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Original Research Article

A cross-sectional study to evaluate ocular manifestations in chronic kidney disease patients in a tertiary care centre

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ABSTRACT

Purpose: Chronic kidney disease (CKD) constitutes a major healthcare issue due to defective microcirculation secondary to systemic hypertension and diabetes mellitus. Hence, the aim is to find the prevalence of ocular pathology, risk factors and its association with the level of kidney function in patients with CKD undergoing haemodialysis.

Materials and Methods: This prospective, cross-sectional study included 105 CKD patients referred to Ophthalmology Department in a tertiary care centre from November 2021 to April 2023. They were evaluated for demographic data, history of systemic comorbidities, visual acuity and ocular pathologies. This was correlated with the stages of CKD which is defined as the presence of glomerular filtration rate (GFR) < 60 mL/min/1.73 m2 and/or proteinuria. Chi-square test or Fischer's exact test was used as test of significance for qualitative data and Independent t test was used as test of significance to identify the mean difference between two quantitative variables. ANOVA was used as test of significance to identify the mean difference between more than two quantitative variables.

Results: Out of 105 [74 (70.5%) male and 31(29.5%) females] CKD patients with mean age 58.43±13.05, ocular pathology was noted in 63 (60%) with hypertensive retinopathy in 47 (44.76%), diabetic retinopathy in 38 (36.19%), mixed retinopathy in 24 (22.85%), cataract in 24 (22.85%), glaucomatous changes in 5 (4.76%), ARMD in 4 (3.8%) and retinal vein occlusion in 3 (2.85%). The mean platelet volume also showed positive correlation with worsening stages of CKD (P-0.015), Hypertensive and diabetic retinopathy (P<0.001).

Conclusion: Higher prevalence of ocular pathology 63 (60%) was observed in this study, re-emphasising that ocular screening is mandatory in all chronic kidney disease patients for early detection and initiation of prompt treatment to prevent ocular morbidity.

1. Introduction

Chronic kidney disease (CKD) a major health problem worldwide, is associated with a wide range of complications leading to adverse health outcomes. The Kidney Disease Outcome Initiative Guidelines from 2002 describe it as kidney damage or a glomerular filtration rate of 60ml/min/1.73m2 for more than 3 months, regardless of the aetiology.[1] Albuminuria, defined as an albumin: creatinine ratio greater than 30mg/g in two of three spot urine samples, can demonstrate renal damage in numerous illnesses.

Studies have found CKD to be associated with ocular disorders like age-related macular degeneration, diabetic retinopathy, glaucoma, and cataract. Also, the retinal microvascular parameters are predictive of chronic kidney

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disease with an undetected progressive loss of renal function over several years resulting in renal failure. Subsequently, the organs' function is seriously impaired necessitating dialysis or renal transplant for the patient's survival.[2–4]

Renal microvascular pathology that plays an important role in the development of renal insufficiency requires invasive procedures for its assessment. The ocular and renal diseases are closely linked as they share structural, developmental and genetic pathways, suggesting their possible association. Hence, the non-invasive examination of retinal vasculature can offer a unique tool to analyse the relationship between systemic microvascular disease and renal function.

Hence, the aim was to determine the prevalence of ocular findings, risk factors and to evaluate and correlate the severity of retinopathy with the renal function in CKD patients.

2. Materials and Methods

This prospective cross-sectional observational hospital-based study was conducted on 105 CKD patients referred for fundoscopy to the department of Ophthalmology from November 2021 to April 2023. This study was performed according to the guidelines of the Declaration of Helsinki, and all subjects gave their written informed consent to participate, which was approved by the Institutional Ethics Committee. All patients aged > 18 years of either gender with Chronic kidney disease were included and those with acute kidney injury, renal transplant and cataracts were excluded from the study.

