JAMA Ophthalmology | Original Investigation

Donor Diabetes and 1-Year Descemet Membrane Endothelial Keratoplasty Success Rate
A Randomized Clinical Trial

Francis W. Price Jr, MD; Loretta B. Szczotka-Flynn, OD, PhD; Marianne O. Price, PhD; Colleen E. Bauza, PhD; Zachariah W. Reed, MS; Baha M. Arafah, MD; Mark A. Greiner, MD; Paula J. Johnson, COA; Devon B. Keeler, COT; Shahzad I. Mian, MD; Sanjay V. Patel, MD, FRC, Ophth; Sudeep Pramanik, MD; Mark C. Soper, CEBT; Mark A. Terry, MD; Michael S. Titus, CEBT; David D. Verdier, MD; Craig Kollman, PhD; Roy W. Beck, MD, PhD; Jonathan H. Lass, MD; for the Diabetes Endothelial Keratoplasty Study Group

IMPORTANCE If the success of Descemet membrane endothelial keratoplasty (DMEK) is not affected by whether the donor has diabetes, then the donor pool should expand.

OBJECTIVE To determine whether the 1-year DMEK success rate is affected by the presence of diabetes in the donor.

DESIGN, SETTING, AND PARTICIPANTS This was a multicenter, double-masked, randomized clinical trial conducted from February 2022 to July 2025 at 28 clinical sites (46 surgeons), with donor corneas provided by 13 eye banks in the US. Included in the study were individuals undergoing low to moderate risk DMEK (95% for Fuchs endothelial corneal dystrophy). Study data were analyzed from April to September 2025.

INTERVENTION DMEK performed with a cornea from a donor without or with diabetes, assigned using a minimization procedure (comparable with randomization) to achieve an approximate 2:1 distribution, respectively.

MAIN OUTCOMES AND MEASURES Graft success at 1 year

RESULTS A total of 1097 individuals (1421 study eyes; median [IQR] age, 71 [66-76] years; 631 female [57.5%]) were included in the study. The 1-year cumulative probability of graft success was 96.3% (95% CI, 95.0%-97.5%) among 912 study eyes (64.2%) receiving tissue from donors without diabetes and 97.1% (95% CI, 95.5%-98.4%) among 509 study eyes (35.8%) receiving tissue from donors with diabetes (difference between groups = 0.7 percentage points; 95% CI, −1.2 to 2.6; *P* = .63). The 1-year cumulative probability of graft success was 96.5% (95% CI, 93.6%-98.9%) in the mild donor diabetes severity subgroup (n = 173) and 97.3% (95% CI, 95.4%-98.8%) in the moderate to severe donor diabetes severity subgroup (n = 336), using a diabetes severity rating scale based on medical history. The rates of primary donor failure, early failure related to surgical complications, and subsequent failure were as follows: 2.5% (23 of 912), 0.7% (6 of 912), and 0.3% (3 of 912), respectively, in recipients of tissue from a donor without diabetes, and 2.6% (13 of 509), 0.4% (2 of 509), and 0%, respectively, among recipients of tissue from a donor with diabetes. There were no failures due to graft rejection.

CONCLUSIONS AND RELEVANCE The 1-year success rate in eyes undergoing DMEK with successfully prepared tissue was very high regardless of donor diabetes status. These results, supported by the separately reported finding that endothelial cell loss and cornea morphometry after 1 year were not affected by donor diabetes status, provide strong support for having no restrictions on the use of tissue from donors with diabetes for DMEK.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT05134480

Visual Abstract
Invited Commentary page 1051
Multimedia
Related article page 1053
Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The members of the Diabetes Endothelial Keratoplasty Study Group appear in Supplement 4.

Corresponding Author: Jonathan H. Lass, MD, University Hospitals Cleveland Medical Center, 11100 Euclid Ave, Cleveland, OH 44106 (deks@case.edu).

JAMA Ophthalmol. 2025;143(12):1043-1051. doi:10.1001/jamaophthalmol.2025.4253
Published online October 17, 2025.

Diabetes is increasingly prevalent among keratoplasty donors and recipients, and the prevalence in donors substantially exceeds that in recipients.[1,2] Over 25% of adults aged 65 years and older in the US have diabetes, and it is the eighth leading cause of death.[3] Studies suggest the prevalence of known diabetes among cornea donors has almost doubled in 2 decades to approximately one-third of the donor supply[2,4,5]; the actual prevalence is probably higher because more than 20% of diabetes cases are thought to be undiagnosed.[3]

Diabetes can adversely affect the corneal endothelium and endothelial mitochondria[6] and increase Descemet membrane thickness, rigidity, and adhesion to the corneal stroma.[7,8] Eye banks have reported 3- to 8-fold higher damage rates when preparing tissue from donors with diabetes for Descemet membrane endothelial keratoplasty (DMEK),[9,10] the most common keratoplasty procedure in the US.[11] Many eye banks and corneal surgeons avoid use of tissue from donors with diabetes, particularly for DMEK. This decision, together with increasing regulations to prevent infectious disease transmission and periodic supply chain disruptions, makes it increasingly difficult to meet the demand for donor corneal tissue.

A secondary analysis of Descemet stripping automated endothelial keratoplasty (DSAEK) outcomes from the Cornea Preservation Time Study (CPTS) found that corneas from donors with diabetes had a lower graft success rate[12] and higher endothelial cell loss (ECL)[13] 3 years postoperatively. However, other studies have not found an association between graft success and the presence of diabetes in the cornea donor.[1,14] Consequently, there is considerable uncertainty about whether donor diabetes should be a factor in determining whether a donor cornea is suitable for keratoplasty.

The Diabetes Endothelial Keratoplasty Study (DEKS) was designed to determine whether donor diabetes affects graft success and ECL with low to moderate risk DMEK. Herein we report the 1-year primary graft success rate from the randomized clinical trial. The effect of donor diabetes on ECL is reported in a companion article.[15]

Key Points

Question Does the presence of diabetes in a cornea donor affect the success of Descemet membrane endothelial keratoplasty (DMEK) 1 year postoperatively?

Findings In this randomized clinical trial including 1097 individuals and 1421 eyes, DMEK was successful at 1 year using corneas from donors with or without diabetes. The success rate among trial recipients did not appear to be influenced by donor diabetes severity.

Meaning DMEK is a highly effective procedure, and the 1-year success rate did not appear to be influenced by the presence of diabetes in the donor.

Methods

Trial Conduct and Oversight

The DEKS trial was a National Institutes of Health–sponsored trial conducted at 28 clinical sites and 13 eye banks in the US. The protocol was approved by the Jaeb Center for Health Research institutional review board; methods were published previously.[2] Supplement 1 includes the protocol, and Supplement 2 includes the statistical analysis plan. Further details on the Diabetes Endothelial Keratoplasty study group are listed in the eAppendix in Supplement 3. Each participant provided written informed consent. A stipend was provided for completion of study visits. An independent data and safety monitoring committee appointed by the National Eye Institute (NEI) provided oversight. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Trial Design and Participants

Eligible recipients were aged 30 years to younger than 91 years with a clinical indication for low to moderate risk DMEK due to endothelial dysfunction, including Fuchs endothelial corneal dystrophy (FECD), pseudophakic corneal edema, or failed DSAEK or DMEK. Complete criteria are in eTable 1 in Supplement 3. Recipients had blood collected at screening and 1-year postoperative visits for hemoglobin A_{1c} (HbA_{1c}) assessment at a central laboratory (Advanced Research and Diagnostics Laboratory [ARDL], University of Minnesota, Minneapolis, Minnesota) and received the results. Those without a history of diabetes were reclassified as having diabetes if the screening HbA_{1c} level was greater than or equal to 6.5% (to convert to proportion of total hemoglobin, multiply by 0.01), based on the American Diabetes Association criteria for diabetes diagnosis.[16] Trial recipients self-identified the following races and ethnicities: African American, American Indian or Alaska Native, Asian, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, multiracial, White, and unknown or not reported. Race and ethnicity data were included to evaluate potential association with outcomes.

Donor corneas met Eye Bank Association of America standards for DMEK and were stored in hypothermic storage solution (eMethods in Supplement 3). The eye bank classified each potential donor as having diabetes or not from a review of medical history and drew blood from each donor for HbA_{1c} measurement at a central laboratory (ARDL). A previous study[17] showed that postmortem HbA_{1c} level corresponded with premortem HbA_{1c} level within 90 days of death. Donors who initially classified as not having diabetes were reclassified as having diabetes if postmortem HbA_{1c} level was greater than or equal to 6.5%. A Diabetes Severity Score was determined based on criteria described by Williams et al[18] to predict DMEK lenticule preparation failure risk and was applied more broadly to graft outcomes (eTable 2 in Supplement 3). The diabetes severity groups were graded 1 to 3 (mild) or 4 to 5 (moderate to severe) per the modified Williams scale.

A minimization procedure was used to assign a donor cornea to each study eye in an approximate distribution of 2:1 without vs with diabetes from tissue available at the eye bank on the day tissue placement was needed. We chose this ratio to approximate the contemporaneous proportion of tissue from

donors with diabetes used for keratoplasty in the US.[5] The assignment was stratified by site, surgeon, and recipient diabetes status. For recipients with 2 study eyes, the minimization procedure was used to assign a donor cornea for the first eye. Whenever the first eye received a cornea from a donor with known diabetes, the second eye received a cornea from a donor without known diabetes, whereas when the first eye received a cornea from a donor without known diabetes, the minimization procedure was used to assign a donor with or without diabetes to the second eye. Participants and surgeons were masked to donor diabetes status.

Tissue Preparation

Individual eye banks followed their standard protocols for tissue preparation, except technicians were masked to donor diabetes status. Specular microscopy was required before preparation during donor screening and was optional after preparation. Technicians documented observations during preparation including membrane tears, tear type, adhesions, scroll tightness, and proportion of cell damage by trypan blue staining after preparation.[2] The same assessments applied to surgeon-prepared tissue, with study-specific certification required for trypan blue staining and scroll tightness assessments. Use of prestripped or preloaded donor tissue was allowed and documented.

Surgical Procedure and Postoperative Care

Surgeons followed their usual technique and documented key operative and postoperative details.[2] Study-specified evaluations, including specular microscopy but not visual acuity, were conducted at 1 month and 1 year postoperatively. At the 1-month visit, all clinical events that occurred from surgery to that visit were recorded; at the 1-year visit, events that occurred between the 1-month and 1-year visits were recorded. Clinical assessments and additional examinations followed the investigator's standard care.

Recipient central stromal clarity was assessed using a standard grading system, categorizing findings as clear, equivocal, or cloudy (eTable 3 in Supplement 3). All investigators underwent formal training, testing, and certification in use of this scale, guided by a validated photographic reference set.

