Ophthalmic Situation of The Patients With Chronic Renal Failure Undergoing Haemodialysis

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Abstract

Haemodialysis(HD) is the unique treatment modality for end stage chronic renal failure (ESCRF) patients. In these patients , refractive changes , dry eye, increased tear osmolarity, conjunctival calcium deposits, band keratopathy, corneal endothelium changes, lenticular opacity, macular edema, ischemic optic neuropathy, elevated intraocular pressure, retinal detachment, and retinal hemorrhage can be seen due to haemodialysis or ESCRF. We aimed to assess the ophthalmological situation of the patients with ESCRF undergoing haemodialysis

Methods:

A total of 504 eyes of 252 patients with ESCRF undergoing haemodialysis were recruited in this study. All patients were asked about demographic factors, renal failure and haemodialysis information. All participants were underwent total ophthalmologic examination

Results:

A hundred and twenty patients were female, the average age was 65.21 ± 13.15 years (range 21-87) and average duration of haemodialysis was 4.95 ± 4.25 years (2-20). The most reasons of the chronic renal failure is hypertension 119/252 (47.2%) eyes were pseudophacic and 170 (33.7%) eyes have cataract in different grades. 120 of 504 (23.8%) eyes have proliferative diabetic retinopathy (DRP) , 28 of 504 (5.5%) have non-proliferative DRP , 20 of 504 (3.9%) have choroidal neovascular membrane (CNVM) , 56 of 504 (11.1%) have geographic atrophy, 36/504(7.1 %) have drusen , and 60/504 (11.9%) have epiretinale membrane. Twenty (7.8%) patients have glaucoma and 94 (37.1%) patients have dry eye disease .

Conclusion:

The most common vision threatening situation in ESCRF patients was cataract. 76.5% of the eyes have still cataract or had cataract surgery. Most common ocular surface problem was dry eye disease (37.1%). In addition ,proliferative DRP rate was more than in all diabetic population, because they are probably at last stages of the organs affected by diabetes mellitus.

Introduction

Chronic kidney diseases (CKD) refer to pathophysiological conditions that have many different 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 (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 3 months with structural and functional abnormalities. End stage renal disease, moreover, is defined as a GFR less than 15 mL/min (1)

However, this definition is not strictly certain because many patients may live years without being symptomatic or needing dialysis even if they had been diagnosed end stage kidney failure(2)

There are various reasons could be included to pathogenesis like hypertension, diabetes mellitus, systemic lupus, rheumatoid arthritis, some medications including non-steroidal anti-inflammatory drugs (NSAIDs), calcineurin inhibitors, and antiretrovirals.

According to a study the number of terminal kidney failure patients is growing worldwide at an average rate of 7% per year. This may be an important indicator of the need for more hemodialysis in the future and the medical problems associated with it. (3)

The main aim with hemodialysis 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 and the eye is one of them. A wide spectrum of pathologies and chronic eye diseases such as diabetic retinopathy, glaucoma, macular degeneration are seen in the list. 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 that outcome. (4)(5)(6)

The effects of end stage kidney disease on visual system has been evaluated and reviewed in the literature since 1960's.The uremic state and dialysis effects have been noted on various ocular tissues like conjunctiva, cornea. Irritated red eyes, corneal clouding, episcleritis, higher ocular pressure, cataract were among ocular manifestations. Moreover the comorbid diseases like diabetes or vascular diseases and the multifactorial reasons in end stage kidney disease pathogenesis could have strong effect on eyes and periocular tissues such as, end stage kidney diseases could present higher incidence with macular degeneration both non exudative and exudative and vein occlusions. Hospital based studies have detected high prevalence of visual impairment and blindness in patients with chronic kidney diseases, and also they found that the more kidney function decreases, the retinal damage leading to visual loss rises.(7)(8)(9)

Due to the high probability of various ocular problems in hemodialysis patients, routine ophthalmological examinations will help to diagnose and treatment of ocular damages that may occur in the acute period, and even alterations can be planned in the hemodialysis treatment for this reason (such as stopping anticoagulants).

