

Retinopathy in Chronic Kidney Disease: A Hospital Based Study

Sujata Priyambada¹, Divya Mohindru², Srabana Kumar Pradhan³,
Pragnya Paramita Mishra⁴

¹Associate Professor, Department of Ophthalmology, Hi-Tech Medical College and Hospital, Rourkela, Odisha, India

²Assistant Professor, Department of Medicine, Hi-Tech Medical College and Hospital, Rourkela, Odisha, India

³Associate Professor, Department of Medicine, Hi-Tech Medical College and Hospital, Rourkela, Odisha, India

⁴Assistant Professor, Department of Pathology, Hi-Tech Medical College and Hospital, Rourkela, Odisha, India

Received: 15-01-2023 / Revised: 21-02-2023 / Accepted: 25-03-2023

Corresponding author: Dr Pragnya Paramita Mishra

Conflict of interest: Nil

Abstract

Introduction: Eye and kidney have structural, developmental and organizational and pathogenic similarities and retinal vessels may reflect renal disease. In our present hospital-based study, we find out the prevalence of retinopathy, the relation of fundus changes with grades of retinopathy and factors associated with retinopathy.

Materials and Methods: It was a retrospective study conducted at Hi-tech Medical College and hospital where data of 152 consecutive patients diagnosed as chronic kidney disease was collected and analyzed. The parameters included their ocular examination details and biochemical parameters. Relation was established between the grades of kidney disease and severity of retinopathy.

Results: After accounting for both conventional and unconventional risk factors, lower estimated glomerular filtration rate (eGFR) was linked to more severe retinopathy. Lower eGFR was also related to a higher incidence of vascular anomalies often linked to hypertension. No significant correlation between average arteriolar or venular calibres and eGFR was discovered.

Conclusion: After adjusting for both conventional and unconventional risk factors for CKD, the results reveal a significant correlation between the severity of retinopathy, its characteristics, and kidney function, indicating that retinovascular pathology mirrors renal illness.

Keywords: Creatinine, eGFR, Diabetic Retinopathy, Hypertensive Retinopathy.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Chronic kidney disease (CKD) has emerged as a leading cause of morbidity and mortality worldwide affecting nearly 843.6 million people. [1] According to The Indian CKD Registry diabetic nephropathy is the commonest cause, followed by CKD

of undetermined etiology, chronic glomerulonephritis and hypertensive nephrosclerosis. [2]

Eye and kidney have structural, developmental and organizational and pathogenic similarities and retinal vessels

may reflect renal disease. [3-3b] Studies have concluded that retinal microvascular abnormalities are significantly associated with renal function deterioration. [4-7] Ocular morbidity in persons with CKD and end-stage kidney disease may be due to risk factors like diabetes, hypertension, metabolic disorders associated with CKD, uremia, anemia and CKD treatment. [8] Qualitative and quantitative changes in the retinal vasculature are associated with markers of renal dysfunction and damage. [9-10]

Various population based studies have found strong association of visual impairment (VI) and ocular fundus pathology with CKD and have emphasized the importance of ocular screening in such patients. [11-13] In another study by Deva et al, retinal abnormalities like diabetic retinopathy, microvascular retinopathy and macular degeneration have been found to be more severe in patients with CKD stage 3 to 5. [14]

In a study conducted in Cuttack district in the state of Odisha, India the prevalence of CKD was 14.3% but we could not find any data regarding prevalence of retinopathy in Odisha. [15] In our present hospital-based study, we find out the prevalence of retinopathy, the relation of severity of retinopathy with grade of CKD and factors associated with retinopathy.

Aim of the Study

1. To determine the prevalence of different type of retinopathy in chronic kidney disease patients.
2. To study the relation between grades of chronic kidney disease and severity of retinopathy.
3. To study the relation between biochemical parameters (urea, creatinine, sodium, potassium, haemoglobin, lipid profile and retinopathy).

