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ORIGINAL ARTICLE

Ophthalmic Situation of the Patients with Chronic Renal Failure Undergoing Hemodialysis

Hemodiyaliz Yapılan Kronik Böbrek Yetmezliği Hastalarının Oftalmolojik Durumları

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ABSTRACT

Aim: Hemodialysis (HD) is a unique treatment modality for patients with end-stage chronic renal failure (ESCRF). A wide range of ophthalmologic findings, such as refractive changes, dry eye, increased intraocular pressure, and retinal hemorrhage, can be seen in these patients. In this study, we aimed to evaluate the ophthalmological status of HD patients.
Methods: A total of 504 eyes of 252 patients with ESCRF undergoing HD were included in the study. Renal failure, HD, and additional disease data were evaluated along with demographic data of all patients. All participants underwent a total ophthalmological examination, including visual acuity, intraocular pressure, and detailed anterior and posterior segment examination.
Results: The mean age was 65.21±13.15 years, and the mean HD time was 4.95±4.25 years. 237 (47.2%) of 504 eyes were pseudo-phakic, and 170 (33.7%) had cataracts at different stages. Diabetic retinopathy (DRP) findings were detected in a total of 148 (26.4%) eyes. Age-related macular degeneration (AMD) findings at various stages were observed in 112 eyes (22.1%), while epiretinal membranes were detected in 60 eyes (11.9%). Dry eye findings were observed in 94 cases (37.1%), and glaucoma was detected in 20 cases.
Conclusions: The most common sight-threatening condition in ESCRF patients appears to be cataract, and the most common ocular surface problem was dry eye disease. Various retinal pathologies were observed in a significant part of the patients.

Keywords: Chronic kidney disease, hemodialysis, ophthalmologic findings, renal failure, visual loss

ÖZ

Amaç: Hemodiyaliz (HD), son dönem kronik böbrek yetmezliği (SDKBY) olan hastalar için özel bir tedavi yöntemidir. Bu hastaların büyük bir kısmında kırma kusurları, göz kuruluğu, göz içi basıncı artışı ve retina kanaması gibi çok çeşitli oftalmolojik bulgular görülebilmektedir. Bu çalışmada hemodiyaliz hastalarının oftalmolojik durumlarını değerlendirmeyi amaçladık.
Gereç ve Yöntemler: Hemodiyalize giren 252 SDKBY hastasının toplam 504 gözü çalışmaya dahil edildi. Tüm hastaların demografik verilerinin yanı sıra böbrek yetmezliği, hemodiyaliz ve ek hastalık verileri de değerlendirildi. Tüm katılımcılara görme keskinliği, göz içi basıncı, detaylı ön ve arka segment muayenesini içeren tam oftalmolojik muayene yapıldı.
Bulgular: Ortalama yaş 65,21±13,15, ortalama hemodiyaliz süresi 4,95±4,25 yıl olarak hesaplandı. 504 gözün 237'si (%47,2) psödofakik iken, 170'inde (%33,7) farklı evrelerde katarakt mevcuttu. Toplam 148 (%26,4) gözde diyabetik retinopati (DRP) bulguları saptandı. 112 gözde (%22,1) çeşitli evrelerde yaşa bağlı makula dejenerasyonu (YBMD) bulguları gözlenirken, 60 gözde (%11,9) epiretinal membran tespit edildi. Olguların 94'ünde (%37,1) kuru göz bulguları, 20'sinde ise glokom saptandı (%3,9).
Sonuçlar: Bu çalışmada SDKBY hastalarında en sık görülen görmeyi tehdit eden durumun katarakt, en sık görülen oküler yüzey sorununun ise kuru göz hastalığı olduğu gözlemlenmiştir. Hastaların önemli bir kısmında çeşitli retina patolojileri tespit edilmiştir.

Anahtar kelimeler: Böbrek yetmezliği, görme kaybı, hemodiyaliz, kronik böbrek hastalığı, oftalmolojik bulgular

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INTRODUCTION

Chronic kidney disease (CKD) refers to pathophysiological conditions that have various etiological causes and generally lead to end-stage renal disease (ESRD). The Kidney Disease Improving Global Outcomes (KDIGO) foundation guidelines define CKD using kidney damage markers such as proteinuria (in which the albumin is greater than 30 mg per gram of creatinine) and glomerular filtration rate (GFR) (less than 60 mL/min) for more than three months with structural and functional abnormalities. Moreover, ESRD is defined as a GFR less than 15 mL/min (1). However, variability can occur in clinical practice, as many patients can live for years without being symptomatic or needing dialysis, even if they have been diagnosed with ESRD (2).

