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A Study of Ocular Manifestations in Diabetic Patients Undergoing Dialysis

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Abstract:

Background: Patients who have ESRD (End Stage Renal Failure) are susceptible to ophthalmic manifestations. This risk is linked to comorbidities such as diabetes mellitus, which is prevalent in ESRD patients, as well as the particular side effects of hemodialysis and the uremic state, which can result in alterations to the conjunctivae, cornea, retina, and macula. Very few studies were available regarding ophthalmic illness among diabetic patients undergoing dialysis. Hence, the present study was conducted to delve into the ocular problems among diabetic patients undergoing dialysis.

Methods: This was a cross-sectional observational study carried out in the Department of Ophthalmology in collaboration with the Department of Nephrology at SRM Medical College and Research Centre, Trichy, over a period of two years (November 2020 to October 2022) among 101 diabetic patients aged more than 20 years attending the nephrology department for dialysis.

Results: There was a statistically significant association of diabetic retinopathy with gender, education, socioeconomic status and residence. Duration of renal disease, duration of dialysis, and duration of DM were significantly associated with diabetic retinopathy, while there was no statistically significant association with stage of renal disease, type of DM, treatment taken for DM or obesity.

Conclusion: Our study concluded that diabetic patients with kidney disease undergoing hemodialysis had a higher proportion of ocular problems. Gender, education, socio-economic status and residence in addition to the duration of renal disease, dialysis, and diabetes were significantly associated with diabetic retinopathy. Further research into ophthalmic examinations both prior to and following hemodialysis would facilitate a better understanding of the effects of dialysis on the eyes.

Keywords: Diabetes Mellitus, ESRD, Hemodialysis, Ocular Manifestations.

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Introduction

The most frequent single condition producing ESRD that necessitates hemodialysis is T2DM (Type 2 Diabetes Mellitus). About 40% of patients who require renal replacement therapy have been found to have diabetic nephropathy. [1] Various visual parameters in ESRD patients may potentially change as a result of these changes. [2] Patients occasionally experience a sudden rise in IOP (Intraocular Pressure) during or after HD, which is accompanied by temporary blurred vision, eye pain, a headache, and other symptoms. Macular edema, ischemic optic neuropathy, retinal haemorrhage, retinal detachment, and other modifications can also be brought on by HD. [3] BCVA (Best Corrected Visual Acuity) has been shown to increase following a single haemodialysis treatment. [4]

According to certain studies, the CMT (Central Macular Thickness) can decrease or even stay the same after hemodialysis. According to other studies, SFCT (Subfoveal Choroidal Thickness) decreased following single hemodialysis. IOP has also been demonstrated in numerous studies to rise, fall, or stay the same. Additionally, it was said that following hemodialysis, retinal venules dilated while retinal arteriole calibre remained the same. [2] Many ophthalmic conditions, including cataracts, glaucoma, ocular surface problems, recurrent stye, non-arteritic anterior ischemic optic neuropathy, diabetic papillopathy, and diabetic retinopathy,

can develop as a result of uncontrolled diabetes. [5] The most prevalent and serious eye complication is diabetic retinopathy, which can cause the retina to suffer vision-threatening damage and finally become blind. [6,7]

Patients who have ESRD are susceptible to ophthalmic manifestations. This risk is linked to comorbidities such as diabetes mellitus, which is prevalent in ESRD patients, as well as the particular side effects of hemodialysis and the uremic state, which can result in alterations to the conjunctivae, cornea, retina, and macula. Very few studies were available regarding ophthalmic illness among diabetic patients undergoing dialysis. So, this study is an opportunity to study the ocular problems among diabetic patients undergoing dialysis.

This study was therefore carried out to determine the prevalence of various ocular manifestations among diabetic patients undergoing dialysis and to find out the association between ocular manifestations and renal involvement.

