

Ocular manifestations in renal allograft recipients: An Indian perspective

Ginu PM, Alok Sati¹, T Murari², Jaya Kaushik, Sanjay Kumar Mishra¹, Vijay Kumar Sharma¹

Purpose: The aim of this study was to report the ocular findings in renal allograft recipients in India. **Methods:** A cross-sectional, comprehensive ophthalmic evaluation was performed, at least three months postrenal transplant, in 152 renal allograft recipients for the ocular findings. In addition, ocular findings were assessed for an association with the clinical variables like major etiologies of end-stage renal disease, pre-transplant dialysis duration, post-transplant duration, and dosage of immunosuppressive drugs. **Results:** 72.36% of the recipients (mean age, 38.16 ± 10.04 years) had at least one ocular finding at 3 ± 2.6 years (range, 0.3-14 years), postrenal transplant. Hypertensive retinopathy was the commonest ocular finding followed by posterior subcapsular cataract (20.4%), nuclear sclerosis (19.7%), diabetic retinopathy (15.1%), dry eye (11.2%), allergic conjunctivitis (9.9%), pterygium (6.6%), open-angle glaucoma (3.3%), meibomitis (3.3%), pinguicula (2.6%), chalazion (1.3%), subconjunctival haemorrhage (1.7%), central serous chorioretinopathy (1.7%), healed ocular toxoplasmosis (1.7%), papilledema (1.7%), and dry ARMD (1.7%). In addition, a significant association existed between some of the ocular findings with major aetiologies of ESRD, post-transplant duration, and dosage of immunosuppressive drugs. However, no association existed between the ocular findings and pre-transplant dialysis duration. **Conclusion:** Ocular findings are seen in 72.36% of the renal transplant recipients with hypertensive retinopathy being the commonest one. Hence, a mandatory regular ophthalmic screening of the recipients is recommended for an early detection and timely intervention to improve the quality of life.

Key words: End-stage renal disease, ocular findings, post-transplant duration, renal allograft recipients

Chronic kidney disease (CKD) refers to a broad spectrum of the pathophysiological process (Stage One to Five) associated with a progressive deterioration in glomerular filtration rate (GFR) due to an abnormal renal function.^[1] Stage five CKD, also referred to as end-stage renal disease (ESRD), is characterized by the accumulation of toxins and invariably results in mortality unless managed either by dialysis or renal transplantation.^[2] Renal transplantation offers the best potential for complete rehabilitation in ESRD patients as compared to dialysis.^[3] In addition, the life expectancy following renal transplantation has improved in view of advances in surgical technique and development of more effective immunosuppressive agents.^[4]

Prolonged survival rate inadvertently exposes the recipients to various factors responsible for ocular morbidity including the underlying causes of ESRD, infections, and immunosuppressants. The evaluation and identification of ocular findings is of paramount importance as this can be timely intervened thus reducing the hardships and improve the recipient's quality of life. The purpose of the current study is to find such ocular abnormalities in renal transplant recipients and to associate them with major etiologies of ESRD, pre-transplant dialysis duration, post-transplant duration, and dosage of immunosuppressive drugs.

Department of Ophthalmology, Armed Forces Medical College, ²Department of Internal Medicine, Armed Forces Medical College, Pune, Maharashtra, ¹Department of Ophthalmology, Army Hospital (Research and Referral), New Delhi, India

Correspondence to: Prof. Alok Sati, Cornea and Anterior Segment Services, Department of Ophthalmology, Army Hospital (Research and Referral), New Delhi - 01, India. E-mail: aloksati_123@rediffmail.com

Received: 23-Apr-2020
Accepted: 30-Sep-2020

Revision: 25-Jul-2020
Published: 16-Mar-2021

Access this article online

Website:
www.ijo.in

DOI:
10.4103/ijo.IJO_1120_20

Quick Response Code:



Methods

This study adheres strictly to the tenets of the Declaration of Helsinki, and prior approval of the institutional ethical committee was received. A cross-sectional ophthalmic evaluation was performed in 152 renal transplant recipients at a tertiary care multidisciplinary hospital in India between October 2017 and December 2019. The above sample size, that is, 152 subjects, was calculated after considering the proportion of interest (p) i.e., ocular manifestation in renal transplant recipients, as 89% (based on the previous study^[4]); Z alpha (Z_α) as 1.96 (corresponding to type I error of 5%, i.e., 0.05); q as 100-p i.e., 11% and experimental error (d) as 5%. The number of patients is as follows:

$$N = Z^2 p q / d^2 = 1.96^2 \times 89 \times 11 / 5^2 \\ = 150.37 (\sim 150 \text{ recipients})$$

Recipients who had completed 3 months postrenal transplantation (for stabilization of renal function) were included in the study. Recipients with graft rejection and less than 3 months postrenal transplantation status, were excluded from the study.

