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DIABETIC RETINOPATHY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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ABSTRACT

Objective: To study and compare the association between the grade of chronic kidney disease (CKD) and a set of parameters including: the stage of diabetic retinopathy (DR), random blood sugar level, insulin versus oral hypoglycemics use, and the history of receiving some ocular treatment for coexisting DR.

Study Design: Cross sectional study.

Place and Duration of Study: Lahore General Hospital, Lahore, form Sep 2016 to Jun 2017.

Material and Methods: Our study included 100 patients diagnosed to have chronic kidney disease (CKD) due to diabetic nephropathy, these patients had fundus photographs, blood sugar random (BSR) check, and inquired about the nature of hypoglycemics used and about the history of receiving treatment for co-existing diabetic retinopathy. The fundus photographs were evaluated for the presence and the grade of diabetic retinopathy. The association between the grade of CKD and these four parameters was compared.

Results: The mean age of our patients is 54.55 ± SD 11.647, 40% are male and 60% are female, 68% of the patients had any diabetic retinopathy, and 22% had severe disease including proliferative diabetic retinopathy (PDR) and advanced diabetic eye disease. Forty six percent had non-proliferative diabetic retinopathy (NPDR), 28% of the patients had random blood sugar levels less than 200 mg/dl and 72% had higher levels making poor glycemic control common among the participants. The stage of retinopathy advanced in accordance with the stage of CKD but could not reach a statistical significance (p=0.134).

Conclusion: Patients with chronic kidney disease due to diabetes mellitus are at risk for diabetic retinopathy and need regular fundus examination and timely treatment to prevent blindness and visual impairment.

Keywords: Chronic kidney disease, Diabetic Retinopathy, Fundus Photographs, Proliferative diabetic retinopathy.

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INTRODUCTION

Diabetes mellitus is a global health problem with a continuously growing load. It is estimated that 2030 will witness a 69% increase in the number of diabetics in the developing countries compared to 2010, whereas a 20% rise will be seen in the developing countries[1]. Diabetic retinopathy will definitely keep the pace with this rising number of the diabetic population[2]. Strong association between diabetic retinopathy and nephropathy have been suggested[3], and it can be utilized to facilitate the multidisciplinary care for the affected population[4].

The progression of diabetic retinopathy and the development of nephropathy each increase the risk for the incidence of the other[3], this suggests the presence of a common pathophysiology. It is also found that proliferative diabetic retinopathy is considered as an independent marker of long-term nephropathy in patients with type 1 diabete[5]. Other studies indicated association of the presence of diabetic retinopathy and increased overall-mortality and cardiovascular events both in type 1 and type 2 diabetes[6].

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MATERIAL AND METHODS

This is a cross-sectional observational study conducted at Lahore General Hospital over 10 months, from September 2016 to June 2017.

Non-probability convenient sampling was done and 100 patients diagnosed to have chronic renal disease (CKD) due to diabetic nephropathy at the department of nephrology with GFR <60 ml/min/1.73 m^2 were included in the study after informed consent.

All the patients had fundus photographs using non-mydriatic fundus camera at the diabetic clinic of the same hospital. All the patients had random blood sugar level check using a glucometer. They were inquired if they were using insulin or oral hypoglycemic medications, they were also asked if they did ever receive any form of treatment for coexisting diabetic retinopathy in the form of intravitreal medications, laser photocoagulation or pars plana vitrectomy.

The fundus photographs were assessed for the presence and the grade of diabetic retinopathy by expert ophthalmologist, retinopathy was graded according to Early Treatment Diabetic Retinopathy Study (ETDRS). Patients with un-gradable fundus photographs or media opacities were excluded from the study. Relevant retinal treatment was provided where needed. Risk factors for renal function and for retinopathy were obtained from nephrology and medical records.

The association between the stage of chronic kidney disease (CKD) with the mentioned four parameters was studied and compared.

Data Analysis

The association between the grade of CKD and the grade of diabetic retinopathy (DR), blood sugar random (BSR), route of hypoglycemics, and history of treatment for coexisting retinopathy was analyzed using SPSS-20 and chi square test was applied. Age of included patients was expressed in terms of mean and standard deviation. Gender, CKD stage, DR stage, BSR levels, use of insulin versus oral hypoglycemics, and history of ocular treatment for coexisting DR was expressed in frequencies and percentages. Chi-square test was applied to determine the association of the stage of CKD with the mentioned parameters and *p*-values were obtained and compared to identify the parametersbetter related to the stage of CKD.

Sample size was calculated using survey monkey online sample size calculator, CKD population visiting Lahore General Hospital per year was assumed to be 10,000. Confidence interval was 95% with 10% margin of error.

RESULTS

We included 100 patients with CKD caused by diabetic nephropathy, their mean age was 54.55 ± SD 11.647. A total of 40% (40) were male and 60% (60) were females.