After obtaining informed consent all patients were assessed for socioeconomic status, risk factors (smoking), medication use and history of systemic diseases, ocular examination for visual acuity, anterior segment examination by slit lamp, retinal examination by indirect ophthalmoscopy and intraocular pressure measurement by Goldman's applanation tonometer. Data was acquired from investigations such as complete blood count, blood urea, serum creatinine, Mean platelet volume (MPV) and serum fasting lipid profile. Any retinal vascular abnormality secondary to metabolic disorders such as diabetes and hypertension was graded according to the Early Treatment of Diabetic Retinopathy Study (ETDRS) protocol[5] and Keith–Wagener–Barker classification[6] respectively.

Assessment of renal function was done by estimating the glomerular filtration rate (eGFR) from the serum creatinine concentration by using the Chronic Kidney Disease Epidemiology Collaboration equation. According to Kidney Disease Improving Global Outcomes 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease, CKD is defined as abnormalities of kidney structure or function, present for >3 months concerning e-GFR,[7] suggesting the following stages:

Table 1: Early treatment diabetic retinopathy study classification of diabetic retinopathy[5]

Category	Description
Mild NPDR	Microaneurysms
Moderate NPDR	Retinal haemorrhages in 1–3 quadrants or mild IRMA, Significant venous beading < 1 quadrant, Cotton-wool spots commonly present
Severe NPDR	Severe haemorrhages in all 4 quadrants, Significant venous beading > 2 quadrants, Moderate IRMA >1 quadrants
Very severe NPDR	Two or more of the criteria for severe NPDR
Mild–moderate PDR	New vessels on the disc (NVD) or elsewhere (NVE)
High-risk PDR	NVD about 1/3 disc area, Any NVD with vitreous haemorrhage, NVE greater than 1/2 disc area with vitreous haemorrhage
Advanced diabetic eye disease	Pre retinal haemorrhage, Tractional retinal detachment & Rubeosis iridis

NPDR – Non proliferative diabetic retinopathy, PDR – Proliferative diabetic retinopathy

Table 2: Keith–Wagener–Barker classification of Hypertensive retinopathy[6]

Grade	Hypertensive retinopathy
Grade 0	No changes.
Grade 1	Barely detectable arterial narrowing
Grade 2	Obvious arterial narrowing with focal irregularities
Grade 3	Grade 2 plus retinal haemorrhages, exudates, cotton wool spots or retinal oedema
Grade 4	Grade 3 plus papilledema

Table 3: Stages of chronic kidney disease[7]

Stage	GFR (ml/min/1.73 m2)	Renal function
1	≥ 90	Normal
2	60 - 89	Mildly decreased renal function
3a	45 - 59	Mild to moderately decreased renal function
3b	30 - 44	Moderate to severely decreased renal function
4	15 - 29	Severely decreased renal function
5	<15	Kidney failure

Sample size calculation was based on the major ocular complication of CKD i,e hypertensive retinopathy (44%) reported in a study by Malleshwari et al.[8] With 95% CI with an absolute error of 5% the calculated sample size is 95. Expecting a non-compliance of 10% the final sample size calculated is 105.

2.1. Statistical analysis

Data entered into MS excel sheet was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions and Chi-square test or Fischer's exact test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation and Independent t test was used as test of significance to identify the mean difference between two quantitative variables. ANOVA was used as test of significance to identify the mean difference between more than two quantitative variables. Probability that the result is true (P value) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