After obtaining informed consent and relevant history, a complete ophthalmic evaluation was performed in all

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Cite this article as: Ginu PM, Sati A, Murari T, Kaushik J, Mishra SK, Sharma VK. Ocular manifestations in renal allograft recipients: An Indian perspective. Indian J Ophthalmol 2021;69:900-5.

recipients including an assessment of visual acuity by Snellen chart, anterior segment evaluation by slit-lamp examination, posterior segment evaluation by indirect ophthalmoscopy and +90D biomicroscopy and intraocular pressure measurement by applanation tonometer. Glaucoma suspect recipients were further evaluated by gonioscopy, ultrasonic pachymeter (DGH Technology Inc., Exton, PA, USA), visual field analyzer (Humphrey, Carl Zeiss Meditec, Inc., USA), and optic nerve head analysis by optical coherence tomography (OCT) (Cirrus HD OCT, Carl Zeiss Meditec, Inc., USA). Retinal lesions, if required, were evaluated in detail by OCT and fundus fluorescein angiography. Dry eye diagnosis was based on ocular symptomatology, tear meniscus height, tear film breakup time, Schirmer test I and II and the ocular surface changes. Hypertensive retinopathy was diagnosed based on Keith Wagner Becker classification. Lens Opacity Classification system II (LOCS II) was used to grade the cataract. Diabetic retinopathy findings were assessed based on the Early Treatment Diabetic Retinopathy Study (ETDRS).

Recipients were primarily evaluated for the ocular abnormalities. In addition, an association of major etiologies of ESRD (chronic glomerulonephritis, hypertension, diabetes mellitus, and chronic interstitial nephritis), pre-transplant dialysis duration (duration is arbitrarily divided as <6 months, 6 months to 1 year and >1 year), post-transplant duration (duration is arbitrarily divided as up to 1 year, >1 year and up to 5 years, >5 years and up to 10 years and >10 years) and total dosage of each immunosuppressive drugs i.e., Tacrolimus, Mycophenolate mofetil (MMF) and Prednisolone (divided into three quartiles); with ocular manifestations, were also analyzed.

Statistical analysis

Data analysis was done by using SPSS (Statistical Package for Social Sciences) version 25.0. Qualitative data variables were expressed using frequency and percentage. Quantitative data variables were expressed using mean and standard deviation. Chi-square test and Fisher's exact test were used to finding association between two qualitative data variables, as per tables. A value of $P < 0.05$ was considered as significant.

Results

The mean age of renal transplant recipients ($n = 152$) was 38.16 ± 10.04 years (range, 18–60 years) with 66.4% ($n = 101$) as male and 33.3% ($n = 51$) as female. The causes of ESRD for renal transplantation were summarized in Table 1. Chronic glomerulonephritis (41%) was the most common indication of renal transplantation. It included Focal segmental glomerulosclerosis (FSGS), Membranoproliferative glomerulonephritis (MPGN), IgA nephropathy and Alport syndrome. It was followed by Hypertensive nephropathy (22%) and Idiopathic causes (12%). The major co-findings associated with renal transplant recipients ($n = 152$) included hypertension (87/152; 57.2%), diabetes mellitus (43/152; 28.3%), hepatitis C virus infection (5/152; 3.2%) and hypothyroidism (3/152; 2%).

