Ocular Findings among the Patients of Renal Transplantation

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ABSTRACT

Introduction: Renal diseases are on rise globally due to increased incidence of non-communicable-diseases as well as primary-kidney diseases and frequent use of nephrotoxic drugs. Only definite treatment of End-Stage-Renal-Disease (ESRD) is renal transplantation. Immuno-suppressive-drugs are prescribed lifelong after renal transplantation especially steroids which can lead to various sight threatening complications.

Methods: This cross sectional, observational study included 62 eyes of 31 patients who had undergone renal transplantation, at least 3 months prior were referred from Nephrology Department. Comprehensive eye evaluation was done at B. P. Koirala Lions Centre for Ophthalmic Studies (BPKLCOS), Department of Ophthalmology, Institute of Medicine.

Results: The average age of participants was 37 ±10.57 years with 77.4 % (n=24) male. Mean duration of renal transplant was 5.10 ± 3.61 years. Fifty-eight percent (n=18) had hypertensive kidney disease. Diabetes Kidney disease, recurrent UTI, CKD of unknown causes and combined case of diabetes plus hypertension were seen in 6.4% (n=2) each. Sixty percent of the patients had some kind of ocular involvement.Twenty-nine percent (n=18) had sub-normal visual acuity of ≤ 6/9. Cataract was seen in 29% (n=18) of eyes followed by pinguecula (17.7%, n=11) and hypertensive-retinopathy (17.7%, n=11). Glaucoma and Diabetic-retinopathy were seen only in 6.4% (n= 4) of each eyes. There was no association seen between ocular findings with cause of renal transplant, duration of transplant and renal function status in bivariate analysis.

Conclusions: Some form of ocular abnormality is commonly seen in patients of renal transplantation who are on immunosuppressive drugs. However, incidence of sight threatening complications are rare.

Keywords: end-stage-renal-disease, non-communicable disease, ocular-morbidity

Financial Interest : Nil
Conflict of Interest : Nil

Received : 11.09..2022
Accepted : 21.12.2022

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Access this article online
Website: www.nepjol.info/index.php/NEPJOPH
DOI: https://doi.org/10.3126/nepjoph.v15i1.52446

ISSN: 2072-6805, **E-ISSN:** 2091-0320

INTRODUCTION

There is an increasing trend of non-communicable diseases, mainly Diabetes and Hypertension which lead to compromised renal function as well as renal failure. Kidney damage can occur in chronic glomerulonephritis, obstructive urinary tract diseases, polycystic kidney diseases, connective tissue diseases and in patients on drugs like non-steroidal anti-inflammatory drugs and antiretroviral agents (Banaga et al, 2015). End stage renal disease (ESRD) occurs due to irreversible loss of kidney function. This might lead to complications like hyperkalaemia or pulmonary oedema within few days to weeks which can have fatal outcome. End stage renal disease can be treated with renal transplantation only (Rodger, 2012). The rejection can be the main reason for failure in those patients who have undergone renal transplant. Intensive Immunosuppressive therapy is usually given for a long period of time following transplant surgery, to avert transplant rejection. The triple therapy consisting of corticosteroids along with mycophenolate mofetil (or azathioprine) and tacrolimus (or cyclosporine) have been used as a mainstay of immunosuppressive drugs after renal transplant. Among these, corticosteroids have been the main immunosuppressive drug widely used after renal transplantation, but these drugs cause many systemic and ocular side effects. Ocular side effects might lead to irreversible vision loss.

Therefore, it is very important to evaluate the ocular findings in these patients at regular intervals. Timely diagnosis of ocular diseases and prompt management save these patients from losing vision and improve their quality of life.

