A Cross Sectional Study of the Prevalence of Retinopathy in Patients with Chronic Kidney Disease on Hemodialysis in a Tertiary Care Centre in Chengalpattu District, South India

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KEYWORDS
Chronic kidney disease, hemodialysis, retinopathy, ocular findings

ABSTRACT
Context: Many studies have reported varying proportions of retinopathy among cases with chronic kidney disease (CKD). Cases with severe grades of CKD were more likely to develop ocular complications, especially diseases which occurs due to small vessel pathology.
Aim: To estimate the prevalence of various types of retinopathies in patients with CKD undergoing hemodialysis in a tertiary care centre in South India.
Settings and Design: The outpatient Department of Ophthalmology and Hemodialysis unit of Nephrology, Karpaga Vinayaga Institute of Medical Sciences from January 2022 to June 2023
A cross-sectional hospital-based observational study in a low resource setting.
Methods and Material: The study consists of 28 patients who were known cases of CKD on hemodialysis. Patients underwent complete ocular evaluation and findings were noted. The pre hemodialysis values of blood urea and serum creatine, hemoglobin, liver function tests and vital parameters were also noted. Data analysis was done utilising version 20 of Statistical Packages for the Social Sciences (SPSS).
Results: 56 eyes of 28 patients on hemodialysis were studied. The mean age was 53 years $\pm$ 10.9 with a male preponderance. 31.6% had retinopathy of which 26.3% had hypertensive retinopathy and 5.3% had diabetic retinopathy. This is contrary to the previous studies that have reported a higher incidence of diabetic retinopathy in patients with end stage CKD. Hypertension resulted in CKD earlier than diabetes.
Conclusion: The results emphasize the importance of frequent eye examination in patients with CKD to identify retinopathy earlier, thus potentially averting permanent vision impairment.

1. Introduction

Chronic kidney disease (CKD) is a major global public health concern that affects 10-16% of adult populations in Asia, Australia, Europe, and the United States.[1] According to a study by P.P.Varma, the prevalence of chronic renal failure (CRF) in India was 17.2%.[2] Causes of CKD are diabetes, hypertension, chronic glomerular nephritis, chronic interstitial disease and vesico-ureteral reflux.[2] Several studies have shown a connection between CKD and diabetes and hypertensive retinopathy.[3,4] When fundus examination shows evidence of diabetic or hypertensive retinopathy, it would indicate long duration of the respective systemic disease and the possible cause of these diseases for CKD.[5]

The renal parameters to define CKD are urine albumin:creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR). Serum creatinine levels are also determined. Normoalbuminuria is defined as UACR <30 mg/g, microalbuminuria is defined as UACR 30-299 mg/g, and macroalbuminuria is defined as UACR >=300 mg/g. eGFR can be determined using the Chronic Kidney Disease Epidemiology Collaboration equation.[6]

In CKD patients, prevalence of DR increases with high urine albumin:creatinine ratio (>10 mg/g), whereas eGFR levels were low (44-30 mL /min/1.73m2). According to a hypothesis, a common pathogenetic mechanism functions towards hypertension related retinal and renal vascular changes. Hence, it is seen that there is an association between hypertensive retinopathy and low GFR. [6-8]

The developmental pathways of the inner retina and the glomerular filtration barrier exhibit notable similarities and structures like the ciliated epithelial cells, basement membrane composed of α3α4α5 Collagen IV, along with extensive capillaries in glomerulus and choriocapillaris. [9-12] Retinopathies can be seen in both inherited as well as acquired renal diseases. Few of the inherited renal conditions causing retinal changes are Alport

Syndrome, reflux nephropathy and MELAS (Myopathy, Encephalopathy, Lactic Acidosis and Stroke-like episodes) syndrome. The various retinal changes seen in these conditions are in the form of drusen, retinitis pigmentosa, crystal deposits and retinal vascular anomalies. [13-14] There are some acquired renal conditions that also cause retinopathy, such as Systemic Lupus Erythematosus, Wegener's granulomatosis, microscopic polyangitis and Good Pasture syndrome. The retinal changes in these conditions are in the form of vasculitis, retinal infarcts or central serous retinopathy. [15-16]

