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Original Article OPEN ACCESS

Association of Renal Functional Status in Different Stages of Diabetic Retinopathy

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Abstract

Introduction: *Diabetic nephropathy (DN) and diabetic retinopathy (DR) are both complications of diabetic microangiopathy with similar pathogenesis and clinical relevance. Many studies have demonstrated an association between diabetic retinopathy and diabetic nephropathy in type 1 diabetes mellitus (T1DM) patients, but this association is less strong in T2DM. There is link exists between different stages of diabetic retinopathy and diabetic nephropathy in T2DM.* ***Aims and Objective:*** *To explore the renal functional status in different stages of diabetic retinopathy.* ***Materials and Methods:*** *This cross sectional study was conducted in the Department of Biochemistry, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh during the period from July 2019 to December 2020. Forty hospitalized type 2 DM with retinopathy were selected. Previously diagnosed case of nephropathy, history of prolong intake of NSAID'S, patient with any acute condition like fever, heart failure, pregnancy were excluded. Serum creatinine, fasting blood sugar, HbA1c, creatinine clearance rate and urinary total protein were measured.* ***Results:*** *The mean age of the patients was 53.66 ± 13.51 years in non- proliferative and 56.21 ± 10.02 years in proliferative diabetic retinopathy; difference was not significant (p=0.538). The mean duration of diabetes was significantly greater in proliferative diabetic retinopathy compared to non- proliferative diabetic retinopathy (7.23 ± 2.86 years versus 11.36 ± 4.70 years; p=0.001). Raised serum creatinine [11 (42.3%) versus 7 (50.0%); p=0.641], decreased creatinine clearance rate [22 (84.6%) versus 14 (100.0%); p=0.278] and raised urinary total protein [21 (80.8%); p=1.000] did not significantly between non-proliferative and proliferative diabetic retinopathy.* ***Conclusions:*** *The renal functional status such as raised serum creatinine, decreased creatinine clearance rate and raised urinary total protein non-significantly greater in proliferative than no-proliferative diabetic retinopathy.*

Keywords: *Diabetic retinopathy, no-proliferative diabetic retinopathy, proliferative diabetic retinopathy, renal function, chronic kidney disease.*

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Introduction:

Type 2 diabetes accounts for 90% of the total cases of diabetes making it one of the largest health care challenges facing many developed and developing countries[1]. The associated morbidity and mortality can be caused by the disease itself or its complications. Severe and not uncommon complications include chronic kidney disease (CKD) and diabetic retinopathy (DR)[2]. Diabetic retinopathy (DR), a disease of the retina, is the fifth primary reason for acquired sightlessness in the world[3]. Diabetic retinopathy is characterised by steady and progressive changes in the vasculature of the retina that results from chronic

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hyperglycaemia[4]. Diabetic retinopathy is probably the most characteristic, easily identifiable and treatable complication of DM and it remains an important cause for visual loss in the developing world. Since type 2 diabetes mellitus remains undiagnosed for several years, a significant number of people,even indeveloped countries, already have retinopathy by the time their diabetes is diagnosed[5]. Retinopathy may begin to develop as early as 7 years before the diagnosis of diabetes in patients with type 2 diabetes[6]. The earliest pathologic changes associated with retinopathy are termed mild nonproliferative diabetic retinopathy. The first signs of mild nonproliferative diabetic retinopathy are microaneurysms, which arise most often in areas of capillary occlusion. Subsequently, increasing vascular permeability leads to retinal blot haemorrhages (round, with blurred edges) and "hard" exudates (sharply defined and yellow). Infarctions of the nerve fiber layer, known as soft exudates or cotton-wool spots, appear as white or gray, rounded swellings[5]. Moderate nonproliferative diabetic retinopathy is characterized by intraretinal microvascular abnormalities, including venous caliber changes, beading, and increased capillary dilation and permeability[5]. Proliferative diabetic retinopathy involves neovascularization, the growth of fine tufts of new blood vessels and fibrous tissue from the inner retinal surface or the optic head. Early proliferative changes are confined to the retina, but later invasion of the vitreous body constitutes high-risk proliferative diabetic retinopathy; during this end stage, fibrosis and contracture of the neovasculature result in retinal detachment and haemorrhage, the most important determinants of blindness[7]. Approximately 40% of people with diabetes develop diabetic nephropathy (DN), which has become the leading cause of end-stage renal disease (ESRD) in developed countries[8]. A close relationship has been observed between retinopathy and nephropathy in diabetes mellitus. The retina and the kidney complications of DM both result from damage to small vessels in these organs[9]. Since retinal and renal vessels are exposed to the diabetic mellitus, it is often assumed that progression of diabetic retinopathy and nephropathy occurs at the same time[10]. Proliferative diabetic retinopathy may be a highly specific indicator for diabetic nephropathy. Studies have shown that the presence of diabetic retinopathy (DR) itself may leave patients at risk for diabetic nephropathy (DN)[9, 11].