The best spectacle-corrected visual acuity (BCVA) in recipients was 0.07 ± 0.16 (range; 0–0.77) logarithm of the minimum angle of resolution (log MAR) (Snellen equivalent (SE), 20/23.49) in the right eye and 0.08 ± 0.13 (range: 0–0.60) log MAR (SE, 20/24.04) in the left eye. Of 152 recipients, 50 recipients had BCVA less than 20/20. It constituted 32.89% of all the recipients. The causes included posterior subcapsular cataract (PSC) (26/50; 52%), nuclear cataract (11/50; 24%), diabetic retinopathy (5/50; 12%), dry eye (2/50; 4%), branch retinal vein occlusion (5/50; 10%) and central serous chorioretinopathy (1/50; 2%). The mean duration between

Table 1: Aetiology of End Stage Renal Disease in Renal transplant recipients

| Aetiology | Number of patients | Percentage (%) |
|-----------------------------------|--------------------|----------------|
| Chronic Glomerulonephritis | 62 | 40.8 |
| Hypertension | 34 | 22.4 |
| Idiopathic | 18 | 11.8 |
| Chronic Interstitial nephritis | 13 | 8.6 |
| Diabetes Mellitus | 11 | 7.2 |
| Polycystic chronic kidney disease | 7 | 4.6 |
| NSAIDS and alternate medication | 4 | 2.6 |
| Obstructive uropathy | 3 | 2.0 |

renal transplantation and the ocular examination was 3 ± 2.66 years (range, 0.3–14 years).

Ocular abnormalities

72.36% of the recipients had at least one ocular manifestation in either of the eyes, other than the correctable refractive error. [Fig. 1] summarises the ocular findings in the recipients. Hypertensive retinopathy (55/152; 36.18%) was the most common ocular finding followed by posterior subcapsular cataract (31/152; 20.40%) and nuclear sclerosis (30/152; 19.70%). According to Keith Wagener Barker grading, hypertensive retinopathy ($n = 55$) existed as grade 1 to 2 (47/55; 85.45%), grade 3 (7/55; 12.72%) and grade 4 (1/55; 1.81%) in 55 recipients. Based on Lens Opacities Classification System II, PSC ($n = 31$) existed as grade 2 to 3 (5/31; 16.12%) and grade 4 (26/31; 83.87%) in 31 recipients whereas nuclear sclerosis ($n = 30$) existed as grade 1 (19/30; 63.33%) and grade 2 (11/30; 36.66%) in 30 recipients. Ocular findings with the least frequency included sub conjunctival haemorrhage (1/152; 0.7%), central serous chorioretinopathy (1/152; 0.7%), ocular toxoplasmosis (1/152; 0.7%), papilledema (1/152; 0.7%) and dry age-related macular degeneration (1/152; 0.7%).

In Table 2, both Fisher's exact test and Chi-square tests were used to examine the significance of the association between ocular findings and major aetiologies of ESRD. Recipients with chronic glomerulonephritis had a significant association with PSC ($P = 0.002$), nuclear cataract ($P = 0.012$), and diabetic retinopathy ($P = 0.005$). With hypertension as an etiology, no significant association existed with the ocular manifestations. Recipients with diabetes mellitus had a significantly higher chance of development of nuclear sclerosis ($P = 0.001$), diabetic retinopathy ($P = 0.002$) and meibomitis ($P = 0.042$). Amongst the ocular findings, with chronic interstitial nephritis as an etiology, recipients had a significant association with hypertensive retinopathy ($P = 0.032$).

Pre-transplant dialysis duration

Using Chi-square test, Table 3 depicts an insignificant association between ocular findings and pre-transplant dialysis duration.

Post-transplant duration

In Table 3, using Chi square test, a significant association existed between ocular findings like hypertensive retinopathy ($P < 0.001$), posterior subcapsular cataract ($P < 0.001$), nuclear sclerosis ($P = 0.012$), diabetic retinopathy ($P = 0.003$), dry eye ($P = 0.012$), and pterygium ($P < 0.001$) with post-transplant duration. In other words, the chance of occurrence of hypertensive retinopathy, posterior subcapsular cataract, nuclear sclerosis, diabetic retinopathy, dry eye, and pterygium altered with a change in post-transplant duration.