Patients were stratified according to their glomerular filtration rate into three groups; mild, moderate and severe CKD. Mild CKD included stage 1 and 2 CKD, moderate CKD group included stage 3 patients, and severe CKD group included stage 4 and 5 patients.

The mild CKD group included 12 patients (12%), the moderate CKD group included 20 patients (20%), and most of the patients belonged to the severe CKD group; 68 patients (68%).

On fundus examination 68% (n=68) had some diabetic retinopathy changes, and in 32 patients (32%) diabetic retinopathy changes were not observed. 22 patients (22%) had advanced retinopathy in any eye including proliferative diabetic retinopathy (PDR) and advanced diabetic eye disease according to ETDRS classification of diabetic retinopathy, and 46 (46%) had mild to moderate non-proliferative diabetic retinopathy (NPDR) (table-I).

On studying the results of random blood sugar levels, 28% of the patients had better glycemic control with random blood sugar levels <200mg/dl, the rest of 72% of the patients had higher levels at the time of fundus examination, this indicates poor glycemic control as a common risk factor among the participants for both retinopathy and nephropathy.

Clinical history revealed that 50% were taking insulin to control their blood sugar levels and 50% were using oral hypoglycemic agents and history also revealed that some ocular intervention was received by 27% of the patients in this study.

Majority of the patients were the patients of type 2 diabetes (93%), while a few number had type 1 diabetes mellitus (7%).

On studying the association between the stage of CKD and patients' parameters, we found

that the stage of diabetic retinopathy was advanced in patients with severe CKD, this can clinically help in evaluating patient's renal functions, but the association did not reach a statistical significance (p= 0.134).

Table-II shows that as the stage of diabetic retinopathy advanced from No DR to NPDR, then to PDR and advanced diabetic eye disease; the fact that patients having severe CKD were unaware of having coexisting diabetic retinopathy requiring treatment, this emphasizes the importance of fundus examination in these patients to facilitate diagnosis and then early treatment of coexisting diabetic retinopathy (table-III).

Among the patients having lower values of the percentage of patients having severe CKD increased from 56.25% to 69.57% and then to 81.81% (p=0.134)

Table-I: Demographics and clinical characteristics.

Parmeter	Groups	Number and frequency
Age	Mean 54.55 years	± SD 11.647
Gender	Male	40 (40%)
	Female	60 (60%)
Stage of CKD	mild CKD	12 (12%)
	moderate CKD	20 (20%)
	severe CKD	68(68%)
Dialysis Status	On dialysis	12 (12%)
	Not on dialysis	88 (88%)
ETDRS Stage of DR	No DR	32 (32%)
	NPDR	46 (46%)
	PDR and advanced	22 (22%)
Ocular Intervention	No ocular intervention received	73 (73%)
	Some ocular intervention received	27 (27%)
	Laser	6 (6%)
	Intravitreal bevacizumab	12 (12%)
	Surgery	2 (2%)
	Laser +Avastin	7 (7%)
Type of Diabetes Mellitus	Type 1	7 (7%)
	Type 2	93 (93%)
Hypoglycemics	Oral	50 (50%)
	Insulin	50 (50%)
Random Blood Sugar	100-<200 mg/dl	28 (28%)
	200-<300	48 (48%)
	300-<400	17 (17%)
	400-<500	6 (6%)
	>500	1 (1%)

Among the patients giving history of receiving some ocular intervention for diabetic retinopathy; 77.78% had severe CKD, however also 64.38% of those who did not receive any diabetic retinopathy treatment were also having severe CKD (p=0.202). This can be attributed to random blood sugar levels from 100-200 mg/dl, 67.8% of them had severe CKD, and among the patients with higher random BSL at the time of examination also 68.06% had severe CKD. Random blood sugar levels could not help in predicting renal function (p=0.418) (table-IV).

The use of insulin for BSL control is neither protective nor harmful regarding the progression of CKD as shown in table-V.

DISCUSSION

We have studied the relationship between the stage of CKD and a group of parameters in diabetic patients. These parameters included: the presence and the stage of diabetic retinopathy and if retinopathy received ocular treatment or not. We also studied the relationship between the grade of CKD and patients' random blood sugar level and the route of hypoglycemic agents used to control blood sugar levels (oral versus insulin).

The percentage of patients with severe CKD increased in patients having severe diabetic retinopathy, but this could not reach a statistical significance (p=0.134). However, the stage of diabetic retinopathy remains a helpful parameter enabling the clinician to look at the kidneys of the diabetic patients through their eyes[7].

Nephropathy and retinopathy share a common etiological background, based on capillary dysfunction and vascular abnormalities associated with inflammation, basement membrane thickening, endothelial dysfunction, leakage and capillary shut down[8].

