Original Article

Association of Retinopathy with Chronic Kidney Disease in Diabetes Mellitus

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Abstract

Background: *Diabetic retinopathy (DR) and nephropathy are two major complications of diabetes mellitus carrying significant morbidity and mortality. In this study DR was investigated in different stages of chronic kidney disease (CKD) to find out possible association of these two devastating complications.*

Methods: *This cross-sectional study was conducted in 150 diabetic patients having CKD in BIRDEM. CKD was defined as estimated glomerular filtration rate (eGFR) of <60ml/min/1.73m^{2}and/or urinary albumin excretion rate (UAER) >30 mg/day in at least two occasions in 3 months apart. Retinopathy was assessed by direct fundoscopic examination and confirmed by color fundus photography. Severe DR (SDR) included proliferative diabetic retinopathy, severe non-proliferative DR and maculopathy; whereas microaneurysm regarded as non-severe retinopathy.*

Results: *Majority (68%) of the respondents had some form of retinopathy (38.35% SDR and 29.65% non-severe). There was strong association between different levels of albuminuria (UAER) and DR (p<0.0001). On the contrary DR did not correspond with stages of CKD (P=0.349). Hypertension (79.5%) and dyslipidaemia (59%) were common co-morbidities.*

Conclusion: *This study concluded that DR prevalence was more in nephropathy along with significant association with UAER. Whereas different stages of CKD was not associated with stages of DR . This finding focused the necessity of regular retinal examination irrespective of the stage of renal involvement.*

Key words: *Diabetic Retinopathy(DR), Chronic Kidney disease(CKD)*

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Introduction

Diabetes mellitus (DM) is one of the most common non-communicable diseases affects around 120 million people worldwide. The late complications of DM result in reduced life expectancy and bear major health costs. The complications of DM are due to both microvascular and macrovascular damage.[1] The metabolic and haemodynamic disturbances in Diabetes result in increased vessel permeability, raised blood pressure, and altered regulation of intracapillary pressure. This microvascular complication is specific to diabetes where small blood vessels throughout the body are affected but the disease process is of particular danger in three sites: retina, renal glomerulus and nerve sheaths. In the kidney, these changes may lead to increased trafficking of plasma proteins across the glomerular membrane and to the appearance of protein in the urine. The strong relationship between proteinuria and a constellation of other diabetic complications supports the view that elevated urinary protein excretion reflects a generalized vascular disturbance. Since retinal and renal vessels are exposed to the diabetic milieu, it is often assumed that progression of diabetic retinopathy and nephropathy occurs at the same time.[2]

Several studies have been done to find out the correlation between these two complications as they share common

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etiological factors.[3,4,5] Significant correlation between retinal and glomerular disease in diabetes were found based on fundoscopic findings with histopathological changes in kidney in type 1 patients.[3] Another study showed that 82% patients with overt proteinuria had retinopathy. [4] Estacio et al aimed to find out overt proteinuria as a predictor of retinopathy previously.[5]

Despite the catastrophic effects of diabetic retinopathy on vision and quality of life, the predictive value of this opthalmological complication for development of chronic kidney disease(CKD) or worsening renal function or vice versa is not fully defined across the spectrum of kidney disease in diabetes.

Bangladesh has the 10th largest number of diabetic patients in the world. [6] Prevention of complication should be emphasized more to reduce the health burden. In this regard we investigated retinopathy in different stages of CKD to find out possible association in the progression of these two devastating complications with an aim to improve quality of life in terms of morbidity and mortality in diabetes.

Methods

This cross-sectional study was conducted in 150 diabetic patients having CKD in BIRDEM. CKD was defined as estimated glomerular filtration rate (eGFR) of <60(ml/min/1.73m$^{2)}$ and/or urinary albumin excretion rate (UAER) >30 mg/day in at least two occasions in 3 months apart. Retinopathy was assessed by direct fundoscopic examination and confirmed by color fundus photography. Severe DR (SDR) included proliferative diabetic retinopathy, severe non-proliferative DR and maculopathy whereas microaneurysm regarded as non-severe retinopathy.