Total Dosage of immunosuppressive drugs

Table 4 depicts the association between the ocular findings and the total dosage of each immunosuppressive drug. Using the Chi-square test, a significant association existed between ocular findings like hypertensive retinopathy ($P < 0.001$), posterior subcapsular cataract ($P < 0.001$) and pterygium ($P < 0.001$) with the total dosage of Tacrolimus. Similarly, a significance in association is present between the ocular findings like hypertensive retinopathy ($P < 0.001$), pterygium ($P < 0.001$), dry eye ($P = 0.01$), nuclear cataract ($P = 0.02$), posterior subcapsular

cataract ($P < 0.001$), and diabetic retinopathy ($P = 0.01$) with the total dosage of Mycophenolate mofetil. Also, a significant association exists between the total dosage of prednisolone and ocular findings like hypertensive retinopathy ($P < 0.001$), nuclear cataract ($P < 0.001$), posterior subcapsular cataract ($P < 0.001$) and diabetic retinopathy ($P < 0.001$).

Discussion

Renal transplantation, the most preferred management of ESRD, leads to a longer survival and a superior quality of life.^[5] The current study highlights at least one ocular finding in 72.6% of the recipients. On the contrary, Kian-Ersi *et al.*^[4] and Berindán *et al.*^[6] had reported the ocular findings in 89.3% and 88% of the recipients respectively. This difference in rate might be attributed to the inclusion of impaired visual acuity as one of the ocular findings in the later studies. Similarly, our observations showed discordance with the findings of Das *et al.*^[7] and Jahadi-hosseini *et al.*^[8] The later studies have reported the ocular findings as 52.5% and 57% respectively and this incompatibility could be due to the difference in number of the recipients being analyzed including the type and dosage of the immunosuppressants administered.

Unlike the existing literature,^[4,7-10] this study proscribed hypertensive retinopathy as the commonest ocular manifestation in renal transplant recipients. This is because hypertension was detected in 87 of 152 recipients at the time of ocular examination. With an increase in dosage of immunosuppressants, our study showed that the chance of occurrence of hypertensive retinopathy increased. This observation could very well be ascribed to the well-known

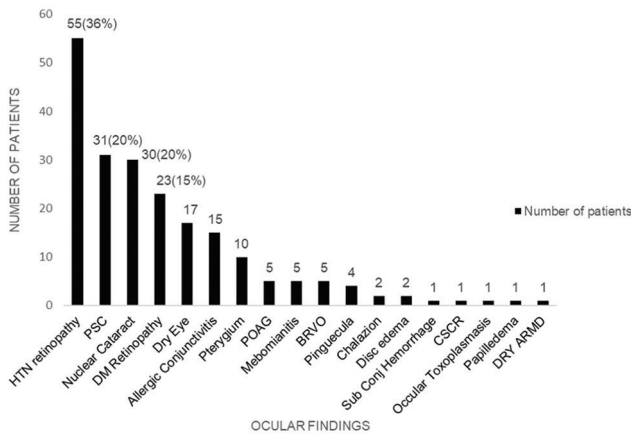


Figure 1: Frequency of ocular abnormalities in renal transplant recipients

Table 2: Frequency of ocular findings based on aetiologies of End Stage Renal Disease

