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KEY WORDS: Diabetes Mellitus, Diabetic Kidney Disease, Diabetic Retinopathy, Non-Proliferative Diabetic Retinopathy, Diabetic Macular Edema.

RENAL FUNCTION AND RETINOPATHY IN TYPE-2 DIABETES MELLITUS: A CASE SERIES

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ABSTRACT

Diabetes Mellitus (DM) is a metabolic disorder characterized by hyperglycemia which is associated with long term damage, dysfunction and failure of various organs viz eyes, kidneys, nerves, heart and blood vessels. Diabetic Kidney Disease (DKD) develops in 40% of patients with type 2 diabetes mellitus (T2DM) and 30% of patients with type 1 diabetes. Diabetic retinopathy (DR) is the leading cause of blindness in working age population and can develop without any serious symptoms. We present a case series of 4 patients with type-2 diabetes mellitus having chronic kidney disease and diabetic retinopathy.

INRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. Chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs viz eyes, kidneys, nerves, heart and blood vessels.[1]The chronic complications of diabetes are broadly divided into microvascular and macrovascular, with the former having much higher prevalence than the latter.[2] Microvascular complications include neuropathy, nephropathy, and retinopathy, while macrovascular complications consist of cardiovascular disease, stroke, and peripheral artery disease (PAD).[2]

Diabetic kidney disease (DKD) also referred to as diabetic nephropathy. The patients with diabetes and chronic kidney disease (CKD) presented a unique cohort of DKD population, which is identified by elevated urine albumin excretion or reduced glomerular filtration rate (GFR) or both.[3] It affects the kidney function and alters the usual process of removal of waste products and excess fluid from the body. Sign and symptoms of kidney disease in people with diabetes include albuminuria (excretion of albumin in the urine), weight gain, swelling of ankle and legs, frequent urination in the night, morning sickness, anaemia, and high blood pressure.[4] DKD develops in 40% of patients with type 2 diabetes mellitus (T2DM) and 30% of patients with type 1 diabetes. DKD is the leading cause of CKD and end-stage renal disease.[5]

Diabetic retinopathy (DR) is the leading cause of blindness in working age population and can develop without any serious symptoms.[6] Risk factors include duration of DM, poor glycemic control, elevated blood pressure, abnormal lipid profile, abnormal renal function test, serum levels of advanced glycation end-products (AGEs), evidence of early-stage atherosclerosis, increased caliber of retinal blood vessels and several genetic factors. In DR, chronic hyperglycemia causes endothelial damage, loss of pericytes, basement membrane thickening, breakdown of blood retinal barrier, platelet aggregation and leukocyte adhesion in retinal capillaries. This leads to vascular hyperpermeability and microaneurysm formation as in Non-Proliferative DR (NPDR). Excessive vascular leakage of fluids, proteins or lipids in the macular area leads to development of Diabetic Macular Edema (DME). As the disease progresses, capillaries close and arteries atrophied, and this causes non perfusion. Chronic hypoxia induces expression of several angiogenic growth factors, which results in retinal neovascularization, resulting in Proliferative DR (PDR)[7].

There is already a paucity of published literature on case report and case series on type-2 diabetes mellitus with chronic kidney disease and diabetic retinopathy. In this article, we describe 4 cases (3 males and 1 female) who were already under treatment for diabetes mellitus , diagnosed with diabetic kidney disease and were found to have diabetic retinopathy on ocular examination.

Case Series

Case: 1

A 57 years male with history of diabetes mellitus for past 25 years with diminution of vision in both eyes for one ear presented in Ophthalmic OPD . He was under treatment with oral hypoglycemics and was diagnosed with diabetic kidney disease (DKD) for one year. Blood test viz fasting blood sugar (FBS), glycosylated Haemoglobin (HbA1c), renal function tests and urine examination for albumin was advised and eGFR was calculated. Posterior segment examination was done with indirect ophthalmoscopy (with 20 D aspheric lens) after obtaining mydriasis by instilling one drop of 1.0% tropicamide and/or with Haag Streit BM 900 slit lamp biomicroscope by using +90 D aspheric volk lens. Fundus photography was done by Fundus camera (Zeiss VISUCAM NM/FA). Central macular thickness was obtained by Optical coherence tomography (Optovue Inc. Co., RTVue 100 model, Fremont, CA). HbA1c was found to be 7.6%, FBS 180 mg/dl, serum creatinine 1.0 mg/dl and eGFR 60.39 ml/min (CKD G2). Fundus and OC examination showed very severe NPDR with CSME bilateral eye (figure 1 &2). He was referred to medicine OPD for further management.

