Infection and Drug Resistance

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ORIGINAL RESEARCH

Incidence and Implications of Culture-Positive Corneoscleral Rims in Corneal Transplantation

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Background: Corneal transplantation is a critical procedure for restoring vision affected by different corneal pathologies. However, postoperative infections threaten graft survival, particularly microbial keratitis and endophthalmitis.

Objective: This study aims to evaluate the incidence of culture-positive corneoscleral rims (CPCR) among transplanted corneas at a tertiary eye hospital and explore its association with death-preservation and preservation-surgery times.

Methods: A retrospective analysis of keratoplasty surgeries performed in 2015 was conducted, involving 603 cases meeting the study criteria.

Results: The incidence of CPCR was found to be 4.6%, predominantly bacterial (68%), with Methicillin-resistant Staphylococcus epidermidis (MRSE) being the most common isolate, followed by fungal (32%) species, notably Candida. However, none of the cases developed subsequent keratitis or endophthalmitis post-transplantation. Statistical analysis revealed no significant association between CPCR occurrence and death-preservation or preservation-surgery times.

Conclusion: The study underscores the reduced impact of contaminated CPCR on graft outcomes, advocating for targeted fungal culturing, intraoperative practices to mitigate post-transplant infections, and maintaining current prophylactic antibiotic regimens, such as optisolGS ™, which contains streptomycin and gentamicin.

Keywords: corneal transplant, keratitis, endophthalmitis, infection, bacterial keratitis

Introduction

Corneal transplantation is the most successful among all human transplants. It restores vision in many blinding diseases, such as corneal decompensation, corneal scars, and fulminant keratitis.[1] Yet, its survival is threatened by postoperative infectious keratitis and endophthalmitis. Both may be transmitted from infected transplants or, more commonly, in relation to sutures.[2] In the literature, culture-positive corneoscleral rims (CPCR) have been linked to post-keratoplasty keratitis.[3] Bacterial infections are the most common, followed by a more devastating fungal etiology.[4–6] The risk of corneal graft viability is significantly increased by graft infection, which can occur due to various factors such as preoperative contamination, lack of aseptic conditions during surgery, or recipient-related factors. Early reports indicated a high prevalence of contamination in untreated donor eyes designated for corneal transplantation, reaching up to 100%.[7] However, advancements in techniques, such as immersion of corneal grafts in antibiotic solutions, have significantly reduced contamination rates to between 2.4% and 61% in recent studies.[8–11] These improvements have been attributed to meticulous aseptic conditions during corneal graft harvesting, along with the implementation of antibiotic-containing solutions for donor ocular surface irrigation and storage media.[4,6,12–15] Several investigations have highlighted the critical role of time intervals between donor death, graft harvesting, and transplantation in corneal button contamination.[6,13,15] While some studies suggest a heightened risk associated with late harvesting or prolonged preservation periods, the direct correlation between contamination and postoperative ocular infections remains debated, particularly regarding the significance of positive cultures from donor corneal grafts in predicting these infections.[6,15,16] In this study, we aim to estimate the incidence of CPCR among all transplanted corneas at a tertiary eye hospital and study its relation with death-preservation and

Received: 5 July 2024
Accepted: 24 January 2025
Published: 12 February 2025

preservation-surgery times. Also, we aim to estimate the incidence of concordant keratitis or endophthalmitis in CPCR in the first six months postoperatively and list the indications and keratoplasty types.