Materials and Methods

This was a cross-sectional observational study carried out in the Department of Ophthalmology in collaboration with the Department of Nephrology, SRM Medical College and Research Centre, Trichy, over a period of two years (November 2020 to October 2022) among 101 diabetic patients aged more than 20 years attending the nephrology department for dialysis. Non-diabetic patients undergoing dialysis, those who are disorientated and unable to understand the questionnaire, and those for whom ocular procedures could not be carried out were excluded from the study.

All patients were examined 30 minutes after hemodialysis. Patients were questioned about their symptoms and demographic determinants by using a semi-structured questionnaire after getting informed written consent. The ocular examination was held using specific ocular instruments appropriate to the procedure. External examination of the eye, including eyelids, extraocular movements and conjunctiva was done by using a torch examination. A Snellen chart was used to measure visual acuity. The patient was positioned 20 feet away from the chart and asked to read the letters from the top. To assess the corrected visual acuity current corrective lenses were used. The anterior segment (cornea, anterior chamber, iris and lens) was best assessed by using a slit lamp examination. Intraocular pressure was measured by using a Goldman applanation tonometer and noncontact tonometry. Schirmer's test was performed using filter paper placed inside the eyes. The fundus was examined after dilatation with tropicamide using indirect ophthalmoscopy with a 20D lens and fundus photography.

Data were expressed in Microsoft Excel 2019 and analyzed using SPSS software 23 version by descriptive and inferential statistics. Continuous variables and categorical variables were expressed as frequencies and percentages respectively. The proportion of ocular manifestations was tested for an association by using the independent t-test (continuous variable) and chi-square test (categorical variable). Multivariate analysis was used for predicting risk factors.

Results

The mean age of the participants was 48.74 ± 13.133 years, ranging from 20 to 69 years. The predominant participants were males (74.3%) in this study. 53.5% of the patients had Stage V renal disease, followed by 24.8% who had stage IV renal disease. The mean duration of renal involvement was 3.35 ± 1.154 years, ranging from 2 to 6 years.

The mean duration of dialysis was 2.277 ± 1.361 years, ranging from 1 to 5 years, with a majority, (30.7%) being on dialysis for 3 dialysis years.

Most of the patients had type II DM (97%). The mean duration of diabetes was 12.21 ± 6.727 years, ranging from 4 to 25 years, with a majority, (31.7%) having diabetes for 6 to 10 years. 46.5% of the patients were prescribed insulin and oral hypoglycemic drugs.

The mean systolic blood pressure was 125.45 ± 14.108 mm hg, ranging from 110 to 140 and the mean diastolic BP was 77. 82 ± 9.960 mm hg, ranging from 60 to 90.

The mean BMI was 27.01 ± 2.583 ranging from 24 to 32. 63.4% and 11.9% of the patients were overweight and obese based on the Asian classification of body mass index.

Participants consulted an ophthalmologist before 27.7% of the patients consulted an ophthalmic surgeon for their complaints.

34.7%, 21.8% and 7.9% of the patients had complaints of blurring of vision, decreased vision and irritation of the eyes respectively.

Ocular Examination

69.3% and 71.3% of the patients had good vision based on WHO criteria in the right and left eye respectively. Impaired vision was observed in 16.8% of the right eye and 20.8% of the left eye. Based on WHO criteria, 21.8% (13.9% right, 7.9% left) were legally blind.

29 eyes (14.35%) had lid edema, while the rest were normal. Only one patient was found to have restricted ocular movements due to proptosis.

35 eyes (17.32%) had pale conjunctiva, while in the rest it was normal. Only 4 eyes had band-shaped keratopathy (3.96%). 89 eyes (44.05%) had presenile cataract and 15 eyes (7.42%) had mature cata-

Statistical Analysis

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ract. 25 eyes (12.37%) had PCIOL implantation. With Schirmer's test 52 eyes (25.74%) had reduced values, which indicated ocular surface disorders.