Method and Materials

It was a hospital-based prospective study conducted on the patients presenting to Medicine Department, Hi-Tech Medical College and Hospital, Rourkela, District Sundergarh, Odisha during the period January 2021 to June 2022. The study was carried out on patients older than 20 years who had been diagnosed with chronic kidney disease for a minimum of 3 months. For the study, patients with estimated glomerular filtration rate (eGFR) less than 60 ml/min/1.73m² was defined as chronic kidney disease. It was a combined study done by ophthalmology and medicine department of the institute.

Study was conducted after due approval from institutional ethics committee.

The demographic details, examination findings and for patient requiring dialysis the pre-dialysis laboratory parameters were considered.

The patients were subjected to detailed ophthalmic examination including visual acuity, subjective and objective refraction, slit lamp examination, direct and indirect ophthalmoscopy, 90D slit-lamp biomicroscopy and OCT wherever required. Laboratory investigations included kidney function test, serum lipid profile, haemoglobin estimation and serum electrolytes. Patients who have undergone kidney transplant were excluded from study. Exclusion criterion also included patients with vision impairment or documented retinopathy prior to diagnosis of CKD. Those who have undergone previous retinal surgery, retinal laser procedure or intravitreal injections for retinopathy were also excluded

International Clinical Disease Severity Scale was used for grading Diabetic Retinopathy, Wong and Mitchell Classification for Hypertensive Retinopathy, and for Age-related Macular Degeneration, NICE recommendation to Modified International Criteria was used. [16-19] Retinal findings which could not be included or classified among the three

major heads were considered in and as Non-specific Retinopathy. In a patient with bilateral retinopathy, eye with more severe retinopathy was taken for consideration.

Results

Data was collected from hospital database of 152 consecutive patients with CKD

during the period January 2022 to June 2022.

There were 69 females and 83 males in this study. Figure 1 Shows the distribution among the patients based on gender.

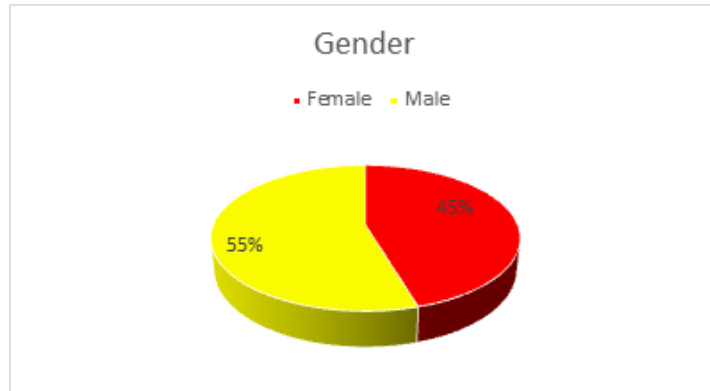


Figure 1: Distribution of Patients based on gender

Table 1 shows distribution of CKD grade amongst the two gender. CKD Grade 4 was the most prevalent in males (58.8%) and females (47.7%), followed by Grade 3 (Male:24.6%; Females 36.5%) and Grade 5 (male:16.6%; Female:15.8%).

Table 1: Gender distribution of grades of ckd patients

Grade of CKD	Male (n%)	Female (n%)	P-value
Grade 3	29 (24.6%)	24 (36.5%)	<0.002
Grade 4	38 (58.8)	34 (47.7%)	
Grade 5	19 (16.6%)	11 (15.8%)	

Of the total 152 patients, Diabetes mellitus was found in 64 patients, while no diabetes mellitus was found in 88 patients and Hypertension was found in 78 patients while no hypertension was found in 78 patients. However, out of 152 patients, only 21 patients had both diabetes and hypertension, while 131 had either present or both absent [Figure 2].

