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A study to correlate hypertensive retinopathy with chronic kidney disease

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Abstract
Background: Chronic Kidney Disease (CKD) is characterized by abnormalities in kidney structure or function, with albuminuria >3 mg/mmol and Glomerular Filtration Rate (GFR) <60 ml/min/1.73 m² for more than three months. Hypertensive nephropathy can lead to end-stage renal disease (ESRD) requiring renal replacement therapy for survival. This study aims to investigate the correlation between hypertensive retinopathy and CKD.
Methods: The study was conducted from January 2016 to June 2017 at Vydehi Institute of Medical Sciences, Bangalore, involving 100 clinically diagnosed CKD patients. Comprehensive ophthalmological examinations, including visual acuity, slit lamp biomicroscopy, intraocular pressure measurement, and fundus examination, were performed. Blood pressure and several blood tests, including serum creatinine, were also conducted to calculate GFR using the Cockcroft-Gault formula. CKD and hypertensive retinopathy were graded according to established classifications.
Results: The study found a significant correlation between hypertensive retinopathy and CKD (P-value <0.001). A decrease in GFR was associated with increased severity of both CKD and hypertensive retinopathy.
Conclusion: The study concluded that hypertensive retinopathy is prevalent in CKD patients, and the severity of hypertensive retinopathy and CKD are inversely proportional to GFR levels.

Keywords: Chronic kidney disease, hypertensive retinopathy, glomerular filtration rate, hypertensive nephropathy, end-stage renal disease

Introduction

Chronic kidney disease (CKD) is a progressive and irreversible condition that ultimately results in end-stage renal disease (ESRD), necessitating renal replacement therapy for patient survival [1]. CKD encompasses various pathophysiological processes that lead to a progressive decline in glomerular filtration rate (GFR), with patients becoming reliant on dialysis or transplantation as their kidney function deteriorates [1].

CKD is intricately associated with aging, and its progression is often accelerated by hypertension, diabetes, obesity, and primary renal disorders [2]. A systematic review and meta-analysis conducted in 2016, which included 6,908,440 patients, highlighted the global prevalence of CKD at different stages. The study found that CKD has a global prevalence of 11-13%, with the majority of cases in stage 3. The prevalence of stages 1 to 5 was 13.4%, with 10.6% in stages 3 to 5 [4].

Hypertension, a significant public health issue worldwide, contributes substantially to the progression of CKD [5]. Poorly controlled hypertension can lead to complications affecting the cardiovascular and cerebrovascular systems, kidneys, and retina, collectively referred to as target organ damage (TOD) [6]. Hypertensive retinopathy, a manifestation of TOD, has long been recognized as a predictor of systemic morbidity and mortality. Epidemiological and clinical studies have demonstrated that markers of hypertensive retinopathy are associated with elevated blood pressure, systemic vascular diseases, and subclinical cerebrovascular and cardiovascular diseases. These markers also predict clinical stroke, congestive heart failure, and mortality due to cardiovascular complications. Importantly, the association between hypertensive retinopathy and other TOD has been shown to be independent of blood pressure and other risk factors, underscoring the importance of retinal vascular changes in risk stratification for individuals with systemic hypertension [6].

Assessing hypertensive nephropathy typically involves routine blood investigations, such as serum creatinine levels, microalbuminuria, and urine microscopy, as well as renal biopsy. However, these methods can be costly and carry procedure-related risks.

Fundoscopy, a non-invasive and cost-effective clinical tool, is recommended in the routine management of hypertensive patients to assess retinal vessels, which are end vessels. This method can be valuable in evaluating the severity of nephropathy. Nonetheless, the utility of fundoscopy as a screening tool for nephropathy has been debated and is considered by some to offer limited additional value [7].

This study aims to evaluate the efficacy of fundoscopy as a screening tool for nephropathy in hypertensive patients, exploring its potential role in the early detection and management of hypertensive nephropathy. By correlating hypertensive retinopathy with chronic kidney disease, we hope to provide insights into its use as a cost-effective, non-invasive method for assessing nephropathy severity in hypertensive individuals.

Objective

To correlate hypertensive retinopathy with chronic kidney disease.

Materials and Methods

This duration-based cross-sectional observational study was conducted from January 2016 to June 2017 in the Department of Ophthalmology at Vydehi Institute of Medical Sciences, Bangalore. It included 100 patients diagnosed with chronic kidney disease (CKD), all of whom provided written consent after meeting the inclusion and exclusion criteria.

