

# Frequency and Grading of Diabetic Retinopathy in Diabetic End Stage Renal Disease Patients

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*Pak J Ophthalmol 2016, Vol. 32 No. 2*

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Received: April 21, 2016  
Accepted: May 22, 2016

**Purpose:** To find out the prevalence of diabetic retinopathy (DR) and its grades in diabetic end stage renal disease (ESRD) patients.

**Study Design:** Descriptive, cross – sectional, study.

**Place and Duration of Study:** The study was conducted in Department of Ophthalmology, Jinnah Hospital, Lahore from May 2015 to November 2015.

**Materials and Methods:** Patients aged 35 – 75 years of either gender with ESRD caused solely by diabetes were included in the study. Retinal examination was done using 90D slit lamp bio microscopy and 20D lens with indirect ophthalmoscope. Presence or absence of DR and grades of retinopathy were documented in each case following ETDRS classification of diabetic retinopathy.

**Results:** There were 100 subjects in the study: 55% males and 45% females. Mean age was  $53.99 \pm 11.88$  years. Frequency of diabetic retinopathy in diabetic ESRD patients was recorded in 51.0% of the cases. Of the diabetic retinopathy patients, 68.63% had non-proliferative (NPDR) while 31.37% had proliferative diabetic retinopathy (PDR). Out of 35 cases with NPDR, 34.29% had mild, 40.0% had moderate and 5.71% had severe NPDR. Out of 16 cases with PDR, 68.75% had mild to moderate PDR while 31.25% had high risk PDR.

**Conclusion:** Diabetic retinopathy is quite prevalent among diabetic end stage renal disease patients. Non-proliferative diabetic retinopathy is significantly higher than proliferative diabetic retinopathy in such cases.

**Key words:** Diabetic end stage renal disease, diabetic retinopathy, frequency.

In Pakistan, the prevalence of diabetes mellitus is increasing and is estimated to be around 7.6 to 11% currently<sup>1</sup>. Diabetic nephropathy, neuropathy and retinopathy are well known complications of the disease<sup>2,3</sup>. Out of 93 million people with diabetic retinopathy (DR), 17 million have proliferative diabetic retinopathy (PDR), 21 million suffer from diabetic macular edema, and 28 million face vision threatening diabetic retinopathy worldwide<sup>4</sup>. As the prevalence of diabetes increases, so is the expected increase in diabetes related end stage renal disease (ESRD)<sup>5</sup>.

In a study done by El-Menyar, it was shown that diabetic retinopathy was present in 45% of the patients who were on regular hemodialysis with ESRD<sup>5</sup>. Solini et al showed that advanced diabetic retinopathy was present only in 15.28% of individuals with chronic kidney disease<sup>6</sup>. Data from various Pakistani studies estimate the prevalence of blindness in Pakistani adults to be around 2.7% and amongst them, 15.3% due to diabetes related various fundal pathologies<sup>3</sup>.

We searched for the topic on PubMed, EMBASE, Cochrane Library, Google Scholar and Pak Medinet, but found that no such study had been published so

far on diabetic retinopathy in ESRD patients solely due to diabetes mellitus in our country. Limitations of previous published studies include small sample size (7 cases only) which gave a good rationale to conduct this study with sample size of 100 cases. The study was conducted with the objective to determine the frequency of diabetic retinopathy and its grades in diabetic end stage renal disease patients. The results of this study are expected to help create awareness about importance of ocular examination and grading of diabetic retinopathy in patients with diabetes related end stage renal disease.

## MATERIAL AND METHODS

This was a descriptive, cross - sectional, hospital based study conducted in department of Ophthalmology, Jinnah Hospital Lahore, Pakistan - a tertiary care teaching hospital, from May 2015 to November 2015. The study was conducted after approval from institutional review board of Allama Iqbal Medical College/ Jinnah Hospital, Lahore following declaration of Helsinki and principles of good clinical practice. 100 patients were included in the study after taking written informed consent. The sample size was calculated using WHO sample size calculator with 95% confidence level, 7% margin of error with an expected percentage of mild grades of diabetic retinopathy as 14%<sup>7</sup> in end stage renal disease (ESRD).

The patients were sampled using non-probability purposive sampling and following strict inclusion criteria: age 35 - 75 years of either gender, patients with diabetes mellitus (type 2) as defined below, patients with diabetic end stage renal disease as defined below.

The following patients were excluded: Patients with end stage renal disease with causative factor other than diabetes e.g. hypertension, glomerulonephritis, renal calculi. Patients who underwent any form of retinal surgery/laser therapy were also not included in the study.

