Ocular Disorders in Renal Transplant Patients

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Purpose: To determine ocular findings in patients with renal transplants and to correlate them with clinical characteristics related to transplantation.
Methods: This cross-sectional study was performed on 150 patients who had received a renal transplant of at least three months' duration with serum creatinine levels < 3 mg/dl. All patients underwent a complete ophthalmologic examination. Clinical variables related to the transplant included cause of renal failure, duration of hemodialysis prior to transplantation and immunosuppressive regimen.
Results: Overall, 91 male and 59 female subjects with mean age of 39±17.7 years were included. At least one ocular abnormality could be detected in 89.3% including visual acuity ≤20/25 (48.6%), conjunctival degeneration in the palpebral fissure (36.6%), posterior subcapsular cataracts (24%), pinguecula (17.3%), retinal pigment epitheliopathy (14%), arteriovenous crossing changes (8.6%), proliferative diabetic retinopathy (6%), central serous chorioretinopathy and retinal vein occlusions (each in 3.3%), and non-proliferative diabetic retinopathy, optic nerve atrophy and diabetic macular edema (each in 2.7%). Abnormal ocular findings were not correlated with the underlying renal disorder or use of cyclosporine and prednisolone, however they were positively correlated with transplant duration, pre-transplant dialysis duration and azathioprine or mycophenolate mofetil consumption.
Conclusion: Ocular disorders are frequent among renal transplant patients especially with older transplants and those with a longer period of pre-transplant hemodialysis.

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INTRODUCTION

Advances in surgical technique and development of more effective immunosuppressive agents have rendered kidney transplantation an effective renal replacement therapy. Nowadays patients with end stage renal disease (ESRD) have better survival rates and enjoy improved quality of life after renal transplantation.[1] Ocular complications following renal transplantation are mainly secondary to the underlying cause of renal failure, accumulation of noxious materials, cytomegalovirus infection and immunosuppressive therapy. These factors can result in significant ocular morbidity secondary to conditions such as cataracts, glaucoma, hypertensive retinopathy, conjunctival deposits, and drug-induced retinitis.[2] Management of ocular complications in renal transplant patients can decrease morbidity and further improve their quality of life. The aim of this study was to determine the prevalence of ocular abnormalities in renal transplant patients and to correlate them with the underlying cause of renal insufficiency, transplant duration, duration of pre-transplantation dia-

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lysis and immunosuppressive regimen.

METHODS

From February 2004 to November 2004, renal transplant patients at Feiz Hospital Nephrology Clinic, Isfahan, Iran who received monthly immunosuppressive therapy or follow up visits were referred for a comprehensive ophthalmologic examination. Only patients who were at least three months post-transplantation and had serum creatinine levels less than 3 mg/dl were included in the study. After obtaining informed consent, all patients underwent a complete ocular examination including autorefraction, best corrected Snellen visual acuity (BCVA), ocular motility and external examination, slitlamp biomicroscopy, applanation tonometry and funduscopy using a non-contact 78 D lens following pupil dilation with tropicamide 1% in hypertensive patients and tropicamide 1% and phenylephrine 5% in normotensive subjects. A vitreoretinal subspecialist performed all ocular examinations.

Ocular findings were classified as diabetes-related complications including clinically significant macular edema, non-proliferative diabetic retinopathy and proliferative diabetic retinopathy; and non-diabetes related complications. Previous nephrologic history including underlying disease causing ESRD, post-transplant duration, duration of pre-transplant dialysis and immunosuppressive regimen were recorded. Data was analyzed using Mann-Whitney U and Chi square tests for comparing differences in mean values and frequencies, respectively. Statistical significance was set at $P<0.05$.

RESULTS

During the study period, 150 renal transplant patients including 91 (60.7%) male and 59 (39.3%) female subjects with mean age of 39.9±17.7 (range 20-72) years were evaluated. There was at least one abnormal ocular finding in 134 subjects (89.3%); in the remaining 16 patients (10.7%) the eye examination was unremarkable. Table 1 summarizes ocular findings in these patients. The most prevalent abnormality was subnormal visual acuity (BCVA $\leq$20/25) in 73 cases (48.7%). Cataracts were present in 45 patients (30.0%) which were predominantly posterior subcapsular (PSC) (37 cases). Cataract surgery was performed in seven cases after renal transplantation. Ocular findings of less clinical importance or lower frequency included lid swelling, blepharoptosis, phthisis bulbi, and pseudotumor cerebri, each in 2 patients (1.3%), and fourth nerve palsy, herpes zoster ophthalmicus, retinal drusen, and corneal leukoma, each in one case (0.7%). No patient had intraocular pressure (IOP) more than 21 mmHg or glaucomatous optic nerve head changes.