Various causes may play a role in the pathogenesis of ESRD, including hypertension, diabetes mellitus (DM), systemic lupus, rheumatoid arthritis, and some drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), calcineurin inhibitors, and antiretrovirals. Considering that the number of patients with terminal renal failure is increasing at an average rate of 7% per year worldwide, it indicates that there will be more need for hemodialysis (HD) and related medical problems in the future, and clinicians should be aware of the problems associated with HD (3).

The main aim of HD treatment is to remove metabolic wastes, excess water, and regulate the electrolyte and acid-base balance. But both dialysis itself and the unstable metabolic status due to end-stage kidney disease could cause side effects on multiple organ systems, including the eyes. A wide range of chronic eye diseases, such as diabetic retinopathy, glaucoma, and macular degeneration, can be seen in this group of patients. Compared to the normal population, ocular pathologies that cause vision loss are more common in patients with chronic kidney disease, and in addition, the dialysis process may contribute to this outcome (4-6). In addition, it has been shown that loss of kidney function and retinal damage, which leads to vision loss, progress in correlation (7-9).

Considering the entire disease process, it is clear that ocular tissues will be affected in various ways due to both HD and other accompanying systemic diseases. Therefore, this study aimed to evaluate the ophthalmologic conditions in patients with end-stage chronic renal failure undergoing HD. Although the topic is indeed well-explored, our study could add value in terms of updated data and a relatively large sample size.

MATERIALS and METHODS

This study was conducted retrospectively, under the principles of the Declaration of Helsinki, with the ethical approval of the Karamanoglu Mehmetbey University Clinical Studies Ethics Committee (Number: 141011, date: 20.06.2023). Written informed consent was obtained from all patients participating in the study. A total of 504 eyes of 252 patients with ESCRF undergoing HD were evaluated in this study. The data, including demographic factors, renal failure, causes of end-stage chronic renal failure, and duration of HD, were obtained for all patients.

All patients underwent detailed ophthalmic examination, including measurement of Snellen best-corrected visual acuity (BCVA), slit-lamp examination, Goldmann applanation tonometry, and dilated fundus examination with +90D lenses. The Lens Opacities Classification System III (LOCS

III) was used for grading cataracts. The presence of any drusen, microaneurysm, hemorrhage, neovascularization, pigment epithelial changes, geographic atrophy, and signs of exudative macular degeneration was noted. The optical coherence tomography (OCT) and fundus fluorescein angiography (FFA) imaging were used for diagnostic purposes when deemed necessary. Patients also completed the Ocular Surface Disease Index (OSDI) at the initial visit. In addition, Schirmer test results, tear break-up time (TBUT), and corneal staining scores (Oxford Scheme) were measured for all patients. For the Schirmer test, a strip of filter paper was placed in the middle and lateral third of the lower eyelid, without any anesthetic or other eye drops instilled into the eye. After five minutes, strips were carefully removed. The length of the moistened area of the strip was measured using the scale. A measurement greater than 10 mm after 5 minutes was considered normal. To measure the TBUT, a fluorescein strip was applied to the lower fornix of the patients' eyes. The lamp is switched to a cobalt blue filter, and the eye is examined under a broad beam covering the whole cornea. The patients were asked to blink once and keep their eyes open. TBUT is noted as the time interval between the last blink and the appearance of the first randomly-distributed dry spot. A value of 10 seconds or greater is considered normal. In addition, the corneal staining scores were classified from 0 to 5, based on the Oxford Scheme (10,11).

RESULTS

A total of 504 eyes of 252 patients with ESCRF undergoing HD were included in the study. The mean age was 65.21±13.15 years (range 21-87) and the average duration of HD was 4.95±4.25 years (2-20). The most common cause of chronic renal failure was hypertension (Table 1). Other etiologic factors are listed in Table 2. Comorbidities are also summarized in Table 3.

Table 1. Demographic features of patients undergoing hemodialysis treatment

	Female	Male
n	120	132
Age(Years)	63.11	66.34
Duration of HD (years)	5.21	4.65
Reason for ESCRF	Hypertension (46.2%)	Hypertension (48.11%)

ESCRF: End-stage chronic renal failure, HD: Hemodialysis.

Table 2. Etiologic causes of end-stage renal failure.

ESCRF Etiology	% (n)
Hypertensive Nephropathy	47.2 (119)
Diabetic Nephropathy	22.7 (57)
Glomerulonephritis	11.6 (29)
Obstructive Nephropathy	5.1 (13)
PKD	4.4 (11)
Chronic Interstitial Nephritis	3.9 (10)
Other Causes	5.1 (13)

ESCRF: End-stage chronic renal failure, PKD: Polycystic kidney disease

Table 3. Comorbidities accompanying ESCRF patients.