Because of both these reasons and co existing other systemic disorders ocular tissues are likely to be affected in various ways so we planned to assess the ophthalmologic situations in end stage chronic renal failure patients undergoing haemodialysis.

Methods

A total of 504 eyes of 252 patients with ESKRF undergoing haemodialysis were recruited in this study. All patients were asked about demographic factors, renal failure and haemodialysis(HD) information including main reason for end stage chronic renal failure, duration of HD.

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 presence of any drusen, microaneusym, hemorrhage, neovascularisation, pigment epithelial changes, geographic atrophy and signs of exudative macular degeneration were noted.

Patients completed the Ocular Surface Disease Index (OSDI) at initial visit.

Schirmer, Tear break-up time (TBUT) and corneal staining scores (Oxford Schme) were measured for all patients. Schirmer test was performed for a duration of 5 min after instillation of topical anesthetic drops (0.5% proxymetacaine, Alcaine). The filter paper strip was placed in the middle and lateral thirds of the lower eyelid. The corneal staining scores were classified as 0 to 5 based on the Oxford Scheme.(10) (11)

This study was conducted in accordance with the Declaration of Helsinki and ethics approval was obtained by the institutional review board of Baskent Training Hospital. Informed consent was obtained from the subjects after verbal and written explanations

Results

A hundred and twenty patients were female, the average age was 65.21 + 13.15 years (range 21–87) and average duration of haemodialysis was 4.95 + 4.25 years (2–20). The most reasons of the chronic renal failure is hypertension. 119/252 (47.2%) eyes were pseudophacic and 170 (33.7%) eyes have cataract in different grades. 120 of 504 (23.8%)eyes have proliferative diabetic retinopathy (PDRP), 28 of 504 (5.5%) have non-proliferative DRP, 20 of 504 (3.9%) have choroidal neovascular membrane (CNVM), 56 of 504 (11.1%) have geographic atrophy(GA), 36/504(7.1%) have drusens in various size, and 60/504 (11.9%) have epiretinale membrane. Twenty (7.8%)patients have glaucoma and 94 (37.1%) patients have dry eye disease .

Table 1
shows the demographic features of patients in terms of duration of hemodialysis and

	FEMALE	MALE
N	120	132
Age (yrs)	63.11	66.34
Duration of HD(yrs)	5.21	4.65
Reason for ESCRf	Hypertension (46.2%)	Hypertension (48.11%)

HD: Hemodialysis. ESCRf: End stage chronic renal failure

Table 1. *Demographic Features of Patients Undergoing Haemodialysys Treatment*

After detailed ophthalmic examinations ,anterior and posterior segment findings were noted.. 237 (47.2%) eyes were pseudophacic and 170 (33.7%) eyes have cataract in different grades. Twenty (7.8%)patients have glaucoma and (37.1%) patients have dry eye disease .

Table 2
Anterior Segment Findings in patients undergoing
Haemodialysis

ANTERIOR SEGMENT FINDINGS	N	%
<i>Phacic</i>	96	19,1
<i>Pseudphacic</i>	237	47.2
<i>Cataract (various grades)</i>	170	33,7
<i>Dry Eye Disease</i>	186	37,1

The patients underwent dilated posterior segment examination .Fundus florescein angiography and optical coherence tomography was performed. One hundred and twenty of 504 (23.8%)eyes have proliferative diabetic retinopathy (PDRP), 28 of 504 (5.5%) have non-proliferative diabetic retinopathy (NPDRP), 20 of 504 (3.9%) have choroidal neovascular membrane (CNVM), 56 of 504 (11.1%) have geographic atrophy, 36/504(7.1%) have drusen, and 60/504 (11.9%) have epiretinale membrane