The study included patients with CKD and pre-existing essential hypertension. Exclusion criteria were diabetes mellitus, retinal vascular abnormalities (excluding hypertensive retinopathy), CKD secondary to glomerulonephritis and systemic sclerosis, and congenital kidney anomalies.

Methodology

An ophthalmological examination was performed on all patients, which included the assessment of visual acuity (BCVA) using Snellen's chart for distance vision and Jaeger's chart for near vision. Anterior segment examination was conducted using a slit lamp biomicroscope. Intraocular pressure was measured using Goldmann's applanation tonometry. Blood pressure was measured using a sphygmomanometer in both sitting and supine positions. The pupils of both eyes were dilated with 1% tropicamide, and a detailed fundus examination of both eyes was done using direct ophthalmoscopy with 78D and 90D lenses and indirect ophthalmoscopy with a +20D lens.

The following investigations and interventions were performed on CKD patients visiting the outpatient department: haemoglobin%, CBC, ESR, blood sugar (FBS, PPBS), urine spot PCR (protein-creatinine ratio), serum albumin, serum urea, urinary volume, serum creatinine (normal levels: 0.6 to 1.2 mg/dL in adult males and 0.5 to 1.1 mg/dL in adult females), serum calcium, serum phosphate, serum electrolytes, ultrasound abdomen, urine routine and microscopy, and lipid profile.

The glomerular filtration rate (GFR) was calculated for males using the formula:

$$\frac{(140 - \text{age}) \times \text{body weight (kg)}}{(72 \times \text{serum creatinine})},$$

and for females using the formula:

$$\frac{(140 - \text{age}) \times \text{body weight (kg)} \times 0.8}{(72 \times \text{serum creatinine})}.$$

Chronic kidney disease was staged based on the chronic kidney disease classification by Cockcroft–Gault on GFR levels (ml/min/1.73 m²).

Statistical analysis

Statistical analysis was conducted using STATA 11.2 (College Station, TX, USA). The association between hypertensive retinopathy grade and CKD stages was measured using the Chi-square test and expressed as frequency and percentage. The Shapiro-Wilk test checked normality. One-way ANOVA assessed the significance of differences between GFR rate with CKD stages and hypertension grades, expressed as mean and standard deviation. A p-value of <0.05 was considered statistically significant.

Results

Table 1: Gender and age distribution of cases.

Gender	**Number of cases**	**Percentage**
Male	67	67%
Female	33	33%
Total	100	100%
Age group	**Number of cases**	**Percentage**
<40	38	38%
≥40	62	62%
Total	100	
Mean age	46.04 (15.72)	(8-75) years

The study included 100 participants, with 67 males (67%) and 33 females (33%). Age distribution showed 38 participants (38%) under 40 years and 62 participants (62%) aged 40 and above. The mean age was 46.04 years (SD 15.72), ranging from 8 to 75 years.

Table 2: Grade of CKD

	Number of cases	**Percentage**
Stage I	0	0%
Stage II	9	9%
Stage III	21	21%
Stage IV	15	15%
Stage V	55	55%
Total	100	

The study classified 100 participants by CKD stage: 0% in Stage I, 9% in Stage II, 21% in Stage III, 15% in Stage IV, and 55% in Stage V. The majority of participants (55%) were in the most severe stage, Stage V.

Table 3: Prevalence of hypertension with ckd

	Stage I	Stage II	Stage III	Stage IV	Stage V	Total	P-value
Grade I	0	0	1 (5%)	0	0	1 (1%)	0.001
Grade II	0	7 (78%)	12 (57%)	7 (47%)	10 (18%)	36 (36%)	
Grade III	0	2 (22%)	4 (19%)	5 (33%)	39 (71%)	50 (50%)	
Grade IV	0	0	4 (19%)	3 (20%)	6 (11%)	13 (13%)	
Total	0	9 (9%)	21 (21%)	15 (15%)	55 (55%)	100	

In Stage I, there were no cases of hypertension. In Stage II, 78% of participants had Grade II hypertension and 22% had Grade III hypertension. Among Stage III participants, 5% had Grade I, 57% had Grade II, 19% had Grade III, and 19% had Grade IV hypertension. For Stage IV, 47% had Grade II, 33% had Grade III, and 20% had Grade IV hypertension. In Stage V, 18% of participants had Grade II, 71% had Grade III, and 11% had Grade IV hypertension. Overall, the distribution showed that 1% of participants had Grade I, 36% had Grade II, 50% had Grade III, and 13% had Grade IV hypertension. The p-value of 0.001 indicates a statistically significant difference in the prevalence of hypertension across CKD stages.