Outcomes

The primary efficacy outcome was graft success at 1 year (ie, graft failure did not occur before 1 year). Graft failure was defined as follows: (1) cornea regrafted for any reason or (2) recipient cornea was classified as cloudy based on the standardized grading scale, without clearing, where the cornea either (1) never cleared postsurgically such that at 1 week postoperatively, it was graded as cloudy, did not clear, and remained cloudy at or after 8 weeks or (2) was initially clear postoperatively but became cloudy, did not clear, and remained cloudy for at least 91 days. The date of graft failure was the first examination during the failure event in which the cornea was cloudy or the date of regraft if the cornea was not documented as cloudy before regraft. Graft failure was initially determined by the certified surgeon-investigator and confirmed by the coordinating center and study chair review of the submitted data to verify that graft failure criteria were met, supplemented by communication with the investigator for clarification when needed. A recipient cornea that was cloudy or equivocal at 1 week and did not clear or required a regraft within 8 weeks was categorized as follows: (1) primary donor failure in the absence of surgical complications or (2) early failure if associated with intraoperative and/or perioperative complications. Failures after 8 weeks were categorized as (1) graft rejection if a recipient cornea that was initially clear became cloudy after an allograft reaction, (2) nonrejection if a recipient cornea that was clear became cloudy due to causes other than an immune event, or (3) refractive/visual.

Sample Size and Power Calculation

Sample size was calculated as 1420 eyes (approximately 947 receiving corneas from donors without diabetes and 473 receiving corneas from donors with diabetes) based on graft failure rates from the CPTS[12] study of 4% for donors without diabetes and 9% for donors with diabetes, 2:1 allocation ratio favoring donors without diabetes, 2-sided α of .05, 90% statistical power, and 10% loss to follow-up.

Statistical Analysis

Statistical analyses were performed using SAS, version 9.4 (SAS Institute), on an intention-to-treat basis; all recipient eyes were included in the primary and secondary analyses unless otherwise noted. One-year graft success rates between donor diabetes status groups were compared using a proportional hazards model while adjusting for cornea diagnosis and accounting for participants with 2 study eyes using a frailty model. The effect of donor diabetes severity on graft success was evaluated within predefined donor diabetes severity categories (0, 1-3, and 4-5 as well as 0, 1, 2, 3, 4, and 5).

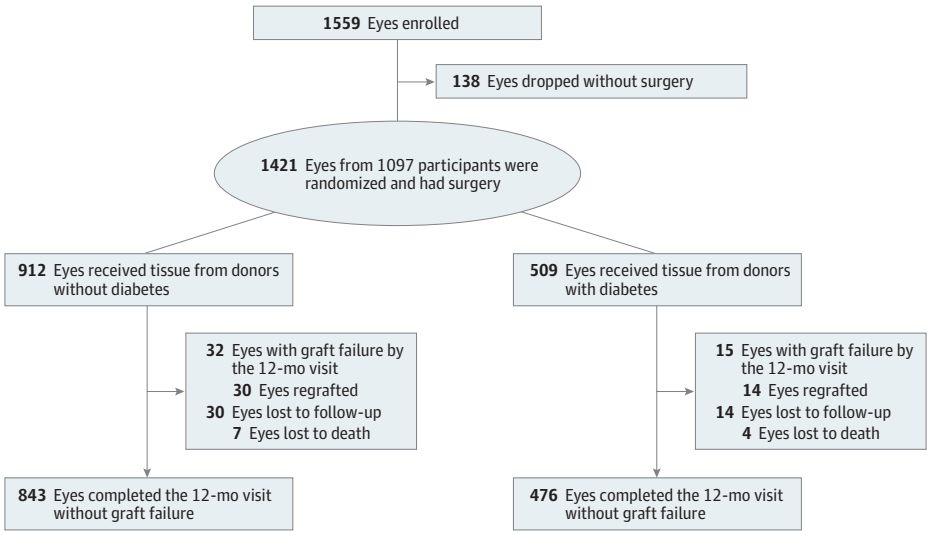
Except for the primary analysis, *P* values were adjusted to control the false discovery rate using the 2-stage Benjamini-Hochberg procedure. Additional statistical methods are described in the eMethods in Supplement 3. Study data were analyzed from April to September 2025.

Results

Baseline Recipient Characteristics

Between February 2022 and July 2024, 1421 eyes from 1097 recipients (324 bilateral cases; median [IQR] age, 71 [66-76] years; 631 female [57.5%]; 466 male [42.5%]) underwent DMEK performed by 46 surgeons at 28 clinical sites; 912 eyes (64.2%) received tissue from donors without diabetes, and 509 eyes (35.8%) received tissue from donors with diabetes (**Figure**). Recipients self-identified the following races and ethnicities: 32 African American (2.9%), 2 American Indian or Alaska Native (0.2%), 3 Asian (0.3%), 1 Native Hawaiian or Other Pacific Islander (0.1%), 4 multiracial (0.4%), 1055 White (96.2%), 0 unknown or not reported, 16 Hispanic or Latino (1.5%), and 1081 not Hispanic or Latino (98.5%) (**Table 1**).[19] A total of 232 of 1097 recipients (21.1%) reported a history of diabetes; 24 of 1097 recipients (2.2%) without a history of diabetes had screening HbA_{1c} level greater than or equal to 6.5% and

Figure. Flowchart of Study Completion



were reclassified as having diabetes. Preoperatively, 776 of 1421 eyes (54.6%) were phakic, 643 of 1421 (45.2%) had a capsule-supported posterior chamber intraocular lens (PC-IOL), and 2 of 1421 (0.1%) had a nonposterior capsule–supported PC-IOL. The most common indication for surgery was FECD, present in 1368 of 1421 eyes (96%). The distributions of key baseline recipient characteristics were similar between donor groups (Table 1).[19]

Baseline Donor Characteristics

Mean (SD) donor age was 65 (7) years (range, 50-75 years), and the mean (SD) eye bank–determined ECD at donor screening was 2709 (275) cells/mm^2 (range, 2304-3759 cells/mm^2). After tissue assignment, 104 of 1154 donors (9%) initially classified as not having diabetes after eye bank medical record review were subsequently reclassified as having diabetes based on a postmortem HbA_{1c} level greater than or equal to 6.5% independently of knowledge of the recipient to whom the tissue was assigned.

Donor Tissue Preparation and Complications

In preparing the donor tissue for surgery, the preparation failed, and the tissue could not be used in 15 of 927 attempts (1.6%) using corneas from donors without diabetes and 33 of 542 attempts (6.1%) using corneas from donors with diabetes ($P < .001$). Among the DMEK lenticules transplanted in the trial, the eye banks prepared 60%, the surgeons prepared 18%, and preparation was initiated by the eye bank and completed by the surgeon with 22%. Median (IQR) tissue preservation time was 6 (5-7) days for both groups. Baseline characteristics were similar for donors with and without diabetes (eTable 4 in Supplement 3).

Intraoperative and Postoperative Procedures and Complications

The frequencies and types of intraoperative procedures performed in addition to DMEK were similar in both donor diabetes groups (eTable 5 in Supplement 3). Surgeons combined cataract extraction and PC-IOL placement with DMEK in 606 of 776 phakic eyes (78%). After DMEK, 1249 of 1421 eyes (87.9%) were pseudophakic with a PC-IOL, and 168 of 1421 eyes (11.8%) were phakic (Table 1).[19] The rate of intraoperative complications was low and similar in both donor diabetes groups (eTable 5 in Supplement 3).

Postoperatively, the rate of air reinjection to treat partial graft detachment was 19% regardless of donor diabetes status (eTable 6 in Supplement 3). Major postoperative complications were rare throughout the first postoperative year. No eye experienced endophthalmitis or microbial keratitis in the early postoperative period (eTable 7 in Supplement 3). Other than air injections, the most common postoperative procedures were air/gas release due to pupillary block or intraocular pressure elevation caused by the air/gas bubble used to temporarily hold the graft in place, cataract surgery, which may be staged after DMEK to optimize uncorrected visual acuity outcomes, and YAG capsulotomy to treat posterior capsule opacification after cataract surgery (eTable 8 in Supplement 3).

Study Completion

Follow-up was completed on July 3, 2025. Overall, 875 study eyes (96%) that were assigned tissue from donors without diabetes and 491 eyes (96%) that were assigned tissue from donors with diabetes either completed the 1-year visit or experienced graft failure (Figure).

Graft Failure

During the 1-year follow-up, 32 of 912 grafts from donors without diabetes and 15 of 509 grafts from donors with diabetes failed. The 1-year cumulative probability of graft success was 96.3% (95% CI, 95.0%-97.5%) and 97.1% (95% CI, 95.5%-98.4%) using tissue from donors without and with diabetes, respectively (difference between groups = 0.7 percentage points; 95% CI, −1.2 to 2.6; $P = .63$) (eFigure in

Table 1. Participant and Study Eye Characteristics by Donor Diabetes Status

Characteristic	Donor diabetes status	
	Without diabetes	With diabetes
Participant characteristics		
No.	782[a]	492[a]
Age when patient enrolled, median (IQR), y[a]	70 (65-75)	71 (66-76)
Sex, No. (%)[a]		
Female	432 (55)	292 (59)
Male	350 (45)	200 (41)
Race, No. (%)[a]		
African American	22 (3)	16 (3)
American Indian or Alaska Native	1 (<1)	2 (<1)
Asian	3 (<1)	0
Native Hawaiian or Other Pacific Islander	1 (<1)	0
Multiracial	2 (<1)	3 (<1)
White	753 (96)	471 (96)
Unknown/not reported	0	0
Ethnicity: Hispanic or Latino, No. (%)[a]	7 (<1)	11 (2)
Self-reported history of diabetes, No. (%)[b]	172 (22)	94 (19)
Current cigarette smoker, No. (%)[b]	34 (4)	28 (6)
Received any immunizations or vaccinations in last 3 mo, No. (%)[b]	137 (18)	80 (16)
Study eye characteristics		
No.	912	509
Prior glaucoma surgery, No. (%)	17 (2)	12 (2)
Glaucoma meds currently being used, No. (%)	49 (5)	32 (6)
Diagnosis, No. (%)		
PCE	12 (1)	11 (2)
Failed DSAEK	8 (<1)	10 (2)
Failed DMEK	9 (<1)	3 (<1)
FECD	883 (97)	485 (95)
FECD grade[2]		
0	2 (<1)	0
1	4 (<1)	0
2	11 (1)	7 (1)
3	16 (2)	6 (1)
4	211 (24)	118 (24)
5	241 (27)	123 (25)
6	398 (45)	231 (48)
Evidence of a corneal abnormality other than FECD, No. (%)		
No	804 (88)	443 (87)
Map-dot fingerprint	62 (7)	39 (8)
Subepithelial scarring	25 (3)	15 (3)
Stromal scarring	9 (<1)	6 (1)
Prior LASIK	6 (<1)	3 (<1)
Keratoconus	2 (<1)	2 (<1)
Other	9 (<1)	5 (<1)
Stromal corneal vessels present (but not visually significant), No. (%)	0	0
Central subepithelial or stromal scarring present (but could not impact postop stromal clarity assessment), No. (%)	33 (4)	21 (4)
Peripheral anterior synechiae present (nongonioscopic), No. (%)	0	1 (<1)
Preoperative lens status, No. (%)		
Phakic	508 (56)	268 (53)
PC-IOL, posterior capsule supported	402 (44)	241 (47)
PC-IOL, nonposterior capsule supported	2 (<1)	0
Postoperative lens status, No. (%)		
Phakic	104 (11)	64 (13)
PC-IOL, posterior capsule supported	805 (88)	444 (87)
PC-IOL, nonposterior capsule supported	3 (<1)	1 (<1)
IOP, median (IQR), mm Hg	13 (11-16)	13 (11-16)

Abbreviations: DMEK, Descemet membrane endothelial keratoplasty; DSAEK, Descemet stripping automated endothelial keratoplasty; FECD, Fuchs endothelial corneal dystrophy; LASIK, laser-assisted in situ keratomileusis; PC-IOL, posterior chamber intraocular lens; PCE, pseudophakic corneal edema.