Table 3
Posterior Segment Findings in ESCRf Patients

POSTERIOR SEGMENT FINDINGS	N	%
<i>Non Proliferative Diabetic Retinopathy</i>	28	5,5
<i>Proliferative Diabetic Retinopathy</i>	120	23,8
<i>Choroidal Neovascular Membrane</i>	20	3,9
<i>Geographic Atrophy</i>	56	11,1
<i>Drusen</i>	36	7,1
<i>Epiretinal Membrane</i>	60	11,9

Discussion

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

As it is known, serum phosphate and calcium levels are found to be increased in hemodialysis patients and this causes accumulation in various tissues such as ocular surface and conjunctiva. This contributes

to tear- ocular surface irregularity and eventually dry eye formation. The tear break up time and schrimers values are found decreased among those patients. Aktas et. al reported that conjunctival deposits may have been a reason for the decreased schirmer or tear break up time values, reduced number of goblet cells and dry eye and also they caused tear-film instability. They found dry eye in 21.3% of population which is quite less than our result. In another study Kal et al found that break up time and schirmer values were significantly lower than control group. They stated that they determined patients with chronic renal failure undergoing hemodialysis had significantly high dry eye prevalence. 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 not be ignored in patients undergoing hemodialysis treatment. (12) (13)

The cataract is a condition of the crystalline lens losing its clarity due to opacification and generally occurs with aging and is still the most common cause of treatable blindness in the world particularly in developing countries (14)

Many factors could be associated with cataract formation such as age, diabetes, uremia, ultraviolet exposure, smoking, and electrolyte imbalances. In end stage renal disease uncontrolled serum calcium deposits , which is generally higher than healthy subjects, accumulates in crystalline lens causing disruption the clear nature thus leading cataract formation in patients undergoing haemodialsys (9)

Regarding the process of cataract formation in patients undergoing hemodialysis another suggested pathway is carbamylation of lens proteins due to oxidative stress. Protein carbamylation refers to the posttranslational modification of proteins or amino acids via adduction with cyanat which is an end product of urea .The structure and function of proteins could change after carbmylation resulting various outcomes such as atherosclerosis, endothelial dysfunction and yellowing of the crystalline lens. Furthermore oxidative stress may contribute to the development of cataracts by paving the way for the formation of oxygen-free radicals. (15)

Diabetes is one of the most common factors in the development of end-stage renal disease. In diabetic patients the increased osmolarity due to high glucose levels results fluid accumulation into tissues like crystalline lens. This disrupts the transparency of the lens and facilitates formation of cataracts. For all these reasons, dialysis patients need to undergo routine ophthalmic examination, although it is not easy. (16)

In our study nearly half of eyes had undergone cataract surgery and one-third of them had cataract in different grades. In a similar manner, in a population based study from Singapore, Wong et. al. reported that 74,6 % of patients with end stage kidney disease had cataract and they suggested that screening for ocular disease and visual impairment is important in patients with kidney failure. (17)

Glycalization and age(advanced glycalized end) products due to high glucose levels in diabetes can cause not only cataracts but also various damages in tissues such as microangiopathy, microaneurysm and other damages. Diabetic Retinopathy is one of the main visual loss reasons among diabetic patients

. It is defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) that lesions including microaneurysms, hemorrhage, cotton wool spots, intraretinal vascular abnormalities, venous beading and hard exudates called non proliferative diabetic retinopathy (NPDR) and if neovascularization exists anywhere in retina than it is called proliferative diabetic retinopathy (PDR).

PDR may cause irreversible visual impairment due to complications like recurrent vitreous retinal hemorrhages, tractional retinal detachment, and neovascular glaucoma. That is why close up monitoring is essential for diabetic patients undergoing hemodialysis treatment. Wong et al. pointed to this important issue about 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 literature. In a study which was conducted among 119 chronic renal failure patients, proliferative diabetic retinopathy was present in 38 diabetic cases (31.6%) and half of them was detected for the first time which also emphasizes the importance of retinal evaluation in renal patients. Likewise Deva et al. determined retinal abnormalities in chronic kidney diseases and they found if the patients have diabetes associated renal failure, they also have retinopathy at the same time. They expressed that 28% patients with chronic kidney disease stages 3 to 5 had a moderate-severe diabetic retinopathy. In another study Ismayilov et al. reported that proliferative diabetic retinopathy was found 21% among hemodialysis patients. (18)(19)

