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Research Article

Clinical Outcomes of Large-Diameter Penetrating Keratoplasty in Microbiologically Proven Fungal Keratitis

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Abstract

Objectives: To evaluate the anatomical and optical outcomes, complications and postoperative management including delayed corticosteroid initiation following Large-Diameter Penetrating Keratoplasty (LDPK) in microbiologically confirmed refractory fungal keratitis cases.

Methods: This prospective observational study included 29 patients with severe fungal keratitis unresponsive to medical therapy who underwent LDPK. Detailed clinical, microbiological and surgical data were collected. Postoperative care involved delayed corticosteroid initiation after 15 days of antifungal therapy. Patients were monitored for graft clarity, rejection, reinfection, intraocular pressure and other complications over the follow-up period. The clinical outcomes were evaluated.

Results: The majority of patients were males (58.6%) with a mean age between 30–70 years. Trauma involving vegetative matter was the most common predisposing factor (44.8%) and *Fusarium* species were isolated in 62.1% of cases. Graft sizes ranged from 10 to 12 mm, correlating with ulcer diameters of 9 to 11 mm. Postoperatively, steroid therapy initiated after 15 days was associated with a 48.3% success rate without reinfection. Graft rejection was observed in 37.9% of cases and graft reinfection in 13.7%, corneal neovascularization in 13.7% and panophthalmitis necessitating evisceration in 10.3%. Anatomical globe preservation was achieved in 89.7% of patients, with 65.5% attaining clear grafts and functional visual outcomes. However, 10.3% required evisceration and 3.4% developed phthisis bulbi.

Conclusions: LDPK is an effective surgical option for severe refractory fungal keratitis, facilitating globe preservation and visual rehabilitation. Despite inherent risks such as graft rejection and postoperative complications, early surgical intervention combined with meticulous technique and individualized postoperative management, including cautious steroid use, can improve outcomes. Larger studies with extended follow-up are needed to further refine treatment protocols.

Keywords: Fungal Keratitis; Large-Diameter Penetrating Keratoplasty; Graft Rejection; *Fusarium*; Corticosteroids; Corneal Ulcer; Globe Preservation; Postoperative Complications; Therapeutic Keratoplasty; Refractive Fungal Keratitis

Introduction

Fungal keratitis, a severe form of corneal infection, is a potentially devastating eye disease [1]. Fungal keratitis is a major cause of vision loss, especially in tropical climates and regions with high agricultural activity. In countries like India, it remains a leading contributor to corneal blindness, with global estimates indicating over one million cases occur each year [1,2]. The most common underlying etiology of fungal keratitis is ocular trauma, particularly when the injured cornea is exposed to soil or vegetative matter. The incidence has also been linked to the overuse of broad-spectrum antibiotics and corticosteroids, which may alter normal ocular flora and immune responses [3]. Another common risk factor associated with fungal keratitis is use of soft contact lens [4]. Fungal keratitis can be caused by a range of fungal pathogens, with *Fusarium*, *Aspergillus* and *Candida species*

being the most frequently identified. The specific organism responsible often varies based on environmental conditions such as climate, temperature and residence (urban or rural setting) [5].

Recent advancements in antifungal therapy, particularly the development of more effective and less toxic agents, have significantly improved the management of both local and systemic fungal infections, especially when accurate diagnosis and timely treatment are achieved [6,7]. However, refractory cases of fungal keratitis remain difficult to treat and may lead to serious complications such as corneal perforation and fungal endophthalmitis. If not managed promptly and effectively, the resulting inflammation can cause extensive iris synechiae (anterior or posterior synechiae), uncontrollable secondary glaucoma and in extreme cases, extrusion of intraocular contents [8,9]. To halt the progression of infection, prevent severe complications and maintain the structural integrity of the eye, therapeutic Penetrating Keratoplasty (PKP) is often recommended in advanced cases of fungal keratitis [10]. However, achieving long-term graft survival remains challenging due to factors such as a highly inflamed ocular environment, delayed initiation of corticosteroid therapy (often postponed to prevent infection recurrence) and the frequent use of lower-quality donor corneas, especially in settings with limited resources. Although anatomical success rates are generally high (ranging from 90% to 97%); functional outcomes, including graft transparency and visual recovery, tend to be less satisfactory [11].