| | Number of recipients with Chronic Glomerulonephritis | | | Number of recipients with Hypertension | | | Number of recipients with Diabetes Mellitus | | | Number of recipients with Chronic Interstitial Nephritis | | |
|------------------------------|--|----|-------|--|----|------|---|----|-------|--|----|-------|
| | P | A | P | P | A | P | P | A | P | P | A | P |
| Major Ocular findings | | | | | | | | | | | | |
| Nuclear Cataract | 6 | 24 | 0.01* | 9 | 21 | 0.33 | 7 | 23 | 0.00* | 0 | 30 | 0.07 |
| PSC | 5 | 26 | 0.00* | 9 | 22 | 0.34 | 5 | 26 | 0.05 | 1 | 30 | 0.31 |
| HTN retinopathy | 21 | 34 | 0.73 | 17 | 38 | 0.07 | 3 | 52 | 0.75 | 1 | 54 | 0.03* |
| Diabetic Retinopathy | 3 | 20 | 0.01* | 7 | 16 | 0.41 | 6 | 17 | 0.00* | 0 | 23 | 0.22 |
| Minor findings | | | | | | | | | | | | |
| Ocular findings | | | | | | | | | | | | |
| Pterygium | 2 | 8 | 0.20 | 5 | 5 | 0.05 | 0 | 10 | 0.62 | 0 | 10 | 0.60 |
| Meibomitis | 0 | 5 | 0.08 | 2 | 3 | 0.58 | 2 | 3 | 0.04* | 0 | 5 | 0.99 |
| Pinguecula | 1 | 3 | 0.64 | 1 | 3 | 0.99 | 0 | 4 | 1.00 | 0 | 4 | 0.99 |
| Dry Eye | 7 | 10 | 0.99 | 5 | 12 | 0.54 | 2 | 15 | 0.61 | 0 | 17 | 0.36 |
| Chalazion | 0 | 2 | 0.51 | 1 | 1 | 0.39 | 0 | 2 | 1.00 | 0 | 2 | 0.99 |
| Allergic Conjunctivitis | 8 | 7 | 0.41 | 4 | 11 | 0.75 | 0 | 15 | 0.38 | 0 | 15 | 0.37 |
| Sub Conj Hge | 1 | 0 | 0.41 | 0 | 1 | 0.99 | 0 | 1 | 1.00 | 0 | 1 | 0.99 |
| BRVO | 2 | 3 | 1.00 | 0 | 5 | 0.35 | 0 | 5 | 0.99 | 0 | 5 | 0.99 |
| CSCR | 1 | 0 | 0.41 | 0 | 1 | 0.99 | 0 | 1 | 0.99 | 0 | 1 | 0.99 |
| Ocular Toxoplasmosis | 1 | 0 | 0.41 | 0 | 1 | 0.99 | 0 | 1 | 0.99 | 0 | 1 | 0.99 |
| Disc edema | 0 | 2 | 0.51 | 0 | 2 | 0.99 | 0 | 2 | 0.99 | 0 | 2 | 0.99 |
| Papilledema | 0 | 1 | 0.99 | 1 | 0 | 0.22 | 0 | 1 | 0.99 | 0 | 1 | 0.99 |
| Dry ARMD | 1 | 0 | 0.41 | 0 | 1 | 0.99 | 0 | 1 | 0.99 | 0 | 1 | 0.99 |

P, present; A, absent; PSC, posterior subcapsular cataract; Sub Conj Hge, subconjunctival haemorrhage; HTN, hypertensive; DM, diabetic; BRVO, branch retinal vein occlusion; CSCR, central serous chorioretinopathy; ARMD, age related macular degeneration. *Significant ($P < 0.05$)

Table 3: Frequency of ocular findings based on pre-transplant and post-transplant duration