[a] If the recipient received a study cornea from a donor with diabetes and a donor without diabetes, the baseline characteristics collected at time of enrollment of the first eye is counted in both columns.

[b] These recipient-level questions were repeated at the time of enrollment of the second eye; therefore, the answers could differ from 1 eye to the next. The most recent answer is reported where applicable.

Supplement 3). The adjusted hazard ratio for graft success was 0.86 for donors without diabetes compared with those with diabetes (95% CI, 0.47-1.59; P = .63). Among donors with diabetes, the 1-year cumulative probability of graft success was 96.5% (95% CI, 93.6%-98.9%) in the mild diabetes severity donor subgroup (n = 173) and 97.3% (95% CI, 95.4%-98.8%) in the moderate to high diabetes severity donor subgroup (n = 336) (**Table 2** and eFigure in Supplement 3). In an analysis based on the original eye bank classification of donor diabetes, with no reclassification based on postmortem HbA_{1c} level, 1-year graft success rates were similar to the primary analysis: 1001 of 1038 (Kaplan-Meier estimate, 96.3%) and 373 of 383 (Kaplan-Meier estimate, 97.4%) for donors without and with diabetes, respectively. Sensitivity analyses adjusting for the correlation between 2 recipients receiving tissue from the same donor, and eyes with surgery by the same surgeon demonstrated similar results.

The rates of primary donor failure, early failure related to surgical complications, and subsequent failure were as follows: 2.5% (23 of 912), 0.7% (6 of 912), and 0.3% (3 of 912), respectively, in recipients of tissue from a donor without diabetes, and 2.6% (13 of 509), 0.4% (2 of 509), and 0%, respectively, among recipients of tissue from a donor with diabetes (**Table 3** and **Table 4**). No failure was due to graft rejection in either donor diabetes group, and the cumulative risk of a definite rejection episode was less than 1% in both groups.

There was no significant interaction of recipient age, indication for keratoplasty (FECD or other), or recipient diabetes status on the effect of donor diabetes status on the 1-year graft success rate (eTable 9 in Supplement 3).

Table 2. Effect of Donor Diabetes Status on 1-Year Graft Success

Status	No.	1-y Graft success rate KM estimate, % (95% CI)	Difference in graft success rate, percentage points (95% CI)	Adjusted hazard ratio (95% CI)[a]	Adjusted *P* value[a]
Donor diabetes status					
Without diabetes	912	96.3 (95.0 to 97.5)	0 [Reference]	1 [Reference]	.63
With diabetes	509	97.1 (95.5 to 98.4)	0.7 (−1.2 to 2.6)	0.86 (0.47 to 1.59)	
Donor diabetes severity group[b]					
Without diabetes	912	96.3 (95.0 to 97.5)	0 [Reference]	1 [Reference]	.78
With mild diabetes	173	96.5 (93.6 to 98.9)	0.2 (−3.0 to 3.0)	1.02 (0.43 to 2.45)	
With moderate to severe diabetes	336	97.3 (95.4 to 98.8)	1.0 (−1.3 to 3.0)	0.78 (0.37 to 1.63)	
Donor Diabetes Severity Score					
Without diabetes	912	96.3 (95.0 to 97.5)	0 [Reference]	1 [Reference]	.94
1	29	96.6 (88.5 to 100)	0.2 (−8.0 to 4.6)	0.97 (0.13 to 7.10)	
2	63	95.2 (89.3 to 100)	−1.1 (−7.1 to 3.7)	1.42 (0.43 to 4.64)	
3	81	97.5 (93.7 to 100)	1.2 (−2.9 to 4.3)	0.74 (0.18 to 3.08)	
4	166	97.0 (94.2 to 99.4)	0.7 (−2.5 to 3.3)	0.89 (0.35 to 2.28)	
5	170	97.6 (95.1 to 99.5)	1.3 (−1.6 to 3.7)	0.67 (0.24 to 1.89)	

Abbreviation: KM, Kaplan-Meier.

[a] The primary analysis used proportional hazards models that adjusted for corneal diagnosis and accounted for participants with 2 eyes included in the study using a frailty model.

[b] A Diabetes Severity Score was calculated for donors with diabetes, as described in eTable 2 in Supplement 3. The sum of the assigned point values produced scores ranging from 1 to 5. A sum of 1 to 3 points was categorized in the mild severity group, and a sum of 4 to 5 points was categorized in the moderate to severe severity group.

Table 3. Categories of Graft Failure Within 1 Year,[a] by Donor Diabetes Status

Graft failure type	Donor diabetes status, No. (%)	
	Without diabetes (n = 912)	With diabetes (n = 509)
Total No. of 1-y graft failures	32 (3.5)	15 (2.9)
Primary donor failure in the absence of surgical complications	23 (2.5)	13 (2.6)
Early failure associated with surgical complications	6 (0.7)	2 (0.4)
Nonrejection graft failure—endothelial decompensation	2 (0.2)	0
Nonrejection graft failure—other	1 (0.1)	0

[a] Prespecified graft failure categorization: a recipient cornea that was cloudy or equivocal at 1 week and did not clear or required a regraft within 8 weeks was categorized as follows: (1) primary donor failure in the absence of surgical complications or (2) early failure if associated with intraoperative and/or perioperative complications. Failures after 8 weeks were categorized as (1) graft rejection if a recipient cornea that was initially clear became cloudy after an allograft reaction, (2) nonrejection if a recipient cornea that was clear became cloudy due to causes other than an immune event, or (3) refractive/visual if the graft was replaced due to inadequate vision while the central recipient cornea remained clear.

Discussion

The DEKS trial was designed to determine whether donor diabetes affects DMEK graft success through rigorous assessment of donor diabetes status and random assignment of corneas from donors with and without diabetes. We found that donor diabetes status and diabetes severity did not affect DMEK success through the first postoperative year. Furthermore, the diabetes status of the donor did not affect endothelial cell loss and morphometry 1 year after DMEK, as reported separately.[15]

Corneal surgeons have been wary of using tissue for DMEK from donors with diabetes, especially from donors with a history of moderate to severe diabetes. These results provide strong evidence that surgeons and patients can have high confidence in the use of successfully prepared donor tissue, regardless of donor diabetes status or severity. The findings should lead to expansion of the pool of suitable donor tissue at a time when the donor supply is under strain because of new regulations and periodic supply chain disruptions.

Prior studies have provided conflicting evidence regarding the effect of donor diabetes on graft success. A secondary analysis[12] from the CPTS study suggested that donor diabetes was associated with a higher primary/early failure rate after DSAEK (5.3% vs 2.5% with vs without donor diabetes, n = 357 and n = 973, respectively). However, a secondary Cornea Donor Study analysis[14] found no significant association between donor diabetes and failure rate at 10 years after penetrating keratoplasty (26% vs 23% with vs without donor diabetes, n = 199 and 891, respectively; *P* = .60). Likewise, a single-center retrospective analysis[1] found no significant association between donor diabetes and failure rate at 4 years after DMEK (9% vs 7% with vs without donor diabetes, n = 504 and n = 1287, respectively; *P* = .15). Differences in findings may reflect differences in keratoplasty procedures. Our finding that recipient diabetes did not significantly affect DMEK success was consistent with prior studies.[1,20] Notably, the DEKS trial used more rigorous methods for classifying donor and recipient diabetes than previous studies.

As the largest (to our knowledge) prospective, multicenter DMEK study conducted to date, the DEKS trial showed that DMEK was a highly effective and safe procedure for treating corneal endothelial dysfunction. Most graft failures in the first year after DMEK were primary donor failures or early failures associated with surgical complications, regardless of donor diabetes status, consistent with prior DMEK studies,[21] and with DSAEK performed by experienced surgeons for similar conditions in the CPTS study.[22] The 97% success rate at 1 year in the current study is comparable with that reported by

Table 4. Categories of Graft Failure Within 1 Year,[a] by Donor Diabetes Severity Score Subgroups and Donor Diabetes Severity Scores

Graft failure type	Donor Diabetes Severity Score subgroups		Donor Diabetes Severity Scores				
	Mild (score 1-3) (n = 173)	Moderate to severe (score 4-5) (n = 336)	1 (n = 29)	2 (n = 63)	3 (n = 81)	4 (n = 166)	5 (n = 170)
Total No. of 1-y graft failures, No. (%)	6 (3.5)	9 (2.7)	1 (3.4)	3 (4.8)	2 (2.5)	5 (3.0)	4 (2.4)
Primary donor failure in the absence of surgical complications, No.	5	8	1	3	1	4	4
Early failure associated with surgical complications, No.	1	1	0	0	1	1	0
Nonrejection graft failure—endothelial decompensation, No.	0	0	0	0	0	0	0
Nonrejection graft failure—other, No.	0	0	0	0	0	0	0

[a] Prespecified graft failure categorization: a recipient cornea that was cloudy or equivocal at 1 week and did not clear or required a regraft within 8 weeks was categorized as follows: (1) primary donor failure in the absence of surgical complications or (2) early failure if associated with intraoperative and/or perioperative complications. Failures after 8 weeks were categorized as (1) graft rejection if a recipient cornea that was initially clear became cloudy after an allograft reaction, (2) nonrejection if a recipient cornea that was clear became cloudy due to causes other than an immune event, or (3) refractive/visual if the graft was replaced due to inadequate vision while the central recipient cornea remained clear.

high-volume single-sites using DMEK for FECD,[21,23] the most common keratoplasty indication in the US.[11] Outcomes with DMEK in the DEKS trial were similar to outcomes with DSAEK in the CPTS: respective overall rates of primary/early graft failure were 3.3% vs 3.1%, rates of air/gas injection to promote graft attachment were 19% vs 11%, and rates of definite graft rejection episodes through 1 year were less than 1% vs 2%.[19]

The tissue preparation failure rates in the DEKS trial were 1.6% with corneas from donors without diabetes vs 6.1% with corneas from donors with diabetes, representing a small but potentially relevant difference with respect to eye bank costs in procuring corneas from donors with diabetes. Tissue preparation for DMEK requires detaching the donor Descemet membrane from the stroma. Donor diabetes increases Descemet membrane rigidity and adherence,[7,8] thus increasing the risk of tearing the tissue during detachment and rendering it unusable. Secondary analyses in the DEKS trial are under way to explore associations between various measures of donor diabetes severity and tissue preparation success, as well as graft success and endothelial cell loss at 1 year.