3. Results

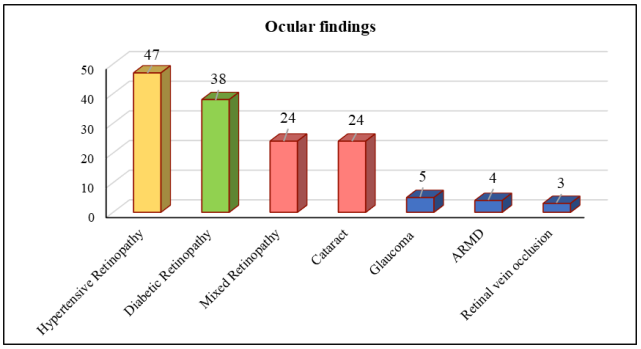
There were a total of 105 patients 74 (70.5%) male and 31(29.5%) females aged from 36 to 80 years, with mean ± SD 58.43±13.05. The prevalence of ocular pathology was 63 (60%) consisting of 72 (68.6%) hypertensive, 64 (61%) diabetic, 15 (14.3%) asthmatic, 4 (3.8%) stroke and 2 (1.9%) Ischemic heart disease patients. The mean log MAR visual acuity is 0.6 + 0.16 and the range of intraocular pressure is 12 – 20mmHg. (Table 1) Ocular examination revealed Hypertensive retinopathy in 49 (46.66%), diabetic retinopathy in 38 (36.19%), mixed retinopathy in 24 (22.85%), cataract in 24 (22.85%), glaucomatous changes in 5 (4.76%), ARMD in 4 (3.8%) and retinal vein occlusion 3 (2.85%).

Table 4: Characteristics of patients with CKD patients (N=105)

Characteristics		N	%
Gender	Female	31	29.5
	Male	74	70.5
Diabetes mellitus		64	61
Hypertension		72	68.6
IHD		2	1.9
Bronchial Asthma		15	14.3
Smoking		15	14.3
Myocardial infarction		6	5.7
Stroke		4	3.8

The results of haematological investigations among the study participants is displayed in Table 2. Low-density lipoprotein (P=0.019) and e-GFR (P=0.049) showed a significant correlation with hypertensive retinopathy.

Relationship of retinopathy changes with e-GFR is presented in Table 3 which shows significant results with reduced e-GFR (P = 0.033.).



Graph 1: Prevalence of ocular disease in CKD patients

The correlation of MPV with various stages of CKD, Hypertensive and Diabetic retinopathy is shown in Table 8. There is difference between CKD stages with regard to MPV values 9.0±2.3, 8.2±2.4, 10.5±2.0, 10.7±1.5, and 10.8±1.3 fL in stage 1-5 CKD, respectively. (P=0.015) The MPV also showed positive correlation with Hypertensive (11.1+1.4) and Diabetic retinopathy (11.6+0.8). P<0.001

4. Discussion

A CKD diagnosis can make a profound impact on life, the treatment of which is lifelong requiring time and patience.[9] This hospital-based study on 105 Chronic kidney disease patients with a mean age of 58.43±13.05 showed a prevalence of 63 (60%) with a male preponderance of 74 (70.5%) similar to studies stating that males have a faster rate of deterioration,[10,11] but a much higher prevalence when compared to other studies.[12] Although CKD is said to be more prevalent in the elderly population younger patients with CKD was observed with uncontrolled glycemic level.

The most common risk factors seen to be associated with them were hypertension 72 (68.6%), diabetes mellitus 64 (61%), Bronchial asthma 15 (14.3%), stroke 4 (3.8%) and Ischemic heart disease 2 (1.9%) patients. (Table 4) Wong et al. observed similar risk factors attributed to ocular diseases like diabetic and hypertensive retinopathy, cataract, glaucoma and age-related macular degeneration.[13]

Various ocular manifestations among patients of CKD are shown in Figure 1. Hypertensive retinopathy was the commonest in 47 (44.76%) followed by diabetic retinopathy in 38 (36.2%), mixed retinopathy and cataract in 24 (22.8%) each, glaucomatous changes in 5 (4.7%), ARMD in 4 (3.8%), Branch retinal vein occlusion in 2 (1.9%) and Central retinal vein occlusion in 1(0.95%) patient. Similarly, a higher prevalence of Hypertensive retinopathy and other ocular features was observed in other studies.[14,15] The mean e-GFR was 23.1+23.75 ml/min/1.73 m2 which was statistically significant with the retinopathy changes. [P=0.049] Lipid profile showed the mean Low-Density Lipoprotein 110.6+32.21 mg/dl which was significantly