100 subjects those fulfilling the inclusion criteria were selected from Dialysis Centre, Jinnah Hospital Lahore, Pakistan. Pupils of both eyes were dilated using tropicamide 1% eye drops. Pre- and post-mydriatic intraocular pressure was measured using Goldmann applanation tonometer. Retinal evaluation was done using the 90D lens with slit lamp biomicroscopy and 20D lens with indirect ophthalmoscope by same consultant ophthalmologists

(MHA, NHB). Presence or absence of retinopathy and grades of retinopathy were documented in each case. Confounders were strictly controlled by following the exclusion criteria and getting the patient evaluated by the same ophthalmologists. Data was analyzed using computer software SPSS version 20.0. The variables included age, gender, presence or absence of retinopathy and grades of retinopathy. Mean and standard deviation was calculated for numerical variables e.g. age, duration of diabetes mellitus and duration of renal disease. Qualitative variables like gender, presence or absence of retinopathy and grading of retinopathy were presented as frequencies and percentages. Data was stratified for age, gender and duration of diabetes to see the effect of these variables on outcome. Chi-square test was used post-stratification with p-value < 0.05 considered as statistically significant.

All the patients of diabetes mellitus were labeled to have diabetic retinopathy after examination with the help of slit lamp biomicroscope with 90D lens and indirect ophthalmoscope showing any one of the following abnormal patterns, according to Early treatment diabetic retinopathy study classification<sup>11</sup>:

### ➤ Non-Proliferative diabetic retinopathy (NPDR)

- **Mild:** Microaneurysms, retinal hemorrhages, exudates, cotton wool spots at least in two quadrants.
- **Moderate:** Severe intraretinal hemorrhages in one to three retinal quadrants or mild intraretinal microvascular abnormalities (IRMA), significant venous beading in no more than 1 quadrant, cotton wool spots.
- **Severe:** ≥ 1 severe hemorrhages in all four retinal quadrants, significant venous beading in two or more retinal quadrants, moderate IRMA in one or more retinal quadrants.

### ➤ Proliferative Diabetic Retinopathy (PDR)

- **Mild-Moderate:** New vessels on the disc (NVD) or new vessels elsewhere (NVE), but extent insufficient to meet high risk criteria.
- **High Risk:** New vessels on 1/3<sup>rd</sup> disc area. NVD with vitreous or pre-retinal hemorrhage, new vessels greater than 1/2 disc area elsewhere with vitreous or pre-retinal hemorrhage.

- **Advanced Diabetic Eye Disease:** Tractional retinal detachment, significant persistent vitreous hemorrhage, neo-vascular glaucoma.

➤ **Diabetic Patients:**

- Already diagnosed patients of type 2 diabetes mellitus with more than 5 years of duration of disease were included.
- The patients having glomerular filtration rate (GFR) less than 15ml/min and were on dialysis were labeled as end stage renal disease (ESRD) patients.
- GFR was calculated according to Cock Croft Equation.<sup>12</sup>  
 $GFR = 140 - AGE \text{ in yrs} \times WEIGHT \text{ in kg} / 72 \times CREATININE \text{ in mg/dl}$

**RESULTS**

There were a total of 100 subjects in the study. Mean age was 53.99 ± 11.88 years. 55% (n=55) of the patients were males and 45% (n=45) were females. 63% (n=63) of the patients had ESRD for 1 - 3 years and 37% (n=37) had ESRD for more than 3 years. Mean ESRD duration was calculated as 3.67 ± 1.09 years. 68% (n=68) of the patients had diabetes mellitus for 6 - 10 years and 32% (n=32) had diabetes for more than 10 years of duration. Mean duration of diabetes was 9.57± 2.65 years (Table 1).

Diabetic retinopathy was seen in 51% (n=51) of the patients with diabetic ESRD while remaining 49% (n=49) had no ophthalmic findings (table 2). Frequency of grades of diabetic retinopathy in diabetic end stage renal disease patients showed that out of 51 cases, 68.63% (n=35) had NPDR while 31.37% (n=16) had PDR (p-value=0.002). Out of 35 cases, 34.29% (n=12) had mild, 40.0% (n=14) had moderate while 25.71% (n=9) had severe NPDR. Out of 16 cases of PDR 68.75% (n=11) had mild to moderate PDR while 31.25% (n=5) had high risk PDR (Table 1).

Stratification for frequency of diabetic retinopathy with regards to age showed that out of 51 cases of diabetic retinopathy 26 (51%) were between 35 - 50 years and 25 (49%) were between 52 - 75 years of age with p-value = 0.30. Frequency of diabetic retinopathy with regards to gender showed that out of 51 cases of diabetic retinopathy 33 (64.7%) were males and 18 (35.3%) were females with p-value 0.04. Frequency of diabetic retinopathy with regards to duration of diabetes showed that out of 51 cases of diabetic retinopathy, 33 (64.7%) had diabetes for 6 - 10 years

and 18 (35.3%) had diabetes for more than last 10 years (p-value = 0.47) (Table 2).