Table 4: CKD stages with GFR value

CKD stages	N	GFR value (mean±SD)	P-value
Stage i	0	0	<0.001
Stage ii	9	69.55±10.71	
Stage iii	21	37.28±5.32	
Stage iv	15	19.73±6.18	
Stage v	55	6.76±2.98	

The study analyzed the glomerular filtration rate (GFR) values across different stages of chronic kidney disease (CKD). In Stage I, no participants were included. In Stage II, the mean GFR was 69.55±10.71. For Stage III, the mean GFR was 37.28±5.32. In Stage IV, the mean GFR was 19.73±6.18. In Stage V, the mean GFR was significantly lower at 6.76±2.98. The p-value of less than 0.001 indicates a statistically significant difference in GFR values across the different CKD stages.

Table 5: Grade of hypertension with stage CKD

	Stage I	Stage II	Stage III	Stage IV	Stage V	Total	P value
Grade I	0	0	1 (5%)	0	0	1 (1%)	0.001
Grade II	0	7 (78%)	12 (57%)	7 (47%)	10 (18%)	36 (36%)	
Grade III	0	2 (22%)	4 (19%)	5 (33%)	39 (71%)	50 (50%)	
Grade IV	0	0	4 (19%)	3 (20%)	6 (11%)	13(13%)	
Total	0	9(9%)	21 (21%)	15 (15%)	55 (55%)	100	

Table 5 shows the distribution of hypertension grades across CKD stages. In Stage I, there's only one case of Grade III hypertension. Stage II primarily has Grade II hypertension (78%) with some Grade III (22%). Stage III shows a mix with Grade II (57%) and Grade III (19%), and some Grade IV (19%). In Stage IV, Grade II decreases (47%), while Grade III (33%) and Grade IV (20%) increase. Stage V has the highest Grade III hypertension (71%) and some Grade IV (11%). The P-value of 0.001 indicates a significant relationship between hypertension grades and CKD stages.

Table 6: Grade of hypertension with stage CKD

	Stage I	Stage II	Stage III	Stage IV	Stage V	Total	P value
Grade I	0	0	1 (5%)	0	0	1 (1%)	0.001
Grade II	0	7 (78%)	12 (57%)	7 (47%)	10 (18%)	36(36%)	
Grade III	0	2 (22%)	4 (19%)	5 (33%)	39 (71%)	50(50%)	
Grade IV	0	0	4 (19%)	3 (20%)	6 (11%)	13(13%)	
Total	0	9 (9%)	21 (21%)	15 (15%)	55 (55%)	100	

Table 6 shows the distribution of hypertension grades across CKD stages. In Stage I, there is only one case of Grade III hypertension. Stage II has 78% with Grade II and 22% with Grade III. Stage III has a mix of 57% with Grade II, 19% with Grade III, and 19% with Grade IV. In Stage IV, Grade II is at 47%, Grade III at 33%, and Grade IV at 20%. Stage V has a high prevalence of Grade III hypertension (71%) and some Grade IV (11%). The total number of patients is 100, with a significant P-value of 0.001, indicating a notable relationship between hypertension grades and CKD stages.

Discussion

In this study, chronic kidney disease (CKD) in 100 patients was examined in the Department of Ophthalmology at Vydehi Institute of Medical Sciences and Research Centre, Whitefield, Bangalore. Of these patients, 67 were males and 33 were females, constituting 67% and 33% of the total CKD cases, respectively. This gender distribution aligns with findings from Kunitoshi Iseki *et al*., [8] who observed a higher incidence and prevalence of end-stage renal disease (ESRD) in men than in women. Additionally, Idan Goldberg *et al*. [9] noted a higher prevalence of chronic renal failure in women (15.1%) compared to men (12.1%), with women also having higher urinary albumin-to-creatinine ratios and lower glomerular filtration rates (GFR). In the study by Li, Jun, *et al*., [10] involving 1070 males and 1894 females, the

mean age of the participants was 63.5 ± 7.3 years.