Table 5: Values of haematological investigation

Parameters	Min	Max	Mean	SD	P value
FBS mg/dl	57	466	105.47	45.95	0.150
e-GFR (ml/min/1.73 m2)	3	124	23.1	23.75	0.049*
LDL in mg/dl	69	196	110.6	32.21	0.019*
HDL in mg/dl	31	49	41.20	3.80	0.665
Total Cholesterol (mmol/L)	114	300	171.3	40.87	0.144
Sr. Creatinine	1	17	5.42	3.36	0.388
Sr. BUN	6	147	53.21	30.5	0.462
Albumin	2	5	3.12	0.56	0.176

*Significant correlation with CKD

Table 6: Relationship of retinopathy with e-GFR

Estimated Glomerular filtration rate	Stages of CKD	Retinopathy			
		Absent		Present	
		N	%	N	%
15 < 29	IV	17	51.7	53	73.6
30-44	III a	4	12.1	8	11.1
45-59	III b	4	12.1	7	9.7
> 60	II	8	24.2	4	5.6

Table 7: Relationship of hypertensive retinopathy with e-GFR (P value 0.049)

e-GFR in ml/min /1.73 sq m	N	Mean	SD	95% Confidence Interval for Mean		Min	Max	P value
				Lower	Upper			
Nil	58	22.93	16.053	16.02	29.84	3	124	0.049
Grade I	14	31.57	20.814	13.78	49.36	3	112	
Grade II	26	21.77	10.676	15.84	27.70	5	58	
Grade III	5	7.60	2.408	4.61	10.59	5	10	
Grade IV	2	18.00	11.556	-121.77	157.77	7	29	
Total	105	22.97	23.793	18.34	27.60	3	124	

Table 8: Association of the Mean platelet volume with variables

Variables		MPV		P value
		Mean	SD	
Chronic Kidney Disease	Stage 1	9.0	2.3	0.015
	Stage 2	8.2	2.4	
	Stage 3	10.5	2.0	
	Stage 4	10.7	1.5	
	Stage 5	10.8	1.3	
Diabetic Retinopathy	No	9.6	1.7	<0.001
	Yes	11.6	0.8	
Hypertensive Retinopathy	No	10.1	1.7	0.001
	Yes	11.1	1.4	

raised in patients with CKD. [P=0.019] unlike Fasting blood sugar, High-density lipoprotein, Total Cholesterol, Sr. Creatinine, Sr. BUN and albumin showed no statistically significant correlation with the ocular findings. (Table 5)

Relationship of retinopathy with e-GFR is shown in Table 6. Stage IV CKD was seen in 53 (73.6%), stage III in 15 (20.8%) and stage II in 4 (5.6%) patients. Hypertensive retinopathy was the frequently observed ocular finding correlating with the stages of CKD. (P = 0.049)(Table 7) As the e-GFR reduced the worsening of retinal vascular changes was noticed (P = 0.033) similar to the observation by Grunwald and Alexander et al. They also noticed worsening of Diabetic retinopathy with deterioration of renal function particularly in patients with poor blood pressure control.[11,15]

Among the 38 (36.2%) diabetic retinopathy patients, 14 (36.8%) had mild NPDR, 12 (31.6%) had moderate NPDR, 9 (23.7%) severe NPDR and 3 (7.9%) showed vision-

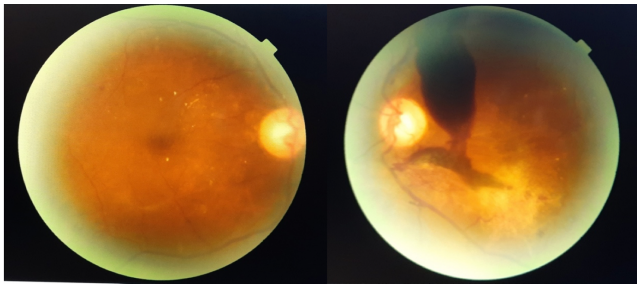


Figure 1: Stage 3 CKD patient showing RE: moderate NPDR, LE: Advanced diabetic eye disease