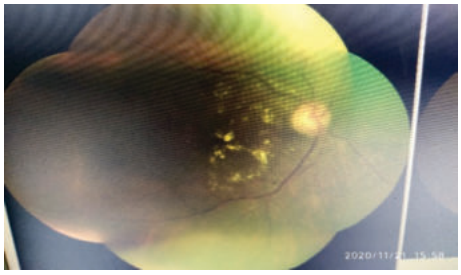

Figure 1: Fundus photograph showing multiple hard exudates with dot blot haemorrhages-suggestive of very severe NPDR.

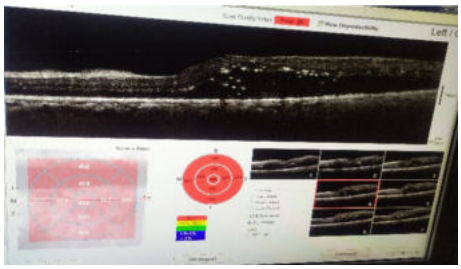

Figure 2: OCT picture showing multiple hyper-reflecting

dots as hard exudates with cystoid macular edema with loss of foveal contour.

Case: 2

A 58 years male with history of diabetes mellitus for past 10 years with diminution of vision in right eye for one year presented in ophthalmic opd . He was under treatment with oral hypoglycemics and was diagnosed with diabetic kidney disease (DKD) for two years. Blood tests viz fasting blood sugar (FBS), glycosylated Haemoglobin (HbA1c), renal function tests and urine examination for albumin was advised and eGFR was calculated. Posterior segment examination was done with indirect ophthalmoscopy (with 20 D aspheric lens) after obtaining mydriasis by instilling one drop of 1.0% tropicamide and/or with Haag Streit BM 900 slit lamp biomicroscope by using +90 D aspheric volk lens. Fundus photography was done by Fundus camera (Zeiss VISUCAM NM/FA). Central macular thickness was obtained by Optical coherence tomography (Optovue Inc. Co., RTVue 100 model, Fremont, CA). HbA1c was found to be 8.6%, FBS 192 mg/dl, serum creatinine 6.92 mg/dl and eGFR 9.87 ml/min (CKD G5). Fundus and OC examination showed severe NPDR right eye with cystoid macular edema (figure 3 & 4). He was referred to medicine OPD for further management.

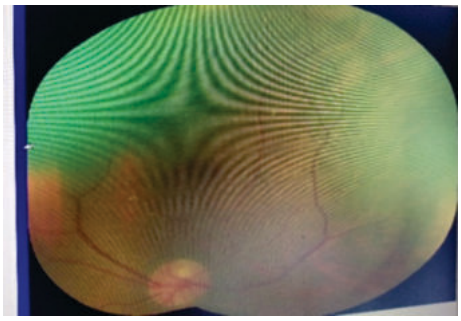

Figure 3: Fundus photograph showing multiple hard exudates with dot blot- haemorrhages-suggestive of severe NPDR.

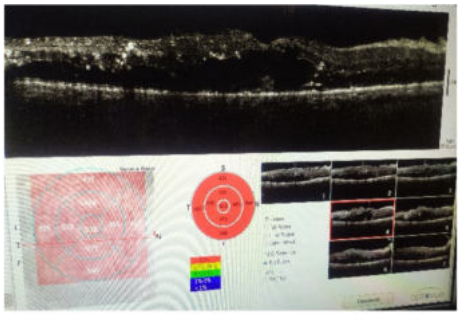

Figure 4: OCT picture showing hard exudates and cystoid macular edema.