In our study, the patients with diabetic retinopathy undergoing hemodialysis were evaluated, the rate of diabetic retinopathy was found to be around 28% which was quite consistent with previous studies. Although the comparison is not totally appropriate because factors like the renal failure levels, hemodialysis treatment existence and co morbid other disease would probably effect the outcomes (20)

Age related macular degeneration (AMD) is the leading visual impairment reason among developed countries. AMD were defined in two stages. Early AMD has slow pigment and soft drusen deposition with degeneration of retinal pigment epithelial cells and any drusen type with areas of depigmentation or hypopigmentation of the retinal pigment epithelium without vascular component.

Late AMD on the other hand, was defined as the presence of exudative macular degeneration or geographic atrophy (the atrophic roundish area without pigment epithelial cells that choroidal vessels can be visible). This is described as dry AMD. When choroidal neovascularization and hemorrhage exist, it is defined as wet AMD in late stages. Endothelial dysfunction, Several factors were found responsible for AMD development like smoking, age, diabetes, hypertension and also oxidative stress, inflammation and genetic factors

The factors mentioned above were also held responsible for kidney disease development. For example hypertension could damage renal vasculature with atherosclerosis and this might contribute kidney

failure progression. Furthermore , due to low glomerular filtration rate in chronic kidney diseases , 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 kidney and eye could explain that they may be affected by common vascular pathologies because both kidney and eye are end-arterial organs. (17)

(21)(22)(23)(24)(25)

The genetic variations which causes tissue damage in both kidney and eye were described in previous studies. The polymorphisms in the complement factor H(CFH) gene, which has an effective role in the complement activation cascade, have been defined for pathologies in both tissues. In particular, self-destruction has been observed in both tissues, since the glomerular basement membrane and bruch membrane have anionic surfaces and complement mediated activation can not be prevented as a result of mutations in the polyanion binding region in the CFH gene. The similar complement activation and the genetic predisposition in this process was described in another study conducted by Seddon et. al.

Also, Weiner et. al pointed out that relative deficiencies in complement Factor H can result in excessive alternative pathway activation and may promote both thrombotic microangiopathy as well as debris deposition which would contribute amd and kidney failure pathogenesis.(26)

(27)(28) (29)(30)

Several studies have shown association between chronic kidney disease anda age-related macular degeneration. Weiner et.al screened over 8000 participants with a kidney disease defined with albuminuria and lower glomerular filtration rate(gfr). About 800 of them had early amd (10.4%) and 51 of them late amd findings (0.7%).In our study late amd findings (choroidal neovscualr membrane , geographic atrophy) was found 15% of all participants. The difference between two studies may result from the patients renal status becuase in our study all patients had end stage chronic renal failure and they had been underwent hemodialysis (26)

Wang et al investigated over 17000 end stage renal disease patients having hemodialsys treatment and they showed that patients with ESRD undergoing long-term dialysis exhibited a 1.72-fold higher hazard of AMD than patients without a history of kidney disease. They also stated that the risks of both nonexudative and exudative AMD were higher in ESRD patients. We did not compare with a control group in our study but we found that nearly 1/5 of patients had AMD findings .

(31)

In another study Leisy et al. investigated the association between reduced renal functions with the presence of geographic atrophy(GA) which is one of the components of late amd and they found that reduced glomerular filtration rate was found significantly associated with geographic atrophy.19% of participants had geographic atrophy in their study, similar to our study which the GA was found 11.9% .

In conclusion the incidence of different eye problems is increasing in patients receiving chronic kidney diseases and related dialysis treatment. Routine ophthalmic examination of these patients will provide preventive treatments and reduce the risk of low vision

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