Original Article

Ocular Manifestations in Hemodialysis Patients: Importance of Ophthalmic Examination in Prevention of Ocular Sequels

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Abstract

Background: Hemodialysis (HD)-associated ocular abnormalities are one of the causes of morbidity among people undergoing HD. This study evaluates the frequency of ocular abnormalities in end-stage renal disease (ESRD) patients undergoing HD and their potential link to HD and demographic parameters. **Methods:** This cross-sectional study examined 242 eyes of 121 patients with ESRD undergoing regular HD after excluding the ineligible subjects. The study was designed in two parts. Medical histories of each patient including age, gender, family history, medication history, past medical history, and duration of HD collected using a structured check list. All patients underwent complete ophthalmologic examination for evaluation of the best corrected visual acuity (BCVA), intraocular pressure (IOP), and anterior and posterior segments. **Results:** In total, 121 patients, including 68 (56.2%) males and 53 (43.8%) females, were enrolled in the study. The mean ± SD age of the patients and their mean duration of dialysis were 51.59 ± 16.01 and 3.40 ± 2.75 years, respectively. The most prevalent etiology for HD was diabetes mellitus (39.67%), followed by hypertension (38.84%), and the most common ocular findings included cataract (142 eyes; 58.7%) and ectopic calcification of the conjunctiva and cornea (78 eyes; %32.2). There was at least one abnormal ocular finding in 89.3% of the cases. The BCVA was equal to or less than finger count in 70 eyes (28.92%). There was a significant relationship between conjunctival calcification and the duration of dialysis (P = 0.02). There was significant association between etiology of HD and conjunctival calcification (adjusted odds ratio, 2.44; 95% CI, 1.05–5.67; and P value, 0.03). Such significant associations were present for corneal calcification (P = 0.009), cataract (P = 0.02), and optic atrophy (P = 0.01). **Conclusions:** Regular ophthalmologic examinations are recommended due to the prevalence of clinical ocular abnormalities in HD patients.

Keywords: *Diabetic retinopathy, eye disease, kidney disease, kidney failure, renal dialysis*

Introduction

Hemodialysis (HD)-associated ocular abnormalities are one of the causes of morbidity among people undergoing HD, but their etiology remains unidentified to date.[1-4]

Several studies have shown the persistence of certain ocular findings among end-stage renal disease (ESRD) patients undergoing HD. Changes in ophthalmologic findings often occur in ESRD patients after HD.[1,4-6]

A potential pathophysiological mechanism is the correlation with increased plasma colloid osmotic pressure (COP), alterations in calcium and phosphor levels during the phase of uremic state, and chronic inflammation.[5,7,8]

Ocular abnormalities include intraocular pressure (IOP) changes associated with HD, corneal and conjunctival abnormalities, metastatic calcification, chronic inflammatory changes, cataracts, and retinal diseases (e.g., retinal detachment, macular leakage, retinal hemorrhage, and optic neuropathy).[7]

Although most complications are not sight-threatening, retinal vascular complications such as hypertensive retinopathy, anterior ischemic optic neuropathy (AION), central retinal artery occlusion (CRAO), central retinal vein occlusion (CRVO), and diabetic retinopathy are major sight-threatening ocular changes.[9,10]

There is either no standard protocol for periodic ophthalmologic evaluation in HD patients, also limited data provided about pattern of ocular complications associated with HD and frequency of eye involvement

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and associated risk factors in HD. So, considering the importance of the diagnosis and management of ocular findings in HD patients and scarcity of the data on ocular manifestations in HD patients, this study was conducted to evaluate the frequency of ocular complications in HD patients and their potential relationship with HD and demographic parameters.

Materials and Methods

Study design and participants

This cross-sectional study was conducted at Feiz ophthalmology referral center affiliated Isfahan University of Medical Sciences (IUMS), in Isfahan, Iran, from September 2016 to September 2017. Before beginning the study, a medical ethics approval was obtained from the Medical Ethics Committee of IUMS (Project Number: 394676).

In total, 121 ESRD patients >18 years undergoing regular HD were referred to Feiz ophthalmology referral center included in the study. All the patients underwent HD three or four times per week on dialysis unit of university hospital of IUMS.