Many global studies have explored the correlation between fundoscopic abnormality and the development of CKD in people with diabetes mellitus, hypertension, or both. The prevalence of hypertensive and diabetic retinopathy in CKD patients was reported to be 7.8%-68% and 22.8%-88.3%, respectively. [17-19] The local literature contains limited information, and one study that only included hemodialysis patients found that the prevalence of diabetic retinopathy was 36% and that of hypertensive retinopathy was 22%.[20] Considering the varied aetiology of CKD, this study aimed to estimate the prevalence of various types of retinopathy in patients with CKD undergoing hemodialysis in a tertiary care centre in South India that catered to the needs of the economically underprivileged**.**

2. Methods

This cross sectional observational study was conducted in the outpatient Department of Ophthalmology and in the Hemodialysis unit of Nephrology at a multi speciality tertiary care in Chengalpattu district. This hospital extends its medical care to a rural population of a very low socioeconomic status. 56 eyes of 28 patients with CKD 5 on hemodialysis were examined for the prevalence of retinopathy. Patients who were extremely sick, post renal transplant patients were excluded from the study

This study adhered to the tenets of the Declaration of Helsinki. The study was commenced after obtaining informed consent from each participants. A detailed medical history of diabetes, hypertension, ischemic heart disease, bronchial asthma and the duration of the systemic disease was taken using a questionnaire. The frequency of hemodialysis was noted. The blood investigations such as blood urea, serum creatinine, hemoglobin, liver function tests from the records of the patients were noted.

All patients underwent complete ocular evaluation including best corrected visual acuity (BCVA), slit lamp examination, intra ocular pressure estimation by Goldman applanation tonometry and fundus examination with + 78D lens. Hypertensive retinopathy (HR) was graded using Keith Wagners classification. Diabetic retinopathy was classified using Early Treatment Diabetic Retinopathy Study (ETDRS) classification. The retinal picture was captured using mydriatic fundus camera. (Canon, CF1, Tokyo, Japan). The ocular examination was done in the Department of Ophthalmology. At times, the dilatation of the pupils of these patients were carried out in the hemodialysis unit itself followed by fundus examination in the department of Ophthalmology.

Statistical analysis was done using Statistical Packages for the Social Science (SPSS) version 20.A P value of < 0.05 was considered significant.

3. Results

56 eyes of 28 patients with CKD stage 5 on hemodialysis were studied for the prevalence of retinopathy. 20 (71.4%) patients were hypertensives, 2 (7.1%) were diabetics, 4 (14.4%) had both diabetes and hypertension, 2(7.1%) had neither hypertension (HT) nor diabetes (DM) or any other systemic disease that could lead to CKD [chart 1]. The mean age of CKD was 53years $\pm$ 10.9 years. The mean duration of CKD was 3 years and 5 months. The mean duration of HT was 4 years and 8 months. The mean duration of DM was 10 years and 9 months. Of the 40 eyes that were examined for hypertensive retinopathy (HR), 28 eyes (11.2%) had no evidence of retinopathy, 12 eyes (4.8%) had HR. Of the 12 eyes, 8 eyes (66.6%) had grade 1 HR, 2 (16.6%) had grade 2 HR and 2 (16.6%) had grade 3 HR [Fig 1 a and 1b]. Of the 2 patients with DM, one had bilateral proliferative diabetic retinopathy (DR), and one had no evidence of DR in either eye. Of the 8 eyes of the patients with DM and HT, one patient had bilateral non proliferative diabetic retinopathy and HR (grade 2 in one eye and grade 3 in the other), which is known as combined retinopathy. 2 cases with HT had age related macular degeneration as well (ARMD) [Figure 2a and 2b] one patient had anaemic retinopathy associated with hypertensive retinopathy. However, there were no vasculitis induced retinopathy in the study group [chart 2].