Strengths and Limitations

This study has several strengths, including a large sample size, random assignment of tissue from a donor without or with diabetes, rigorous classification of donor diabetes status including postmortem HbA_{1c} testing,[17] masking of the lenticule preparation technician, surgeon, participant and coordinating center to the donor diabetes status, experienced surgeons in both academic and private practice setting, high participant retention, and standardized methods of assessing recipient corneal stroma clarity and graft failure.[2]

However, this study also has some limitations. As noted previously, chance, confounding, and bias are unlikely sources of error due to the precision of the point estimates by having a large sample size, random assignment of cornea tissue, and masking of the surgeon and participant to donor diabetes status, respectively. Regarding generalizability, the DEKS cohort consisted principally of FECD cases (96%), but we know of no biologically plausible reason to expect that the effect of donor diabetes on DMEK success would be different for other corneal conditions. The 1-year follow-up was the main limitation. Longer follow-up of a subset of DEKS participants through funding provided by the NEI will provide valuable information about whether donor and/or recipient diabetes affect long-term graft success.

Conclusions

This randomized clinical trial confirms that DMEK is a highly effective and safe procedure for treatment of corneal endothelial dysfunction. The 1-year success rate in eyes undergoing DMEK principally for FECD was very high irrespective of donor or recipient diabetes status or donor diabetes severity. In addition, the finding that endothelial cell loss and morphometry 1 year after DMEK were not affected by diabetes status of the cornea donor suggests that the results observed after 1 year with respect to donor diabetes status will be sustained with longer follow-up. These findings support the use of tissue across the full spectrum of donor diabetes severity for DMEK, the most common keratoplasty procedure performed in the US. Acceptance of these results by the cornea community should expand the pool of donor tissue, which has been shrinking because of new regulations, eg, new sepsis exclusion criteria,[24] and which has long been inadequate to meet demand worldwide.

ARTICLE INFORMATION

Accepted for Publication: September 4, 2025.

Published Online: October 17, 2025. doi:10.1001/jamaophthalmol.2025.4253

Author Affiliations: Price Vision Group, Indianapolis, Indiana (F. W. Price); Department of Ophthalmology and Visual Sciences, Case Western Reserve University School of Medicine and University Hospitals Eye Institute, Cleveland, Ohio (Szczotka-Flynn, Lass); Cornea Research Foundation of America, Indianapolis, Indiana (M. O. Price); Jaeb Center for Health Research, Tampa, Florida (Bauza, Reed, Kollman, Beck); Department of Medicine, Case Western Reserve

University School of Medicine and University Hospitals Cleveland Medical Center (Arafah); Department of Ophthalmology and Visual Sciences, Carver College of Medicine, University of Iowa Hospitals & Clinics, Iowa City (Greiner); Verdier Eye Center, Grand Rapids, Michigan (Johnson, Keeler, Verdier); Kellogg Eye Center, University of Michigan, Ann Arbor (Mian); Department of Ophthalmology, Mayo Clinic, Rochester, Minnesota (Patel); Mid-Atlantic Cornea Consultants, Baltimore, Maryland (Pramanik); VisionFirst, Indianapolis, Indiana (Soper); Now with Lions Eye Bank of the Northeast, Albany, New York (Soper); Devers Eye Institute, Portland, Oregon (Terry); Eversight, Ann Arbor, Michigan (Titus).

Author Contributions: Dr Bauza and Mr Reed had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Szczotka-Flynn, M. Price, Bauza, Greiner, Soper, Terry, Titus, Verdier, Kollman, Beck, Lass.
Acquisition, analysis, or interpretation of data: F. Price, Szczotka-Flynn, M. Price, Bauza, Reed, Arafah, Greiner, Johnson, Keeler, Mian, Patel, Pramanik, Terry, Titus, Verdier, Kollman, Beck, Lass.
Drafting of the manuscript: Szczotka-Flynn, M. Price, Bauza, Reed, Patel, Terry, Verdier, Beck, Lass.
Critical review of the manuscript for important intellectual content: F. Price, Szczotka-Flynn, M. Price, Bauza, Arafah, Greiner, Johnson, Keeler, Mian, Patel, Pramanik, Soper, Terry, Titus, Verdier, Kollman, Lass.
Statistical analysis: Bauza, Reed, Verdier, Kollman.
Obtained funding: Szczotka-Flynn, Bauza, Lass.
Administrative, technical, or material support: F. Price, Szczotka-Flynn, M. Price, Bauza, Johnson, Keeler, Patel, Soper, Titus, Verdier, Lass.
Supervision: F. Price, Szczotka-Flynn, M. Price, Bauza, Mian, Patel, Pramanik, Titus, Verdier, Kollman, Beck, Lass.

Conflict of Interest Disclosures: Dr F. Price reported receiving grants from National Eye Institute (NEI) during the conduct of the study; personal fees from EyeYon and Alcon; and stock ownership in RxSight. Dr Szczotka-Flynn reported receiving grants from the National Institutes of Health (NIH) and LensTechs during the conduct of the study and personal fees from Epion outside the submitted work. Dr M. Price reported receiving personal fees from EyeYon and stock ownership in RxSight outside the submitted work. Dr Bauza reported receiving grants from the NEI during the conduct of the study. Dr Reed reported receiving grants from the NIH during the conduct of the study. Dr Mian reported receiving grants from the NEI and Kowa during the conduct of the study. Dr Patel reported receiving grants from the NEI during the conduct of the study; personal fees from Santen, Design Therapeutics, Emmecell, Thea, and Iris Medicine (ended in 2024), and Invirsa (ended in 2024) outside the submitted work; and being the developer of V-FUCHS, which is licensed by Mayo Clinic to: Santen, Design Therapeutics, Iris Medicine, and Kowa Research Institute. Dr Soper reported receiving grants from the NEI and being an employee of VisionFirst Eye Bank (retired in October 2023) outside the submitted work. Dr Terry reported receiving grants from the NEI; royalties on instruments used in Descemet stripping automated endothelial keratoplasty (DSAEK) surgery but not Descemet membrane endothelial keratoplasty (DMEK) surgery from Bausch and Lomb outside the submitted work. Dr Titus reported receiving grants from Jaeb Center for Health Research Foundation Inc during the conduct of the study and employee-related fees from Eversight outside the submitted work. Dr Verdier reported that NIH Verdier Eye Center has been provided funds to cover usual and customary expenses for patients receiving care in the DEKS study. Dr Kollman reported receiving grants from the NIH during the conduct of the study. Dr Beck reported receiving grants from the NIH during the conduct of the study. Dr Lass reported receiving grants from the NEI; a donation to Case Western Reserve University to support additional expenses beyond NIH funding from Eye Bank Association of America, The Cornea Society, Cleveland Eye Bank Foundation, Beauty of Sight, CorneaGen, Eversight, Eye Bank for Sight Restoration, Eye Bank for Kentucky, Gift of Sight, Iowa Lions Eye Bank, Kenneth Maverick, MD, Lions Eye Bank of Wisconsin, San Antonio Eye Bank, San Diego Eye Bank, Utah Lions Eye Bank, VisionFirst, and VisionGift; and nonfinancial support as board member from Eversight and Cleveland Eye Bank Foundation. No other disclosures were reported.

Funding/Support: This work was supported by cooperative agreements with the National Eye Institute, National Institutes of Health, Department of Health and Human Services (EY030030 5 and EY030039). Sponsors: Eye Bank Association of America, The Cornea Society, Cleveland Eye Bank Foundation, Beauty of Sight (formerly Florida Lions Eye Bank), CorneaGen, Eversight, Eye Bank for Sight Restoration, Eye Bank of Kentucky, Gift of Sight, Iowa Lions Eye Bank, Kenneth Maverick MD, Lions Eye Bank of Wisconsin, San Antonio Eye Bank, San Diego Eye Bank, Utah Lions Eye Bank, VisionFirst, and VisionGift.

Role of the Funder/Sponsor: The National Eye Institute, National Institutes of Health, Department of Health and Human Services had roles in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; and decision to submit the manuscript for publication. The following sponsors had no role the design, conduct, management, analysis, interpretation or publication of the study data, but provided additional support for ancillary work pertaining to this study: Eye Bank Association of America, The Cornea Society, Cleveland Eye Bank Foundation, Beauty of Sight (formerly Florida Lions Eye Bank), CorneaGen, Eversight, Eye Bank for Sight Restoration, Eye Bank of Kentucky, Gift of Sight, Iowa Lions Eye Bank, Kenneth Maverick MD, Lions Eye Bank of Wisconsin, San Antonio Eye Bank, San Diego Eye Bank, Utah Lions Eye Bank, VisionFirst, VisionGift.

Group Information: The members of the Diabetes Endothelial Keratoplasty Study Group appear in Supplement 4.

Meeting Presentation: This paper was presented at the Cornea and Eye Banking Forum on October 17, 2025, and the AAO 2025 on October 18, 2025; Orlando, Florida.

Data Sharing Statement: See Supplement 5.

Additional Contributions: We thank the study participants for their important contribution to the conduct of this study. A stipend was provided for completion of study visits for each recipient.