Case: 3

A 65 years male with history of diabetes mellitus for past 5 years with diminution of vision in both eyes for one year presented in ophthalmic opd . He was under treatment with dialysis and was diagnosed with diabetic kidney disease (DKD) for one year. Blood tests viz fasting blood sugar (FBS), glycosylated Haemoglobin (HbA1c), renal function tests and urine examination for albumin was advised and eGFR was calculated. Posterior segment examination was done with indirect ophthalmoscopy (with 20 D aspheric lens) after obtaining mydriasis by instilling one drop of 1.0% tropicamide and/or with Haag Streit BM 900 slit lamp biomicroscope by using +90 D aspheric volk lens. Fundus photography was done by Fundus camera (Zeiss VISUCAM NM/FA). Central macular thickness was obtained by Optical coherence tomography (Optovue Inc. Co., RTVue 100 model, Fremont, CA). HbA1c was found to be 7.2%, FBS 120 mg/dl, serum creatinine 4.65 mg/dl and eGFR 10.5 ml/min (CKD G5). Fundus and OC examination showed severe NPDR with CSME bilateral eye (figure 5&6). He was referred to medicine OPD for further management.

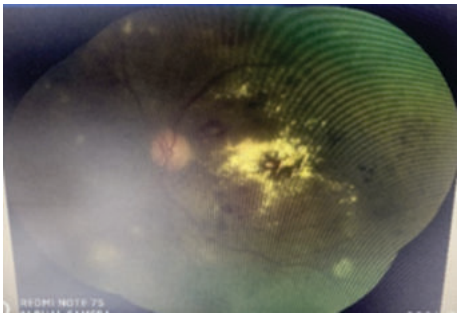

Figure 5: Fundus photograph showing severe NPDR.

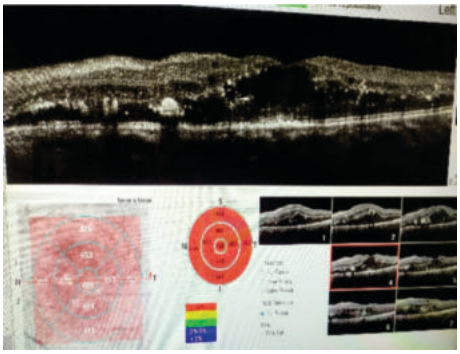

Figure 6: OCT picture showing loss of foveal contour with hard exudates with cystoid macular oedema with epiretinal membrane.

Case: 4

A 58 years female with history of diabetes mellitus for past 16 years with diminution of vision in both eyes for one year presented in ophthalmic opd . She was under treatment with dialysis and was diagnosed with diabetic kidney disease (DKD) for one year. Blood tests viz fasting blood sugar (FBS), glycosylated Haemoglobin (HbA1c), renal function tests and urine examination for albumin was advised and GFR was calculated. Posterior segment examination was done with indirect ophthalmoscopy (with 20 D aspheric lens) after obtaining mydriasis by instilling one drop of 1.0% tropicamide and/or with Haag Streit BM 900 slit lamp biomicroscope by using +90 D aspheric volk lens. Fundus photography was done by Fundus camera (Zeiss VISUCAM NM/FA). Central macular thickness was obtained by Optical coherence tomography (Optovue Inc. Co., RTVue 100 model, Fremont, CA). HbA1c was found to be 7.8%, FBS 148 mg/dl, serum creatinine 2.0 mg/dl and eGFR 36.1 ml/min. Fundus and OCT examination showed moderate NPDR with CSME bilateral eye (figure 7&8). He was referred to medicine OPD for further management. Details of all four cases has been summarized in table1.

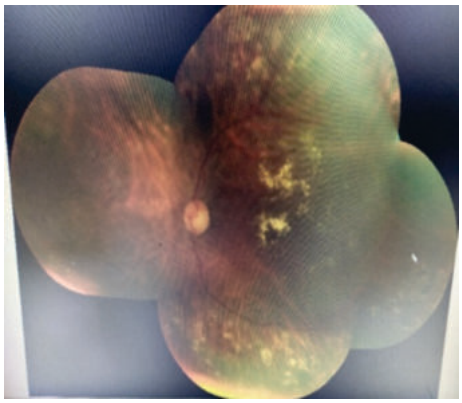

Figure 7: Fundus photograph showing Moderate NPDR.

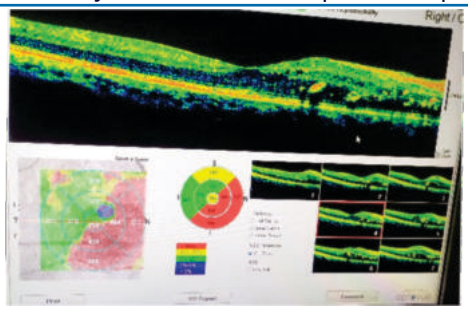

Figure 8: OCT picture showing hard exudates and inter-retinal fluid.