Fundus Findings

56 eyes (27.7%) had hypertensive changes (A-V changes) and 82 eyes (40.6%) had diabetic retinopathy. 7 eyes (3.46%) reported age-related macular degeneration. 9 eyes (4.45%) had diabetic mac-

ular edema. 6 eyes (2.97%) were complicated with vitreous hemorrhage. One eye reported optic atrophy (0.49%) and branch retinal vein occlusion (0.49%). Clinically significant macular edema was seen in six eyes (2.97%). DM retinopathy was seen in 41.6% of eyes in the right eye of patients. DR was seen in 39.6% of eyes in the left eye of patients. ME was seen in 5% of eyes on the right and 4% of the left eye of patients. (Table 1).

Table 1: Fundus Examination Findings				
Fundus Examination	Right Eye		Left Eye	
	Frequency	Frequency	Frequency	Proportion
Age-related Macular Degeneration	4	3.96%	3	2.97%
Hypertensive Changes (A-V changes)	25	24.75%	31	30.69%
Diabetic Retinopathy (DR)	42	41.58%	40	39.6%
BRVO (Branch Retinal Vein Occlusion)	1	0.9%	-	-
Macular Edema (ME)	5	4.95%	1	0.99%
Vitreous Hemorrhage	2	1.98%	4	3.96%
Clinically Significant Macular Edema	3	2.97%	4	3.96%
No View	4	3.96%	3	2.97%
Media Hazy	5	4.95%	7	6.93%
Normal	20	19.8%	21	20.79%

Grading of Diabetic Retinopathy

36.58%, 14.63%, 25.6%, and 23.17% of eyes were diagnosed with mild NPDR, moderate NPDR, severe NPDR, and PDR, respectively. The findings in the right and left eyes are as shown in Table 2.

Table 2: Grading of Diabetic Retinopathy (N = 82 Eyes)				
Sl. No.	Findings	Right Eye	Left Eye	Total
1	Mild NPDR	17 (20.73%)	13 (15.85%)	30 (36.58%)
2	Moderate NPDR	6 (7.31%)	6 (7.31%)	12 (14.63%)
3	Severe NPDR	10 (12.19%)	11 (13.41%)	21 (25.6%)
4	PDR	10 (12.19%)	9 (10. 97%)	19 (23.17%)

The mean value of blood sugar was 170.21 ± 33.541 , ranging from 101-304. The mean value of serum creatinine was 8.283 ± 1.40 , ranging from 0.6 to 70. The mean value of blood urea was 120.48 ± 60.52 ranging from 21-312. The mean value of hemoglobin was 8.222 ± 1.407 .

Association of Retinopathy with Baseline Characteristics.

There was a statistically significant association between diabetic retinopathy and gender, education, socio-economic status and residence as shown in Table 3.

Table 3: Association between Demographic Determinants and Diabetic Retinopathy (N = 202 Eyes)

Variables		DR Yes	DR No	Total	P-Value
Gender	Male	67(44.7%)	83(55.3%)	150	0.045
	Female	15(28.8%)	37(71.2%)	52	
Education	Primary	2 (11. 1%)	16(88.9%)	18	0.005
	Middle	18(33.3%)	36(66.7%)	54	
	High/ Hr sec	15(37.5%)	25(62.5%)	40	
	Graduates	47(52.2%)	43(47.8%)	90	
Socio-	Upper middle	23(67.6%)	11(32.4%)	34	0.001
Economic	Middle	33(35.9%)	59(64.1%)	92	
Status	Lower middle	20(30.3%)	46(69.7%)	66	
	Lower	6 (60%)	4 (40%)	10	
Marital Status	Married	81(41.8%)	113(58.2%)	194	0.235
	Unmarried	1 (16. 7%)	5 (83. 3%)	6	
	Widower	0	2 (100)	2	
Residence	Urban	67(48.6%)	71(51.4%)	138	0.001
	Rural	15(23.4%)	49(76.6%)	64	

Duration of renal disease, duration of dialysis, and duration of DM were significantly associated with diabetic retinopathy, while there was no statistically significant association with stage of renal disease, type of DM,