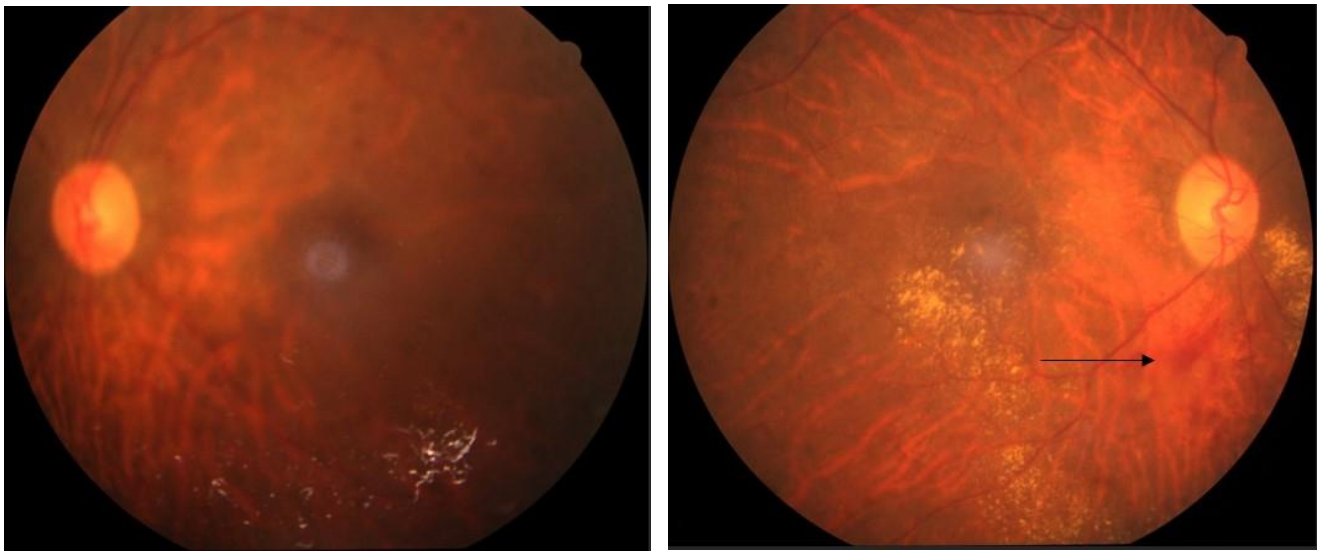

Figure 1a and 1b - Grade 3 Hypertensive retinopathy, in a patient with CKD undergoing hemodialysis. Superficial haemorrhages are noted along the inferior vascular arcade (black arrow).