| Major Ocular findings | Number of recipients based on pre-transplant dialysis duration (% of related ocular findings) | | | | Number of recipients based on post-transplant duration in years (% of related ocular findings) | | | | |
|-------------------------|---|--------------|-----------|-------|--|-----------|-----------|-------|--------|
| | ≤ 6 mo | 6 mo -1 year | >1 year | P | ≤1 | >1-5 | >5-10 | >10 | P |
| HTN retinopathy | 2 (20) | 2 (20) | 6 (60) | 0.421 | 9 (16.4) | 28 (50.9) | 18 (32.7) | 0 (0) | <0.001 |
| PSC | 1 (20) | 2 (40) | 2 (40) | 0.850 | 5 (16.1) | 13 (41.9) | 11 (35.5) | 2 (6) | <0.001 |
| Nuclear Cataract | 2 (50) | 2 (50) | 0 (0) | 0.239 | 7 (23.3) | 12 (40) | 9 (30) | 2 (6) | 0.012 |
| Diabetic Retinopathy | 3 (17.6) | 8 (47.1) | 6 (35.3) | 0.072 | 6 (26.1) | 8 (34.8) | 7 (30.4) | 2 (8) | 0.003 |
| Minor findings | | | | | | | | | |
| Dry eye | 2 (100) | 0 (0) | 0 (0) | 0.180 | 1 (5.9) | 8 (47.1) | 8 (47.1) | 0 (0) | 0.012 |
| Allergic Conjunctivitis | 7 (23.3) | 6 (20) | 17 (56.7) | 0.127 | 2 (13.3) | 12 (80) | 1 (6.7) | 0 (0) | 0.063 |
| Pterygium | 9 (29.03) | 5 (16.1) | 17 (54.8) | 0.155 | 2 (20) | 0 (0) | 8 (80) | 0 (0) | <0.001 |
| Meibomitis | 5 (33.3) | 3 (20) | 7 (23.3) | 0.839 | 2 (40) | 3 (60) | 0 (0) | 0 (0) | 0.736 |
| Pinguecula | 1 (100) | 0 (0) | 0 (0) | 0.599 | 2 (50) | 2 (50) | 0 (0) | 0 (0) | 0.726 |
| BRVO | 17 (30.9) | 12 (21.8) | 26 (47.3) | 0.422 | 1 (20) | 2 (40) | 2 (40) | 0 (0) | 0.109 |
| Chalazion | 7 (30.4) | 7 (30.4) | 9 (39.1) | 0.881 | 0 | 0 (0) | 2 (100) | 0 (0) | 0.052 |
| Disc edema | 2 (40) | 0 (0) | 3 (60) | 0.446 | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 0.172 |
| Sub Conj Hg | 1 (100) | 0 (0) | 0 (0) | 0.599 | 0 (0) | 1 (100) | 0 (0) | 0 (0) | 0.999 |
| CSCR | 0 (0) | 0 (0) | 1 (100) | 0.999 | 0 (0) | 1 (100) | 0 (0) | 0 (0) | 0.999 |
| Ocular Toxoplasmosis | 1 (50) | 1 (50) | 0 (0) | 0.516 | 0 (0) | 0 (0) | 1 (100) | 0 (0) | 0.178 |
| Papilledema | 0 (0) | 1 (100) | 0 (0) | 0.257 | 0 (0) | 1 (100) | 0 (0) | 0 (0) | 0.999 |
| Dry ARMD | 0 (0) | 1 (100) | 0 (0) | 0.257 | 0 (0) | 1 (100) | 0 (0) | 0 (0) | 0.999 |

mo, months; HTN, hypertensive; PSC, posterior subcapsular cataract; BRVO, branch retinal vein occlusion; Sub Conj Hge, subconjunctival haemorrhage; CSCR, central serous chorioretinopathy; ARMD, age related macular degeneration. *Significant (P<0.05)

hypertensinogenic effect of both Prednisolone and Tacrolimus; however, this observation is not clear with MMF. We perceived it being a biased observation, as all three drugs are co-administered as a Triple Therapy.

Posterior subcapsular cataract was the second most common ocular manifestation in our study. However, most of the studies in literature labeled it as the most frequent anatomical disorder.^[7-10] This difference in observation could be ascribed to the fact that most of these studies were conducted in the late twentieth century and of late lifestyle diseases like hypertension is on rise especially in the developing world. For many years, cataract formation postrenal transplant has been linked with dose-dependent relationship with corticosteroid^[4,7-10]; and the same is being highlighted in the current series. In addition, our study has also shown dose-dependent relationship between Tacrolimus and cataract. This unusual observation is in line with the preclinical toxicity studies in rats which have shown tacrolimus as cataractogenic, secondary to diabetes-induced sorbitol accumulation in the lens.^[11] Though our study showed a similar dose-dependent relation between MMF and cataract, we could not find any literature substantiating this observation. We presumed that this observation could either be an incidental finding or a biased result due to the co-administration of drugs as a triple therapy.

Nuclear sclerosis was the next prevalent complication in our study. The existing literature mentions PSC as a form of cataract post-renal transplant,^[4,6-10] however, none of them reported nuclear sclerosis and to the best of our knowledge, we are reporting it for the first time. We presumed that the development of nuclear sclerosis in postrenal transplant recipients may be multifactorial. First, it might be age related as some of the patients in our study is more than 50 years. Second, immunosuppressive agents like prednisolone and tacrolimus, which form the part of triple therapy, had been incriminated

as diabetogenic,^[11,12] and was a well-known fact that incidence and progression of nuclear sclerosis is common in diabetic patients.^[13,14] The later presumption is further substantiated in our study as we found a significantly higher frequency of nuclear cataract with diabetes mellitus and a significant dose-dependent relationship between prednisolone and nuclear sclerosis. In addition, the significant dose-dependent relationship between nuclear cataract and MMF, as observed in our study, was presumed to be incidental.