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Variables		DR Yes	DR No	Total	P-Value
Stage of	Stage I	4 (33. 3%)	8 (66. 7%)	12	0.646
renal dis-	Stage II	1 (16. 7%)	5 (83. 3%)	6	
ease	Stage III	9 (34. 6%)	17(65.4%)	26	
	Stage IV	22 (44%)	28 (56%)	50	
	Stage V	46(42.6%)	62(57.4%)	108	
Duration of	2 years	19 (38%)	31 (62%)	50	0.0001
renal dis-	3 years	13(23.2%)	43(76.8%)	56	
ease	4 years	14(30.4%)	32(69.6%)	46	
	5 years	35(76.1%)	11(23.9%)	46	
	6 years	1 (25%)	3 (75%)	4	
Duration of	Less than one year	9 (37. 5%)	22(62.5%)	24	0.0001
dialysis	1 year	18(33.3%)	36(66.7%)	54	
	2 years	7 (25%)	21 (75%)	28	
	3 years	25(40.3%)	37(59.7%)	62	
	4 years	7 (38. 9%)	11(61.1%)	18	
	5 years	16 (100%)	0	16	
Type DM	Ι	1 (16. 7%)	5 (83. 3%)	6	0.226
	II	81(41.3%)	115(58.7%)	196	
Treatment	OHA	29 (50%)	29 (50%)	58	0.248
taken for	Insulin	35 (38%)	57 (62%)	92	
DM	Both	18 (36%)	32 (64%)	50	
Duration of	≤ 10 years	37(34.3%)	71(65.7%)	108	0.049
DM	> 10 years	45(47.9%)	49(52.1%)	94	
Obesity	Normal	20 (40%)	30 (60%)	50	0.717
-	Overweight	54(42.2%)	74(57.8%)	128	
	Obesity I	8 (33. 3%)	16(66.7%)	24	

treatment taken for DM or obesity. The results are as shown in Table 4.

Table 4: Association	between	Comorbid Illne	ess and Diabetic	Retinopathy

Biochemical values like blood sugar, urea, creatinine, and haemoglobin did not show any significant association with diabetic retinopathy.

Discussion

This study was conducted among 101 patients who underwent hemodialysis with different stages of chronic renal disease and the comorbid status of DM, to assess ocular manifestations. The observations of the present study and those of similar studies are as follows:

Ocular Examination

Chougule N et al. [8] found that the most common symptom reported by patients was blurring of vision (a loss of good vision) which was similar to our study results.

Our study reported that 38 eyes (18.81%) had impaired vision and 21 eyes (10.39%) were legally blind based on WHO criteria. A study by Chougule N et al. [8] in Karnataka among the eyes of fifty DM patients undergoing hemodialysis identified that about 47% of patients had eyesight worse than 6/24. The majority of them began gradually, and 53% of the remaining patients had vision between 6/6 and 18/24. The prevalence was high in Chougule N et al. study, which shows contrast results might be due to patient characteristics. Our study showed that 89 eyes (44.05%) had presenile cataract and 15 eyes (7.42%) had mature cataract. 25 eyes (12.37%) had PCIOL implantation. In patients with diabetes mellitus having endstage kidney disease, the cataractous lens (Grade II-IV nuclear sclerosis [NS]) and posterior subcapsular cataract were present in 53% of cases, according to Chougule N et al., which was similar to our study results. Anterior segment findings include presenile cataract (1.5%), senile cataract (68.1%), and other types of cataracts (3%) by Yasaswini et al. and show a higher prevalence of mature cataract compared with our results. This variation might be due to a higher rate of cataract surgery in our area.

Fundus Examination in Diabetics

Our study reported that 82 eyes (40.6%) had diabetic retinopathy. 36.58%, 14.63%, 25.6% and 23.17% of eyes were diagnosed with mild NPDR, moderate NPDR, severe NPDR and PDR respectively.

The most prevalent ocular illnesses were DR in 19 patients, cataract in 17 patients, and others in 5 patients, according to a survey of diabetic patients with ESRD receiving hemodialysis (38 patients) in Japan by Kimura M et al. [9] Our study reported 40.6% of diabetic retinopathy and 51% of cataracts among patients. The prevalence was high in our

study because of the larger sample size (n = 101) included in it.