Materials and Methods

The Institution Research Board of King Khalid Eye Specialist Hospital (KKESH) approved this study, which complies with the Declaration of Helsinki. Since it was a retrospective chart review, patients' informed written consent was waived, and their identities were kept confidential. We reviewed charts of all keratoplasty surgeries performed in 2015 in KKESH. The inclusion criteria were all keratoplasty patients. The exclusion criteria were as follows: a history of prior glaucoma surgery, uveitis, keratitis (either infectious or immune-related), connective tissue disease, cicatrizing diseases, trichiasis, and severe blepharitis. Similarly, patients who underwent therapeutic, tectonic, or patch grafts were excluded. Finally, patients who developed post-keratoplasty infection secondary to a known etiology (suture-related and trauma) were also excluded. We elected to put those exclusion criteria to limit the confounding factors that may make donors' cornea susceptible to infections. Data collection is comprised of demographics of both donor and recipient, death preservation time, preservation date, cause of donor death, transplant surgery date, transplant surgery type, transplant indication, corneal rim culture result, development of post-transplant keratitis, duration between transplant surgery and infection, development of endophthalmitis and its management. The incidence of CPCR and the concordant postoperative infection was estimated. The association between the occurrence of CPCR and death-preservation time and preservation surgery time was tested for statistical significance using the Mann–Whitney test. All statistical analyses were performed using SPSS version 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

Results

Our study included 603 cases that met the study criteria and were analyzed (Tables 1–3).

The incidence of CPCR is 4.6% (95% Confidence Interval 3.0–6.3). Sixty-eight percent of those were bacterial, and 32% were fungal. None of those have developed either keratitis or endophthalmitis after keratoplasty (Table 4).

The incidence of fungal CPCR is 1.5%; the most common fungal species was candida, with 6 cases out of 9 (66%).

Table 1 Descriptive Analysis of the Donors' Data

Donors' Characteristics		
	N	**%**
Gender		
Male	351	58%
Female	252	42%
Age (years)		
Median	58	
Minimum	2	
Maximum	86	
Cause of death		
Cardiac	216	36%
Cancer	178	30%
Others	136	27%
Stroke	41	9%
Road Traffic Accident	32	5%

(*Continued*)

Table 1 (Continued).

Donors' Characteristics		
	N	%
Death-preservation time (hrs.)		
Median	8	
Min	1	
Max	16	

Table 2 Descriptive Analysis of the Recipients' Data

Recipients' Characteristics	**N**	%
Gender		
Male	337	56%
Female	266	44%
Age (years)		
Median	33	
Minimum	4	
Maximum	102	
Keratoplasty type		
Penetrating Keratoplasty (PKP)	317	53%
Lamellar Keratoplasty (LKP)	213	35%
Descemet Stripping Automated Endothelial Keratoplasty (DSEAK)	73	12%
Preservation- Surgery time (days)		
Median	10	
Min	2	
Max	22	
Indication for keratoplasty		
Keratoconus	368	61%
Bullous keratoplasty (phakic/ pseudophakic)	88	15%
Corneal scar	62	10%
Failed graft	51	9%
Corneal dystrophy	34	6%

https://doi.org/10.2147/IDR.S485717

Table 3 Descriptive Analysis of Rim Cultures

Culture Results	N	%
Negative	575	95.4%
Positive	28	4.6%
BacteriaL	19	3.1%
Fungal	9	1.5%
Virus/protozoa	0	

Table 4 The Microbiology Analysis That Lists the Microbial Organisms Found in CPCR and Their Frequencies

Organism	N (%)
Bacteria	**19/28 (68)**
Staphylococcus aureus	1
Methicillin-resistant Staphylococcus epidermidis (MRSE)	7
Streptococcus oralis	4
Finegoldia Magna	1
Bacillus	1
Enterococcus faecium	4
Stenotrophomonas maltophilia	1
Fungal	**9/28 (32)**
Candida parapsilosis	1
Candida glabrata	4
Candida albicans	1
Rhodotorula mucilaginosa	1
Cryptococcus Uniguttulatus	1
Mixed fungal Rhodococcus mucilaginosa with Cryptococcus laurentii	1

Abbreviations: CPCR, culture-positive corneoscleral rims; KKESH, King Khalid Eye Specialist Hospital.

There was no statistically significant association between CPCR and death preservation time (Mann–Whitney test P=0.8). Moreover, there was no statistically significant association between CPCR occurrence and preservation-surgery time (Mann–Whitney P=0.1).