We reported diabetic retinopathy in 15.1% of the recipients which was almost in line with the previous study.^[4] Its development might be either pre-transplant related (diabetes leading to ESRD) or it evolved in posttransplant phase. Diabetes in post-transplant duration is invariably related to Prednisolone as exhibited by a significant dose-dependent relationship between prednisolone and diabetic retinopathy in the current study. However, this relationship between diabetic retinopathy and MMF, as observed in our study, is presumed to be incidental.

Dry eye, though less reported postrenal transplant,^[6] is seen in 11.2% of the recipients in our study. Its development postrenal transplant mainly seemed to be by chance or rarely could be the ongoing impact of long-term hemodialysis in the post-transplant period.^[15]

Allergic conjunctivitis and pterygium were the next prevalent ocular findings. The mechanism behind allergic conjunctivitis postrenal transplant is not well understood, however, it is hypothesized that it could either be a coincidental finding or an allergic manifestation of Tacrolimus mediated IgE sensitization.^[16] Tacrolimus mediates this sensitization by selective suppression of Th1 lymphocytes, thereby promoting Th2 lymphocytes, which in turn triggers B-cells to produce IgE antibodies for an IgE mediated allergic response.

Table 4: Frequency of ocular findings based on dosage of immunosuppressive drugs

| Ocular findings | Number of recipients based on total dosage of Tacrolimus in grams | | | | Number of recipients based on total dosage of MMF in grams | | | | Number of recipients based on total dosage of Prednisolone in grams | | | | P | | |
|----------------------|---|-------------------|-------------------|-----------|--|----------|----------|-----------|---|-------|-------|-----------|----|-----------|-------|
| | <23 30 | 23 30-46 12 | 46 13-65 02 | >65 02 | P | <8 55 | 855-1160 | 1161-1905 | >1905 | P | <3655 | 3655-5850 | | 5851-9667 | >9667 |
| Pterygium | 2 | 0 | 0 | 8 | 0.00* | 2 | 0 | 0 | 8 | 0.00* | 2 | 0 | 0 | 8 | 0.00* |
| Meibomitis | 0 | 4 | 1 | 0 | 0.01* | 0 | 4 | 1 | 0 | 0.04* | 1 | 3 | 1 | 0 | 0.13 |
| Pinguecula | 2 | 0 | 2 | 0 | 0.33 | 2 | 0 | 2 | 0 | 0.21 | 2 | 0 | 2 | 0 | 0.25 |
| Dry Eye | 1 | 4 | 4 | 8 | 0.07 | 1 | 7 | 1 | 8 | 0.01* | 1 | 5 | 3 | 8 | 0.06 |
| Chalazion | 0 | 0 | 0 | 2 | 0.18 | 0 | 0 | 0 | 2 | 0.17 | 0 | 0 | 0 | 2 | 0.11 |
| Nuclear Cataract | 5 | 9 | 4 | 12 | 0.07 | 5 | 11 | 2 | 12 | 0.02* | 6 | 10 | 1 | 13 | 0.00* |
| PSC | 3 | 3 | 8 | 17 | 0.00* | 2 | 6 | 6 | 17 | 0.00* | 4 | 5 | 4 | 18 | 0.00* |
| Allergic Conj | 0 | 7 | 4 | 4 | 0.05 | 1 | 6 | 3 | 5 | 0.29 | 1 | 4 | 5 | 5 | 0.30 |
| Sub Conj Hge | 0 | 1 | 0 | 0 | 0.24 | 0 | 1 | 0 | 0 | 0.99 | 0 | 1 | 0 | 0 | 0.73 |
| HTN retinopathy | 9 | 7 | 15 | 24 | 0.00* | 9 | 9 | 13 | 24 | 0.00* | 6 | 12 | 15 | 22 | 0.00* |
| Diabetic Retinopathy | 4 | 6 | 3 | 10 | 0.11 | 4 | 9 | 0 | 10 | 0.01* | 5 | 8 | 0 | 10 | 0.01* |
| BRVO | 1 | 0 | 2 | 2 | 0.63 | 1 | 2 | 0 | 2 | 0.75 | 1 | 2 | 0 | 2 | 0.65 |
| CSCR | 0 | 0 | 1 | 0 | 0.74 | 0 | 0 | 1 | 0 | 0.22 | 0 | 0 | 1 | 0 | 0.23 |
| Ocular Toxoplasmosis | 0 | 0 | 0 | 1 | 0.74 | 0 | 0 | 0 | 1 | 0.73 | 0 | 0 | 0 | 1 | 0.48 |
| Disc edema | 2 | 0 | 0 | 0 | 0.24 | 2 | 0 | 0 | 0 | 0.11 | 2 | 0 | 0 | 0 | 0.24 |
| Papilledema | 0 | 0 | 1 | 0 | 0.74 | 0 | 0 | 1 | 0 | 0.22 | 0 | 0 | 1 | 0 | 0.23 |
| Dry ARMD | 0 | 0 | 1 | 0 | 0.74 | 0 | 0 | 1 | 0 | 0.22 | 0 | 0 | 1 | 0 | 0.23 |

