Posterior Segment changes of eyes in Diabetic patients undergoing Hemodialysis: An Observational study.

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KEYWORDS

Hemodialysis, Diabetes mellitus, Diabetic retinopathy.

ABSTRACT:

Background:

Renal and retinal circulations share similar anatomic, physiologic and pathologic features; hence evaluating the retinal microvasculature can help identify early microcirculatory changes associated with Chronic kidney disease (CKD). In End-stage renal disease (ESRD) visual system is affected as a result of uraemia, metabolic imbalance, hypertension or hemodialysis (HD). One of the major risk factor for ESDR is Diabetes mellitus (DM), and it's prevalence has increased in India. Diabetic retinopathy (DR) and nephropathy are two frequent complications of DM and they add burden of CKD and blindness respectively. Objectives of the study were to assess the posterior segment status of eye and severity of diabetic retinopathy in diabetics undergoing hemodialysis.

Methods:

Observational cross-sectional study was conducted in the Nephrology Unit at a tertiary care hospital and included 120 diabetics undergoing hemodialysis twice weekly. Ocular examination included visual acuity using Snellen's chart, Intra ocular pressure (IOP) using applanation tonometry and posterior segment evaluation after dilating with tropicamide and phenylephrine.

Results:

Mean age of diabetic patients undergoing dialysis was 55.77 years with SD of 9.42. 65% of the patients were known to be diabetic for duration of less than 5 years. Moderate NPDR (37.91%) constituted the major group, followed by mild NPDR (23.33%) and severe NPDR (18.33%).76 eyes (31.66%) showed clinically significant macular edema (CSME). Association between diabetic retinopathy severity and duration of DM was found to be significant (P value = 0.028). Association of duration of hemodialysis and severity of DR was also significant (P value = 0.037).

Conclusions:

Moderate NPDR is the most common retinopathy in patients undergoing hemodialysis. Significant association was noted between duration of DM and severity of DR and between duration of HD and severity of DR. It is important for patients with diabetic ESRD to undergo ophthalmological evaluation regularly prior to the development of irreversible vision loss.

Main Manuscript Text:

Background

Eye is a mirror that reflects the pathological changes occurring in many parts of the body. Examination of eye is important part of clinical assessment of the patient with renal disorder. "End-stage renal disease (ESRD), with a glomerular filtration rate lower than 15 ml/ (min*1.73 m), is the 5th stage of disease and the final outcome of disease progression in chronic kidney disease (CKD) patients." a variety of clinical

manifestations, such as hypertension, anemia, and edema, and metabolic and endocrine disorders can occur in this stage; thus, renal replacement therapy, such as hemodialysis (HD), is needed to remove excess water and metabolic wastes from the extracorporeal blood and to maintain the electrolyte and acid-base balance.[1]

Renal and retinal circulations share similar anatomic, physiologic and pathologic features; hence assessment of retinal microvasculature gives opportunity to find early microcirculatory changes associated with chronic kidney disease. In ESRD visual system is affected as a result of uraemia, metabolic imbalance, hypertension or HD.[2]

Chronic kidney disease leads to a lot of systemic effects that affects a variety of systems in the body. The eye also shows changes due to long standing kidney disease. Some systemic diseases such as diabetes, hypertension (HTN) and autoimmune disorders affect the kidneys as well as the eye. Ocular manifestation occurs as a result of the primary diseases causing renal failure or as a result of the secondary effects of renal failure itself.[3]

Diabetes mellitus is one of the major risk factors causing ESRD and its prevalence has increased in India. Diabetic retinopathy and nephropathy are two frequent complications of diabetes mellitus, and they add burden of CKD and blindness respectively. Some authors have found association between complications and one complication being risk factor for the other. Some of the posterior segment changes in ESRD are retinopathy, Central Retinal Vein Occlusion (CRVO), Branch Retinal Vein Occlusion (BRVO), Central Retinal Artery Occlusion (CRAO), disc edema and glaucomatous optic atrophy. Among them deterioration of eyesight is mainly due to worsening of diabetic or hypertensive retinopathy. Blindness due to proliferative retinopathy or maculopathy is approximately five times more common in diabetic patients with nephropathy compared with normoalbuminuric patients. Diabetic retinopathy (DR) tends to deteriorate with falling renal function, poorly controlled blood pressure and in patients in whom no retinal treatment has been given before.[4,5]

The negative impact of CKD on the patient's eye is complex and diverse. Studies have shown that HD, as a relief and treatment of CKD, can improve certain ocular symptoms in ESRD patients. It has been reported that best corrected visual acuity (BCVA) improves after a single HD session, and patients with diabetes tend to have more obvious improvements.[6]