Discussion

Keratoplasty helps restore vision, especially when the cornea loses its vital transparency. Postoperatively, graft clarity and survival are threatened by infection. The incidence of post-keratoplasty microbial keratitis is 7%, whereas the endophthalmitis incidence ranges from 0.41% to 0.61%.[17,18] Although suture-related infections are the most common etiology, the transmission of microbes, especially bacteria and fungi, from contaminated donor rims has been reported.[3,6,19–22] Moreover, the risk of developing post-keratoplasty endophthalmitis increases to 12–22 times with

CPCR.[6,21] At KKESH in 1991, a report calculated the CPCR rate of 29%;[6] in that report, 5 out of 2210 (0.23%) PKPs had concordant CPCR and culture-positive endophthalmitis within the first post-operative month. Three cases had candida species, and two had staph aureus. They concluded that a patient with CPCR is at 12 times the risk of developing postoperative endophthalmitis. Contrary to their findings, this report shows a lower incidence rate of CPCR (4.6%) and no risk of developing post-operative infection. This disagreement could be explained by the implementation of serial updates by the Eye Bank Association of America (EBAA), organized historically as follows: in 1993, streptomycin was added to the preservation media (Optisol GS), this provided better antibacterial coverage, in mid-1995, preservation of in-situ corneoscleral tissue replaced whole donor eye enucleation and lastly, in 1996–1997, immersion of whole globe in 5% povidone-iodine for 2 minutes then two sterile saline rinses, then serial irrigation with povidone-iodine.[23] Moreover, the advent of more powerful post-operative antibacterial medication, which is prescribed routinely as a prophylaxis, may have contributed to decreasing the incidence.

In regard to bacterial CPCR, this report agrees with the published data that it is the most common type of infection. Yet, there is no clinically significant risk of concordant post-transplant infection.[2,6,18] On the other hand, although fungal CPCR is less than bacterial ones, it is more clinically significant. This has recently been shown in a large study with 3414 samples focused on post-keratoplasty mycosis. The report calculated the incidence of fungal CPCR to be 2.1%; 4 out of the 70 fungal CPCR cases developed mycotic keratitis, and none had progressed to endophthalmitis. Also, the study indicated that prophylactic antifungal use in CPCR patients decreased the risk of developing postoperative mycosis from 15.8% in untreated to 1.9% in treated cases. Despite that, no specific regimen was advocated.[20] Moreover, another report concluded that having a fungal CPCR increases the risk of developing concordant mycosis on the graft 247 times.[24] Similarly, a large local study done over 17 years on 7488 patients, aimed at estimating the incidence of microbial endophthalmitis after keratoplasty, showed that only six patients had CPCR and only one patient had concordant infection (candida glabarata).[17] In another local report, only one out of 9 CPCRs had progressed to mycotic keratitis in the graft; again, it was a candida etiology.[22] Similarly, international reports showed that fungal CPCR has a higher positive predictive value for the development of post-transplant infection than bacterial CPCR.[19,20,24,25] Overall, those studies suggest that having a positive fungal CPCR is a greater determinant of developing keratitis after the keratoplasty compared to bacterial contamination.

As preventive and protective measures against CPCR-related post-graft infections, a local study reported for the first time that LKP could be a safer choice, if possible, than PKP with regard to developing postoperative endophthalmitis.[17] Similarly, different preservation methods carry variable risks. The incidence ranged from 0.2% to 1.3% in the hypothermic preservation method, whereas the organ culture preservation method had only 0.1%.[26] Moreover, pre-cut DSEAK grafts were noted to have fungal CPCR. This could indicate that manually preparing DSEAK lenticules intraoperatively may have a lower risk of post-transplant infection compared to onsite prepared pre-cut DSEAK.[20] In regard to the microbiology profile, we report that 68% of CPCR was bacterial, followed by 32% fungal. This agrees with previous reports.[4,6,17] The bacteriology analysis showed that most isolates grew Methicillin-resistant Staphylococcus epidermidis (MRSE). The sensitivity of which showed resistance to prophylactic antibacterial medications given postoperatively. Yet none of the cases developed either keratitis or endophthalmitis. This finding may indicate that the positivity of MRSE could have been caused by contamination while handling the rims from the time of opening the container until culturing in the laboratory rather than a genuine infection from the donor.