MMF, Mycophenolate Mofetil; P val, P; PSC, posterior subcapsular cataract; Allergic Conj, allergic conjunctivitis, Sub Conj Hge, sub conjunctival haemorrhage; HTN, hypertensive; BRVO, branch retinal vein occlusion; CSCR, central serous chorioretinopathy; ARMD, age related macular degeneration. *Significant (P<0.05)

Unlike the existing literature,^[7-10] the current study reported raised IOP in addition to optic nerve damage in recipients with Open Angle Glaucoma (OAG) and is being presumed to be secondary to prolonged intake of oral steroid.

Though rarely reported, the current study reports some of the ocular findings with an extremely lower frequency like branch retinal vein occlusion (BRVO), pinguicula, chalazion, disc edema, subconjunctival hemorrhage, central serous chorioretinopathy (CSCR), ocular toxoplasmosis, papilledema, and dry age-related macular degeneration (dry ARMD). Amongst them, papilledema was secondary to malignant hypertension in the current series and subconjunctival hemorrhage is probably either due to hypertension or diabetes or both as this ocular morbidity was found in a recipient with both the systemic disorders. CSCR, the known ocular morbidity in renal transplant recipient,^[17] may be secondary to the long-term administration of oral steroid.

The current study is unique in many aspects. First, to the best of our knowledge, the current series is the largest from India and third in the world, highlighting the ocular findings following renal transplantation.^[7,18] Herein, we expect a variation from the developed world because of variability in causes of ESRD and post-transplant management protocol (steroid-free protocol more common in developed world). Second, to the best of our knowledge, we are reporting certain ocular findings like nuclear sclerosis, allergic conjunctivitis, pterygium, chalazion, disc edema, and subconjunctival hemorrhage, post-renal transplant for the first time. Third, unlike earlier Indian studies,^[7,18] the current series did not report any active opportunistic ocular infection and this declining trend may be secondary to a better follow-up protocol in addition to a better titration of immunosuppressive agents with the blood level in the post-transplant period. Like any other study, this study was not without limitations. First, being a cross-sectional study, it was difficult to analyze the behavior of ocular findings over a period of time. Moreover, the timing of the snapshot may not guarantee the true representative of the ocular findings. Second, though the patients are on triple therapy for immunosuppression, an effort was made to associate the ocular manifestations with the drugs individually, the observations, therefore, may not be exclusive since it is a combination therapy. In other words, though the association might not be the true representative, however, it highlighted the probable trend in terms of ocular manifestations. Third, though a significant association existed between different pathologies and ocular manifestations, the same can be interpreted with a caution as most of these pathologies have multiple risk factors in addition to the selection bias, being the cross-sectional study. Fourth, an arbitrary time frame of 3 months was taken post-transplant to include the subjects as that was thought to stabilize the graft, however, that hadn't been established in the literature and moreover significant immune-mediated reactions were possible in the immediate post-operative phase which might go unnoticed.

Conclusion

To conclude, the current study reported at least one ocular finding in 72.36% of the renal transplant recipients with hypertensive retinopathy being the commonest one. Considering the higher percentage of ocular findings in renal transplant recipients, it is recommended to have a mandatory regular screening of the recipients by the Ophthalmologist especially in the developing world and the Ophthalmologist

should be made an important member of the renal transplant team.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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