Studies have reported that HD can relieve macular edema in patients with kidney failure caused by diabetes.[7] However, in most cases, the negative impact of hemodialysis on the eye in CKD patients seems to be far beyond its positive impact, and it can cause macular edema, ishemic optic neuropathy, retinal haemorrhages and retinal detachments.[8]

Retinopathy is often asymptomatic in its most treatable stage; delay in diagnosis can result in significant increase in the patient's risk of visual loss. Ocular condition is also an indicator of the metabolic control of the disease process. Similarly, an unknown case of chronic renal failure, with its ocular complications, may first present to an ophthalmologist. The objective of the study was to access the posterior segment status of eye and to access the severity of diabetic retinopathy among diabetics undergoing HD and to determine the importance of ocular examination so that necessary treatment /advice can be given at proper time before irreversible visual loss occur.

Methodology

This was a hospital-based observational cross-sectional study conducted in the Nephrology Unit and outpatient department of ophthalmology at a tertiary care hospital, in Mandya, a Southern Indian district, in 2019. In the dialysis unit, 80 patients were undergoing hemodialysis in a month, twice weekly. On daily basis three sessions were carried out. New input of patients every month was three, on an average since past 6 months prior to the study. Taking into consideration mortality and patient's refusal,

study included 120 diabetics undergoing hemodialysis twice weekly. They were evaluated for posterior segment changes in their eyes. The study was initiated after obtaining approval from the Institutional Ethics Committee. The patients were explained the importance of ocular examination, the plan and intention of the study in the language best known to them. Written informed consent was obtained. Detailed history was taken regarding their complaints, duration of dialysis, duration of diabetes and other co-morbidities and ocular examination was conducted. Diabetics were defined according to the American Diabetes Association guidelines: Fasting plasma glucose >126 mg/dl, 2-hour Post prandial blood glucose > 200 mg/dl, HbA1c> 6.5% and Random blood sugar > 200 mg/dl. Type 2 diabetics defined patients on diet therapy or oral hypoglycemic agents for control of sugars. If on insulin therapy, should have onset of diabetes after 40 years, with body wait excess than ideal at the time of diagnosis. Ocular examination included visual acuity using Snellen's chart, Intra ocular pressure (IOP) using applanation tonometry and posterior segment was evaluated using direct ophthalmoscope, indirect ophthalmoscope, slit lamp using 90D after dilating with tropicamide and phenylephrine. Diabetic retinopathy was graded using Early Treatment Diabetic Retinopathy Study (ETDRS) system.

The statistical analysis was done using the SPSS software. Descriptive statistics like percentage, mean, standard deviation was used to describe results. Chi square test / fisher exact test was used as and when required for finding the association between various parameters, and $p<0.05$ was considered statistically significant.

Results

A total of 120 diabetics undergoing hemodialysis twice weekly were included in the study. Table:1 presents the demographic and clinical characteristics of the study participants. A majority of participants were aged between 51 to 60 years (34.17%), followed by 41 to 50 years (31.67%), 61 to 70 years (29.16%) and a small proportion aged 71 to 80 years (5.00%). Males constituted a majority 63.33%, while females accounted for 36.67%. In terms of the duration of diabetes mellitus, a majority of study participants reported having diabetes for 0–5 years (65.00%), followed by 6–10 years (20.83%) and 11–15 years (14.17%).

Table 1: Demographic and clinical characteristics of the study participants.

	No. of participants (n = 120)	**Percentage**
Age (in years)		
41 - 50	38	31.67 %
51 - 60	41	34.17 %
61 - 70	35	29.16 %
71 - 80	6	5.00 %
Sex		
Male	76	63.33 %
Female	44	36.67 %
Duration of Diabetes Mellitus		
0 - 5	78	65.00 %
6 - 10	25	20.83 %
11 - 15	17	14.17 %

Table:2 shows grading of diabetic retinopathy changes according to ETDRS classification. Out of 240 eyes (120 subjects), 20 eyes (8.33%) had no diabetic retinopathy changes, whereas 220 eyes (91.67%) had diabetic retinopathy. Moderate NPDR (37.91%) constituted the major group, followed by mild NPDR (23.33%) and

severe NPDR (18.33%). Advanced diabetic eye disease was seen in 3 eyes (1.25%). There were no patients with advanced diabetic eye disease in the left eye.

Table 2: Distribution of severity of diabetic retinopathy of the study participants.