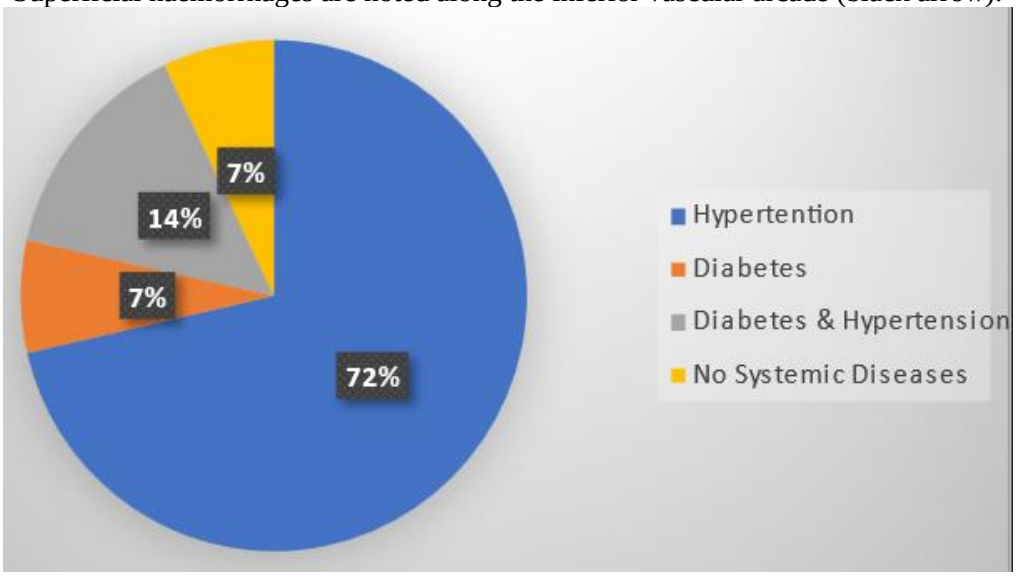

Chart 1: Prevalence of systemic diseases in patients with CKD on hemodialysis

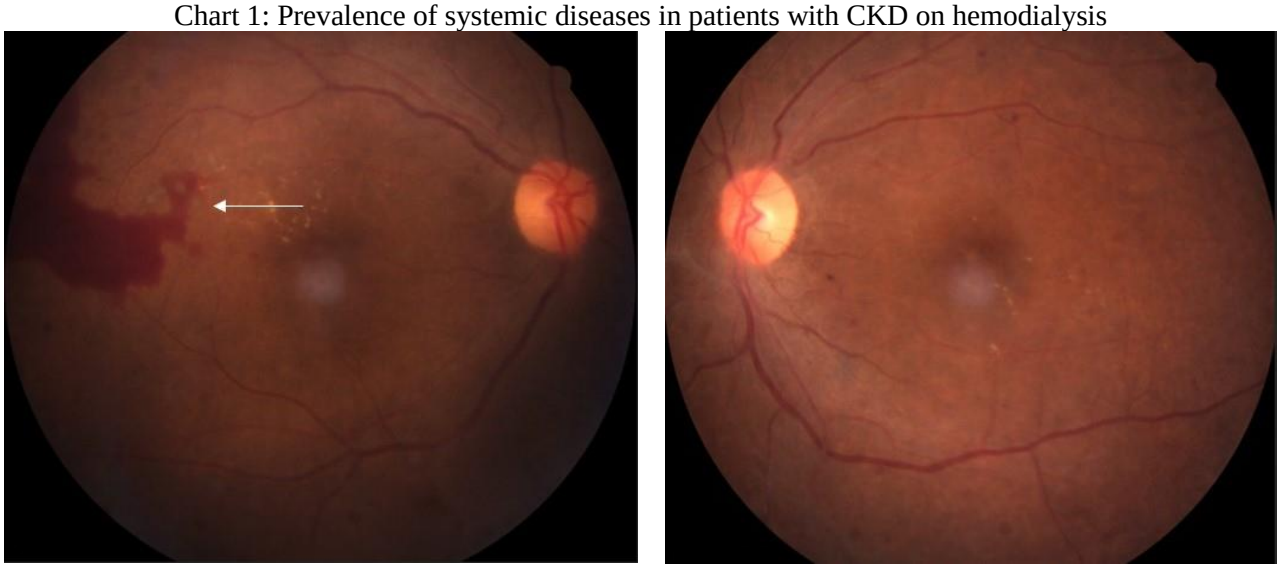

Figure 2a - Pre retinal hemorrhage (white arrow) in the right fundus of type 1 diabetic, which developed during her course of hemodialysis. There are hard exudates in the macula involving the foveal centre. Figure

2b - Proliferative Diabetic Retinopathy left eye post pan retinal photocoagulation status.

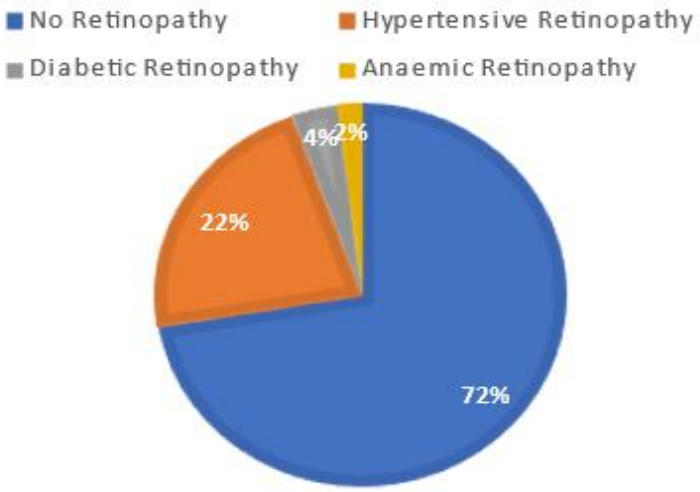

Chart 2: Prevalence of Retinopathy in patients with CKD on hemodialysis

We noted fresh pre retinal haemorrhage in a 43 year old type 1 diabetic [Fig 3a and 3b], a known case of proliferative diabetic retinopathy post laser status during her course of hemodialysis. She was advised fill in laser and a more frequent retinal examination (2 monthly)

The frequency of hemodialysis of these patients were twice a week. Two patients had pleural effusion and this necessitated thrice a week regimen of hemodialysis. Of the blood parameters, the mean value of urea was 93.8 $\pm$ 47.3, creatinine 10.2 $\pm$ 3.5. All the patients on hemodialysis were anaemic with the mean hemoglobin of 7.2 $\pm$ 1.9.

In the present study, longer duration of CKD was found to be significantly high among the cases with retinopathy; cases with hypertension and diabetes mellitus were found to have retinopathy compared to non-hypertensive and non-diabetic CKD cases. However, parameters like age, gender, bronchial asthma, IHD, anaemia, frequency of dialysis, vitals and laboratory parameters were found to be similar among the cases with and without retinopathy [Table 1].