MATERIALS AND METHODS

This hospital-based analytical cross-sectional study was conducted from May 2021 to October 2021 in the department of ophthalmology, BP Koirala Lions Center for Ophthalmic Studies, Maharajgunj, Kathmandu, Nepal. Non-probability convenience sampling was done. Patients were referred from Nephrology department of Tribhuvan University Teaching Hospital, who had undergone renal transplantation at least 3 months prior. Patients having significant ocular morbidities before transplantation were excluded from the study. This study included 62 eyes of 31 patients. The approval to conduct the study was taken from the institutional review committee beforehand. After taking the informed consents and detailed history, all patients were examined thoroughly and ocular findings were recorded. Aetiology of ERDS and comorbidities, pretransplant dialysis duration, post-transplant duration, renal function status, and total dosage of steroids were also analysed. Auxiliary tests (Optical coherence tomography, Visual field examination) were also performed as per need for associated ocular findings. Type of cataract was noted, Early Treatment Diabetic Retinopathy Study (ETDRS) classification was used for diabetic retinopathy grading and Keith Wagner Becker classification system used for grading of hypertensive retinopathy.

After compilation of data, IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, N.Y., USA)was used for the analysis. Chi-square test and Fishers exact test were used for bivariate analysis. P value of <0.05 was considered as significant.

RESULTS

Sixty two eyes of 31 renal transplant patients were included. Average age of the participants was 37 years (SD ± 10.57 years, rang:19 - 62 years). More than two-thirds of the participants were male (male 77.4%, n=24) and female (22.6% n=7). Mean duration of renal transplant was 5.10 years (SD ± 3.61 years) ranging from three months to 13 years. Best corrected visual acuity was subnormal (≤6/9) and was seen in 29% (n=18) of eyes.

More than half (n=18, 58%) had only hypertensive kidney disease as the cause for renal failure. Diabetes Kidney disease, recurrent urinary tract infection (UTI), chronic kidney disease (CKD) of unknown causes and combined cases of diabetes and hypertension were seen in 6.4% (n=2) each. Other causes seen were pyelonephritis, Non Steroidal anti inflammatory drugs (NSAID) induced glomerulonephritis, diabetic kidney disease with small kidney and CKD due to neurogenic bladder and Churg Strauss syndrome (3.2% , n=1 in each).

Some kind of systemic disease association was found in 96.8% of patients. Among them 68% (n=21) of the patients had associated systemic hypertension and 16.1% (n=5) had diabetes mellitus. One (3.2 %) patient had neurogenic bladder and Churg Strauss syndrome.

Renal function status is determined by serum creatinine value. The cut off value is 62-115 micro mole per litre. In our study population, 45.2% (n=14) of patients had abnormal renal function.

60% (n=37) eyes had some form of ocular abnormality. Most common ocular abnormality was cataract accounting for 29% (n=18) of eyes followed by pinguecula 17.7% (n=11), hypertensive retinopathy in 17.7% (n=11). Glaucoma and diabetic retinopathy were seen only in 6.4% of each eye.