**Table 1:** Characteristics of the patients in the study.

Parameters	No. of Patients n (%)
<b>Age (years)</b>	
35-50	46 (46)
51-75	54 (54)
Total	100 (100)
Mean ± SD	53.99± 11.88
<b>Gender</b>	
Male	55 (55)
Female	45 (45)
Total	100 (100)
<b>Duration of ESRD (years)</b>	
1-3	63 (63)
>3	37 (37)
Total	100 (100)
Mean ± SD	3.67± 1.09
<b>Duration of diabetes (years)</b>	
6-10	68 (68)
>10	32 (32)
Total	100 (100)
Mean ± SD	9.57± 2.65
<b>Diabetic retinopathy</b>	
Yes	51 (51)
No	49 (49)
Total	100 (100)
<b>Grades of Diabetic Retinopathy</b>	
<b>NPDR: 35 (68.63%)</b>	
Mild	12(34.29)
Moderate	14 (40)
Severe	9 (5.71)
<b>PDR: 16 (31.37%)</b>	
Mild to moderate	11 (68.75)
High risk	5 (31.25)

**DISCUSSION**

The main objective of the study to determine the frequency of diabetic retinopathy and its grades in diabetic ESRD patients was successfully met. To the best of our knowledge, no such study has earlier been published on diabetic retinopathy in solely diabetic ESRD patients in our country.

**Table 2:** Relationship of diabetic retinopathy with different variables.

Age (years)	Diabetic Retinopathy (n=51)		p-value
	Yes	No	
35 - 50	26	20	0.30
51 - 75	25	29	
<b>Gender</b>			
Male	33	22	0.04
Female	18	27	
<b>Duration of diabetes (years)</b>			
6 - 10	33	35	0.47
>10	18	14	

The frequency of diabetic retinopathy was calculated to be 51.0% in our study. The result is in agreement with a study conducted by Grunwald on 925 participants with diabetes mellitus. Out of 925 subjects, 456 (49%) had diabetic retinopathy; the presence of retinopathy was associated with lower glomerular filtration rate (GFR) ( $p < 0.001$ ); with the lowest estimated glomerular filtration rate (i.e. less than 15 ml/min) in patients with proliferative retinopathy. This association even existed after adjustment for traditional and non-traditional risk factors ( $p = 0.005$ )<sup>7</sup>.

Another study by Mohmad et al showed that the commonest abnormality in diabetic patients was non-proliferative diabetic retinopathy (ranging from mild, moderate and severe) on fundus examination in patients having diabetic nephropathy<sup>8</sup>. Mild Diabetic retinopathy was mostly seen in mild chronic renal failure group but moderate and severe proliferative diabetic retinopathy were seen in higher grades of chronic renal failure. Our results are in agreement

with this study as well since the maximal frequency was found to be of NPDR in 68.32% of the patients out of which 34.29% had mild, 40.0% had moderate while 25.71% had severe NPDR.

A study conducted by Bajracharya et al included only 7 patients of end stage renal disease and showed that 29% of subjects had PDR and 71% had NPDR<sup>9</sup>. When patients of end stage renal disease were evaluated for grades of non-proliferative diabetic retinopathy, it was observed that mild grade was seen in 14%, moderate in 42.85% and severe in 14% of the cases. For proliferative diabetic retinopathy mild to moderate grade was noted in 14% and high risk in 14% of cases with end-stage renal disease<sup>9</sup>. Limitation of this study was its small sample size (only 7 cases). Our study overcame this shortcoming by evaluating more cases (100 cases). Our findings correlate with this study in overall frequency of various types of diabetic retinopathy (NPDR and PDR) but differ in frequency of individual grades of various types of diabetic retinopathy (mild, moderate, and severe). The patients in our study had more severe grades of DR. Severe PDR was observed in 14% of the patients in aforementioned study versus 68.75% in our study. This indicates that patients present late with advanced disease in our part of the world. It is recommended to conduct further research in this area to find out reasons of such delayed presentation with advanced stage of the disease.

Lee WJ et al<sup>13</sup>. Studied the association between diabetic retinopathy and progression of chronic kidney disease. 21.6% and 13.7% of their subjects had PDR and high - risk PDR at baseline respectively. They concluded that patients with extensive retinal ischemia and capillary non-perfusion had a greater risk for progression of chronic kidney disease (hazard ratio = 6.64;  $p = 0.002$ ). Frequencies of PDR and its high risk grade were calculated to be 31.37% and 31.25% in our study respectively which were relatively higher as compared to the aforementioned study.

In a recent study conducted by Wong et al, the prevalence of diabetic retinopathy in patients with chronic kidney disease due to diabetes mellitus was shown to be 34.7% after adjusting for various co-morbidities<sup>14</sup>. Many other studies have also shown various risk factors of diabetic retinopathy and end stage renal disease in diabetic patients<sup>15-20</sup>.

In light of the above studies and our results it is evident that frequency of diabetic retinopathy is higher among patients with diabetic ESRD. However, ocular screening of these patients may be helpful in

preventing irreversible visual loss and severe visual impairment. With timely management of diabetic retinopathy, the progression of the disease can be monitored and controlled as well. People need to be educated for their regular ophthalmic examinations to detect the disease at an earlier, treatable and reversible stage.

## CONCLUSION

We conclude that the diabetic retinopathy is present in a significant proportion of diabetic ESRD patients. Non-proliferative diabetic retinopathy is seen significantly more as compared with proliferative diabetic retinopathy. Steps should be taken to diagnose the disease earlier to prevent irreversible vision loss in all such patients. Further research should be conducted to check the level of awareness of diabetic patients about diabetic retinopathy and reasons of delayed presentation with advanced stage of the disease.

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