Materials and Methods:

This cross-sectional study was conducted in Department of Biochemistry, Sylhet MAG Osmani Medical College during the period between July 2019 and June 2020. Forty diagnosed cases of diabetic retinopathy admitted in the Department of Medicine, Sylhet MAG Osmani Medical College Hospital fulfilled the inclusion criteria were enrolled. The clinical histories of the patients were noted. Each patient was examined thoroughly. All the findings, previous history, reports and investigations were analyzed. Detailed history and examination regarding exclusion criteria were also taken. Dilated retinal examination was performed using ophthalmoscope. Any form of diabetic retinopathy was recorded. Diagnosis and staging of retinopathy were confirmed by consultant physician of the respective units of Department of Medicine. Patient was asked to stay overnight fast and in the next morning after a fasting period of 8 hours, 6 ml of venous blood was collected from ante-cubital vein by plastic disposable syringe under aseptic precaution and was transferred into separate plain glass tubes. Blood samples were kept in room temperature for one hour. After clot retraction centrifugation of the blood was done at a relative centrifugal force of 3000 rpm for 30 minutes. Afterward, serum was removed by disposable pasture pipettes and transferred into air tight tube. Patient was asked to place all his/her urine in a plastic jug for 1 day from 8:00 am to 8:00 am next morning, then researcher herself collected it to measure creatinine clearance rate and urinary total protein. All biochemical analysis of blood and urine samples were performed in the Department of Biochemistry, Sylhet MAG Osmani Medical College, Sylhet by researcher herself with technical assistance of department staff. Serum creatinine, fasting blood sugar, urinary total protein and creatinine clearance rate were measured by Automated Biochemistry Analyzar, Vitros 350 machine with calibration. **Statistical Analysis:** Collected data were checked and edited first. They were processed and analyzed with the help of Statistical Package for Social Science (SPSS) Version 25. Quantitative data were expressed as mean and standard deviation. Qualitative data were expressed as frequency and percentage. **Ethical Implications:** An approval of the study protocol was obtained from Ethical Review Committee of Sylhet MAG Osmani Medical College after commencement of the study. Informed written consent was taken from each patient after explaining all procedures.

Results:

The mean age of the patients was 53.66 ± 13.51 years in non- proliferative and 56.21 ± 10.02 years in proliferative diabetic retinopathy; difference was not significant (p=0.538) (Table-I).

The mean duration of diabetes was 7.23 ± 2.86 years in non-proliferative and 11.36 ± 4.70 years in proliferative diabetic retinopathy and duration of diabetes was significantly greater in proliferative diabetic retinopathy compared to non-proliferative diabetic retinopathy (t=-3.460 p=0.001) (Table- I).

In the study serum creatinine was raised in 11 (42.3%) patients of non-proliferative diabetic retinopathy and 7 (50.0%) patients of proliferative diabetic retinopathy; difference was not significant (p=0.641) (Table- II).

Creatinine clearance rate was decreased in 22 (84.6%) patients of non-proliferative diabetic retinopathy and 14 (100.0%) patients of proliferative diabetic retinopathy; difference was not significant (p=0.278) (Table- II).

Urinary total protein was raised in 21 (80.8%) patients of non-proliferative diabetic retinopathy and 12 (85.7%) patients of proliferative diabetic retinopathy; difference was not significant (p=1.000) (Table- II).

Table- I Characteristics of the patients by stage of retinopathy (n = 40).

Characteristics of the patients	Non-proliferative (n=26)	Proliferative (n=14)	p-value
Age (years)	53.66 ± 13.51	56.21 ± 10.02	p=0.538*
Duration of DM (years)	7.23 ± 2.86	11.36 ± 4.70	p=0.01*

*Statistical analysis was done by Unpaired t test and †Fisher's Exact test. P<0.05 was considered as significant.

Table- II : Renal function status of the patients by stage of retinopathy

Biochemical parameters	Non-proliferative (n=26)	Proliferative (n=14)	p-value
Serum creatinine (mg/dl)			
Raised	11 (42.3%)	7 (50.0%)	*p=0.641
Normal	15 (57.7%)	7 (50.0%)	
Creatinine clearance rate (ml/min)			
Decrease	22 (84.6%)	14 (100.0%)	†p=0.278
Normal	4 (15.4%)	0 (0.0%)	
Urinary total protein (gm/day)			
Raised	21 (80.8%)	12 (85.7%)	†p=1.000
Normal	5 (19.2%)	2 (14.3%)	

*Chi-Square test and †Fisher's Exact test were applied to determine the level of significance. P<0.05 was considered as significant

Discussion:

Type 2 diabetes mellitus (DM) is a common chronic disease worldwide[12]. The associated morbidity and mortality can be caused by the disease itself or its complications. Severe and not uncommon complications include chronic kidney disease (CKD) and diabetic retinopathy (DR). DR separately has been noted as a major public health problem worldwide as well[13,14]. The associated problems include disability, increased healthcare costs, and socioeconomic burdens[15, 16]. Currently, many studies have demonstrated an association between diabetic nephropathy and DR in T1DM patients, but this association is less strong in T2DM[17,18]. Hence, currently the associations of renal function with DR and its severity in T2DM are inconclusive[19]. We found the age of the patients was 53.66 ± 13.51 years in non-proliferative diabetic retinopathy and 56.21 ± 10.02 years in proliferative diabetic retinopathy; difference was not significant (p=0.538). Cho et al.[20] found that the age of the patients was 60 ± 11 years in non-proliferative diabetic retinopathy and 57 ± 11 years in proliferative diabetic retinopathy; difference was significant (p=0.003). In our study the duration of diabetes was 7.23 ± 2.86 years in non- proliferative diabetic retinopathy and 11.36 ± 4.70 years in proliferative diabetic retinopathy; duration of diabetes was significantly greater in proliferative diabetic retinopathy compared to non- proliferative diabetic retinopathy (p=0.001). Park et al.[21] found that the duration of diabetes was 11.9 ± 8.0 years in non- proliferative diabetic retinopathy and 12.0 ± 8.2 years in proliferative diabetic retinopathy; duration of diabetes was significantly greater in non-proliferative diabetic retinopathy compared to proliferative diabetic retinopathy (p<0.001). Cho et al.[20] found that the duration of diabetes was 12.2 ± 8.3 years in non- proliferative diabetic retinopathy and 11.9 ± 7.9 years in proliferative diabetic retinopathy; duration of diabetes was significantly greater in non-proliferative diabetic retinopathy compared to proliferative diabetic retinopathy (p<0.001).

In this study serum creatinine was raised in 42.3% patients of non-proliferative diabetic retinopathy and 50.0% patients of proliferative diabetic retinopathy; difference was not significant (p=0.641). Park et al.[21] found that serum creatinine increased in non-proliferative diabetic retinopathy than proliferative diabetic retinopathy. In our study creatinine clearance rate was decreased in 84.6% patients of non-proliferative diabetic retinopathy and 100.0% patients of proliferative diabetic retinopathy; difference was not significant (p=0.278). Park et al.[21] found that deterioration of renal function in proliferative diabetic retinopathy than non-proliferative diabetic retinopathy measured by eGFR. Difference may be due to small sample size in the present study. It is well known that the association between diabetic retinopathy and CKD is strong and the presence of CKD almost always accompany diabetic retinopathy. A large amount of cross-sectional studies demonstrated that the presence of diabetic retinopathy is associated with concurrent renal dysfunction[22-24]. However, only a few studies have evaluated causal relationship between diabetic retinopathy and CKD. Trevisan et al.[25] demonstrated that the rate of renal function decline was larger with those who have retinopathy and proteinuria compared to those without retinopathy. Another study evaluated the effect of retinopathy upon renal outcome in elderly group and showed that retinopathy even affects faster renal function decline in non-DM subjects[26]. There can be some possible explanation about why diabetic retinopathy severity affects renal function deterioration. Firstly, DR and diabetic CKD are both microvascular complication which lead to extravasation and inflammation. Previous study by Matsuyama et al.[27] suggested that pigment epithelium-derived factor, an inhibitor for angiogenesis, is significantly elevated in the type 2 DM patients with diabetic retinopathy and CKD, which may indicate microvascular damage. Another study by Yang et al.[28] also suggested that retinal damage marker found in urine proteome reflect renal progression in type 2 DM patients. However, other recent study by McKay et al.[29] showed that mere retinal microvascular parameters including vascular caliber, tortuosity, and fractal dimension cannot predict renal outcome in type 2 DM patients. Moriya et al.[30] suggested that microalbuminuria together with DR result in glomerulosclerosis and renal progression. In the present study urinary total protein was raised in 21 (80.8%) patients of non-proliferative diabetic retinopathy and 12 (85.7%) patients of proliferative diabetic retinopathy; difference was not significant (p=1.000). This was our observation but other studies did not analyse such correlation. Our results support the common pathogenetic mechanism of diabetic retinopathy and diabetic nephropathy in type 2 diabetic patients. The microvascular changes in both the retina and glomerulus are thought to be initiated by the chronic hyperglycemia, followed by the progressive narrowing and eventual occlusion of vascular lumina, subsequently leading to

inadequate perfusion of affected tissues. In the glomerulus, the widespread capillary occlusion and podocyte loss caused urinary protein loss and renal function decline. In the retina, this induces programmed cell death of Muller and ganglion cells, the losses of endothelial cells in capillaries, together with the losses of pericytes, and eventually leads to the development of retinal microvascular signs including microaneurysms, cotton-wool spots, hemorrhage, arteriovenous nicking, and focal and generalized narrowing[31].

Conflict of Interest: None

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