REFERENCES

1. Price MO, Lisek M, Feng MT, Price FW Jr. Effect of donor and recipient diabetes status on Descemet membrane endothelial keratoplasty adherence and survival. *Cornea*. 2017;36(10):1184-1188. doi:10.1097/ICO.0000000000001305

2. Price MO, Szczotka-Flynn LB, Bauza CE, et al; Writing Committee for the Diabetes Endothelial Keratoplasty Study Group. Diabetes Endothelial Keratoplasty Study: methods and impact on the use of corneas from donors with diabetes for Descemet membrane endothelial keratoplasty. *Cornea*. 2025. doi:10.1097/ICO.0000000000003776

3. Centers for Disease Control and Prevention. Leading causes of death. Accessed August 31, 2024. https://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm

4. Lass JH, Szczotka-Flynn LB, Ayala AR, et al; Writing Committee for the Cornea Preservation Time Study Group. Cornea Preservation Time Study: methods and potential impact on the cornea donor pool in the US. *Cornea*. 2015;34(6):601-608. doi:10.1097/ICO.0000000000000417

5. Rand GM, Polla DJ, Patel SH, et al. Donor diabetes mellitus severity and corneal transplant suitability in a US eye bank donor population. *Cornea*. 2019;38(10):1203-1208. doi:10.1097/ICO.0000000000002047

6. Aldrich BT, Schlötzer-Schrehardt U, Skeie JM, et al. Mitochondrial and morphologic alterations in native human corneal endothelial cells associated with diabetes mellitus. *Invest Ophthalmol Vis Sci*. 2017;58(4):2130-2138. doi:10.1167/iovs.16-21094

7. Kingsbury KD, Skeie JM, Cosert K, et al. Type II diabetes mellitus causes extracellular matrix alterations in the posterior cornea that increase graft thickness and rigidity. *Invest Ophthalmol Vis Sci*. 2023;64(7):26. doi:10.1167/iovs.64.7.26

8. Schwarz C, Aldrich BT, Burckart KA, et al. Descemet membrane adhesion strength is greater in diabetics with advanced disease compared to healthy donor corneas. *Exp Eye Res*. 2016;153:152-158. doi:10.1016/j.exer.2016.10.015

9. Greiner MA, Rixen JJ, Wagoner MD, et al. Diabetes mellitus increases risk of unsuccessful graft preparation in Descemet membrane endothelial keratoplasty: a multicenter study. *Cornea*. 2014;33(11):1129-1133. doi:10.1097/ICO.0000000000000262

10. Vianna LM, Stoeger CG, Galloway JD, et al. Risk factors for eye bank preparation failure of Descemet membrane endothelial keratoplasty tissue. *Am J Ophthalmol*. 2015;159(5):829-34.e2. doi:10.1016/j.ajo.2015.01.030

11. Eye Bank Association of America. *2024 Eye Banking Statistical Report*. Eye Bank Association of America; 2025.

12. Terry MA, Aldave AJ, Szczotka-Flynn LB, et al; Cornea Preservation Time Study Group. Donor, recipient, and operative factors associated with graft success in the Cornea Preservation Time Study. *Ophthalmology*. 2018;125(11):1700-1709. doi:10.1016/j.ophtha.2018.08.002

13. Lass JH, Benetz BA, Patel SV, et al; Cornea Preservation Time Study Group. Donor, recipient, and operative factors associated with increased endothelial cell loss in the Cornea Preservation Time Study. *JAMA Ophthalmol*. 2019;137(2):185-193. doi:10.1001/jamaophthalmol.2018.5669

14. Lass JH, Riddlesworth TD, Gal RL, et al; Cornea Donor Study Research Group. The effect of donor diabetes history on graft failure and endothelial cell density 10 years after penetrating keratoplasty. *Ophthalmology*. 2015;122(3):448-456. doi:10.1016/j.ophtha.2014.09.012

15. Lass JH, Benetz BA, Verdier DD, et al; Diabetes Endothelial Keratoplasty Study Group. Endothelial cell loss 1 year after successful DMEK in the diabetes endothelial keratoplasty study: A randomized clinical trial. *JAMA Ophthalmol*. Published online October 17, 2025. doi:10.1001/jamaophthalmol.2025.4261

16. American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes—2020. Accessed April 20, 2021. https://care.diabetesjournals.org/content/43/Supplement_1/S14

17. Soper MC, Marcovina SM, Hoover CK, et al. Validity of postmortem glycated hemoglobin to determine status of diabetes mellitus in corneal donors. *Cornea*. 2017;36(8):942-947. doi:10.1097/ICO.0000000000001211

18. Williams RS, Mayko ZM, Friend DF, Straiko MD, Clay RD, Stoeger CG. Descemet membrane endothelial keratoplasty (DMEK) tissue preparation: a donor diabetes mellitus categorical risk stratification scale for assessing tissue suitability and reducing tissue loss. *Cornea*. 2016;35(7):927-931. doi:10.1097/ICO.0000000000000892

19. Stulting RD, Lass JH, Terry MA, et al; Cornea Preservation Time Study Group. Factors associated with graft rejection in the Cornea Preservation Time Study. *Am J Ophthalmol*. 2018;196:197-207. doi:10.1016/j.ajo.2018.10.005

20. Janson BJ, Terveen DC, Benage MJ, et al. DMEK outcomes using nondiabetic grafts for recipients with diabetes mellitus. *Am J Ophthalmol Case Rep*. 2019;15:100512. doi:10.1016/j.ajoc.2019.100512

21. Vasiliauskaite I, Kocaba V, van Dijk K, et al. Long-term outcomes of Descemet membrane endothelial keratoplasty: effect of surgical indication and disease severity. *Cornea*. 2023;42(10):1229-1239. doi:10.1097/ICO.0000000000003130

22. Rosenwasser GO, Szczotka-Flynn LB, Ayala AR, et al; Cornea Preservation Time Study Group. Effect of cornea preservation time on success of Descemet stripping automated endothelial keratoplasty: a randomized clinical trial. *JAMA Ophthalmol*. 2017;135(12):1401-1409. doi:10.1001/jamaophthalmol.2017.4989

23. Price DA, Kelley M, Price FW Jr, Price MO. Five-year graft survival of Descemet membrane endothelial keratoplasty (EK) vs Descemet stripping EK and the effect of donor sex matching. *Ophthalmology*. 2018;125(10):1508-1514. doi:10.1016/j.ophtha.2018.03.050

24. Federal Register. Recommendations to reduce the risk of transmission of disease agents associated with sepsis by human cells, tissues, and cellular and tissue-based products. Accessed August 20, 2025. https://www.federalregister.gov/documents/2025/05/05/2025-07752/recommendations-to-reduce-the-risk-of-transmission-of-disease-agents-associated-with-sepsis-by-human

Invited Commentary

Impact of the Diabetes Endothelial Keratoplasty Study

Kathryn A. Colby, MD, PhD; Andrea L. Blitzer, MD

As the prevalence of diabetes increases in the population and thus in the corneal transplant donor pool, there has been increased interest in understanding how the diabetic status of the donor affects graft outcomes. The Diabetes Endothelial Keratoplasty Study (DEKS) provides the strongest evidence to date, to our knowledge, for addressing this question. The DEKS is a well-designed randomized clinical trial with excellent participant retention and a primary outcome of Descemet membrane endothelial keratoplasty (DMEK) graft success at 1 year.[1] Secondary outcomes of endothelial cell loss (ECL) and cell morphologies are reported in a companion article.[2] Both studies reached the same conclusion: the diabetic status of the donor did not adversely affect graft survival or health at 1 year.

Multimedia

Related articles pages 1043 and 1053

Diabetes affects more than 38 million US individuals, and its increasing prevalence is mirrored in the donor pool for corneas impacting approximately one-third of the donor supply.[3] Concerns about using tissue from donors with diabetes center on 2 issues: (1) the effect on tissue preparation and the resulting burden on eye banks, and (2) surgeon concerns about a possible increased risk of graft failure and ECL. Diabetes causes structural changes to the Descemet membrane, increasing its thickness, rigidity, and stromal adhesion.[4] Studies have shown that tissue from donors with diabetes is more prone to tears during DMEK graft preparation, with up to a 9-fold higher rate of graft preparation failure.[5] The Cornea Preservation Time Study's secondary analysis found that grafts from donors with diabetes had a lower success rate and higher ECL at 3 years.[6,7] For these reasons, corneal transplant surgeons and eye banks may opt to avoid tissue from donors with diabetes in the absence of level 1 evidence. Results from the DEKS show that the diabetes status of donors did not affect graft survival or ECL at 1 year, which should help allay surgeon concerns.

A key strength of the DEKS is its rigorous study design. This National Institutes of Health–sponsored trial enrolled 1097 individuals (1421 eyes) across 28 clinical sites and 13 eye banks, with 96% of study eyes completing the full year of follow-up.[1] Eye bank technicians, surgeons, and participants were masked to donors' diabetes status. Tissue was randomized to reflect the approximately 2:1 distribution of donors without vs with diabetes in the US donor pool. The postmortem hemoglobin A_{1c} concentration was obtained to capture donors with undiagnosed diabetes. To reduce confounding factors that may affect graft health and success, only low- to moderate-risk cases were included. Because higher-risk transplants were excluded, Fuchs endothelial corneal dystrophy (FECD) was overrepresented in the DEKS (96% of cases). Secondary measures of ECL and endothelial cell morphology were performed at a central image analysis reading center.

The DEKS found no difference in graft success at 1 year (96.3% [95% CI, 95.0%-97.5%] success in donors without diabetes vs 97.1% [95% CI, 95.5%-98.4%] in donors with diabetes).[1] Stratification by recipient diabetes status or severity of diabetes in the donor showed similar results. ECL and cell morphology were similarly unaffected by the donor's diabetes status or diabetes severity or by the recipient's diabetes status. The mean (SD) ECL at 1 year was found to be 28.3% (16.1%) in the donor group without diabetes and 28.0% (17.0%) in the donor group with diabetes. This secondary outcome is of significant importance as ECL reflects long-term graft health. Studies have shown that the ECL of endothelial keratoplasty (EK)

The Ocular Surface 41 (2026) 37–42

Contents lists available at ScienceDirect

The Ocular Surface

journal homepage: www.elsevier.com/locate/jtos

Keratitis due to pigmented *vs.* Nonpigmented fungi: Clinical features and outcome

Shalvika Gupta [a], Smruti Rekha Priyadarshini [a], Himansu Sekhar Behera [b], Sujata Das [a,*]

[a] *Cornea and Anterior Segment Service, L V Prasad Eye Institute, Bhubaneswar, Odisha, 751024, India*
[b] *Ocular Microbiology Service, L V Prasad Eye Institute, Bhubaneswar, Odisha, 751024, India*

ARTICLE INFO

Keywords:
Fungal keratitis
Pigmented fungus
Non-pigmented fungus
Outcome
Therapeutic penetrating keratoplasty

ABSTRACT

Purpose: To compare the demographics, clinical characteristics, and treatment outcomes of pigmented versus non-pigmented fungal corneal ulcers.
Methods: A retrospective analysis was carried out on 100 consecutive culture-proven cases of keratomycosis (pigmented [$n = 50$] and non-pigmented [$n = 50$]) who presented between Jan-2024 to Jun-2024 at the L V Prasad Eye Institute, Bhubaneswar, India.
Results: There was no significant difference in ulcer size or presenting visual acuity between the two groups. Macroscopic pigmentation was observed in only 16% of eyes with keratitis due to pigmented fungus. Both groups responded favorably to medical therapy with similar rates of infiltrate resolution and scar formation. The final visual acuity was not significantly different between the groups. However, number of patients requiring surgical intervention was significantly more in non-pigmented group than pigmented ($P = 0.03$). Also, a trend towards higher frequencies of therapeutic penetrating keratoplasties and eviscerations was observed in the non-pigmented group compared to the pigmented group.
Conclusion: Macroscopic pigmentation was proven to be an unreliable diagnostic indicator. The requirement for surgical interventions differed significantly between two groups. These findings highlight the importance of species-specific treatment protocols and need for aggressive management of deep ulcers to improve visual outcomes.

1. Introduction

Fungal keratitis is a severe corneal infection that contributes significantly to ocular morbidity and vision loss worldwide, particularly in tropical and subtropical regions. Fungal keratitis is particularly common in agricultural societies where ocular trauma following vegetative matter is frequently reported. Epidemiologically, fungal keratitis is more prevalent in males compared to females, with studies from India indicating that fungi are responsible for 34% to 44% of all keratitis cases [1–7]. In tropical regions, including India, approximately 8% to 17% of keratitis cases are attributed to dematiaceous fungi [8].