The majority of our severe CKD patients were the victims of type 2 diabetes mellitus (95.59%), which is in the favor with the hypothesis that CKD victimizes type 2 diabetics with prolonged duration as patients of type 2 diabetes have higher incidence of albuminuria and decreased glomerular filtration[9].

The frequency of diabetic retinopathy was calculated to be 68% which is relatively high compared to other studies[10-12]. This can be explained with the fact that 72% of our patients had BSR above 200mg/dl at the time of examination, poor glycemic control was a common factor among our patients. Grunwald *et al*[10] studied the presence of retinopathy in the Chronic Renal Insufficiency Cohort (CRIC) and found that 49% of the diabetic patients in the cohort had retinopathy, they also elaborated a stronger relationship between the CKD stage and the stage of retinopathy in diabetic versus non-diabetic

Table-II: Association between the stage of CKD and the stage of diabetic retinopathy.

	Mild to moderate CKD (n=32)	Severe CKD (n=68)	*p*-value
Stage of retinopathy			
No DR (n=32)	14 (43.75%)	18 (56.25%)	*p*=0.134
NPDR (n=46)	14 (30.43%)	32 (69.57%)	
PDR and Advanced diabetic eye disease (n=22)	4 (18.18%)	18 (81.81%)	

Table-III: Association between the stage of CKD and history of receiving ocular intervention for diabetic retinopathy.

Ocular Intervention	Mild to moderate CKD (n=32)	Severe CKD (n=68)	*p*-value
None (n=73)	26 (35.62%)	47 (64.38%)	0.202
Some intervention for DR (n=27)	6 (22.22%)	21 (77.78%)	

Table-IV: Association between the stage of CKD and random blood sugar level at the time of fundus photography.

	Mild CKD	Moderate CKD	Severe CKD	*p*-value
100-<200 (n=28)	5 (17.85%)	4 (14.28%)	19 (67.8%)	0.418
200 and more (n=72)	7 (9.72%)	16 (22.22%)	49 (68.06%)	

Table-V: Association between the stage of CKD and the route of hypoglycemics.

	Mild CKD	moderate CKD	Severe CKD	*p*-value
Insulin (n=50)	6 (12%)	10 (20%)	34 (68%)	*p*=1.000
Oral (n=50)	6 (12%)	10 (20%)	34 (68%)	
Total	12	20	68	

patients. Mathew *et al*[11] included diabetic and non-diabetic patients with CKD, they reported that 42% of the patients with CKD had diabetic retinopathy, among them 28.5% had diabetic retinopathy alone as the prominent retinal finding and 13.5% had combined features of diabetic and hypertensive retinopathy. Another study conducted in Pakistan found that 51% of the diabetic patients with end stage renal disease had diabetic retinopathy among which non-proliferative diabetic retinopathy (NPDR) was more prevalent compared to PDR[12]. Al-Menyar *et al* emphasized on the importance of diabetic retinopathy as an independent predictor of morbidity and 3 years mortality in patients dependent on hemodialysis[13].

We found 22% advanced diabetic retinopathy (including PDR and advanced diabetic eye disease according to ETDRS) in patients with any CKD, and 26.47% advanced diabetic retinopathy in patients with stage 5 CKD, whereas Penno *et al*[14] found 15.28% advanced diabetic retinopathy in patients with any CKD. On reverse observation they found 58.64% CKD in patients diagnosed to have advanced diabetic retinopathy in the multicenter Italian study.

Our higher frequency of any diabetic retinopathy and advanced retinopathy may be attributed to the fact that 72% of our patients had poor control on blood sugar levels with random BSL of 200mg/dl or more, and this emphasizes upon the need for more careful and strict screening ophthalmic examination required by CKD patients in this part of the world, this may help to address the increasing burden of visual impairment and preventable blindness[15,16].

Mohmad *et al*[17] found retinopathy more frequent compared to nephropathy (71.2% versus 50.7%) in patients with longstanding diabetes mellitus, making retinopathy a probable possibility in the majority of diabetic patients with CKD in Sudan and this also supports the higher incidence of retinopathy in our study.

In summary our study demonstrates that the stage of retinopathy advances in accordance with the stage of CKD as both of them share similar pathological grounds and risk factors, making it important to screen the patients with CKD for retinal changes in order to detect diabetic retinopathy at an earlier, reversible stage, and minimize the burden of blindness and visual impairment caused by diabetic retinopathy.

CONCLUSION

Patients with chronic kidney disease due to diabetes mellitus are at high risk for diabetic retinopathy and need regular fundus examination and timely treatment to prevent blindness and visual impairment.

Retinopathy staging is of clinical and prognostic value regarding coexisting renal status.

RECOMMENDATIONS

Patients with chronic kidney disease due to diabetes mellitus are at risk for diabetic retinopathy and need regular fundus examination and timely treatment to prevent blindness and visual impairment.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any authors.

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