Severity of diabetic retinopathy	No. of eyes		
	Right eye (n = 120)	Left eye (n = 120)	Both eyes (n = 240)
No retinopathy	9 (7.50%)	11 (9.17%)	20 (8.33%)
Mild NPDR	28 (23.33%)	28 (23.33%)	56 (23.33%)
Moderate NPDR	45 (37.50%)	46 (38.33%)	91 (37.92%)
Severe NPDR	18 (15.00%)	26 (21.67%)	44 (18.33%)
Very severe NPDR	2 (1.67%)	2 (1.67%)	4 (1.67%)
Early PDR	11 (9.17%)	5 (4.16%)	16 (6.67%)
High risk PDR	4 (3.33%)	2 (1.67%)	6 (2.50%)
Advanced diabetic eye disease	3 (2.50%)	0 (0%)	3 (1.25%)

Table:3 shows that among 240 eyes of study subjects undergoing hemodialysis, 76 eyes (31.66%) showed clinically significant macular edema (CSME). Out of 76 eyes, CSME was predominantly seen in eyes with Severe NPDR 29 (38.16%) and Moderate NPDR 26 (34.21%). CSME was least in eyes with Mild NPDR, very severe NPDR and advanced diabetic eye disease with 2.63% in each group.

In our study we found posterior segment changes other than diabetic retinopathy. Among them normal fundus was the predominant posterior segment change. Hypertensive retinopathy was seen in 36 eyes (15.00%), vein occlusions like BRVO was seen in 2 eyes (0.83%) and CRVO in one eye. Exudative retinal detachment was seen in one eye (0.41%). 3 eyes (1.25%) had tractional retinal detachment. In 6 eyes (2.50%) posterior segment changes could not be seen due to hazy media.

Table 3: Distribution of clinically significant macular edema in association with the severity of diabetic retinopathy in both eyes.

Severity of diabetic retinopathy	No. of right eyes with CSME (n = 38)	No. of left eyes with CSME (n = 38)	Total (n = 76)
WNL	0 (0%)	0 (0%)	0 (0%)
Mild NPDR	1 (2.63%)	1 (2.63%)	2 (2.63%)
Moderate NPDR	12 (31.58%)	14 (36.84%)	26 (34.21%)
Severe NPDR	12 (31.58%)	17 (44.74%)	29 (38.16%)
Very severe NPDR	1 (2.63%)	1 (2.63%)	2 (2.63%)
Early PDR	9 (23.68%)	4 (10.53%)	13 (17.11%)
High risk PDR	1 (2.64%)	1 (2.63%)	2 (2.63%)
Advanced diabetic eye disease	2 (5.26%)	0 (0%)	2 (2.63%)

Table:4 shows relationship between duration of diabetes and severity of diabetic retinopathy. In our study majority of patient undergoing HD had duration of DM less than 5 years, followed by 6 - 10 years and 11 - 15 years. Majority of the patients had NPDR changes in their eyes, followed by PDR and advanced diabetic eye disease. As the duration of diabetes increased, number of patients undergoing HD decreased. Association between diabetic retinopathy severity and duration of DM was significant with p value of 0.028.

Table 4: Distribution of diabetic retinopathy grade according to duration of diabetes mellitus.

Severity of Diabetic retinopathy	Duration of DM			Chi square (p value)
	0 - 5 years (n = 143)	6 - 10 years (n = 45)	11 - 15 years (n = 32)	
NPDR	132 (92.32%)	35 (77.78%)	28 (87.50%)	10.86 (p=0.028)
PDR	9 (6.29%)	10 (22.22%)	3 (9.38%)	
Advanced diabetic eye disease	2 (1.39%)	0 (0%)	1 (3.12%)	

Table:5 shows that majority, 75% of the patients had been undergoing hemodialysis for a duration of one year. Among them, 142 (86.06%) eyes had NPDR and 23 (13.93%) eyes had PDR changes. Among patients undergoing HD for more than a year (25%), NPDR changes were seen in 53 (96.36%) eyes and PDR in 2 (3.64%) eyes. Association between duration of hemodialysis and severity of DR was significant with a p value of 0.037.

Table 5: Distribution of severity of diabetic retinopathy according to duration of hemodialysis.