Within fungal keratitis, the subset of infections caused by dematiaceous fungi, produce darkly pigmented colonies. It is characterized by dark-colored hyphae and spores due to the presence of melanin in their cell walls. The presence of pigmentation in fungal pathogens may have implications for pathogenesis, immune response, and treatment outcomes, although these aspects are not yet fully understood. These fungi are typically found in soil and decaying plant material, making agricultural workers particularly vulnerable. Published studies have reported that pigmented fungal keratitis may differ from non-pigmented cases in clinical presentation, severity, and response to treatment [1–4].

The clinical outcomes of non-pigmented fungal keratitis have been extensively studied and reported. However, there is limited published data on the clinical profile and treatment outcomes of dematiaceous fungal keratitis, particularly when compared to a non-pigmented counterpart. The majority of available studies on dematiaceous fungal keratitis consist of case reports or small case series, many of which were published more than a decade ago [5,9,10]. Furthermore, the regional epidemiological patterns of dematiaceous fungal infections are known to vary significantly, and there is a lacuna of head-to-head comparison between the two groups within the same ecosystem which has been conducted in this current paper.

Understanding the clinical characteristics, microbiological profile, and treatment outcomes of dematiaceous fungal keratitis is critical for

* Corresponding author.
E-mail address: sujatadas@lvpei.org (S. Das).

https://doi.org/10.1016/j.jtos.2026.04.005
Received 30 October 2025; Received in revised form 15 April 2026; Accepted 17 April 2026
Available online 17 April 2026

improving diagnostic accuracy and therapeutic management. This study aims to bridge this knowledge gap by comparing the clinical presentation, microbiological findings, and treatment outcomes of dematiaceous fungal keratitis with those caused by non-pigmented fungus. This research will contribute valuable insights into the management of fungal keratitis, particularly in regions with a high prevalence of agricultural activity.

2. Material and methods

This retrospective observational study analyzed 100 consecutive culture-proven keratomycosis cases (pigmented [$n = 50$] and non-pigmented [$n = 50$]) who presented between Jan-2024 to Jun-2024 at the L V Prasad Eye Institute, Bhubaneswar, India. The study was approved by the Institutional Ethics Committee (IEC# 2024-208-BHR-9) and the study followed the principles outlined in the Declaration of Helsinki. In order to have a comparable analysis, we selected 50 consecutive cases from each group who fulfilled the study's inclusion criteria with complete documentation and complied to follow-up. The records of these patients were collected from the Electronic Medical Record (EMR) database of the Institute and reviewed for demographic features, occupation, predisposing factors including history of ocular trauma, best corrected visual acuity (BCVA) at presentation and after treatment (evaluated using logMAR chart), clinical characteristics, microbiological reports, medical treatment including the first-line drug prescribed, duration of treatment, surgical interventions, and the final outcome.

Clinical parameters evaluated at presentation included the size (maximum vertical and horizontal diameters were measured separately) and depth of the corneal infiltrate, its location, the presence of hypopyon, clinically visible pigmentation, and the presence of an endothelial plaque. Patients were excluded if they had incomplete documentation or were unable to comply with follow-up visits necessary for the outcome assessment.

Infiltrate dimensions which were recorded using slit-lamp biomicroscopy. Corneal scrapings were collected from both the ulcer margins and base using a sterile #15 surgical blade (Bard Parker handle) under topical anesthesia (0.5% proparacaine hydrochloride) under slit-lamp magnification. Smear examination was performed as a part of the routine microbiological workup. Samples were subjected to both Gram staining and 10% potassium hydroxide (KOH) and calcofluor white (CFW) wet mount preparations. Gram-stained smears were examined under × 1000 magnifications using bright field microscopy, while KOH + CFW mounts were assessed with × 400 magnifications.

For fungal isolation, the specimens were inoculated onto 5% sheep blood chocolate agar, 5% sheep blood agar, Sabouraud dextrose agar (SDA), brain heart infusion broth, and thioglycolate medium. These cultures were incubated at both 25 °C and 37 °C, monitored regularly for up to 14 days, and discarded if no growth was observed. Dematiaceous fungi were identified based on both the criteria, the presence of darkly pigmented colonies on SDA and the presence of melanin-containing structures (hyphae or conidia), using lactophenol cotton blue (LPCB) mount. Many a times the pigmentation of a dematiaceous fungus appears late, and in the early stage it looks like a hyaline fungus. As the fungus matures it starts developing the melanin pigments, and therefore, pigmented fungus might not have clinical pigmentation always.

Fungal pigmentation is influenced by multiple factors, including media composition, carbon-to-nitrogen ratio, temperature, and light exposure [11]. As a routine practice in our laboratory, all these conditions are maintained uniformly for all fungal isolates. Variations in these conditions can result in noticeable phenotypic changes in hyaline fungi, leading to differences in colony morphology and pigmentation. In contrast, dematiaceous fungi typically exhibit stable dark pigmentation, appearing black to dark grey, which is relatively less affected by routine variations in culture conditions.

Initial antifungal management was guided by clinical presentation and smear findings. Topical 5% natamycin was the primary treatment administered hourly. In cases with deeper or more extensive stromal involvement, topical 1% voriconazole and/or systemic antifungal therapy (oral ketoconazole) was added to the regimen. Systemic ketoconazole 200 mg twice a day were given after doing baseline blood investigation in the form of liver function test. The surgical interventions included intrastromal voriconazole 0.1 cc which was given when the infiltrate extends deep into the stroma whereas cases with hypopyon and endo-exudates intracameral voriconazole 0.1 cc were given. Those patients who did not respond to medical and other surgical interventions or had large perforations, therapeutic penetrating keratoplasty was done. A microbial culture was considered significant if it met one or more of the following criteria: growth of the same organism in two or more solid media, confluent growth at the site of inoculation on a single medium, consistency with findings from direct microscopy.

2.1. Statistical analysis

Data was analyzed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables, such as age, visual acuity (in logMAR units), infiltrate size, symptom duration, and time intervals, were expressed as mean ± standard deviation and compared between the pigmented and non-pigmented groups using the independent samples *t*-test. Categorical variables, including gender distribution, occupation, risk factors, ulcer location, depth of infiltrate, presence of hypopyon, endothelial plaque, pigmentation, perforation, treatment modalities, and outcomes, were presented as frequencies and percentages, with intergroup differences assessed using the chi-square test or Fisher's exact test for small, expected frequencies. A *P*-value of less than 0.05 was considered statistically significant for all comparisons.

3. Results

3.1. Incidence

During the 6-month study period (January to June 2024), cases of non-pigmented fungal keratitis were more prevalent, comprising 133 eyes (63.6%) of the total, while pigmented (dematiaceous) fungi accounted for 76 cases (36.3%).

3.2. Demography

In terms of age distribution, the mean age in the pigmented group

Table-1
Demographic profile and risk factors.

Demographics	Pigmented ($n = 50$)	Non-Pigmented ($n = 50$)	*P*-value
(i) Mean Age (±SD) in Years	56.5 ± 16.8	49.9 ± 12.4	0.028
(ii) Gender (Female:Male)	1:1.77 (32, 64%)	1:1.94 (33, 66%)	0.835
(iii) Occupation			
(a) Farmer	17	16	0.832
(b) Housewife	17	17	1.000
(c) Private Sector Employee	—	1	0.317
(d) Student	4	3	0.697
(e) Business	—	3	0.080
(f) Truck Driver	—	1	0.317
(g) Mason	—	1	0.317
(h) Manual Laborer	2	2	1.000
(i) Fisherman	—	1	0.317
(iv) Ocular Risk Factor			
(a) Ocular Trauma			
▪ Vegetative Matter	23	16	0.153
▪ Insect	2	7	0.082
▪ Iron Particle	1	1	1.000
(b) Chemical Injury	1	1	1.000

was 56.5 ± 16.8 years (Range: 7-82 years), while it was 49.9 ± 12.4 years (Range: 18-75 years) in the non-pigmented group (Table-1). A male predominance was observed in both cohorts: 32 patients (64%) in the pigmented group and 33 patients (66%) in the non-pigmented group. Occupationally, agricultural workers and housewives represented the most frequently affected populations. The leading predisposing factor was a history of ocular trauma, particularly with vegetative material or insect exposure, observed in 26 eyes (52%) with pigmented fungi and 24 eyes (48%) with non-pigmented fungi.

3.3. Clinical features

At presentation, the average visual acuity was 1.71 ± 1.06 logMAR in eyes with pigmented fungal keratitis and 1.92 ± 1.03 logMAR in those with non-pigmented keratitis, with no statistically significant difference between the groups ($P = 0.318$) (Table-2).

There was no significant difference between the two groups based on ulcer location, area of infiltrate (length x breadth) and the depth of infiltration (Fig. 1a–e). Hypopyon and endothelial plaque were significantly more observed in the pigmented group and presence of pigments in the pigmented fungi group. Perforated corneal ulcer was seen in 8 eyes (16%) in each group (Table-2).

Only natamycin eye drop was given throughout the treatment in 14 cases (28%) in pigmented and 9 cases (18%) in non-pigmented fungus corneal ulcer. ($P = 0.237$). Systemic ketoconazole was added to natamycin in 19 (38%) of pigmented cases and 25 (50%) of non-pigmented cases. Topical voriconazole along with ketoconazole and natamycin eye drops were given in 10 pigmented cases (20%) and in 13 non-pigmented cases (26%) ($P = 0.478$) (Table-3).

Tissue Adhesive and Bandage Contact Lens were applied in cases of impending perforation and small perforation (<2 mm) which was in 17 (34%) cases in pigmented and 18 (36%) non-pigmented group which was almost similar in both the groups. ($P = 0.835$). Intrastromal voriconazole 0.1 cc was given for 3 (6%)cases in pigmented and 7 (14%) cases of non-pigmented fungal keratitis ($P = 0.185$) when the infiltrate extends deep into the stroma whereas in cases with hypopyon and endoexudates intracameral voriconazole 0.1 cc was given for 7 (14%) pigmented cases and 10 (20%) non-pigmented cases ($P = 0.427$) (Table-3).

Therapeutic penetrating keratoplasty was performed in patients who did not respond to medical therapy or other surgical interventions. TPK was required in 34% (17/50) of pigmented ulcers and 46% (23/50) of non-pigmented ulcers ($P = 0.223$). Evisceration was performed for cases where the ulcer progressed to endophthalmitis, and the eye was not salvageable. This was 2 (4%) cases in the pigmented group and 4 (8%) cases in the non-pigmented group ($P = 0.402$) (Table-3).

The mean presenting visual acuity in the medically managed group was 1.24 ± 1.04 logMAR ($n = 30$), whereas patients in the surgically managed group presented with significantly poorer vision 2.18 ± 0.97 ($n = 70$) logMAR (P=<0.0001). Similarly, the mean area of corneal infiltrate at presentation was smaller in the medically managed cohort (28.3 ± 22.5 mm^2) compared to the surgically managed group, which demonstrated larger and more extensive infiltrates (39.2 ± 36.1 mm^2) at initial evaluation ($P = 0.129$).

