



## Original Research Article

## Association between diabetic retinopathy and diabetic nephropathy among type II diabetics

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## ARTICLE INFO

## Article history:

Received 13-11-2019

Accepted 09-12-2019

Available online 26-12-2019

## Keywords:

Diabetic retinopathy (DR)  
 Chronic kidney disease (CKD)  
 Macro albuminuria  
 e GFR

## ABSTRACT

**Aim:** Diabetic retinopathy and diabetic nephropathy are two major microvascular complications of DM causing significant morbidity and mortality. The aim is to study prevalence of DR in diabetics with CKD and its association in different stages of CKD.

**Materials and Methods:** Total of 80 diabetic pts were examined. Type 2 Diabetes mellitus was defined as FBS >126mg/dl or RBS of >200mg/dl with symptoms of diabetes. DR graded by ETDRS classification. CKD was defined as eGFR of less than <60ml/min/1.73m<sup>2</sup> or the presence of proteinuria for three or more months and/or parenchymal changes on USG. CKD staging was done by eGFR. Macro-albuminuria was assessed by the urine strip (URISCAN) method.

**Results:** Among 80 patients 37 had CKD of these 24 (64.86%) had DR of variable severity. Among 43 pt with out CKD 12 patients (27.9%) had DR. Compared to pts with out CKD pts with CKD had higher prevalence of DR (p<0.0012) but DR did not corresponded with different stages of CKD(p 0.688). There was strong association between macroalbuminuria and diabetic retinopathy.

**Conclusion:** DR prevalence was more in nephropathy irrespective of staging of CKD. It warrants regular retinal examination irrespective of stage of CKD especially when associated with proteinuria.

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## 1. Introduction

Diabetes is a potential epidemic in India, with more than 62 million diabetic individuals currently diagnosed with the disease.<sup>1,2</sup> It is a metabolic disease in which insulin is lacking or, the body's cells are insensitive to its effects. Late complications of DM are microvascular like diabetic retinopathy, diabetic nephropathy, peripheral neuropathy, and macrovascular complications like CVA, IHD, peripheral vascular disease.

Diabetic Retinopathy (DR) and Diabetic Nephropathy (DN) are the main microvascular complications of diabetes, representing the leading cause of blindness<sup>3</sup> and CKD(chronic kidney disease),<sup>4</sup> respectively. The prevalence of both DR and CKD increases proportionally with the duration of diabetes.<sup>5,6</sup> They also have similar pathogenesis and are clinical manifestations of similar

microvascular lesions in the glomerular and retinal vessels.<sup>7,8</sup> So it is reasonable to say that the presence of the development of DR may predict the development and progression of CKD in diabetics. Many studies have shown an association between diabetic nephropathy and DR in T1DM patients, but this association is less strong in T2DM.<sup>9</sup>

In this regard, we investigated retinopathy in different stages of CKD in type 2 diabetics to find out possible association in the progression of these two devastating complications to improve quality of life in terms of morbidity and mortality in diabetic patients.

## 2. Materials and Methods

This is a cross-sectional study conducted on 80 diabetic patients aged between 38 to 80yrs.

Inclusion criteria: all diabetic patients.

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Exclusion criteria: patients with acute and chronic infections, collagen vascular disorders and malignancies, and any other pre-existing ocular diseases. Patients with hazy media that obscured the view of fundoscopy were excluded.

Type 2 Diabetes mellitus was defined as FBS > 126mg/dl or RBS of > 200mg/dl with symptoms of diabetes. CKD was defined as e GFR of less than < 60ml/min/1.73m<sup>2</sup> or the presence of proteinuria for three or more months and/or parenchymal changes on USG. eGFR was calculated by the Cockcroft Gault formula as follows  $GFR = \frac{(140 - \text{age}) (\text{wt kg})}{(72 \times \text{Scr})}$  in ml/min. If female multiply by 0.85. Macroalbuminuria was assessed by the urine strip (URISCAN) method. A result of positive 1+ or more was affirmed (1+ indicated 30mg of protein in 100 ml of urine). Patients whose urine with white blood cell > 5 /HP were excluded from the present study.

Diabetic retinopathy was diagnosed by retinal examination after pupil dilatation. Retinopathy is graded according to ETDRS classification into NPDR, PDR, and maculopathy.