The age distribution of the study participants ranged from 8 to 75 years, with 38% being under 40 and 62% being 40 or older. The mean age was 46.04 years with a standard deviation of 15.72. This corresponds with findings from Qiu-Li Zhang *et al*., [11] who reported a median CKD prevalence of 7.2% in individuals aged 30 or older, and higher prevalence rates in those aged 64 or older.

CKD staging in the study revealed that 55% of patients were in stage 5, 15% in stage 4, 21% in stage 3, and 9% in stage 2. No patients were found in stage 1. Hypertensive retinopathy was prevalent among these patients, with 50% exhibiting grade 3 retinopathy, most commonly in stage 5 CKD (71%). Grade 2 retinopathy was present in 36% of patients, predominantly in stage 2 CKD (78%). Grade 4 retinopathy was seen in 13% of patients, mostly in stage 5 CKD (11%). Only 1% had grade 1 retinopathy, found in stage 3 CKD.

The correlation between GFR and CKD severity was evident. Stage 5 CKD patients had a mean GFR of 6.76±2.98 ml/min/1.73m², stage 4 had 19.73±6.18 ml/min/1.73m², stage 3 had 37.28±5.32 ml/min/1.73m² and stage 2 had 69.55±10.71 ml/min/1.73m². No stage 1 CKD patients were observed. This inverse relationship between GFR and CKD stage is consistent with findings from Christian Thomas *et al*., [12] who emphasized the clinical importance of early recognition of low GFR to prevent progression to end-stage renal failure.

Hypertensive retinopathy grades showed a positive correlation with CKD stages. Grade 3 hypertensive retinopathy was most prevalent in stage 5 CKD, while grade 2 retinopathy was more common in earlier stages. The severity of retinopathy also correlated with lower GFR values. Grade 4 hypertensive retinopathy patients had a mean GFR of 18.57±15.02 ml/min/1.73m², grade 3 had 13.20±16.83 ml/min/1.73m², and grade 2 had 31.82±21.68 ml/min/1.73m². Grade 1 retinopathy was rare, with a GFR of 30 ml/min/1.73m². Suryachandra, M., *et al*. [13] also demonstrated that advanced stages of CKD are highly affected by hypertensive retinopathy changes. Out of 104 eyes, hypertensive retinopathy changes were seen in 13.46% of Stage 3 CKD patients, 9.6% of Stage 1 CKD patients, and 7.69% of Stage 2 CKD patients. Similarly, Chillo P, *et al*. [14] reported that the proportions of patients with stage 3, 4, and 5 CKD were 21.4%, 19.6%, and 58.9%, respectively. Hypertensive retinopathy was present in 157 (70.1%) of these patients, with the proportions for grade I, grade II, grade III, and grade IV retinopathy being 17.9%, 18.8%, 19.6%, and 13.8%, respectively.

This study confirms that the severity of hypertensive retinopathy is closely linked to the severity of CKD and reduction in GFR. Grunwald Juan E. *et al*. [15] also reported a strong association between retinopathy severity and kidney function, suggesting that retinovascular pathology reflects renal disease. These findings underscore the importance of monitoring retinopathy and GFR in CKD patients to manage disease progression effectively.

Limitations

The study has several limitations:

1. The study included only 100 patients, which may limit the generalizability of the findings.
2. It was conducted at a single institution, which may not represent broader populations.
3. The study design only provides a snapshot of CKD and hypertensive retinopathy, without tracking changes over time.
4. Patients with diabetes mellitus and certain kidney anomalies were excluded, potentially missing relevant data on these conditions.
5. The study did not track the progression of CKD or retinopathy over time, limiting insights into disease progression.
6. The study did not include some clinical parameters that could affect CKD and retinopathy, such as medication use and lifestyle factors.

Conclusion

This study highlights a significant association between chronic kidney disease (CKD) stages and hypertensive retinopathy. A higher prevalence of severe retinopathy grades was observed in patients with advanced CKD stages, indicating that worsening kidney function correlates with increased severity of hypertensive retinopathy. The study also confirmed that lower glomerular filtration rates (GFR) are associated with more severe retinopathy. These findings suggest that regular ophthalmological evaluations could be beneficial for CKD patients to monitor and manage retinal changes and potentially slow disease progression. Further research with larger and more diverse populations is needed to validate these results and explore the underlying mechanisms connecting CKD and retinopathy.

Conflict of Interest

Not available

Financial Support

Not available

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