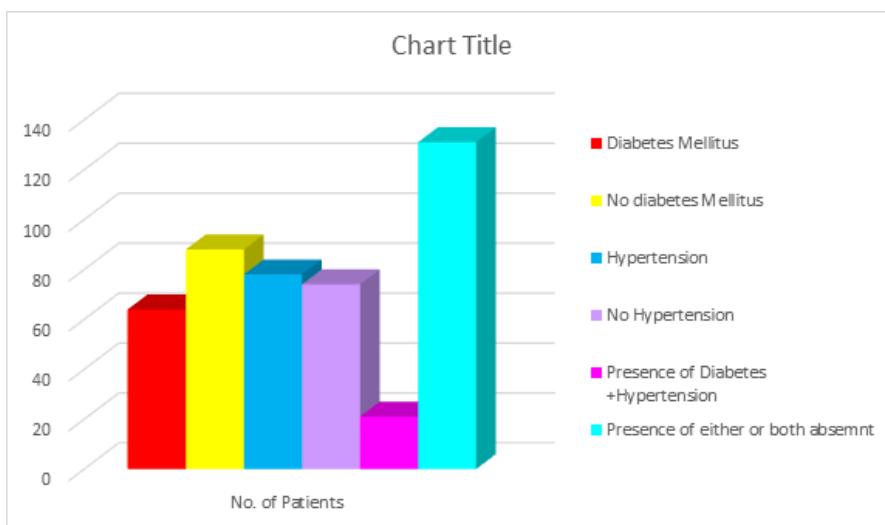


Figure 2: Prevalence of Retinopathy in CKD Patients

Table 2: Shows the prevalence of types of retinopathy in patients

Category	No. of Patients
Diabetes Retinopathy	
DR 1	5
DR 2	5
DR 3	6
DR 4	4
Hypertensive Retinopathy	
HTN 1	7
HTN 2	10
HTN 3	20
HTN 4	7
DR3P (MOD NDPR+ Molecular Edema)	6
ARD	6
ARD 1	4
DR6	1
Non-Specific Retinopathy	16
No Retinopathy	55

Hypertensive retinopathy 3 was most prevalent in patients, followed by Hypertensive retinopathy 2 and equal patients in Hypertensive retinopathy 1 and Hypertensive retinopathy 4. Non-specific retinopathy was seen in 16 patients,

whereas, no retinopathy was seen in 55 patients.

Table 3 shows the distribution of fundus changes according to grades of CKD.

Table 3: Distribution of Fundus according to CKD Grades

Category	No. of Patients
Cotton Wool Spots	
Cotton wool spots	32
No cotton wool spots	120
AV Changes	
AV changes	45
No AV Changes	107
Hard Exudates	
Hard Exudates	45
No Hard Exudates	107
Retinal Hemorrhage	
Retinal Hemorrhage	48
No Retinal Hemorrhage	104
Micro-aneurysm	
Micro-aneurysm	27
No Micro-aneurysm	125
Molecular Edema	
Molecular Edema	17
No molecular Edema	135
Disc Edema	
Disc Edema	10
No Edema	142

Retinal hemorrhage was the most commonly seen fundus, whereas, Disc edema was the least seen fundus.

Discussion:

The retinal pathology in this cohort of CKD patients with a variety of kidney dysfunction is the subject of the first in-depth investigation. According to our research, lower eGFR and worse ETDRS retinopathy scores are significantly correlated. When controlling for both conventional and non-conventional CKD risk variables, this link is still substantial, indicating that the severity of retinopathy adds to our understanding of the severity of CKD. The correlation is higher among those who have had a diabetes diagnosis in the past. Participants without diabetes who have retinopathy have reduced eGFR, but not statistically significantly. Without accounting for the substantial number of risk factors taken into account in our analysis, other studies have demonstrated relationships between retinal and kidney illness [16].

Inflammatory processes and endothelial dysfunction in the retina are linked to pathologic characteristics that include impaired vascular responsiveness and circulatory abnormalities [17, 18]. Basement membrane [19] and muscle layer thickness, as well as increased leakage, are features of both retinopathy and nephropathy [20]. The impact of these pathologic and hemodynamic anomalies on the retinal vasculature may serve as effective indicators of accumulative microvascular damage from processes such as hypertension, inflammation, diabetes, and other conditions [21]. Additionally, a recent study has revealed that diabetes patients may share common hereditary susceptibilities to retinopathy and CKD [22].