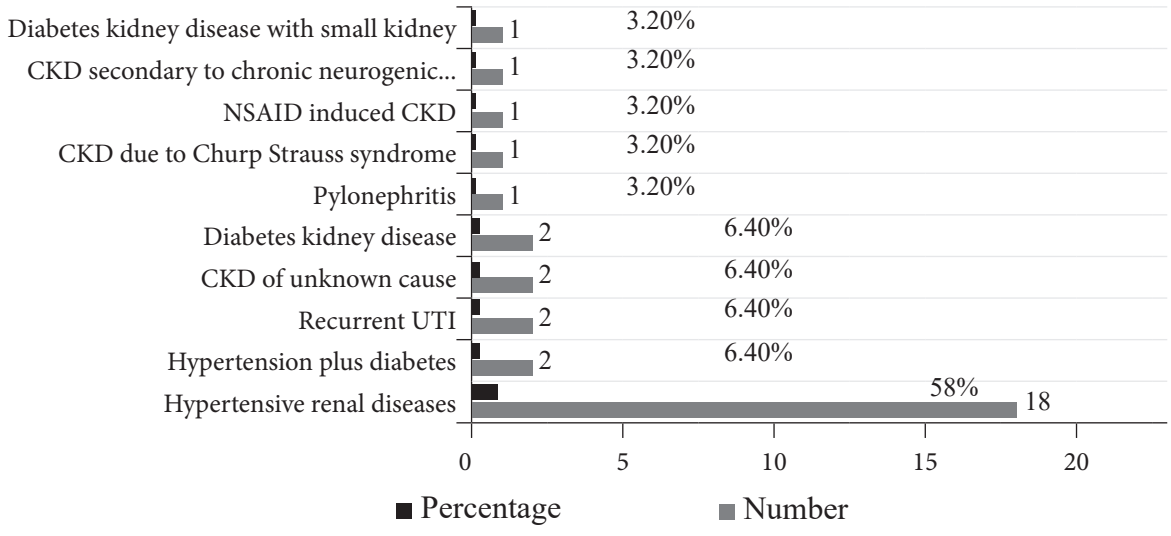

Figure 1: Aetiologies of end stage renal disease

Table 1: Spectrum of ocular findings in patients with renal transplantation

Ocular findings	Number	%
Cataract	18	29.1
Pinguecula	11	17.7
Vitreous degeneration	12	19.4
Hypertensive retinopathy	11	17.7
Diabetic retinopathy	4	6.4
Glaucoma	4	6.4
Blepharitis	3	4.8
Pseudophakia	2	3.2
Pterygium	1	1.6
Superficial punctate Keratopathy	1	1.6

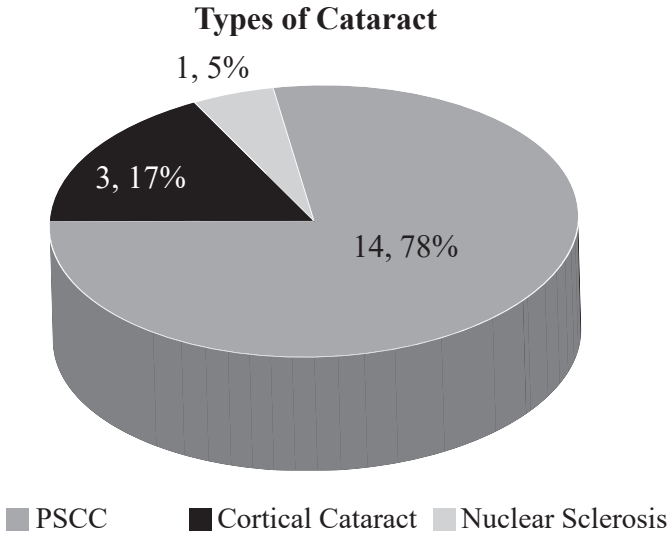

Figure 2: Types of cataract seen in patients with renal transplantation

Posterior sub capsular cataract (PSCC) was the commonest type of cataract seen in 77.7% (n=14), followed by cortical cataract in 16.6% (n=3) and nuclear sclerosis in 5.5%(n=1).

Hypertensive retinopathy was seen in 17.7% eyes (n=11) among which one had hypertensive retinopathy grade 3 changes and 16.1% (n=10) had hypertensive retinopathy grade 1 changes. Diabetic retinopathy was seen in 6.4% (n=4) eyes among which 1.6% (n=1) had mild non proliferative diabetic retinopathy (NPDR) and 4.8% (n=3) had moderate NPDR. Glaucomatous optic disc changes were seen only in 6.5% (n=4). Chorioretinal scar was present in 1.6% (n=1) secondary to laser photocoagulation for branch retinal vein occlusion.

Table 2: Retinal findings in patients with renal transplantaion

Retinal findings	Number	%
Normal	42	67.9
Mild NPDR	1	1.6
Moderate NPDR	3	4.8
Hypertensive retinopathy Gr1	10	16.1
Hypertensive retinopathy Gr3	1	1.6
Glaucomatous disc	4	6.5
Chorioretinal scar due to photocoagulation	1	1.6
Total	**62**	**100**

In all eyes, intra ocular pressure was within normal limit, ranging from 9-19 mmHg with a mean of 15.24 ±2.37 mmHg.

All patients were on oral maintenance steroids following renal transplant (duration more than three months). Patients on high maintenance doses of steroids had more lenticular and retinal problems than patients on low maintenance doses.