Prior to entering the study, all the participants signed a written informed consent form in accordance with the ethical standards of the 2000 revision of the Declaration of Helsinki. The exclusion criteria consisted of (1) renal transplantation during the study; (2) a history of malignancy or primary hyperparathyroidism; (3) irregular HD sessions; and (4) incomplete data.

Study variables

Medical histories of each patient including age, gender, family history, medication history, past medical history, and duration of HD collected using a structured check list.

A complete ophthalmologic examination was performed by vitreo-retina specialist. This examination included measurements of the best corrected visual acuity (BCVA), IOP, biomicroscopic examination (anterior segment and lens), and direct fundus biomicroscopy for evaluation of retina, optic disc, macula, and vitreous. BCVA was assessed using a Snellen scale. IOP was measured using a slit-lamp-mounted Goldmann applanation tonometer. Biomicroscopic examination was performed using slit-lamp and direct fundus biomicroscopy was performed using 90 diopter magnification lenses in seated position. Ocular complication included conjunctival calcification, corneal calcification, glaucoma, cataract, optic atrophy, retinal vein occlusion, proliferative diabetic retinopathy, macular edema, vitreous hemorrhage, and hypertensive retinopathy.

Statistical analysis

Ophthalmologic data were collected from both eyes of all the patients. SPSS-17 (Chicago, IL) was used to perform all the statistical analyses. *P* values <0.05 were considered statistically significant.

The results were reported as mean ± standard deviation (SD) for the quantitative variables and percentage for the categorical variables. Independent samples' *t*-test applied to compare the means of

Table 1: Demographic characteristics, BCVA, and frequency of each ocular complication of the patients

Age (years)		
Mean±SD	51.59±16.01	
Median	54	
Range	18-87	
Duration of dialysis (years)		
Mean±SD	3.40±2.75	
Median	2.50	
Range	1-15	
Times in week, *n* (%)		
Three times	72 (59.5)	
Two times	49 (40.5)	
Gender		
Male	68 (56.2)	
Female	53 (43.8)	
Etiology of ESRD, *n* (%)		
DM	27 (22.3)	
HTN	26 (21.5)	
DM and HTN	21 (17.4)	
Infection	10 (8.3)	
Urinary tract problems	9 (7.4)	
Nephrotic syndrome	9 (7.4)	
Polycystic kidney disease	5 (4.1)	
Lupus nephritis	2 (1.7)	
Unknown	12 (9.9)	
BCVA	Right eye, *n* (%)	Left eye, *n* (%)
8/10-10/10	35 (28.9)	33 (27.3)
5/10-7/10	14 (11.6)	23 (19.0)
1/10-4/10	37 (30.6)	22 (18.2)
FC	20 (16.5)	23 (19.0)
HM	5 (4.1)	8 (6.6)
LP	4 (3.3)	3 (2.5)
NLP	2 (1.7)	5 (4.1)
UC	4 (3.3)	4 (3.3)
Ocular complication (eyes), no. %)		
Conjunctival calcification	78 (32.2)	
Corneal calcification	78 (32.2)	
Glaucoma	18 (7.4)	
Cataract	142 (58.7)	
Optic atrophy	46 (19)	
Retinal vein occlusion	6 (2.5)	
Proliferative diabetic Retinopathy	70 (28.92)	
Macular edema	51 (21.07)	
Vitreous hemorrhage	28 (11.57)	
Hypertensive retinopathy	54 (22.31)	

ESRD=End-stage renal disease, DM=Diabetes mellitus, HTN=Hypertension, BCVA=Best corrected visual acuity, FC=Finger count, HM=Hand motion, LP=Light perception, NLP=No light perception, UC=Uncooperative

continuous variables between groups and the Chi-square test and Fisher's Exact Test were used for comparing categorical data. For possible effects of risk factor, Crude and adjusted odds ratios (ORs) were applied to report magnitude of probable association via fitting simple and multiple logistic regression models.

Results

In total, 242 eyes and 121 patients, including 68 (56.2%) males and 53 (43.8%) females, with ESRD undergoing regular HD were recruited after excluding the ineligible patients. Table 1 presents the demographic characteristics, BCVA and frequency of each ocular complication of the patients.

