27	09.13
	Patients with proliferative DR	09	70.22	09.96

Key:- n=Number of patients DR=Diabetic retinopathy

proliferative diabetes retinopathy, or episodes of vitreous haemorrhage. These complications are devastating and can lead to decreased visual acuity and if not properly treated may lead to blindness.

Keeping in view the creeping effects of DM we aimed to identify the stage of DR at the time of diagnosis to find out relationship between DR and glycaemic control at the time of presentation.

In this study 250 diabetic patients were examined for BSL and stages of retinopathy .

According to stage of diabetic retinopathy, WESDR showed non-proliferative DR in 71% and proliferative DR in 23% of the younger onset group, whereas in older onset group non-proliferative DR was observed in 39% and proliferative DR in 3%. In our study the rate of non-proliferative DR was 86.55% (Background DR 56%, pre-porliferative DR 30.55%) and proliferative DR was 12.55%.

It is important to identify the stage of Retinopathy because the risk of progression of moderate non-porliferative DR to proliferative DR is 12.27% and risk of progression to high risk proliferative DR within 5 years is 33%. In severe non-proliferative DR the risk of progression to proliferative DR is 75% within 1 year. Patients with mild to moderate non-proliferative DR generally are not candidates for scatter Laser surgery therapy and can be followed at 3 month intervals safely, while those with severe non-proliferative DR (without neo-vascularization) require follow-up at short intervals of 2 months and Laser Therapy is indicated. These results indicate the importance of regular follow-up with the identification of the stage of diabetic retinopathy which influences the management of DR and helps in prevention of this sight threatening complication of diabetes.

The frequency and severity of DR increases with increasing duration of DM. Our study showed DR in 19% patients having duration of DM <10 years, 26.92% having duration between 10-15 years while 77.27% had duration of 15-20 years. In fact, 97.4% patients with diabetes for 20 or more years had DR. The stage of DR advances from background to pre-proflierative to proflierative DR with increasing duration of diabetes mellitus. The WESDR showed the four and ten years incidence of DR increases with increasing duration of the diabetes at baseline (118,119mg/dl). It further showed that after 20 years nearly all patients with type-1 (IDDM) and more than 60% of type-2 (NIDDM) had some degree of retinopathy.[1,2,3]

There is a strong relationship between glycaemic control and diabetic retinopathy. Epidemiological studies (UKPDS, DCCT) have consistently demonstrated an association between good glycaemic control and the incidence and progression of DR.[7,8] The WESDR data demonstrated that lower BSL at any stage of DR at any duration of DM was associated with lower incidence of DR. In our study DR was 3.85% in those having BSL of 120 mg/dl, 19.46% with BSL of 121-200 mg/dl and 56% in those having BSL >200 mg/dl. These results reflect that the rate of DR is more with uncontrolled BSL while with good glycaemic control this complication is less frequent.

With such sight threatening complications of diabetes mellitus which could be delayed by good glycaemic control and early treatment, we aimed to know why people are not coming for treatment at early stages of DR. Most of these patients were not told about complications of DM at the time of diagnosis, especially the eye complication like DR which is sight threatening. So the treating physician must be trained to do ophthalmoscopy and identify

the stage of DR to help prevent blindness in diabetics.

Conclusion

In this study, the rate of diabetic retinopathy was calculated to be 28.8%. The background DR was noted in 56%, pre-proliferative in 30.55% and proliferative in 12.5% of diabetics with mean BSL being higher for proliferative then non-proliferative (background, pre-proliferative). Males had a higher rate of DR than females while no significant difference was noted in the rate of DR among type-1 and type-2 diabetics in this study.

The study population had little awareness about this sight threatening complication and even the small percentage who were aware of this, did not come for follow-up. Faced with current inability to prevent or cure DR, the main concern for all doctors should be to focus on early detection of DR so that its progression could be delayed by good glycaemic control and laser therapy (if required). It is therefore very important that treating physician should be able to identify stages of DR so that the required management could be offered to prevent blindness in diabetics.

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