Comorbidities	% (n)
Hypertension	83.3 (210)
DM	36.5 (92)
CVD	52.3 (132)
Anemia	67 (169)
Mineral and Bone Disorder	73.8 (186)
Dyslipidemia	68.2 (172)
Hyperparathyroidism	33.3 (84)

CVD: Cardiovascular disease, DM: Diabetes mellitus, ESCRF: End-stage chronic renal failure

When the anterior segment findings are evaluated, it was found that 237 (47.2%) eyes were pseudo-phakic and 170 (33.7%) eyes had a cataract in different grades. Table 4 summarizes the grading of each type of cataract in the study group. Posterior segment findings were as follows: 120 of 504 (23.8%) eyes had proliferative diabetic retinopathy (PDRP), 28 of 504 (5.5%) had non-proliferative DRP, 20 of 504 (3.9%) had choroidal neovascular membrane (CNVM), 56 of 504 (11.1%) had geographic atrophy (GA), 36/504 (7.1 %) had drusen in various size, and 60/504 (11.9%) had epiretinal membrane. Twenty (7.8%) patients have glaucoma, and 94 (37.1%) patients had dry eye disease (Tables 5 and 6). Etiologic causes of glaucoma are summarized in Table 7.

Table 4. Grading of different types of cataracts in ESCRF patients using the LOCS III grading system

Type of Cataracts	Grade 1 % (n)	Grade 2 % (n)	Grade 3 % (n)	Grade 4 % (n)	Grade 5 % (n)
Nuclear Opacity Predominant	20.6 (35)	18.3 (31)	10 (17)	5.8 (10)	1.1 (2)
Cortical Opacity Predominant	7.6 (13)	10.6 (18)	4.2 (7)	2.9 (5)	N/A
Posterior Subcapsular Predominant	4.2 (7)	7 (12)	3.5 (6)	4.2 (7)	N/A

ESCRF: End-stage chronic renal failure, LOCS III: Lens opacities classification system

Table 5. Anterior segment findings in patients undergoing hemodialysis

Anterior Segment Findings	n	%
Phakic	96	19.1
Pseudo-phakic	237	47.2
Cataract (Various Grades)	170	33.7
Dry Eye Disease	186	37.1

Table 6. Posterior Segment Findings in ESCRF Patients.

Posterior Segment Findings	n	%
Non-Proliferative Diabetic Retinopathy	28	5.5
Proliferative Diabetic Retinopathy	120	23.8
Choroidal Neovascular Membrane	20	3.9
Geographic Atrophy	56	11.1
Drusen	36	7.1
Epiretinal Membrane	60	11.9

ESCRF: End-stage chronic renal failure

Table 7. Causes of glaucoma in ESCRF patients.

Causes of Glaucoma	% (n)
Primary Open Angle Glaucoma	65 (13)
Secondary Glaucoma due to Hemodialysis	15 (3)
Steroid-induced Glaucoma	10 (2)
Neovascular Glaucoma	10 (2)

ESCRF: End-stage chronic renal failure

DISCUSSION

Patients with end-stage renal disease may have various ocular pathologies as a result of both the high uremic milieu caused by the pathology of the disease and the fluid-electrolyte irregularities caused by HD treatment, and also co-morbid diseases like DM or hypertension. These ocular symptoms may differ from simple conjunctivitis to sight-threatening retinal problems.

As it is known, serum phosphate and calcium levels are found to be increased in HD patients, and this causes accumulation in various tissues such as the ocular surface and conjunctiva. This contributes to tear-ocular surface irregularity and eventually dry eye formation. The tear break-up time and Schirmer test measurements are found to decrease among those patients. Aktas et. al reported that conjunctival deposits

may have been a reason for the decreased Schirmer or TBUT values, reduced number of goblet cells, and dry eye, and they caused tear-film instability (12). They found dry eye in 21.3% of the population, which is quite lower than our results. In another study, Kal et al. found that TBUT and Schirmer values were significantly lower than the control group (13). They stated that the prevalence of dry eye was significantly higher in chronic renal failure patients undergoing HD. In our study, nearly one-third of our population had dry eye disease, which is consistent with previous study results. Dry eye disease is an important condition that affects the quality of life and should be taken into account in patients undergoing HD treatment.