Table 1 Frequency of ocular finding in renal transplant patients

Ocular finding	No.	%
BCVA $\leq$ 20/25	73	48.7
Conjunctival degeneration and depositions	55	36.7
Cataract or cataract extraction	45	30.0
Pinguecula	26	17.3
Retinal pigment epitheliopathy	21	14.0
Arteriovenous cross changes	13	8.7
Proliferative diabetic retinopathy	9	6.0
Central serous chorioretinopathy	5	3.3
Central/branch retinal vein occlusion	5	3.3
Non-proliferative diabetic retinopathy	5	3.3
Clinically significant macular edema	4	2.7
Non-glaucomatous optic nerve atrophy	4	2.7

BCVA, best-corrected visual acuity

Hypertension (HTN) was the most frequent cause of ESRD and was present in 38 patients (25.3%), of whom 35 (92.1%) had abnormal ocular findings (table 2). Ocular complications unrelated to diabetes were found in 90% of diabetic and 86% of non-diabetic patients (P= 0.48). Diabetes-related ocular complications were seen in 40% of diabetic subjects.

The post-transplant immunosuppressive regimen consisted of single therapy in 9 (6.0%), dual therapy in 34 (22.7%) and triple therapy in 107 (71.3%) patients. The rates of ocular abnormalities in patients with single, dual and triple immunosuppressive therapy were 100%,

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94.1%, and 86.9%, respectively. The mean number of immunosuppressive agents was 2.93 and 2.67 in patients with and without ocular complications (P= 0.006). Ocular findings are cross tabulated with immunosuppressive agents in table 3. Ocular complications were not significantly different in patients under treatment with regimens containing cyclosporine or prednisolone, however they were more prevalent in patients who received azathioprine or mycophenolate mofetil.

Mean post-transplant duration was 4.1±3.6 years in patients with ocular findings vs 2.9±3.6 years in patients without ocular findings (P<0.05). Table 4 summarizes the frequency of ocular complications based on post-transplant duration and shows that only the incidence of central serous chorioretinopathy (CSCR) was significantly positively correlated with the duration of renal transplant.

Table 2 Etiology of renal failure and ocular complications in renal transplant patients

Primary etiology	Number (% of total) of primary etiology	Number (%) of ocular finding in each etiologic group
Hypertensive nephropathy	38 (25.3)	35 (92.1)
Glomerulonephritis	23 (15.3)	22 (95.7)
Diabetes mellitus	20 (13.3)	20 (100)
Inherited and congenital diseases	19 (12.7)	16 (84.2)
Pyelonephritis	8 (5.3)	7 (87.5)
Obstructive nephropathy	6 (4.0)	6 (100)
Tubulointerstitial diseases	4 (2.7)	4 (100)
Unknown causes	37 (24.7)	29 (78.4)

Table 3 Frequency of ocular complications in renal transplant patients with respect to immunosuppressive agent

Immunosuppressive agent	Number (% of related drug group)		P value*
	with ocular findings	without ocular findings	
Cyclosporine (n= 142, 94.7%)	126 (88.7)	16 (11.3)	0.396
Prednisolone (n= 137, 91.3%)	122 (89.0)	15 (11.0)	0.585
Mycophenolate mofetil (n= 77, 51.3%)	63 (81.8)	14 (18.2)	0.02
Azathioprine (n= 50, 33.3%)	48 (96.0)	2 (4.0)	0.05
Total (n= 150, 100%)	134 (89.3)	16 (10.7)	