The advancement of diabetic retinopathy, inadequate glycemic management, obesity, inflammation, and endothelial dysfunction

have all been linked to retinal venular dilatation [23].

No significant correlation between eGFR and venular calibres was found, suggesting that the effects of impaired kidney function may balance the effects of diabetes mellitus on vascular diameter. Arteriolar narrowing has been linked to both current and previous blood pressure in numerous investigations [24]. Both kidney and cardiac arterioles have undergone similar modifications [25,26].

Conclusion

In conclusion, this study shows a considerable correlation between retinopathy and impaired kidney function, emphasising the importance of eye examinations in CKD patients. Due to the cross-sectional character of our investigation, our data are compatible with the theory that renal vascular pathology may reflect retinovascular pathology but do not prove this association. Further research is required to determine whether the presence of retinopathy in CKD patients provides predictive information about the quickening loss of renal function.

Bibliography

1. Klein R, Klein BE. Vision disorders in diabetes. *Diabetes in America*. 1995 Jul 1;1:293.
2. Kofoed-Enevoldsen A, Jensen T, Borch-Johnsen K, Deckert T. Incidence of retinopathy in type I [insulin-dependent] diabetes: association with clinical nephropathy. *Journal of Diabetic Complications*. 1987 Jul 1;1(3):96-9.
3. Nathan DM, Genuth S, Lachin J, Cleary P, Crofford O, Davis M, Rand L, Siebert C. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329(14):977-86.

4. Chavers BM, Mauer SM, Ramsay RC, Steffes MW. Relationship between retinal and glomerular lesions in IDDM patients. *Diabetes*. 1994 Mar 1;43(3):441-6.
5. Klein R, Klein BE, Moss SE, Cruickshanks KJ, Brazy PC. The 10-year incidence of renal insufficiency in people with type 1 diabetes. *Diabetes Care*. 1999 May 1;22(5):743-51.
6. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive therapy. *New England Journal of Medicine*. 2000 Feb 10; 342 (6):381-9.
7. Wong TY, Coresh J, Klein R, Muntner P, Couper DJ, Sharrett AR, Klein BE, Heiss G, Hubbard LD, Duncan BB. Retinal microvascular abnormalities and renal dysfunction: the atherosclerosis risk in communities study. *Journal of the American society of nephrology*. 2004 Sep 1;15(9):2469-76.
8. Sabanayagam C, Shankar A, Koh D, Chia KS, Saw SM, Lim SC, Tai ES, Wong TY. Retinal microvascular caliber and chronic kidney disease in an Asian population. *American journal of epidemiology*. 2009 Mar 1;169(5):625-32.
9. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, Van Lente F, Levey AS. Prevalence of chronic kidney disease in the United States. *Jama*. 2007 Nov 7;298(17):2038-47.
10. Lash JP, Go AS, Appel LJ, He J, Ojo A, Rahman M, Townsend RR, Xie D, Cifelli D, Cohan J, Fink JC. Feldman HIChronic Renal Insufficiency Cohort (CRIC) Study Group: Chronic Renal Insufficiency Cohort (CRIC) Study: Baseline characteristics and associations with kidney function. *Clin J Am Soc Nephrol*. 2009;4:1302-11.
11. Lash JP, Go AS, Appel LJ, He J, Ojo A, Rahman M, Townsend RR, Xie D, Cifelli D, Cohan J, Fink JC. Feldman HIChronic Renal Insufficiency Cohort (CRIC) Study Group: Chronic Renal Insufficiency Cohort (CRIC) Study: Baseline characteristics and associations with kidney function. *Clin J Am Soc Nephrol*. 2009;4:1302-11.
12. Feldman HI, Appel LJ, Chertow GM, Cifelli D, Cizman B, Daugirdas J, Fink JC, Franklin-Becker ED, Go AS, Hamm LL, He J. The chronic renal insufficiency cohort (CRIC) study: design and methods. *Journal of the American Society of Nephrology*. 2003 Jul 1;14(suppl 2):S148-53.
13. Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs—an extension of the modified Airlie House classification: ETDRS report number 10. *Ophthalmology*. 1991 May 1;98(5):786-806.
14. Hubbard LD, Brothers RJ, King WN, Clegg LX, Klein R, Cooper LS, Sharrett AR, Davis MD, Cai J, Atherosclerosis Risk in Communities Study Group. Methods for evaluation of retinal microvascular abnormalities associated with hypertension/sclerosis in the Atherosclerosis Risk in Communities Study. *Ophthalmology*. 1999 Dec 1;106(12):2269-80.
15. Wong TY, Klein R, Islam FA, Cotch MF, Folsom AR, Klein BE, Sharrett AR, Shea S, Multi-Ethnic Study of Atherosclerosis (MESA. Diabetic retinopathy in a multi-ethnic cohort in the United States. *American journal of ophthalmology*. 2006 Mar 1;141(3):446-55.
16. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D, Modification of Diet in Renal Disease Study Group*. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation.