Time interval between first presentation and therapeutic keratoplasty (TPK) was around 23.7 ± 21.4 days in the pigmented group which was significantly more than non-pigmented group 15.6 ± 13.7 days ($P = 0.026$) (Table-4). A clinical recurrence was seen significantly more in pigmented cases 7 (7/17; 41%) cases as compared to 2 (2/23; 8.7%) cases in non-pigmented fungus group ($P = 0.0002$).

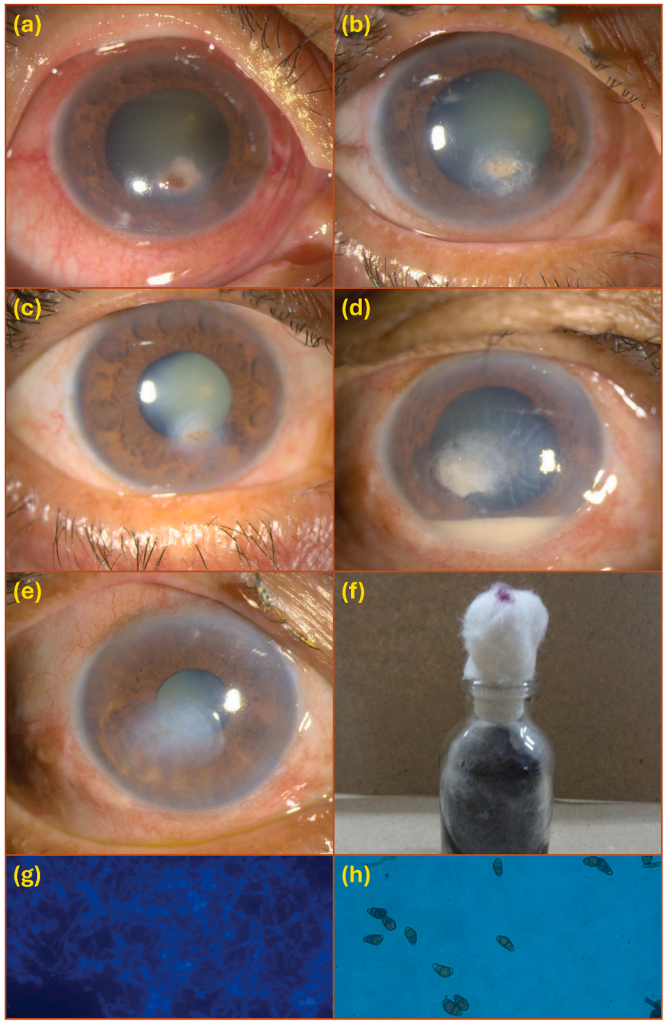


Fig. 1. (a) Clinically pigmented fungal ulcer with thinning at presentation. (b) Four-weeks follow-up after Tissue Adhesive and Bandage Contact Lens (TA + BCL) where the infiltrate is scarring. (c) Infiltrate has scarred completely in two-months, TA + BCL removed. (d) Clinically right eye looks like non-pigmented fungal ulcer with infiltrate 3×3.5 mm infiltrate with 1.5 mm hypopyon at presentation. However, the culture grew *Curvularia lunata*. (e) Infiltrate is scarred at 2-months. (f) Potato Dextrose Agar (PDA) slant culture showing woolly, greyish to black colonies. (g) 10% Potassium Hydroxide (KOH) and Calcofluor White (CFW) mount of corneal scraping (40×) demonstrating septate hyphae suggestive of fungal elements. (h) Lactophenol Cotton Blue Stain (LPCB) mount showing pigmented multiple cells curved poroconidia with the central cell noticeably larger and darker than the end cells consistent with *Curvularia sp*.

Table-2
Clinical characteristics.

Clinical Presentation	Pigmented (n = 50)	Non-Pigmented (n = 50)	P-value
(i) Visual Acuity at Presentation (Mean LogMAR)	1.71 ± 1.06	1.92 ± 1.03	0.318
(ii) Ulcer Location			
(a) Central Only	18 (36%)	14 (28%)	0.394
(b) Central and Paracentral	25 (50%)	26 (52%)	0.842
(c) Limbal	6 (12%)	6 (12%)	1.000
(d) Total	1 (2%)	4 (8%)	0.171
(iii) Mean Size of Infiltrate (mm^2)	35.15 ± 31.9	38.97 ± 33.9	0.563
(iv) Depth of Infiltrate			
(a) Anterior One-Third	15 (30%)	11 (22%)	0.364
(b) Anterior Two-Third	21 (42%)	25 (50%)	0.425
(c) Full Thickness	14 (28%)	14 (28%)	1.000
(v) Hypopyon	18 (36%)	38 (76%)	0.0001
(vi) Endothelial Plaque	14 (28%)	30 (60%)	0.001
(vii) Presence of Pigments	8 (16%)	0 (0%)	0.003
(vii) Perforated Corneal Ulcer	8 (16%)	8 (16%)	1.000

Table-3
Treatment – medical and surgical.

Clinical Presentation	Pigmented (n = 50)	Non-Pigmented (n = 50)	P-value
(i) Topical Natamycin only	14 (28%)	9 (18%)	0.237
(ii) Topical Natamycin + Oral Ketoconazole	19 (38%)	25 (50%)	0.229
(iii) Topical Natamycin + Topical Voriconazole + Oral Ketoconazole	10 (20%)	13 (26%)	0.478
(iv) Topical Natamycin + Topical Antibiotic	7 (14%)	3 (6%)	0.185
(v) Glue + Bandage Contact Lens	17 (34%)	18 (36%)	0.835
(vi) Intrastromal Voriconazole	3 (6%)	7 (14%)	0.185
(vii) Intracameral Voriconazole	7 (14%)	10 (20%)	0.427
(viii) Therapeutic Penetrating Keratoplasty	17 (34%)	23 (46%)	0.223
(ix) Evisceration	2 (4%)	4 (8%)	0.402

Table-4
Outcome post therapeutic keratoplasty.

Outcome Post Therapeutic Keratoplasty	Pigmented (n = 17)	Non-Pigmented (n = 23)	P-value
(i) Time Interval Between First Presentation and Therapeutic Keratoplasty (in Days)	23.7 ± 21.4	15.6 ± 13.7	0.026
(ii) Recurrence after Therapeutic Keratoplasty	7 (41%)	2(8.7%)	0.0002
(iii) Interval between Therapeutic Keratoplasty and Recurrence (in Days)	21 ± 17.6	10.5 ± 9.5	0.0003
(iv) Graft Clarity	8 (47%)	8 (34.7%)	0.213

3.4. Outcome

Twenty (40%) eyes in the pigmented group and ten (20%) eyes in the non-pigmented group responded to medical therapy with resolution of the infiltrate and scar formation ($P = 0.029$). No significant difference was seen in the visual outcome between the two groups, in terms of logMAR value 1.58 ± 1.10 *vs* 1.50 ± 1.21 was seen in pigmented *vs* non-pigmented fungal ulcer group ($P = 0.730$).

The graft clarity post-TPK was similar in both the groups, with 8 cases each in both pigmented and non-pigmented groups having clear graft ($P = 0.213$).

3.5. Microbiology

Most common fungal pathogens isolated in each group are presented in Table-5. The most frequently identified species of non-pigmented fungi were *Fusarium solani* (n = 25; 50%), *Aspergillus flavus* (n = 9; 18%) and *Acremonium sp.* (n = 4; 8%). In the pigmented fungi group the most common isolates included unidentified pigmented fungus (n = 34; 68%), *Curvularia lunata* (n = 6; 12%), *Bipolaris sp.* (n = 4; 8%) and *Colltotrichum sp.* (n = 3; 6%) (Fig. 1f–h).

Table-5
Identified species of fungal pathogens.

Pigmented Fungus (n = 50)	n (%)	Non-Pigmented Fungus (n = 50)	n (%)
Unidentified pigmented	34 (68%)	*Fusarium solani*	25 (50%)
Curvularia lunata	6 (12%)	*Aspergillus flavus*	9 (18%)
Colletotrichum sp.	3 (6%)	*Acremonium sp.*	4 (8%)
Cladosporium sp.	1 (2%)	*Unidentified hyaline fungus*	2 (4%)
Bipolaris sp.	4 (8%)	*Aspergillus fumigatus*	2 (4%)
Epicoccum sp.	1 (2%)	*Penicillium sp.*	1 (2%)
Stachybotrys chartarum	1 (2%)	*Aspergillus nidulans*	2 (4%)
		Aspergillus niger	2 (4%)
		Aspergillus terreus	1 (2%)
		Scedosporium apiospermum	1 (2%)
		Cylindrocarpon lichenicola	1 (2%)

4. Discussion

Fungal keratitis remains a significant cause of visual impairment, especially in tropical and subtropical regions like India [9,12–14]. While historically, non-pigmented fungi have been the predominant causative agents, recent studies suggest a rising importance of pigmented fungi in fungal corneal ulcers [12]. A clear understanding of keratitis caused by these two groups of fungi is essential for prompt diagnosis and effective management.

In our study the proportion of pigmented fungal keratitis was noted to be higher, i.e. 36.3%, compared to 8-17% reported in earlier studies from India [12]. Sengupta et al. reported a 31.3% incidence of pigmented fungal keratitis in their study, which is lower than our finding [12]. Garg et al. in their large retrospective series from LV Prasad Eye Institute, Hyderabad (1991–1996), reported a prevalence of 15.7% for dematiaceous fungal keratitis [15]. This observed increase in our cohort may reflect evolving regional microbiological trends, environmental factors, or improved detection and reporting in recent times. Echoing previous research, agricultural workers and housewives were the most affected occupations in both groups, with ocular trauma involving vegetative matter or insect being the primary predisposing factor [12].

The clinical characteristics of fungal corneal ulcers in our study showed variations between the two groups. While the mean infiltrate area was similar, hypopyon was more frequently observed in the non-pigmented group 76% (38/50) compared to the 36% (18/50) in the pigmented group. Notably, clinically detectable pigmentation was rare and was seen only in 16% of the eyes (n = 8) in the pigmented group. This finding supports the observations made by Sengupta et al., [12] who also reported low rates of visible pigmentation (14.5%) in their cohort and the study by Garg et al. where pigmentation was observed in only 27.3% of eyes [15]. Given the unreliable nature of macroscopic pigmentation, microbiological confirmation is crucial for all suspected cases of fungal keratitis. Relying solely on clinical appearance can lead to misdiagnosis and inappropriate treatment.

In our study, all smear-positive patients received initial treatment with topical natamycin and if required systemic antifungals in the form of oral ketoconazole following established guidelines. However, for larger or deeper ulcers, we enhanced therapy with topical voriconazole and systemic ketoconazole. This approach is similar to older studies like Sengupta [12] et al. where itraconazole was mainly used alongside natamycin. The number of patients responding to medical therapy was significantly different in both the groups, with 20 (40%) and 10 eyes (20%) in the pigmented and non-pigmented group, respectively, showing resolution of the infiltrate and scar formation ($P = 0.03$).