The mean ± SD age of the patients was 51.59 ± 16.01 years. The mean ± SD duration of dialysis was 3.40 ± 2.75 (range: 1–15) years in the patients. The most prevalent etiology for HD was diabetes mellitus (DM), followed by hypertension (HTN). Of the 242 examined eyes, the BCVA was equal to or less than finger count in 70 eyes. Table 1 presents the distribution of BCVA in each eye. The most common ocular findings included cataract 58.7% (142 eyes), conjunctive calcification 32.2% (78 eyes), and corneal calcification 32.2% (78 eyes); [Table 1].

There was at least one abnormal ocular finding in 89.3%, and 13 patients had unremarkable findings in their ophthalmologic examination. Four patients had six ocular abnormalities**.**

Table 2 presents the relationships between ocular abnormalities in HD and variables including age, duration of dialysis, gender, and disease etiology. A significant relationship was found between conjunctival calcification and the duration of dialysis (P = 0.02), but there was no statistically significant relationships between conjunctival calcification and age (P = 0.22), gender (P = 1.00), and the ESRD etiology (P = 0.07); [Table 2].

A significant relationship was also observed between DM with or without HTN and all the ocular abnormalities, including corneal calcification (P = 0.009), cataracts (P = 0.005), optic atrophy (P = 0.004), and proliferative diabetic retinopathy (P < 0.001), excluding conjunctival calcification (P = 0.07) and glaucoma (P = 1.0); [Table 2].

The crud and adjusted OR for risk factors and ocular complications are illustrated in Table 3. There was significant association between etiology of HD and conjunctival calcification (adjusted OR, 2.44; 95% CI, 1.05–5.67; and P value, 0.03). Such significant associations were present for corneal calcification (P = 0.009), cataract (P = 0.02), and optic atrophy (P = 0.01).

Discussion

The most prevalent etiology for HD was DM, followed by HTN. The most common ocular findings were cataracts, followed by ectopic calcification of the conjunctiva and cornea.

There is a category of diseases which affect both the eyes and the kidneys; examples include congenital oculorenal syndromes, acquired autoimmune disorders (e.g., systemic lupus erythematosus), and DM.[7]

The effects of HD on the eyes of CKD and HD patients can vary widely,[11] and pathologies of the cornea, conjunctiva, lens, and retina can develop during an HD period.[4,12]

Diabetic retinopathy is one of the most common and serious ophthalmic problems in patients with renal disease.[13,14] In this study, about 50% of the participants had DM with and without HTN.

Unique ocular abnormalities were found in patients who progressed toward diabetic retinopathy, including proliferative diabetic retinopathy, vitreous hemorrhage, and diabetic macular edema,[7] which is compatible with the present findings.

Table 2: Relationships between ocular abnormalities in HD and variables including age, duration of dialysis, gender, and disease etiology

Characteristics		Age		Duration of dialysis		Gender			Etiology		
		Mean±SD	*P*	Mean±SD	*P*	Male	Female	*P*	DM±HTN	Other	*P*
Conjunctival calcification	Yes	53.95±13.04	0.22	4.24±3.13	0.02	22 (56.4%)	17 (43.6%)	>0.99	19 (48.7%)	20 (51.3%)	0.07
	No	50.46±17.21		3.00±2.47		46 (56.1%)	36 (43.9%)		55 (67.1%)	27 (32.9%)	
Corneal calcification	Yes	50.59±14.75	0.62	3.73±2.95	0.38	23 (59.0%)	16 (41.0%)	0.70	17 (43.6%)	22 (56.4%)	0.009
	No	52.06±16.65		3.24±2.65		45 (54.9%)	37 (45.1%)		57 (69.5%)	25 (30.5%)	
Glaucoma	Yes	51.89±14.69	0.93	3.66±1.67	0.84	6 (66.7%)	3 (33.3%)	0.73	6 (66.7%)	3 (33.3%)	>0.99
	No	51.42±16.21		3.47±2.91		56 (56.6%)	43 (43.4%)		60 (60.6%)	39 (39.4%)	
Cataract	Yes	57.01±12.85	<0.001	3.63±2.86	0.26	37 (52.1%)	34 (47.9%)	0.35	51 (71.8%)	20 (28.2%)	0.005
	No	43.89±17.01		3.07±2.58		31 (62.0%)	19 (38.0%)		23 (46.0%)	27 (54.0%)	
Optic atrophy	Yes	55.70±18.18	0.17	4.22±2.99	0.11	14 (60.9%)	9 (39.1%)	0.65	20 (87.0%)	3 (13.0%)	0.004
	No	50.62±15.41		3.20±2.67		54 (55.1%)	44 (44.9%)		54 (55.1%)	44 (44.9%)	
PDR	Yes	53.97±12.08	0.22	2.66±1.90	0.02	20 (57.1%)	15 (42.9%)	>0.99	35 (100%)	0 (0%)	<0.001
	No	50.62±1 7.33		3.70±2.99		48 (55.8%)	38 (44.2%)		39 (45.3%)	47 (38.8%)	