Although larger grafts are often necessary in cases involving extensive or centrally located corneal lesions, their higher risk of complications such as rejection and glaucoma requires dedicated study to guide clinical decisions and surgical planning [12]. Recent improvements in donor tissue quality, antifungal therapies and diagnostic tools may positively influence surgical outcomes compared to older data. A contemporary, region-specific evaluation will help update clinical protocols and expectations. This study aims to address these gaps by evaluating the anatomical and optical outcomes, complications and postoperative steroid response patterns following large-diameter therapeutic or tectonic Penetrating Keratoplasty (PK) in microbiologically confirmed fungal keratitis, offering insights that may inform surgical strategies and postoperative management in similar clinical contexts.

Methodology

The present study was conducted as a facility based prospective observational study on 29 cases presenting with refractory fungal keratitis (not responding to antifungal treatment) and were scheduled for LDPK. After obtaining ethical clearance from Institute's ethical committee, all the patients with fungal keratitis who were scheduled for large diameter penetrating keratoplasty were included whereas patients not willing for surgery and not willing to participate in the study were excluded. Detailed data was obtained regarding sociodemographic variables, clinical history, trauma, course of infective pathology and previous treatment and documented in proforma. They underwent a series of routine and special ocular investigations. Thorough slit lamp examination was done, which included the size and depth of the stromal infiltrate, type of ulcer, margins of ulcer, mobility, type of a hypopyon and the findings were recorded. Digital Intraocular Pressure (IOP) assessment was done. This was followed by fundus examination (if media was clear) or BSCAN (if media was not clear) to rule out posterior segment abnormality (retinal detachment, vitreous hemorrage).

Conjunctival swab and corneal scraping were retrieved and sent for culture and sensitivity. Microbiological diagnosis was confirmed with corneal scrapings examined by Gram stain, Giemsa stain, 10% potassium hydroxide wet mount and cultures on Sabouraud's dextrose agar. Systemic investigations were done to rule out any septic foci. Special care was taken in corneal perforation when performing these investigations.

Written informed consent was taken to explain guarded prognosis, complications, necessity of secondary procedures and compliance in regular follow ups. Antibiotics according to culture and sensitivity, cycloplegics and anti-glaucoma drugs were started in each case. Intravenous mannitol 20%, 1 g/kg body weight, was given preoperatively to reduce the intraoperative IOP. Surgical procedure was carried out under local anesthesia in all the cases whereas general anesthesia was used in uncooperative patients.

All surgical procedures were conducted by a single, highly experienced ophthalmic surgeon. In recipient, conjunctival peritomy was performed at the site involvement and host bed preparation was done, which involved removing the diseased corneal tissue. Depending on the size of the infiltrates, appropriate size of trephine button was made using disposable trephines. In this, a

trephine was centered over infiltration and partial thickness groove was made (about 80% depth) and entry into the anterior chamber was made through side port. Excision of full thickness host button using curved scissors was done, then corneal button was removed using corneal scissors or completed trephination. The removed corneal buttons were sent for both microbiological culture and histopathological analysis. Any fibrous or exudative membranes present over the iris or lens were carefully removed and the anterior chamber, posterior chamber and angle of the anterior chamber were thoroughly irrigated with intracameral amphotericin B 0.05%and intracameral moxifloxacin. The donor corneal grafts used were 1.0 mm larger than the recipient bed. Donor trephination was done from endothelial side and the donor button was created. The donor cornea was then secured in place with 10-0 nylon sutures onto the recipient bed, equidistantly placed at approximately 90% thickness and buried into the recipient's bed. Associated procedures were done based upon intraoperative condition such as synechiolysis, iris reconstruction in case of intraoperative severe damage to iris, cataract removal in case of lens changes and vitrectomy in case of vitreous in anterior chamber and Peripheral iridectomy was performed in all eyes to avoid postoperative glaucoma.

Postoperatively, all patients were given systemic and topical antibiotics according to culture and sensitivity report along with cycloplegics, anti-glaucoma and lubricating drops. We refrained from administering corticosteroids in any form for a minimum of 15 days, postoperatively. Frequent follow ups were done to record signs of recurrence of infection. If no infection was noted within 15 days, low potency corticosteroids (Fluorometholone 0.1% eye drops) were administered three times a day for a week under close observation. In cases of reinfection, steroids were stopped and after a week, steroid were given again. In case of no untoward finding, higher dose of corticosteroids (prednisolone acetate 1% eye drops) in frequency up to six times a day was given and gradually tapered in 9–12 months. For cases where rejection appear, we administered pulse therapy with IV methylprednisolone at 1 gm every 24 hours for 3 days, then transitioned to oral coticosteroids (1g/kg body weight) based on the patient's weight, with regular monitoring of RBS and BP throughout. During final follow up, patients were assessed for recurrence of disease; signs suggestive of persistent inflammation, graft rejection and reinfection; suture related complications; graft clarity; visual acuity; IOP; need for secondary procedures; and other complications. Appropriate medical and surgical interventions were done as and when required. Good response refers to no signs of graft reinfection while using corticosteroid. While no response refers to persistent inflammation despite adequate corticosteroid use whereas reversal of rejection is successful control and resolution of immune mediated attack on the graft, primarily with prompt and adequate corticosteroid therapy.