Alternatively, the currently implanted regime at KKESH of prescribing postoperative prophylactic antibiotics (fluoroquinolones) seems effective. A study in India, however, found that most gram-negative bacteria, particularly Pseudomonas spp., displayed resistance to all fluoroquinolones, aminoglycosides, 3rd generation cephalosporins, and meropenem. One-third were resistant to imipenem, but all were sensitive to colistin.[27]

We found no association between CPCR development and both death-preservation and preservation-surgery times. This contrasts with the interval reported of five days between preservation and surgery.[6]

The study had the following limitations: All donor corneas were from the US; hence, significant time elapsed during transportation, which subjected them to different climatic, altitudinal, and other environmental factors. These factors may affect the microbiology of preserved corneas. Similarly, comparative studies, which have the merit of local corneal preservation and faster surgeries, would be more representative than our study.

Conclusion

Contaminated CPCR still occurs despite the advancement in preservation techniques and protocols. Yet, it does not pose a major impact on the graft after transplantation. We recommend limiting the routine culturing of cornea-scleral rims to be for fungal only. This is due to the fact that fungal CPCR is more clinically relevant than bacterial counterparts, as shown above. Also, we recommend the maintenance of the current practices, the regimen of prescribing prophylactic post-transplant antibiotics, and preparing DSEAK lenticules intraoperatively rather than buying pre-cut tissues. Moreover, many leading endothelial keratoplasty centers are advocating for updating the current corneal preservation protocols, implementing compulsory fungal culturing after preservation, and adding an anti-fungal agent to the storage media to counteract the increasing incidence of post-transplant fungal infection in DMEK and DSEAK. Our study supports that those additional steps are not necessary.

Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Mannis MJ, Holland EJ. *Cornea*. Fourth edition.. Edinburgh: Elsevier; 2017. 2volumes.
2. Edelstein SL, DeMatteo J, Stoeger CG, et al. Report of the eye bank association of America medical review subcommittee on adverse reactions reported from 2007 to 2014. *Cornea*. 2016;35(7):917–926. doi:10.1097/ICO.0000000000000869
3. Rehany U, Balut G, Lefler E, et al. The prevalence and risk factors for donor corneal button contamination and its association with ocular infection after transplantation. *Cornea*. 2004;23(7):649–654. doi:10.1097/01.ico.0000139633.50035.cf
4. Farrell PL, Fan JT, Smith RE, et al. Donor cornea bacterial contamination. *Cornea*. 1991;10(5):381–386. doi:10.1097/00003226-199109000-00004
5. Aldave AJ, DeMatteo J, Glasser DB, et al. Report of the eye bank association of America medical advisory board subcommittee on fungal infection after corneal transplantation. *Cornea*. 2013;32(2):149–154. doi:10.1097/ICO.0b013e31825e83bf
6. Antonios SR, Cameron JA, Badr IA, et al. Contamination of donor cornea: post-penetrating keratoplasty endophthalmitis. *Cornea*. 1991;10(3):217–220. doi:10.1097/00003226-199105000-00006
7. Polack FM, Locatcher-Khorazo D, Gutierrez E. Bacteriological study of "donor" eyes: evaluation of antibacterial treatments prior to corneal grafting. *Arch Ophthalmol*. 1967;78(2):219–225. doi:10.1001/archopht.1967.00980030221018
8. Paton R. *Keratoplasty*. New York: McGraw-Hill; 1955.
9. Hj R Jr, Stocker FW. Bacterial flora in donor corneas. *Am J Ophthalmol*. 1965;59:247–249.
10. Doctor D, Hughes I. Neosporin for donor eyes. *Am J Ophthalmol*. 1958;46(3):351–353. doi:10.1016/0002-9394(58)90260-5
11. Rycroft P. Method for the preservation and sterilization of fresh donor material for full thickness keratoplasty. *Br J Ophthalmol*. 1965;49(5):251–258. doi:10.1136/bjo.49.5.251
12. Mathers WD, Lemp MA. Corneal rim cultures. *Cornea*. 1987;6(3):231–233. doi:10.1097/00003226-198706030-00016
13. Armitage WJ, Easty DL. Factors influencing the suitability of organ cultured corneas for transplantation. *Invest Ophthalmol Vis Sci*. 1997;38(1):16–24.
14. Wiffen SJ, Weston BC, Maguire LJ, et al. The value of routine donor corneal rim cultures in penetrating keratoplasty. *Arch Ophthalmol*. 1997;115(6):719–724. doi:10.1001/archopht.1997.01100150721003
15. Borderie VM, Laroche L. Microbiologic study of organ cultured donor corneas. *Transplantation*. 1998;66(1):120–123. doi:10.1097/00007890-199807150-00020
16. Dubovy SR, Edorovich S, Miller D. Efficacy of microbiology culture vs. histopathology in recovery of bacterial and fungal pathogens in post-keratoplasty corneal buttons. Presented at the Association for Research in Vision and Ophthalmology Meeting. Fort Lauderdale, Florida, May 5–10, 2002.
17. Alharbi SS, Alrajhi A, Alkahtani E. Endophthalmitis following keratoplasty: incidence, microbial profile, visual and structural outcomes. *Ocul Immunol Inflamm*. 2014;22(3):218–223. doi:10.3109/09273948.2013.841956
18. Wagoner MD, Al-Swailem SA, Sutphin JE, et al. Bacterial keratitis after penetrating keratoplasty: incidence, microbiological profile, graft survival, and visual outcome. *Ophthalmology*. 2007;114(6):1073–1079. doi:10.1016/j.ophtha.2006.10.015
19. Hassan SS, Wilhelmus KR. Eye-banking risk factors for fungal endophthalmitis compared with bacterial endophthalmitis after corneal transplantation. *Am J Ophthalmol,2005*. 2005;139(4):685–690. doi:10.1016/j.ajo.2004.12.016
20. Vislisel JM, Goins KM, Wagoner MD, et al. Incidence and outcomes of positive donor corneoscleral rim fungal cultures after keratoplasty. *Ophthalmology*. 2017;124(1):36–42. doi:10.1016/j.ophtha.2016.09.017
21. Leveille AS, McMullan FD, Cavanagh HD. Endophthalmitis following penetrating keratoplasty. *Ophthalmology*. 1983;90(1):38–39. doi:10.1016/S0161-6420(83)34601-7
22. Al-Assiri A, Al-Jastaneiah S, Al-Khalaf A, et al. Late-onset donor-to-host transmission of Candida glabrata following corneal transplantation. *Cornea*. 2006;25(1):123–125. doi:10.1097/01.ico.0000164777.80879.07
23. Everts RJ, Fowler WC, Chang DH, Reller LB. Corneoscleral rim cultures: lack of utility and implications for clinical decision-making and infection prevention in the care of patients undergoing corneal transplantation. *Cornea*. 2001;20(6):586–589. doi:10.1097/00003226-200108000-00006
24. Wilhelmus KR, Hassan SS. The prognostic role of donor corneoscleral rim cultures in corneal transplantation. *Ophthalmology*. 2007;114(3):440–445. [PubMed PMID: 17324694]. doi:10.1016/j.ophtha.2006.09.006

25. Keyhani K, Seedor JA, Shah MK, Terraciano AJ, Ritterband DC. The incidence of fungal keratitis and endophthalmitis following penetrating keratoplasty. *Cornea*. 2005;24(3):288–291. doi:10.1097/01.ico.0000138832.3486.70
26. Pels E, Beele H, Claerhout I. Eye bank issues: II. Preservation techniques: warm versus cold storage. *Int Ophthalmol*. 2008;28(3):155–163. doi:10.1007/s10792-007-9086-1
27. Chaurasia S, Sri S, Srinivas K, et al. Trends in infectious adverse events after elective optical keratoplasty (PK, EK, and ALK) - Ten years' analysis from an eye bank. *Indian*. *J Ophthalmol*. 2024;72(9):1254–1260.