DM=Diabetes mellitus, HTN=Hypertension, PDR=Proliferative diabetic retinopathy

Table 3: Relationship between risk factors and complications in terms of crude and adjusted odds ratio

Variables	Odds ratio (95% CI)											
	Conjunctival calcification		Corneal calcification		Glaucoma		Cataract		Optic atrophy		PDR	
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Sex (female)	1.01 (0.47-2.18)	1.35 (0.58-3.14)	1.18 (0.54-2.55)	1.37 (0.59-3.13)	0.62 (0.14-2.60)	0.57 (0.13-2.53)	1.49 (0.71-3.13)	1.38 (0.59-3.25)	1.45 (0.56-3.78)	1.95 (0.67-5.62)	1.00 (0.44-2.26)	0.71 (0.26-1.93)
Age (year)	0.98 (0.96-1.01)	0.97 (0.95-1.00)	1.00 (0.98-1.03)	0.99 (0.97-1.02)	1.00 (0.95-1.04)	1.00 (0.95-1.04)	1.06 ** (1.03-1.09)	1.05 ** (1.02-1.09)	0.97 (0.94-1.00)	0.98 (0.95-1.01)	0.98 (0.96-1.01)	1.00 (0.97-1.04)
Duration of dialysis (year)	0.85 * (0.74-0.98)	0.85 * (0.73-0.98)	0.93 (0.82-1.07)	0.94 (0.81-1.09)	1.03 (0.82-1.30)	1.06 (0.83-1.35)	1.08 (0.94-1.24)	1.10 (0.94-1.29)	0.89 (0.77-1.04)	0.83 (0.70-1.00)	1.12 (0.94-1.34)	1.13 (0.91-1.41)
Etiology (Other)	2.14 (0.98-4.67)	2.44 * (1.05-5.67)	2.95 ** (1.34-6.49)	2.98 ** (1.31-6.80)	1.29 (0.30-5.44)	1.31 (0.29-5.86)	2.99 ** (1.40-6.39)	2.55 * (1.10-5.94)	0.19 * (0.05-0.71)	0.18 ** (0.04-0.72)	-	-

DM=Diabetes mellitus, HTN=Hypertension, PDR=Proliferative diabetic retinopathy. *$P \leq 0.05$. **$P \leq 0.01$

Also, in line with this study, Jayamanne *et al*. evaluated the ocular morbidity following renal transplantation and reported diabetes mellitus, followed by HTN, as the most common causes of renal failure.[15]

The most frequent ocular abnormalities in this study were cataracts (60% of the eyes). The incidence of this ocular complication has varied from 5% to 62.5% in different studies.[15,16] One explanation for this wide difference in the prevalence of cataracts in HD may be the different mean age of the patients and the different administration rates of certain medications such as glucocorticoids.

The second most prevalent ocular abnormality in this study was ectopic calcification, including corneal and conjunctival calcification. These abnormalities may result from the accumulation of toxic materials in the body and metabolic changes.[7]

One of the main challenges in HD patients is the occurrence of hyperphosphatemia, which plays a central role in ectopic calcification caused by an abnormal balance of calcium and phosphorus metabolism.[17,18] Since this abnormal balance is a common finding in HD patients, ectopic calcification is believed to be the cause of inflammatory reactions. Nonetheless, few reports have compared ocular abnormalities before and after HD.

The limitations of this study include the retrospective nature of the research and the relatively small sample size; future studies are recommended to be designed in a prospective format and with larger sample sizes.

Conclusions

The results of this study highlight the need for periodic ophthalmological examinations to determine the presence of HD-associated ocular manifestations and prevent their related complications.

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Conflicts of interest

There are no conflicts of interest.

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