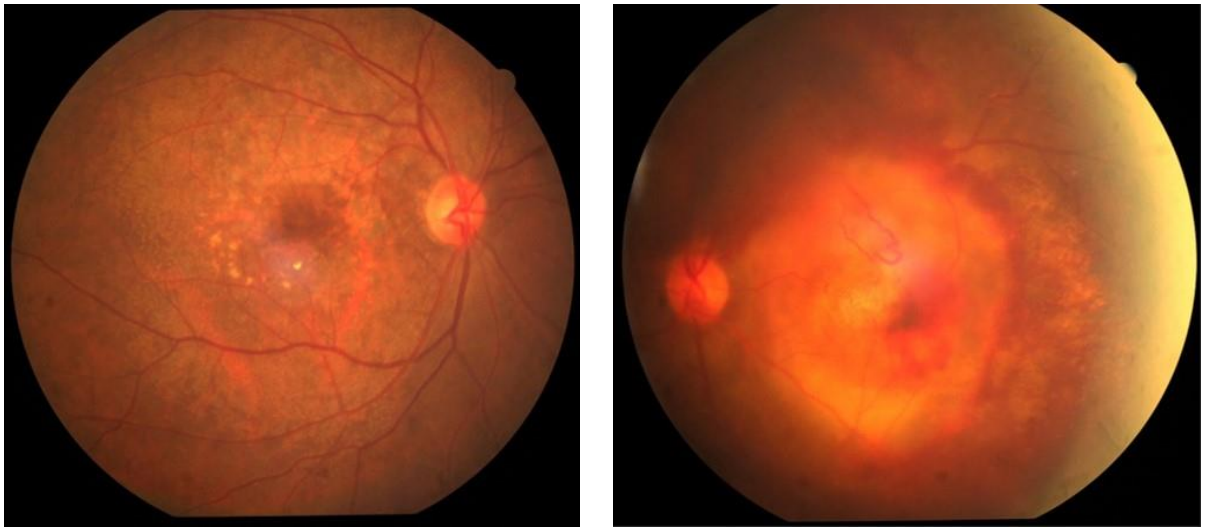

Figure 3a and 3b - Fundus picture showing Dry ARMD in the right eye and exudative ARMD in the left eye.

Table 1: Comparison of Clinical Parameters with Retinopathy

Comparison of Clinical Parameters with Retinopathy							p value <0.05 is significant
No.	**Parameter**	**Retinopathy present N=15**		**Retinopathy absent N=13**		**P Value**	
1	Mean age (years)	53.75(+/-)4.6		50.36(+/-)13.8		0.3775	
2	Gender						
	Male	11	39.3%	7	25.0%	0.2831	
	Female	4	14.2%	6	21.4%		
3	Weight						
	Male	60.1(+/-)9.4		53.7(+/-)13.4		0.1512	
	Female	46.7(+/-)5.1		58.8(+/-)21.4		0.0431	
4	Duration of CKD (months)	41.3(+/-)21.5		60.0(+/-)29.4		0.0634	
5	Duration of Haemodialysis (months)	29.9(+/-)21.4		20.9(+/-)19.8		0.2612	
6	Duration of Hypertension(months)	6.6(+/-)5.6		3.3(+/-)1.5		0.0499	
7	Duration of Diabetes(months)	14.0(+/-)5.3		20		0.0061	
8	Lab Parameters						
	Urea	96.2(+/-)33.0		110.4(+/-)44.5		0.3422	
	Creatinine	9.7(+/-)3.8		9.9(+/-)3.6		0.8879	
	Haemoglobin	6.3(+/-)0.8		8.4(+/-)3.0		0.0147	
9	Vitals						
	Systolic Blood pressure	145(+/-)9.7		133(+/-)20.0		0.0491	
	Diastolic Blood pressure	83(+/-)4.8		82.2(+/-)10.9		0.7989	
	Pulse Rate	79(+/-)2.2		76.6(+/-)2.9		0.0196	

4. Discussion

Of the 28 patients with CKD stage 5 on hemodialysis who were studied for the prevalence of retinopathy. 20 (71.4%) patients were hypertensives. This concurred with the observation by Naikar *et al* [21] that in under developed countries, HT contributed more to CKD than DM whereas DM contributed more to CKD in developed countries. In India, the prevalence of HT in CKD is 64.5% and DM in CKD is 31.6% and there is a male preponderance. [22] There was a male preponderance with 18 subjects being male and 11 (39.3%) of them having retinopathy in our study.