Results

Total patients were 150 with mean age of 45±10.3 years. The mean duration of DM was 9.4 ±6.7. (Table I) Among the co-morbidities HTN was common in the population (79.5%) ,dyslipidaemia (59%), ischemic heart disease (43.6%) and stroke (12.8%) were other co morbid conditions found among the study group (Fig 1). Among 150 respondents, 102(68%) had some form of retinopathy. Among the 68% of retinopathy, severe diabetic retinopathy (SDR)(PDR, severe NPDR, maculopathy) was present in 38.35% and 29.65% were having non severe retinopathy(NDR). NPDR was 45.5%, severe NPDR was 18.2%, PDR was 31.8%, and maculopathy was 4.5% (Fig - 2). The association of 24 hours urinary total protein (24h UTP) and frequency of retinopathy was assessed (Table II). In microalbuminuric (albuminuria <300mg/day)stage only 36% had retinopathy. Whereas in overt proteinuric (0.3 to 3.5 gm/day) and nephrotic stage (>3.5gm/day) it rose to 86.48% and 76.93% respectively with significant association ($p<0.05$). The association between eGFR and retinopathy was unremarkable ($p>0.05$). The frequency of retinopathy in different stages of CKD was variable. The frequency was 73.34% in stage 3 and 67.86% and 58.83% in stage 4 and 5 respectively (Table III)

Table I Baseline characteristics of study population (N-150)

Parameters	n (%)	Mean±SD
Age (years)		
< 50	44(29.3%)	45(±10.3)
≥50	106(70.6%)	
Gender		
Male	80(53.33%)	
Female	70(46.66%)	
Duration of DM (years)		
<5	34(22.66%)	9.4 (±6.7)
5-10	62(41.33%)	
>10	54(36%)	
Glycemic status		
HbA1c (%)		
<7	30(20%)	9.2 (±5.8)
>7	120(80%)	
Area of residence		
Urban	103(68.66%)	
Rural	47(31.33%)	
Treatment		
Only OAD	40(26.66%)	
Insulin ±OAD	110(73.3%)	

[OAD = Oral anti diabetic drugs]

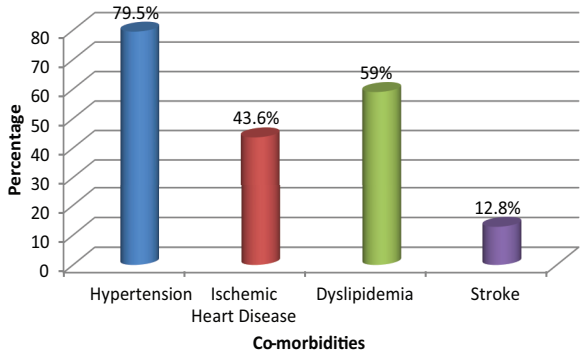

Figure 1 Co-morbidities among the study subjects (N=150)

Among the 150 respondents 58(38.35%) had severe diabetic retinopathy (Severe DR), 44 (29.65%) had non severe diabetic retinopathy (Non severe DR) and only 48(32%) had no retinopathy(No DR).

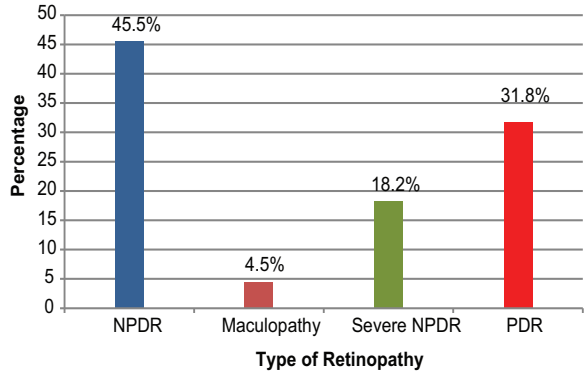

Figure 2 Type of retinopathy among the study subjects (N=150)

Table II Association of 24 hours urinary total protein with retinopathy

UTP (gm /24 hours)	DR n (%)	No DR n (%)	Total	P value
0.03-0.3	32 (64%)	18 (36%)	50(100%)	0.00001
0.3-3.5	10 (13.52%)	64 (86.48%)	74(100%)	
>3.5	6 (23.07%)	20 (76.93%)	26(100%)	
Total	48(32%)	102(68%)	150 (100%)	

Pearson Chi-Square value = 36.1028

Table III Association between eGFR and retinopathy

eGFR	No retinopathy	DR	Total
30 - 59	16(26.66%)	44(73.34%)	60 (100.0)
15 - 29	18(32.14%)	38(67.86%)	56 (100.0)
< 15	14(41.17%)	20(58.83%)	34 (100.0)
Total	48(32%)	102(68%)	150 (100.0)