**3. Results**

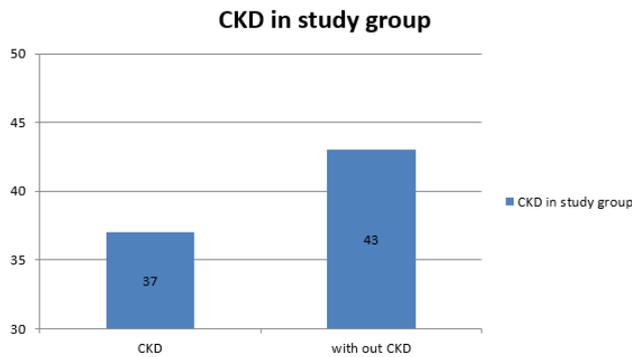
A total of 80 people with diabetes were included in our study with a mean age of 56.47 ± 10.47 yrs, of which 57 were males, and 23 were females.

The mean duration of diabetes was 10.47 ± 8.12. Table 1 demonstrates that the duration of diabetes was strongly associated with the presence of retinopathy

Among 80 patients 37 were with CKD and 43 were without CKD [Figure 1].

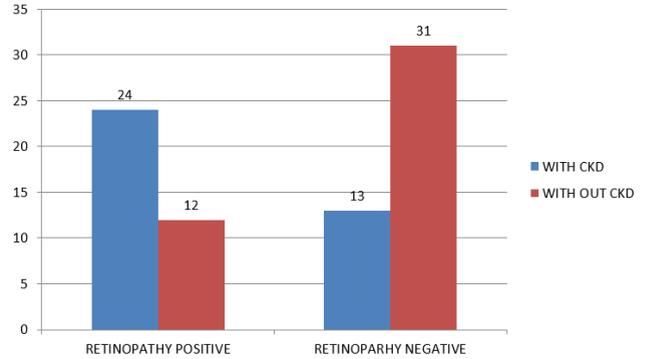
Among 37 CKD patients, 24 had DR, and 13 had no DR. Among 43 patients without CKD 12 had DR, and 31 had no DR [Table 2]

In our study, when compared the patients with CKD and patients without CKD, the patient with CKD had a higher prevalence of retinopathy (p < 0.0012).



**Fig. 1:** CKD in group study

Among those 24 diabetic pts with CKD 22 had NPDR, 2 had PDR, and one been associated with



**Fig. 2:** Relation between DR and CKD

maculopathy.[Table 3]

Among those 12 retinopathy pts without CKD, 11 had NPDR, 1 had

PDR and one been associated with maculopathy.

Among 80, 21 patients showed macroalbuminuria of which patients had DR. Our study showed a significant relation between DR and macroalbuminuria (odds ratio 4.7, p value < 0.0016)[Table 4]

The frequency of retinopathy in different stages of CKD was variable. The frequency was 60% in stage 3, 70 % in stage 4 and 66.7 % stage 5, respectively. The association between eGFR and retinopathy was unremarkable.[Table 5]

**4. Discussion**

The incidence of blindness in diabetic patients is 25 times higher than the general population.<sup>10</sup> Every patient with diabetes will develop diabetic retinopathy at some point, with an incidence of 25-44%. The incidence and prevalence of renal failure caused by diabetes are rising, and its outcome is poor.<sup>11</sup> This leads to increased morbidity, mortality, and cost of treatment.

The DR prevalence in patients with diabetes type 2 was determined by many studies showing different rates between 16-53.4%.<sup>12,13</sup> Our study showed a prevalence rate of 45%. In the study conducted by Grunwald on 925 participants with DM, out of 925 subjects, 456 (49%) had diabetic retinopathy.<sup>14</sup>

The prevalence of retinopathy in the present study was 31.3% (16/51) in patients with diabetes type 2 of less than ten years and 68.9%(20/29) in patients with diabetes of more than ten years (Table 1). Our result is in agreement with the study conducted by Jenchitr et al. They reported the prevalence rate of 22.91% and 42.86% of retinopathy in patients with diabetes type 2 less and more than ten years, respectively.<sup>12</sup>

The present study showed that patients with CKD had a higher prevalence of retinopathy (64.86%)[Table 2] compared to patients without CKD (27.90%) [p < 0.0012]. This was comparable to the results of the cross-sectional

**Table 1:** Rel between DR and duration of diabetes

Duration	Diabetic retinopathy		Total
	Yes	No	
1-5	4(16.6%)	20(83.3%)	24(100%)
6-10	12(44.4%)	15(55.5%)	27(100%)
11-15	9(75%)	3(25%)	12(100%)
16-20	5(50%)	5(50%)	10(100%)
>20	6(85.7%)	1(14.21%)	7(100%)

**Table 2:** Relation between DR and CKD

DR	CKD positive		CKD negative	
	no	%	no	%
positive	24	64.86%	12	27.90%
negative	13	35.13%	31	72.09%
Total	37		43	