The mean age of CKD was also in a younger age group. Apart from hypertension and diabetes, there was no other systemic disease that caused CKD in these patients.[23] The study also found that patients with HT progressed to CKD much earlier than diabetes and the retinopathy in these patients was not as advanced as in the case of diabetic retinopathy. The mean duration of hypertension in CKD was 4 years and 8 months and the most common hypertensive retinopathy was of grade 1(66.6%). Cases with both DM and HT were found to have advanced retinopathy in comparison to cases of either DM or HT alone. Parameters such as age, gender, bronchial asthma, IHD, vital signs, and laboratory parameters were found to be similar between the cases with and without retinopathy. Ocular findings such as intraocular pressure, BCVA, and lens pathologies were also found to be similar between the cases with and without retinopathy.

Gao B *et al* [24] reported that individuals with chronic kidney disease exhibited a greater prevalence of retinopathy, glaucoma suspect, ARMD, and general ocular disease than people without CKD. Wang TJ *et al* [25] also looked at the frequency and risk of a few specific ocular co-morbidities in CKD patients and found that patients with CKD had remarkably higher rates of retinopathy (16.62% vs. 9.70%) than patients without CKD. They also concluded that patients with CKD had a significantly higher incidence of retinal abnormalities, uveitis, glaucoma, and cataract than patients without CKD. Liew *et al* [26] inferred that CKD increases the risk of ARMD. In our study, we found two patients with ARMD with significant involvement of macula in one.

Shafi ST *et al*, [27] found that patients with CKD who were not receiving hemodialysis or peritoneal dialysis were at a higher risk of developing both diabetic and hypertensive retinopathy. The study included 124 patients

in total. The prevalence of stage V CKD was 85.7%. Of these patients, 67% had DM. Of these, 46.4% had DR. 69.1%, (NPDR)10.2%, and 23.1% of patients, respectively, had non-proliferative diabetic retinopathy, proliferative diabetic retinopathy (PDR), and macular edema. The patients with HR were found in 49.5% of cases. Of these patients, 31.3% had Grade I HR, whereas 41.2% had Grade II, 21.6% had Grade III, and 5.8% had Grade IV. They reported a higher incidence of grade 2 HR whereas we found a higher incidence of grade 1 HR. The patients with HR had a higher systolic and diastolic blood pressure than those without retinopathy and the systolic parameter was statistically significant.

We did not have any case of vasculitis as a cause of CKD in our study group. A possible explanation could be that the patients with vasculitis undergo treatment in government hospitals where the cost of treatment is subsidised and could have been missed.

All the study participants were found to have anaemia. Only one patient was identified to have anaemic retinopathy in association with hypertensive retinopathy. Anaemia is defined by WHO as hemoglobin (Hb) less than <12 g/dL in women and <13 g/dL in men. The mean HB amongst the CKD patients in our study was 6.3% in patients with retinopathy and 8.4% in patients without retinopathy which was statistically significant.[28] Anaemia in CKD is attributed to reduced production of erythropoietin. The presence of anaemia not only causes compromise on the quality of life but also increases the cardiovascular morbidity and mortality in patients with CKD.[29]

Screening protocols have been established for DR but not for HR. Screening for DR is recommended annually when there is no DR, again annually in mild DR, every six months in moderate DR, every three months in severe sight threatening DR. [30]

5. Conclusion

This study is a pilot study undertaken among participants who were of low socio-economic status and carried out in a low resource setting. CKD impairs the quality of life. Presence of anaemia, sight threatening retinopathy further compounds morbidity. Patients with CKD, especially those with end stage CKD on hemodialysis, should be encouraged to have a comprehensive eye examination. We recommend retinal screening to be performed in the hemodialysis unit itself. In patients undergoing hemodialysis, a more vigorous retinal screening protocol can be followed. Since Hypertensives progress to CKD earlier, fundus examination should be made mandatory in these patients to rule out HR. Half yearly retinal examination can be initiated in patients undergoing hemodialysis. Those with sight threatening DR can be followed every two months than the usual three months to detect progression. Vision testing, slit lamp biomicroscopy and dilated fundus examination and appropriate management or referral would help preserve vision and enhance the quality of life in these patients.

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