Out of 36 eyes who had hypertensive kidney disease, 7 had ocular surface disorder (OSD) and lens disorder and five had retinal problems. Lid, conjunctival, corneal, tear film problems are included in OSD.

Table 3: Involvement of ocular structures with different maintenance doses of steroid

Dose of oral steroid	Diagnosis category%(n)						Total
	OSD	Lens disorders	Retinal disorders	Lens and glaucoma	Lens and retina	normal	
5.00mg	20.9(n=13)	17.7(n=11)	9.6(n=6)	8(n=5)	1.6(n=1)	41.9(n=26)	100(62)
7.50mg			32.2.(n=20)		32.2(n=20)	33.8(n=21)	100(62)
10.00mg		50.0(n=31)			16.7(n=10)	33.8(n=21)	100(62)

Table 4: Ocular diagnosis in various causes of renal failure

Cause of renal failure	Ocular Diagnosis %(n)						Total
	OSD	Lens disorders	Retinal disorders	Lens and glaucoma	Lens and retina	Normal	
Hypertensive kidney disease	19.4(n=7)	19.4(n=7)	13.8%(n=5)	5.5%(n=2)	8.3%(n=3)	33.3(n=12)	100(n=36)
Diabetic kidney disease	33.3(n=2)	33.3(n=2)	0	0	0	33.3(n=2)	100(n6)
Urinary tract infection	0	16.6(n=1)	33.3(n=2)	0	16.6(n=1)	33.3(n=2)	100(n=6)
Others	10(n=1)	20(n=2)	0	0	0	70(n=7)	100(n=10)
Diabetic +hypertension Kidney disease	0	0	0	50(n=2)	0	50(n=2)	100(n=4)

Table 5: Association between ocular findings with etiology of renal transplant, duration, and renal function status

Variables	Categories	Ocular findings, n (%)		P value
		Normal	Abnormal	
Aetiology of renal transplant	Hypertensive kidney disease	7 (38.9)	11 (61.1)	0.409 [a]
	Other	7 (53.8)	6 (46.2)	
Duration of transplant	<5 years	9 (45.0)	11 (55.0)	0.636 [b]
	≥5 years	5 (45.5)	6 (54.5)	
Renal function status	Normal	10 (58.8)	7 (41.2)	0.092[a]
	Abnormal	4 (28.6)	10 (71.4)	

[a] *Chi-square test,* [b]*Fisher's exact test* *Significant <0.05*

Bivariate analysis was carried out to see the association between ocular findings with cause of renal transplant, duration and renal function status.

Fifty-eight percent (n=18)of renal transplant was done due to hypertensive renal disease but association was not found between causes of renal disease and ocular findings by Bivariate Analysis. Similarly, no association of ocular findings were found between duration of transplant as well as status of renal function.

DISCUSSION

In our study, at least one ocular abnormality was present in 61% (n = 38) of the eyes, similar to 52.5% ocular involvement reported by (Das et al, 1991). However, the incidence of ocular involvement was much less than reported by Berindán et al (2017) which was 88%, and Kian-Ersi et al (2008) reported 89.3%. As in both the studies impaired vision even due to refractive error was taken into account, the reported incidence of ocular involvement was higher.

Sub normal visual acuity less than 6/9 was seen in only 29% (n=18) of the eyes, similar to 20/25 reported by Kian-Ersi et al (2008), 84 letters in ETDRS chart reported by van Dijk et al (2017). The possibility of visual problems occurs significantly more with aging. Mean age of 37.42.±10.57 years was seen in our study population, which is relatively young. The visual threatening retinal complications which are seen more in older age groups were not seen in our study population (Berindán et al, 2017; Porter et al, 1972).

Degenerative conditions of conjunctiva such as pinguecula, which is a frequent finding in chronic renal failure according to many reports (Wang et al, 2012; Kian-Ersi et al, 2008; Pahor et al, 1995). In our study too, we had a high number of conjunctival degenerations. Conjunctival degenerative lesions are usually caused by the long-term radiation from ultraviolet rays. However, this association in ESRD could not be fully explained. Vitreous degeneration was also seen in high numbers in our study, though it could be a confounding

finding with multifactorial aetiologies. It had not been reported previously, though serous retinal detachment has been reported.