Severity of Diabetic retinopathy	< 1 year HD (n = 165)	> 1 year HD (n = 55)	Chi square (p value)
NPDR	142 (86.06%)	53 (96.36%)	4.34 (p = 0.037)
PDR	23 (13.93%)	2 (3.64%)	

Discussion

Out of 240 eyes (120 subjects), 20 eyes did not have diabetic retinopathy changes which constituted 8.33%, and whereas 220 eyes (91.67%) had diabetic retinopathy changes. Prevalence of diabetic retinopathy among diabetics on hemodialysis in the present study was found to be 91.67%. A study conducted by Bajracharya et al[9] found that, 7 diabetic patients undergoing dialysis had retinopathy changes in their eyes with the prevalence of 100%. Prevalence of diabetic retinopathy in diabetic patients on hemodialysis was 71.4% in Malleshwari et al[10] study and 73.68% (14 of 19) in study conducted by Mahmood et al[11]. The prevalence rates of DR in the present study are comparable to the other studies but due to small sample size of all the studies, prevalence may not be appropriate.

In the present study, moderate NPDR (37.91%) constituted the major group, followed by mild NPDR (23.33%) and severe NPDR (18.33%). Advanced diabetic eye disease was seen in 1.25%. Similar findings were seen in a study conducted by Sandhya et al[12], where majority of the eyes had NPDR changes (61.4%) including mild, moderate and severe NPDR. PDR changes were found in 38.6%.

In Bajracharya et al[9] study, NPDR was found in 71.2% and PDR in 28.5% of study participants. In Dahal P et al[13] study, prevalence of NPDR was 75% and PDR was 25%. In Mithun Thulasidas et al[2] study, prevalence of NPDR was 70.4% and PDR was 29.4%. In Malleshwari et al[10] study NPDR constituted 76.5% and PDR 23.5%. In our study majority of the patients were on dialysis for less than a year, hence retinopathy status was not severe. The other limitation in the study was that the status of diabetic retinopathy was not evaluated at initiation of hemodialysis and the influence of metabolic derangements associated with chronic kidney disease on retinopathy was not considered.

In the present study, among 240 eyes of study subjects undergoing hemodialysis, 31.66% of eyes had CSME. It was predominantly seen in eyes with severe NPDR (38.15%) and moderate NPDR (34.21%). CSME was least in eyes with mild NPDR. In study conducted by Sandhya et al[12], DME was found predominantly in eyes with DR of severe NPDR grade (46.7%) which was similar to our study findings.13 eyes (28.8%) had moderate NPDR retinopathy. 21 eyes (46.7%) with severe NPDR grade had DME and 11 eyes (24.5%) with PDR had DME. It is due to dilated and hyperpermeable capillaries at macula. It is not proportional to severity of retinopathy. It can be seen in any stage of retinopathy.

In the present study, among the subjects undergoing HD, majority (75%) of the patients had been undergoing HD for a duration of less than 1year. Most of them had NPDR changes. A significant association was seen between duration of HD and DR changes with the p value of 0.03. In a study conducted by Chougule et al[14], 14% of the patients had duration of dialysis more than 2 years and 32% of the patients had duration of <6 months. The remaining 24% of the patients had duration between 6 and 12 months and 16% of the patients had 12–18 months. In a study conducted by Sandhya et al[12], all diabetic patients were undergoing hemodialysis for the duration ranging from 2 months to 8 years. Majority of the patients had been undergoing hemodialysis for a duration of 1 month to 2 years (68.6%). It was observed from the study that as the duration of dialysis increased, the number of patients undergoing dialysis declined. This could be attributed to patient's poor compliance, low socioeconomic status, uncontrolled diabetes mellitus, hypertension, anemia, secondary infections, and mortality.

In our study majority of patients undergoing HD had duration of DM less than 5 years, followed by 6-10 years and 11-15 years. Majority of the patients had NPDR changes in their eyes, followed by PDR and advanced diabetic eye disease. Study showed statistically significant association between DR severity and duration of DM. In study conducted by Bansal P et al[15], presence of diabetic retinopathy was found to be minimal (9.44%) in less than 5 years of diabetes age. It was more in patients having diabetes of duration 20-25 years (76.47%) and in all patients with duration of diabetes more than 25 years. PDR was found to be present more in patients having DM of longer duration. In our study as the duration of diabetes increased, the number of eyes showing diabetic retinopathy changes decreased. This is because majority of the diabetics undergoing HD were within 5 years of diabetic duration, followed by duration in the range of 6-10 years, it could be attributed to increased mortality in ESRD.

Conclusions

Moderate NPDR was the most common retinopathy in patients undergoing hemodialysis. CSME contributed to visual morbidity. Significant association was noted between duration of diabetes mellitus, duration of hemodialysis and the severity of diabetic retinopathy. This emphasises the role of periodic ophthalmic examination in diabetic patients on hemodialysis for ESRD that may be helpful in early diagnosis of sight threatening diabetic retinopathy and maculopathy. Timely ophthalmic intervention in such patients can prevent visual loss.

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