- Annals of internal medicine. 1999 Mar 16;130(6):461-70.
17. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Retinopathy and nephropathy in patients with type 1 diabetes four years after a trial of intensive therapy. *New England Journal of Medicine*. 2000 Feb 10;342 (6):381-9.
 18. Klein BE, Knudtson MD, Tsai MY, Klein R. The relation of markers of inflammation and endothelial dysfunction to the prevalence and progression of diabetic retinopathy: Wisconsin epidemiologic study of diabetic retinopathy. *Archives of Ophthalmology*. 2009 Sep 14;127 (9): 1175-82.
 19. Wong TY, Islam FA, Klein R, Klein BE, Cotch MF, Castro C, Sharrett AR, Shahar E. Retinal vascular caliber, cardiovascular risk factors, and inflammation: the multi-ethnic study of atherosclerosis (MESA). *Investigative ophthalmology & visual science*. 2006 Jun 1;47(6):2341-50.
 20. Islam A, Klein R, Klein BE, Cotch MF, Castro C, Sharrett AR, Shahar E, Wong TY. Retinal Vascular Caliber, Cardiovascular Risk Factors and Inflammation: The Multi-Ethnic Study of Atherosclerosis (MESA). *Investigative Ophthalmology & Visual Science*. 2006 May 1;47(13):934-.
 21. Grunwald JE, Riva CE, Sinclair SH, Brucker AJ, Petrig BL. Laser Doppler velocimetry study of retinal circulation in diabetes mellitus. *Archives of Ophthalmology*. 1986 Jul 1;104(7):99 1-6.
 22. Grunwald JE, Riva CE, Brucker AJ, Sinclair SH, Petrig BL. Altered retinal vascular response to 100% oxygen breathing in diabetes mellitus. *Ophthalmology*. 1984 Dec 1;91(12):1447-52.
 23. Silva FG. Acute Postinfectious Glomerulonephritis and Glomerulonephritis Complicating Persistent Bacterial Infection. *Heptinstall's Pathology of the Kidney*. 1998:389-453.
 24. Olson JL. The nephrotic syndrome: minimal change disease, focal segmental glomerulosclerosis and miscellaneous causes. *Heptinstall's Pathology of the Kidney*. 1998:187-257.
 25. Sun C, Wang JJ, Mackey DA, Wong TY. Retinal vascular caliber: systemic, environmental, and genetic associations. *Survey of ophthalmology*. 2009 Jan 1;54(1):74-95.
 26. Tamubango Kitoko, H. (2023). Marqueurs de définition du statut martial néonatal. *Journal of Medical Research and Health Sciences*, 2023; 6(2): 2441–2449.