In ESRD, uncontrolled serum calcium deposits, which are generally higher than in healthy subjects, accumulate in the crystalline lens, disrupting the clear nature, thus leading to cataract formation in patients undergoing HD (9). Furthermore, oxidative stress may contribute to the development of cataracts by paving the way for the formation of oxygen-free radicals (14). DM is one of the most common factors in the development of cataract in ESRD. In diabetic patients, the increased osmolarity due to high glucose levels results in fluid accumulation in tissues like the crystalline lens. This disrupts the transparency of the lens and facilitates the formation of cataracts. Similar to our study, in a population-based study from Singapore, Wong et. al. reported that 74,6 % of patients with ESRD had cataracts, and they suggested that screening for ocular disease and visual impairment is important in patients with kidney failure (15).

Glycalization and advanced glycatized-end products due to high glucose levels in DM may cause not only cataracts but also various damages in tissues, such as microangiopathy, microaneurysm, and other damages. For this reason, close-up monitoring is essential for diabetic patients undergoing HD treatment. Wong et al. pointed to this important issue about the visual loss in diabetic patients and they stated that the increased severity of retinal complications in diabetic renal failure emphasizes the need for regular monitoring because the retinopathy is asymptomatic, may progress rapidly if untreated, and visual loss can be prevented or limited with treatment (6).

There are different results in terms of the incidence of diabetic retinopathy in patients with renal failure in the literature. In a study conducted among 119 chronic renal failure patients, PDRP was present in 38 diabetic cases (31.6%), and half of them were detected for the first time, which also emphasizes the importance of retinal evaluation in renal patients (16). Likewise, Deva et al. (17) evaluated retinal abnormalities in chronic kidney diseases (CKDs), and they found that if the patients have DM-associated renal failure, they also have retinopathy at the same time. The authors expressed that 28% of patients with CKD stages 3 to 5 had moderate-severe diabetic retinopathy. In another study, Ismayilov et al. (18) reported that proliferative diabetic retinopathy was found in 21% of HD patients. In our study, the rate of diabetic retinopathy was found to be around 28%, which was consistent with previous studies, although the comparison is not appropriate because factors like renal failure levels, HD treatment existence, and co-morbid disease would probably affect the outcomes.

The factors that were found responsible for AMD development, like smoking, age,

DM, hypertension, and also oxidative stress, inflammation, and genetic factors, were also held responsible for kidney disease development. For example, hypertension could damage renal vasculature with atherosclerosis, and this might contribute to the progression of kidney failure. Furthermore, due to the low glomerular filtration rate in CKDs, excessive waste products and other free radicals cause oxidative stress, which is highly promotive of particularly wet AMD development. Anatomical and functional similarities in the vascular structures of the kidney and eye could explain why they may be affected by common vascular pathologies, because both the kidney and eye are end-arterial organs (15,18-23).

The genetic variations causing tissue damage in both kidneys and eyes were described in previous studies. The polymorphisms in the complement factor H (CFH) gene, which have an effective role in the complement activation cascade, have been defined for pathologies in both tissues. The similar complement activation and the genetic predisposition in this process were described in another study conducted by Seddon et. al. (21). Several other studies also pointed out that relative deficiencies in complement Factor H can result in excessive alternative pathway activation and may promote both thrombotic microangiopathies as well as debris deposition which would contribute to AMD and kidney failure pathogenesis. (21,24-27)

Several studies have shown an association between CKD and age-related macular degeneration. Weiner et.al (24) screened over 8000 participants with a kidney disease defined as albuminuria and lower glomerular filtration rate (GFR). About 800 of them had early AMD (10.4%), and 51 of them had late AMD findings (0.7%). In our study, late AMD findings (choroidal neovascular membrane, geographic atrophy) were found in 15% of all participants. The difference between the two studies may result from the patient's renal status because in our study, all patients had end-stage chronic renal failure and had undergone HD. Wang et al. investigated over 17000 end-stage renal disease patients having HD treatment and they showed that patients with ESRD undergoing long-term dialysis and the incidence of AMD was 1.72 times higher than in patients without a history of kidney disease (6). In another study, Leisy et al. investigated the association between reduced renal function and the presence of geographic atrophy (GA), which is one of the components of late AMD; they found that reduced GFR was significantly associated with geographic atrophy (26). 19% of participants had geographic atrophy in their study; similar to our study, GA was found at 11.9%.

In conclusion, the incidence of different eye problems increases in patients with CKD undergoing dialysis treatment. Routine ophthalmic examination of these patients will provide preventive treatments and reduce the risk of low vision due to complications.

Highlights

1. The incidence of eye pathologies increases in patients with CKD undergoing HD.

2. Pathologies can range from benign ocular surface diseases to sight-threatening conditions.

3. Routine eye examination of these patients will allow preventive treatment and reduce the risk of vision loss due to complications.

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