Table 1: Details of laboratory and clinical findings of all cases.

Characteristics	Case 1	Case 2	Case 3	Case 4
Age (years)	57	58	65	58
Gender	Male	Male	Male	Female
Duration of diabetes (years)	25	10	5	16
Treatment	OHAs	OHAs	Dialysis	Dialysis
CKD duration (years)	1	2	1	1
HbA1c (%)	7.6	8.6	7.2	7.8
FBS (mg/dl)	180	192	120	148
S.Creatinine (mg/dl)	1.0	6.92	4.65	2.0
eGFR(ml/min)	60.39	9.87	10.5	36.1
Fundus and OCT findings	Very severe NPDR wih CSME bilaeral eye	Severe NPDR with CSME bilateral eye	Severe NPDR with CSME bilateral eye	Moderate NPDR with CSME bilateral eye

DISCUSSION

Diabetes has progressively increased in India and around the world over the last quarter-century, with India accounting for a significant portion of the worldwide burden.[8,9] The prevalence of diabetes today is 8.8% among adults, nearly double the rate of 4.7% than in 1980 and it is expected to rise up to 9.9 per cent till 2045.[10] Type 2 diabetes incidence indicates higher rates in males in comparison to females, may be due to sex-related difference in sensitivity, obesity, and other causative factors like raised blood pressure or habits like consuming alcohol or smoking may be increased the risk of diabetes in males.[11]

Numerous studies have consistently demonstrated a strong association between DN and DR in type 2 diabetes mellitus patients. DR severity is found to be significantly associated with reduced kidney function and increased risk of CKD in type 2 diabetes.

Joju et al [12] conducted a descriptive, observational and non-interventional hospital-based study on diabetes-related chronic renal failure patients undergoing regular haemodialysis to evaluate the occurrences of ocular manifestations and to know whether ocular screening was useful. A cross-sectional study was conducted. Hundred patients who were diabetic and undergoing treatment for chronic renal failure were taken. Detailed history was collected, and clinical examination was done. Diabetic Retinopathy (DR) was noted in 95% cases, and of this, 64% of diabetic retinopathy were detected for the first time and were advised to undergo treatment. More severe grades of DR were detected with increasing severity of renal disease. Seventeen percent patients showed Age-Related Macular Degeneration (ARMD) changes. Chronic Renal Failure (CRF) patients are at increased risk of visual loss since this condition causes worsening of diabetic retinopathy changes.

Sapkal et al [13] assessed the association of ocular manifestations with chronic kidney disease and correlating it with the stages of chronic kidney disease. It was a cross-sectional study carried out in tertiary medical college in Central Maharashtra. A total of 84 patients were examined over a period of 18 months. Detailed ocular and systemic examinations were undertaken. Out of 168 eyes of 84 patients, 111 eyes had posterior segment involvement, 25 eyes had anterior segment involvement and 22 eyes had both anterior and posterior segment involvement. Most common posterior segment pathology was hypertensive retinopathy followed by diabetic retinopathy. Anterior segment findings did not correlate with the stage of the disease whereas severe stage of diabetic retinopathy was present in later stages of chronic kidney disease. This study showed a strong association of ocular manifestation in chronic kidney disease.

Gupta et al [14] in a meta-analysis reported that DR was significantly associated with DKD progression with a pooled HR of 2.42 (95% CI: 1.70-3.45) and a pooled OR of 2.62 (95% CI: 1.76-3.89). There was also a significant association between the severity of DR and risk of progression of DKD with a pooled odd ratio (OR) of 2.13 (95% CI: 1.82-2.50) for nonproliferative DR and 2.56 (95% CI: 2.93-.33) for proliferative DR. The study suggested that presence of DR is a strong predictor of risk of kidney disease progression in DKD patients. Furthermore, the risk of DKD progression increases with DR severity.

CONCLUSION

Ocular involvement in CKD patients if not detected early can lead to permanent and irreversible visual loss. Declining renal function is associated with DR progression in patients with T2DM, suggesting that investigation of DR status should be recommended for patients with declining renal function to reduce risk of visual loss and thereby to improve patient's quality of life.

Declaration of Conflicting Interests

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Informed Consent

Verbal informed consent was obtained from the patient for their anonymized information to be published in this article.

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