Renal function improves after renal transplantation in most patients; however, unavoidable administration of immunosuppressive drugs can lead to ophthalmic manifestations along with aetiologies behind kidney disease. Renal function as indicated by serum creatinine, which was abnormal in 45.2% (n=14) of cases following renal transplantation in our study. Normal serum creatinine might indicate less ocular complications. Some previous studies have reported positive associations with increased creatinine level and cataracts (Beiran et al, 1994; Harding and van Heyningen, 1987) whereas others reported statistically nonsignificant results (Ughade et al and Klein et al, 1998).

Patients who had hypertensive kidney disease as a cause of renal failure had more retinal findings as compared to patients who had diabetic kidney disease requiring renal transplant in the present study. Hypertensive retinopathy has been found to be common in renal transplant patients in a study conducted by Berindán et al (2017) which was 16%, similar to our study. However they did not find any diabetic retinopathy (Berindán et al, 2017). Many literatures have mentioned various vision threatening retinal findings like central serous chorioretinopathy, epiretinal membrane, Central retinal vein occlusion, Retinal pigment epithelial detachment which were not present in our study population (Ginu et al, 2021; van Dijk et al, 2017).

Even though, 6.6% (n=4) of eyes had glaucomatous disc findings, all the eyes had IOP within the normal range with mean IOP of 15.24± 2.37 mm of Hg among whom two of the cases were already on anti-glaucoma treatment. This IOP finding is similar to 14.7±4.1 mm Hg seen by Berindán et al (2017). Use of steroids for a prolonged period is a risk factor steroid induced glaucoma (Woods, 1950). But there were no cases of steroid induced glaucoma in a study done by Kian-Ersi et al (2008). However, Jayamanne and Porter (1998) reported high IOP in only 1.4%. Cases of increased IOP are less common when a patient is on oral steroid as compared to the patients on topical steroid (Phulke et al, 2017). That may be one of the reasons for not finding steroid induced glaucoma in our study population.

Long-term steroid use also has a strong correlation with cataract, especially Posterior Sub Capsular Cataract (PSCC), which was seen in 22.7% (n=14) out of 29% (n=18) of total cataract, and it correspond with reports by other researches (Das *et al.*, 1991; Jayamanne and Porter, 1998; Kian-Ersi *et al*., 2008). One study has mentioned more than half (57.1%) of incidence of cataract in their patients but the type of cataract was not classified (Berindán et al, 2017). ESRD patients need to have immunosuppression for survival of donor kidney and this may lead to various opportunistic infections with eye involvement. Sight threatening retinal complications of infective origin like cytomegalovirus retinitis have been reported in older literature by Das et al (1991) and Porter et al (1972), but such cases are not seen in our study. Opportunistic infections by herpes virus, fungus, toxoplasma were also not observed in our study.

Patients on maintenance oral steroid dose of 7.5 mg for more than three months had more retinal

disorders than patients on 5mg and 10 mg. Similarly, patients on oral maintenance steroid of 10 mg for more than three months showed more lens problems, mainly cataract which cannot be concluded as a definitive association, as our sample size was very small. Moreover, we have not taken cumulative doses of steroid for comparison.

Duration of kidney transplant and renal status had no association with ocular findings in our study.

This study consisted of the patients from a single institution, with convenience sampling and ocular findings before the renal transplantation could not be quantified. It would have been more interesting to compare the pretransplant and post-transplant ocular status. However, the fact that the findings has been collected from patients who underwent kidney transplant from a single referral centre, this can serve as a basis for future multicentric studies with larger sample size.

CONCLUSION

In conclusion, our study suggests that ocular disorders like cataract, hypertensive retinopathy, and vitreous degeneration are frequent findings among patients with renal transplantation. However, incidence of sight threatening complications are rare. Regular ophthalmic examination should be considered in these patients to identify the ocular abnormalities early and prevent untreatable blinding ocular complications.

ACKNOWLEDGEMENTS

Ms. Sulata Karki, Research officer, HERD International, Nepal.

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