Odds ratio 4.76, p value &lt;0.0012

**Table 3:** Stages of DR in CKD and non CKD groups

	CKD Positive		CKD Negative	
	n	%	n	%
NPDR	22	90.9 %	11	85.71 %
PDR	2	9.09 %	1	14.28 %
Maculopathy	1	6.06 %	1	14.2 %
Total	24		12	

**Table 4:** The relation between Macroalbuminuria and DR

Macroalbuminuria	DR Positive		DR Negative		Total total
	n	%	n	%	
Positive	21	67.7%	10	32.25%	31
Negative	15	30.61 %	34	69.38 %	49
total	36		44		80

Odds ratio 4.7 p value &lt;0,0016

**Table 5:** Relation between e GFR and DR

e GFR	DR		NO DR		
	N	%	N	%	
30- 59	9	60%	6	40%	15
15- 29	7	70%	3	30%	10
<15	8	66.7%	4	33.3%	12
	24		13		37

study of Biria Gao et al., where the prevalence of DR was found to be 32% among participants with CKD and was significantly higher than that of participants without CKD.<sup>15</sup>

In CKD patients, the main cause of blindness is due to PDR and maculopathy. In our study, we found 8.6% of patients with CKD had proliferative diabetic retinopathy, and 8.6% of patients had diabetic maculopathy among CKD patients.

Gradual changes occur in the retinal microvasculature due to chronic hypoglycemia, leading to retinal nonperfusion, increased vascular permeability, and pathologic

proliferation of retinal vessels.<sup>16</sup> This type of alterations are also commonly observed in diabetic kidney disease (DKD).<sup>17</sup> Similar to DR, widespread capillary occlusion in DKD can result in podocyte death, leading first to urinary protein loss.

The prevalence of macroalbuminuria in the present study is 38.75 %, showing a significant relation between macroalbuminuria and DR in diabetic patients. A study conducted by Manaviat MR et al. reported the incidence of 14.5% of macroalbuminuria in diabetes type 2 and showed a significant relationship between retinopathy and macroalbuminuria.<sup>13</sup> A study by Padmaja K Rani et al. concluded

that subjects with microalbuminuria were 2 times more likely to have DR than those without microalbuminuria, and the risk increased to almost six times in the presence of macroalbuminuria.<sup>18</sup> In the above-mentioned studies, albuminuria had been considered as a risk marker of diabetic retinopathy. Thus excretion of albumin in the urine can be regarded as a sign of kidney involvement and can reflect generalized small vessel damage in the body.

Our study found no association of retinopathy in different stages of CKD. We conclude that though DR was more prevalent in nephropathy, the progression of damage in these two target organs may not coincide. In CRIC study conducted based on subsequent adjusted multivariate analysis, they concluded the presence and severity of DR might not provide any additional prognostic information regarding the risk of CKD progression and vice versa, which is similar to the current study.<sup>19</sup> Goldstein et al. showed that a decline in renal function was not followed by the same decline in retinopathy.<sup>20</sup> Chen et al.<sup>21</sup> and Sabanayagam et al.<sup>22</sup> found that lower levels of eGFR were associated with DR only in the presence of albuminuria. It is worth noting that the studies demonstrating no significant independent relationships between eGFR and DR in type 2 diabetes (Chen et al.<sup>21</sup> and Sabanayagam et al.<sup>22</sup>) were conducted in participants of Asian ethnicity, while studies reporting the converse (Penno et al.<sup>23</sup> and Grunwald et al.<sup>24</sup>) were conducted in participants of Caucasian/non-Asian ethnicity.

Our study had limitations, including a relatively small sample size and a single center. This may have resulted in overestimation of the frequency of retinopathy as the patients with advanced CKD are more likely to have underlying microvascular complications. Also, the urine strip method for estimating macroalbuminuria is less specific.

## 5. Conclusion

In this study, diabetic retinopathy was more prevalent in nephropathy irrespective of stages of renal failure. Macroalbuminuria is a significant predictor for the development of retinopathy. This finding focused on the necessity of regular retinal examination in diabetic patients regardless of any stage of CKD, particularly who has albuminuria to protect vision, thus improving the quality of life in diabetic patients.

## 6. Source of funding

None.

## 7. Conflict of interest

None.

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**Cite this article:** Sowmya P, Moizuddin M, Priya NV. Association between diabetic retinopathy and diabetic nephropathy among type II diabetics. *Int J Ocul Oncol Oculoplasty* 2019;5(4):176-180.

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