Chougule N et al. [8] reported that diabetic retinopathy was seen commonly among the patients (48%) with diabetes mellitus having end-stage kidney disease, followed by 12% with hypertensive retinopathy. This prevalence was somewhat high compared with our study results. Our study reported that 56 eyes (27.7%) had hypertensive retinopathy and 82 eyes (40.6%) had diabetic retinopathy. This variation might be due to patients' characteristics.

In a hospital-based study among diabetic patients with CKD receiving hemodialysis in Karnataka, Yasaswini et al. [10] discovered that 60.6% of all research participants had previously seen an ophthalmologist for their symptoms. But our study showed that only 27.7% of participants had consulted with ophthalmologists before. This might be due to non-adherence and non-utilization of ophthalmic services among long-term illness patients in our setup.

Posterior segment findings include mild NPDR (22.7%), moderate NPDR (27.3%), severe NPDR (12.1%), PDR (3%) in the Yasaswini et al. [10] study. 36.58%, 14.63%, 25.6% and 23.17% of eyes were diagnosed with mild NPDR, moderate NPDR, severe NPDR and PDR respectively in our study. 20, 16, 54, 38, and 68 eyes were diagnosed as no DR (10.2%), mild DR (8.1%), moderate DR (27.6%), severe DR (19.4%) and PDR (34.7%) respectively by Sandhya CS et al. There is a variation in the prevalence of DR compared with our study results, which might be due to a difference in sample size (Table 5)

Present Study	82 eyes (40.6%) had diabetic retinopathy. / eyes (3.46%) reported age- related macular degeneration. 9 eyes (4.45%) had diabetic macular edema. 6 eyes (2.97%) complicated with vitreous hemorrhage. One eye reported optic atrophy (0.
	edema was seen in 6 eyes (2.97%).
Chougule N et al. [8]	Diabetic retinopathy (48%) 12% hypertensive retinopathy. Cataract in 9% of pa- tients, maculopathy in 5%, 4% each had tractional retinal detachment and vitreous
	degeneration (ARMD).
Kimura M et al. [9]	DR in 19 patients, cataract in 17 patients, and others in 5 patients,
Yasaswini et al. [10]	Presenile cataract (1. 5%), senile cataract (68.1%), and other types of cataracts (3%). Posterior segment findings include mild NPDR (22.7%), moderate NPDR (27.3%), severe NPDR (12.1%), PDR (3%), maculopathy (10.6%), glaucoma (4.5%), myopic fundus (3%) and hazy media (4.5%). 65.2% of eyes showed DR changes.
Kumar J. et al. [11]	Diabetic retinopathy (48.70%) was the most prevalent ocular manifestation, fol- lowed by cataract (38.22%), meibomitis (31. 91%), dry eye (15.33%), neovascu- larization of iris(7.33%), glaucoma (4.62%), keratopathy (4.17%), retinal occlu- sive disease (2.37%), optic neuropathy (1.58%) and ocular movement disorder (1.01%).
Umarani S et al. [12]	Diabetic retinopathy (DR) is the most frequent consequence (36.8%), followed by cataracts (35.4%), glaucoma (4.6%), and other diseases such as conjunctivitis, recurrent hordeolum, and dacryocystitis
Singh et al. [13]	Diabetic retinopathy (65.27%), primary open angle glaucoma (1.38%), recurrent styes (1.38%), cataract (23.61%), extra ocular muscle palsy (2.77%), optic atro- phy (1.38%), and recurrent lacrimal abscess (1.38%).

 Table 5: Comparison of Fundus Examination in Diabetics with Other Studies

Our study reported that 36.58%, 14.63%, 25.6% and 23.17% of eyes were diagnosed with mild NPDR, moderate NPDR, severe NPDR and PDR respectively. According to the Romero P. et al. [14] follow-up study conducted in Spain after type 1 diabetes had been present for fifteen years, mild diabetic retinopathy was found to be 27.7% common, followed by moderate diabetic retinopathy at 6.3%, severe diabetic retinopathy at 4.5%, and proliferative diabetic retinopathy at 16.1%.