* Chi square test

Table 4 Distribution of ocular complications based on post-transplant duration

Ocular complications	Number (% of related ocular finding) of patients based on duration of transplant (year)			P value*
	< 1	1-5	> 5	
BCVA < 20/25 (n= 73)	14 (19.2)	37 (50.7)	22 (30.1)	0.27
Conjunctival degeneration (n= 55)	16 (29.1)	24 (43.6)	15 (27.3)	0.47
Cataract or cataract extraction (n= 45)	8 (17.8)	19 (42.2)	18 (40.0)	0.057
Pinguecula (n= 26)	4 (15.3)	10 (38.4)	12 (46.1)	0.10
Retinal pigment epitheliopathy (n= 21)	7 (33.3)	4 (19.1)	10 (47.6)	0.17
Arteriovenous cross changes (n= 13)	5 (38.5)	3 (23.0)	5 (38.5)	0.18
Proliferative diabetic retinopathy (n= 9)	2 (22.2)	6 (66.7)	1 (11.1)	0.19
Non-proliferative diabetic retinopathy (n=5)	1 (20.0)	4 (80.0)	0	0.13
Central serous chorioretinopathy (n= 5)	0	2 (40.0)	3 (60.0)	0.012
Clinically significant macular edema (n= 4)	0	4 (100)	0	-

BCVA, best-corrected visual acuity

* Fisher exact test

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Mean duration of pre-transplantation dialysis was 18.3±22.9 and 6.6±7.2 months in patients with and without ocular complication, respectively (P<0.0001). Corresponding figures were 2.1±2.5 and 1.0±1.1 months in patients with and without conjunctival degeneration, respectively (P< 0.001).

DISCUSSION

In the current study only patients with good transplant function (serum creatinin <3 mg/dl) were selected to avoid interference by ocular complications associated with renal failure per se. HTN was the most prevalent underlying etiology of chronic renal failure; however it can be a complication of the renal disease. Based on previous reports, the most common cause of renal failure is diabetes mellitus followed by HTN.[3]

Subnormal visual acuity (BCVA < 20/25) was the most prevalent functional ocular disorder (47%) in our series which can also be a sign of various conditions. Shimmyo et al[4] reported BCVA of 20/20 in most of their patients.

The most frequent anatomical disorders in the present study were conjunctival degenerations and depositions (36.7%). Conjunctival degenerative lesions often result from ultraviolet radiation,[5] but in renal transplant patients they seem to be mainly correlated with hemodialysis. In a study on patients who were on hemodialysis treatment, the most frequently observed anterior segment abnormality was also conjunctival deposits (66.6%).[6] These conjunctival lesions may result from accumulation of toxic materials in the body. We found a significant relationship between this complication and pre-transplant dialysis duration.

Posterior subcapsular cataract was the next prevalent complication (30%). The incidence of this complication varies from 5% to 62.5% in different studies.[2,4,7] Early studies reported a dose-dependent relationship between corticosteroid treatment and cataracts, however with the increased use of cyclosporine, evidence supporting this relationship is weak.[8] Some studies also reported a direct dose-dependent relationship between steroid treatment and severity of cataract.[9] We did not find any significant relationship between the use of oral prednisolone and cataracts. This may be due to the tapering of prednisolone because of coadministration of immunosupp-ressive agents.

Our study showed a decrease in ocular complications by increasing the number of immunosuppressive agents, such that all cases under single therapy versus 86.9% of patients receiving triple therapy had ocular abnormalities. This may be due to the associated decrease in individual drug dosage when used in combination therapy.

Although IOP rise is a common side effect of topical steroids, systemic corticosteroid treatment rarely causes glaucoma.[10,11] Based on the current series and similar studies[2,4], the rate of IOP rise secondary to systemic corticosteroids in renal transplant patients does not seem to be higher than the general population. However keeping in mind other reports on the relatively high incidence of IOP rise[7,12], special attention is necessary in these particular cases. We found non-glaucomatous optic disc changes in 2.7% of our patients which is consistent with other studies.[2]

Our study, as well as others[2], showed that certain ocular complications are directly related to post-transplant survival. The strongest association was seen between CSCR and post-transplant survival which may indicate a direct relation between renal transplantation and this entity. In a study on 60 CSCR patients, three cases (5%) had previously undergone renal transplantation[13] which also suggests a relationship between these two entities.

In conclusion, the incidence of ocular complication in renal transplant patients is relatively high. Although most complications are not sight-threatening, regular ophthalmologic examinations can result in early detection, better management and improved quality of life.

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