In cases demonstrating inadequate response to topical therapy or deep stromal involvement, adjuvant antifungal delivery was employed. Among hyaline fungal keratitis, intrastromal and intracameral voriconazole were administered in 7 and 10 eyes, respectively. In contrast, intrastromal voriconazole was used in 3 eyes and intracameral voriconazole in 7 eyes with pigmented fungal keratitis. Additionally, tissue adhesive with bandage contact lens (BCL) application was used for eyes with impending perforation or small perforations (<2 mm). This intervention was required in 17 eyes (34%) in the pigmented group and 18 eyes (36%) in the non-pigmented group, indicating comparable rates of corneal structural compromise between the two groups.

Notably, of the 35 eyes that underwent timely tissue adhesive application with BCL, 20 did not require any further surgical intervention. This observation underscores the importance of early tectonic stabilization in preventing disease progression and highlights tissue adhesive with BCL as an effective interim measure in appropriately selected cases.

Patients who ultimately responded to medical therapy presented

with better baseline visual acuity compared to those requiring surgery, who had poorer vision and larger ulcers. Together, these findings suggest that the need for surgical intervention was driven by disease severity and was undertaken when clinically warranted.

We noted a trend toward more therapeutic penetrating keratoplasties ($n = 23$) and more eviscerations ($n = 4$) in the non-pigmented group, which indicates more disease severity in this group which is also supported by more number of cases presenting with hypopyon and endothelial plaque in non-pigmented fungus group. The time interval between presentation and TPK was significantly shorter in the non-pigmented group (15.6 ± 13.7 days) compared to the pigmented group (23.7 ± 21.4 days) ($P = 0.026$), potentially reflecting a more rapid disease progression or a lower threshold for surgical intervention in these cases. Recurrence after TPK was more frequent in the pigmented group (7 cases) than in the non-pigmented group (2 cases) ($P = 0.0002$), the higher recurrence rate in pigmented fungal TPK cases (41% *vs* 8.7%) may be explained by several biological and microbiological factors like role of melanin as a virulence factor which protects fungi from host immune responses (oxidative stress, phagocytosis) and reduce susceptibility to antifungal agent which may allow residual organisms to persist in host tissue even after TPK, contributing to recurrence [16]. In spite of the above differences, the final visual acuity did not differ significantly between the two. This result aligns with the findings of Sengupta [12] et al., who also reported no difference in final visual acuity among healed ulcers.

The rate of therapeutic penetrating keratoplasty (TPK) was notably higher in our pigmented group (40%) compared to 15.3% reported by Garg [15] et al. This discrepancy may be attributed to differences in disease severity at presentation, delayed referrals, or a more aggressive surgical approach adopted in recent years.

Interestingly, while our study showed that 40% of pigmented fungal ulcers responded to medical therapy alone, Garg et al. reported a significantly better response rate of 72%, particularly in cases with superficial stromal involvement [15]. Despite these differences, both studies underline that deep stromal infiltration and late presentation continue to be key indicators for poor prognosis and surgical need. Importantly, our final visual outcomes between the pigmented and non-pigmented groups were comparable, consistent with previous observations, where most grafts post-TPK had suboptimal clarity. This highlights the ongoing challenges in managing advanced fungal keratitis, regardless of etiology, and calls for early intervention to optimize outcomes [12,15,17].

The microbiological profile in our study reaffirms *Fusarium sp*. and *Aspergillus sp.* as the dominant pathogens in non-pigmented fungal keratitis, with *Fusarium* accounting for 50% and *Aspergillus flavus* for 18% of cases. This is consistent with findings by Sengupta et al., who reported *Fusarium* (52.3%) and *Aspergillus* (37.9%) as the leading non-pigmented isolates in their large comparative series [12]. In contrast, the pigmented group in our cohort showed a predominance of unidentified dematiaceous fungi (68%), followed by *Curvularia lunata* (12%), and *Bipolaris* (8%). Although *Curvularia* was less frequently isolated in our series, it remains the most implicated dematiaceous species in the literature, including both Sengupta et al. and Garg et al., who highlighted its widespread presence in Indian soil and agricultural environments [12,15].

The substantial proportion of unidentified pigmented fungi (68%) in our study may reflect limitations in speciation using conventional culture methods or regional differences in environmental exposure. This underscores the need for better molecular identification techniques to enhance fungal classification, especially in tertiary eye care centers. The observed spectrum of isolates in our series also supports the evolving microbiological landscape of fungal keratitis in eastern India, suggesting a possible shift compared to older data from southern or northern parts of the country.

Our study has some limitations. The retrospective nature of the data collection may introduce bias. Additionally, while we adhered to a standardized treatment protocol, some management variations may have occurred based on individual patient characteristics and clinical response. Despite these limitations, our study has several strengths. We analyzed a relatively large sample size of 100 culture-proven cases of fungal keratitis out of a total 209 cases in the 6-month period, with comprehensive follow-up data and inclusion of both medical and surgical management and outcomes.

5. Conclusion

In conclusion, our study highlights that the clinical presentation and final visual outcomes of pigmented and non-pigmented fungal keratitis are broadly comparable, despite differences in underlying microbiological characteristics. The unreliable nature of macroscopic pigmentation underscores the indispensable role of microbiological confirmation for accurate diagnosis and targeted therapy. However, important distinctions were observed in management and post-surgical courses. Non-pigmented fungal keratitis required a significantly higher rate of surgical intervention, including therapeutic penetrating keratoplasty, suggesting deep stromal involvement and a more aggressive clinical course. Conversely, pigmented fungal keratitis exhibited a higher rate of recurrence following keratoplasty, highlighting the potential for persistent or residual infection, possibly related to intrinsic pathogen factors such as melanin-associated resistance. These findings underscore that while visual prognosis may ultimately be similar, the clinical course and therapeutic challenges differ between the two groups. Therefore, both the likelihood of requiring surgical intervention in non-pigmented cases and the risk of recurrence in pigmented infections should be carefully considered when planning management strategies. Overall, microbiological confirmation remains essential, and a tailored, etiology-specific approach is critical to optimize outcomes in fungal keratitis.

CRediT authorship contribution statement

Shalvika Gupta: Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation. **Smruti Rekha Priyadarshini:** Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation. **Himansu Sekhar Behera:** Writing – original draft, Visualization, Validation, Supervision, Resources, Methodology, Investigation, Formal analysis, Data curation. **Sujata Das:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Methodology, Investigation, Formal analysis, Conceptualization.

Support

Hyderabad Eye Research Foundation, Hyderabad, India.

Ethics statement

This study involves human participants and was approved by the Institutional Ethics Committee of L V Prasad Eye Institute, Bhubaneswar, Odisha, India (ID# 2024-208-BHR-9).

Authorship statement

All the authors included in this paper fulfil the criteria of authorship.

Funding statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Competing interest

None to declare.

References

[1] Satpathy G, Ahmed NH, Nayak N, Tandon R, Sharma N, Agarwal T, Vanathi M, Titiyal JS. Spectrum of mycotic keratitis in North India: sixteen years study from a tertiary care ophthalmic centre. J Infect Public Health 2019;12(3):367–71.

[2] Srinivasan M, Gonzales CA, George C, Cevallos V, Mascarenhas JM, Asokan B, Wilkins J, Smolin G, Whitcher JP. Epidemiology and aetiological diagnosis of corneal ulceration in Madurai, South India. Br J Ophthalmol 1997;81(11):965–71.

[3] Basak SK, Basak S, Mohanta A, Bhowmick A. Epidemiological and microbiological diagnosis of suppurative keratitis in Gangetic West Bengal, eastern India. Indian J Ophthalmol 2005;53(1):17–22.

[4] Bharathi MJ, Ramakrishnan R, Meenakshi R, Padmavathy S, Shivakumar C, Srinivasan M. Microbial keratitis in South India: influence of risk factors, climate, and geographical variation. Ophthalmic Epidemiol 2007;14(2):61–9.

[5] Chander J, Singla N, Agnihotri N, Arya SK, Deep A. Keratomycosis in and around Chandigarh: a five-year study from a north Indian tertiary care hospital. Indian J Pathol Microbiol 2008;51(2):304–6.

[6] Saha S, Banerjee D, Khetan A, Sengupta J. Epidemiological profile of fungal keratitis in urban population of West Bengal, India. Oman J Ophthalmol 2009;2(3):114–8.

[7] Tilak R, Singh A, Maurya OP, Chandra A, Tilak V, Gulati AK. Mycotic keratitis in India: a five-year retrospective study. J Infect Dev Ctries 2010;4(3):171–4.

[8] Srinivasan M. Fungal keratitis. Curr Opin Ophthalmol 2004;15(4):321–7.

[9] Kumar A, Khurana A, Sharma M, Chauhan L. Causative fungi and treatment outcome of dematiaceous fungal keratitis in North India. Indian J Ophthalmol 2019;67(7):1048–53.

[10] Ganesan N, Narayana S, Gubert J, Bhosale NK, Sundar B. Clinical, microbiologic, and treatment outcomes of dematiaceous fungal keratitis - a retrospective study. Indian J Ophthalmol 2024;72(12):1721–7.

[11] Palacio-Barrera AM, Areiza D, Zapata P, Atehortúa L, Correa C, Peñuela-Vásquez M. Induction of pigment production through media composition, abiotic and biotic factors in two filamentous fungi. Biotechnol Rep 2019;21:e00308.

[12] Sengupta S, Rajan S, Reddy PR, Thiruvengadakrishnan K, Ravindran RD, Lalitha P, Vaitilingam CM. Comparative study on the incidence and outcomes of pigmented versus non pigmented keratomycosis. Indian J Ophthalmol 2011;59(4):291–6.

[13] Sarkar KC, Naskar TR, Bhattacharyya S, Sarkar P, Biswas MC. Randomized trial for fungal corneal ulcer - a comparison of outcome between two regimes of medical treatment with topical natamycin and topical voriconazole in a tertiary care centre. Panacea J Med Sci 2021;11(2):289–96.

[14] Joshi RK, Goyal RK, Kochar A. A prospective study of clinical profile, epidemiology and etiological diagnosis of corneal ulcer in North-West Rajasthan. Int J Community Med Public Health 2017;4(12):4544–7.

[15] Garg P, Gopinathan U, Choudhary K, Rao GN. Keratomycosis: clinical and microbiologic experience with dematiaceous fungi. Ophthalmology 2000;107(3):574–80.

[16] Taborda CP, da Silva MB, Nosanchuk JD, Travassos LR. Melanin as a virulence factor of Paracoccidioides brasiliensis and other dimorphic pathogenic fungi: a minireview. Mycopathologia 2008;165(4–5):331–9.

[17] Garg P, Rao GN. Corneal ulcer: diagnosis and management. Community. Eye Health 1999;12(30):21–3.