Pearson Chi-Square value = 2.1006. P = 0.349836

Discussion

This cross-sectional study was carried out to observe the correlation between diabetic retinopathy in different stages of CKD in DM. It was found that among the 150 patients 68% patients had some form of diabetic retinopathy. More than half (56.4%) were suffering from vision threatening severe form of retinopathy. The result is in agreement with a study conducted by Grunwald on 925 participants with DM. Out of 925 subjects, 456 (49%) had diabetic retinopathy. [7] In a recent study conducted by Wong et al, the prevalence of diabetic retinopathy in patients with CKD due to DM was shown to be 34.7% after adjusting for various co-morbidities.[8]

Our study found proteinuria as a strong predictor of retinopathy. Several studies supported this evidence. Cruickshanks et al, carried out a prospective study on 1139 diabetic patients who did not have hematuria or a history of renal disease, to find out the association between albuminuria and diabetic retinopathy. After a mean follow up period of 4 years, it was found that participants with microalbuminuria were 1.7 to 3.2 times as likely to have retinopathy as those without microalbuminuria, in univariate analyses. This relationship remained after controlling for other potential confounders such as glycemia, hypertension, smoking and duration of diabetes. [9] Manaviat et al studied 590 type 2 diabetes patients for retinopathy and albuminuria and found that there was significant association between them .[10] Vigstrup et al, conducted a prospective cohort study on 43 patients and concluded that that even a slightly raised UAE (Urinary Albumin Excretion) is a strong predictor with respect to development of proliferative diabetic retinopathy, as well as nephropathy. Their study recommends using UAE to select those patients needing a closer control

and follow up. [11] In the above-mentioned studies albuminuria had been considered as a risk marker of diabetic retinopathy. Thus excretion of albumin in urine can be regarded as a sign of kidney involvement and can reflect generalized vessel damage throughout the body.

On the contrary this study found no association of retinopathy in different stages of CKD. We concluded though DR was more prevalent in nephropathy, the progression of these two target organ damage may not coincide. In CRIC study baseline unadjusted analysis showed significant association between retinopathy and CKD suggesting retinovascular pathology as a reflection of disease of other vascular beds, including kidneys. But in subsequent adjusted multivariate analysis the association of these two waned. They concluded presence and severity of DR may not provide any additional prognostic information regarding risk of CKD progression and vice versa which is similar with the current study.[12] Previously same observation was found in different studies. Goldstein et al showed that a decline in renal function was not followed by the same decline in retinopathy.[13] Some also found that rapid decline in renal function with or without significant proteinuria were inconsistent with natural history of DR. Some patients with advanced retinopathy had little or no renal disease. They emphasized on regular fundoscopic screening particularly in presence of proteinuria irrespective of stages of nephropathy which is consistent to this study. [13-15]Among the co morbidities, HTN and dyslipidaemia were common. It has been observed that hypertension independent of hyperglycaemia up regulates the vascular endothelial growth factor expression in retinal endothelial cells and ocular fluids and increase the risk of developing CKD than those without hypertension. Another study also found that dislipidemia plays a major role in developing complications of DM. Patients with combined dislipidemia have an increased incidence of retinal abnormalities similar to the present study. [16,17]

Hba1c was found more than 7% in 80% respondents in this study. Manaviat et al, found that HbA1c has got significant association with the occurrence of retinopathy. [10] Stratton et al, found that there was a highly significant positive association of HbA1c with incidence and progression of retinopathy in both univariate and multivariate analysis. [12] Wong et al also found similar results. [15] Our study showed that the frequency of retinopathy is more in the age group of >50 years. That age is a risk factor for retinopathy as well as other vascular complications of diabetes is a well known fact. Manaviat et al found in their study that increasing age is significantly associated with the development of diabetic retinopathy (P= 0.014). [10] Sobngwi et al found that diabetic retinopathy is significantly associated with age (P<0.001). [18] Mean duration of DM was 9.4 (±6.7) in our study. Previous studies have demonstrated that both hypertension and duration of diabetes were independent risk factors for diabetic retinopathy. Yau et al found that the prevalence of any diabetic retinopathy increased with diabetes duration ,HbA1c and blood pressure. [19] Thus we found aging, longer duration of DM are non modifiable risk factors whereas HTN and poor glycemic status are modifiable risk factors for development of both retinopathy and nephropathy in DM.

Conclusion

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

Conflict of interest: Nothing to declare.

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