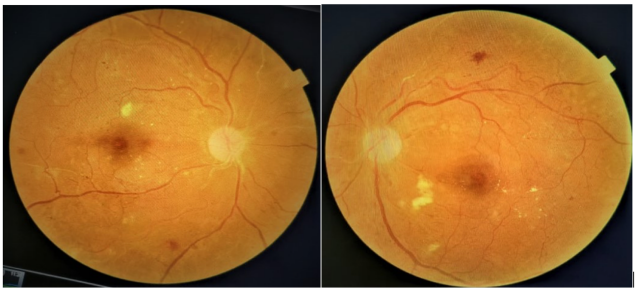


Figure 2: Stage 2 CKD patient showing BE: Grade 3 hypertensive retinopathy

threatening PDR. Mixed retinopathy was seen in 24 (22.8%) participants. On the contrary to hypertensive retinopathy, the worsening diabetic retinopathy as well as mixed retinopathy was not statistically correlating with the decrease in the eGFR. [P= 0.790 and P=0.605 respectively]

This is lesser than observations by Rajeev and Mohamad et al., where moderate to severe NPDR was seen in 41 (28%) patients with CKD stages 3 to 5 when compared to 16 (11%) patients with CKD stages 1 to 2 (p = 0.001). Also, the diabetic retinopathy changes worsened as renal function deteriorated in CKD stages 3 to 5 (p = 0.001).[16]

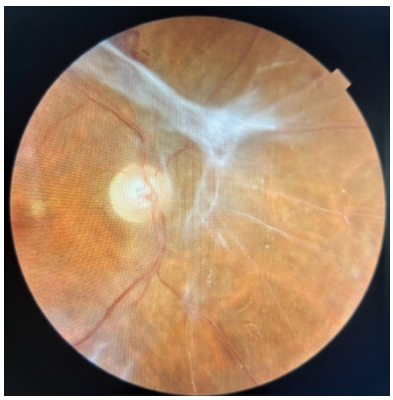


Figure 3: Stage 4 CKD showing RE: High-risk PDR

All patients with cataracts were operated after glycaemic and hypertensive control and one of the high-risk PDR cases received 3 sittings of pan-retinal photocoagulation.

Further the relationship between MPV and GFR was evaluated in these patients where a progressive increase in MPV was noted as the GFR declined in various stages of CKD. There were significant differences in MPV in CKD patients with diabetes and hypertension compared to patients with no comorbidities.(Table 8) Similar results were obtained in several studies suggesting that this simple laboratory test can serve as a biomarker indicating that CKD is a prothrombogenic state that causes increased cardiovascular and ocular morbidity and mortality.[17–19]

Evidence suggests that dysfunction of renin-angiotensin system, atherosclerosis and oxidative stress along with upregulation of proinflammatory markers due to increased levels of angiotensin II[20] and serum cystatin C,[21] advanced glycation end products activation,[22] and deficiency of vitamin D[23] are common etiologies causing chronic kidney disease and ocular manifestations.

5. Conclusion

Elderly patients with advanced stages of CKD had higher prevalence of retinopathy than in the early stages. The primary outcome of this study is Hypertensive and diabetic retinopathy, a common end-organ microvascular complication of CKD associated with rapid progression of renal damage. Decreasing the MPV level could be a new treatment strategy in such patients. This study emphasise the importance of comprehensive eye screening in all patients with CKD and frequent monitoring to initiate appropriate timely treatment to reduce ocular morbidity.

6. Source of Funding

None.

7. Conflicts of Interest

Nil.

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