Fundus Examination in Patients on Hemodialysis

The findings of the fundus examination in patients who have undergone hemodialysis are as shown in Table 6. There was a variation in the prevalence of ocular symptoms across the studies. This might be due to the inclusion of participants with or without DM undergoing hemodialysis.

Present	7 eyes (3.46%) reported age-related macular degeneration. 9 eyes (4.45%) had diabetic
Study	macular edema. 6 eyes (2.97%) complicated with vitreous hemorrhage. One eye reported
	optic atrophy (0.49%) and branch retinal veinocclusion (0.49%). Clinically significant
	macular edema was seen in 6 eyes (2. 97%).
Kianersi et	32.2% of the patient's eyes reported conjunctival calcification, 32. 2% of them had corneal
al. [15]	calcification, 7.4% of them had glaucoma, 58.7% presented with cataract, 19% of them had
	optic atrophy, 2.5% of them had retinal vein occlusion, 28.92 % of them reported with pro-
	liferative diabetic retinopathy, 21.07% were presented with macular edema, 11.57% were
	reported vitreous hemorrhage and 22.31% of them had hypertensive retinopathy.
Zaheer W.	93 people (43.66%) without any eye disorders, 79 (37.08%) with cataracts, and 41
et al. [16]	(19.24%) with retinal disorders. Of the 41 cases of retinal disorders, 17 (41.46%) involved
	hypertensive retinopathy and 24 (58.53%) involved diabetic retinopathy.
Mansour	Yellow sclera (75% of cases), cataract (61.4%), lid edema (56.8%), dry eye (43.2%), con-
et al. [17]	junctival congestion (47.7%), and pterygium (13.6%) were the most frequent findings. Re-
	garding the posterior segment, diabetic retinopathy (38.6% of cases), hypertensive reti-
	nopathy (4.5%), AMD (2.3%), and macular haemorrhage (2.3%)
Okolo OE	Hypertensive retinopathy 33.3%, retinal oedema 20.8%, and diabetic retinopathy 11.5%.
et al. [18]	
Malleswari	Pterygium (14%), pinguecula (3%), conjunctival congestion (6%), cataracts (38%), reti-
B et al.	nopathy changes (44%) and diabetic retinopathy (31%), as well as NPDR (20%), PDR
[19]	(6%), diabetic maculopathy (5%), BRVO (2%), and glaucomatous optic atrophy (3%),
	were the most prevalent ocular findings among HD patients.

Table 6: Comparison of Fundus Examination in Patients on Hemodialysis with Other Studies

Association between Baseline Characteristics and DR

Our study reported that gender, education, socioeconomic status and residence were significantly associated with diabetic retinopathy. Duration of renal disease, dialysis, and DM were also significantly associated with diabetic retinopathy.

According to a study by Muller M. et al. [20] among type 2 diabetics receiving hemodialysis in Germany, the probability of developing DR was 1.71 times greater in patients with hypertension, and 1.08 times higher in patients with longer DM durations, which shows similar results. According to research by Romero P. et al.[14] conducted in Spain, the duration of diabetes mellitus (p = 0.001), was found to be significant in the development of diabetic retinopathy, which was similar to our study results. Umarani S et al.[12] conducted in Karnataka, also stated that the duration of diabetes has been shown statistically to be the best predictor of the prevalence of retinopathy in people with type 2 diabetes.

Conclusion

Our study concluded that diabetic patients with kidney disease undergoing hemodialysis had a higher proportion of ocular problems. Gender, education, socio-economic status and residence in addition to the duration of renal disease, dialysis, and diabetes were significantly associated with diabetic retinopathy. Further research into ophthalmic examinations both prior to and following hemodialysis would facilitate a better understanding of the effects of dialysis on the eyes.

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