Statistical Analysis

Data was compiled using MsExcel and analysed using IBM SPSS software version 20. Categorical data was expressed as frequency and proportions. The LDPK outcome after the surgery was assessed in terms of anatomical success and, thus, achievement of globe integrity.

Results

The study was conducted on total of 29 eyes of 29 patients with fungal keratitis. In the present study, the majority of patients belonged to 60 to 70 years of age (20.7%) and we documented male predominance for refractory fungal keratitis (58.62%). Majority of males belonged to 30 to 40 years of age (13.7%) whereas majority of females belonged to 40 to 50 years of age (13.7%) (Table 1).

The most common underlying etiological factor was vegetative matter (44.8%), followed by corneal graft injection and foreign body in 10.34% cases each. Fusarium was the most commonly isolated organism, present in 19 cases (62.1%) and 6 patients (20.7%) presented with mixed infections. Hypopyon was present in 5 patients (17.2%) (Table 2).

As observed from Table 3, majority of recipients had corneal ulcer of 9 mm and 10 mm (34.4% each), followed by 13.8% cases each having corneal ulcer of 9.5 mm and 11 mm. Only 1 (3.5%) case had corneal ulcer of 10.5 mm and the graft size was 1 mm larger than the ulcer area.

In this study, steroid trial was given to all the patients postoperatively and of them, 14 patients (48.3%) showed no signs of reinfection whereas 13 (44.8%) cases experienced reinfection, which could not be controlled in 4 patients and one out of these four cases developed phthisis. Remaining 9 cases with reinfection showed response to low patency corticosteroid. However, 2 cases (6.9%) experienced rejection, which could be reversed with the help of corticosteroid (Fig. 1).

Wound dehiscence occurred in 3.4% of cases for which wound resuturing was done, while 6.8% of patients experienced a persistent epithelial defect for which autologous topical serum were started. Corneal neovascularization near limbus along with sutures was observed in 13.7% of cases. Phthisis bulbi occurred in 3.4% of patients. Graft rejection was the most common complication (37.9%), followed by graft reinfection (13.7%) (Fig. 2,3).

In our study, 6 patients (20.6%) achieved tectonic results, while 19 patients (65.5%) obtained optical outcomes. Unfortunately, 3 patients (10.3%) required evisceration and 1 patient (3.44%) developed phthisis bulbi (Table 4).

Age (years)	No. (%)	Male (%)	Female (%)
30–40	5 (17.2)	4 (13.7)	1 (3.4)
40–50	5 (17.2)	1 (3.4)	4 (13.7)
50–60	5 (17.2)	3 (10.3)	2 (6.8)
60–70	6 (20.7)	3 (10.3)	3 (10.3)
70–80	3 (10.3)	3 (10.3)	0
≥80	5 (17.2)	3 (10.3)	2 (6.8)

Table 1: Distribution of cases according to age and sex.

Variables		Number of Eyes (n=29)	Percentage
Etiological factor	Vegetative material	13	44.8
	Corneal graft infection	3	10.3
	Foreign body	3	10.3
	Chemical injury	1	3.5
	No history	9	31.0
Micro-organisms	Fusarium	13	44.8
	Aspergillus	6	20.7
	Candida	4	13.8
	Mixed infections	6	20.7
Hypopyon	Present	5	17.2
	Absent	24	82.8

Table 2: Distribution of eyes according to etiology and characteristics of fungal keratitis.

Recipient (mm)	Donor (mm)	No. of Eyes	Percentage
9.0	10.0	10	34.4
9.5	10.5	4	13.8
10.0	11.0	10	34.4
10.5	11.5	1	3.5
11.0	12.0	4	13.8

Table 3: Graft sizes of recipients and donors.

Outcome	No. of eyes (n=29)	Percentage
Optical clarity	19	65.5
Tectonic integrity	6	20.7
Evisceration	3	10.3
Phthisis bulbi	1	3.4

Table 4: Final outcomes in patients following LDKP.

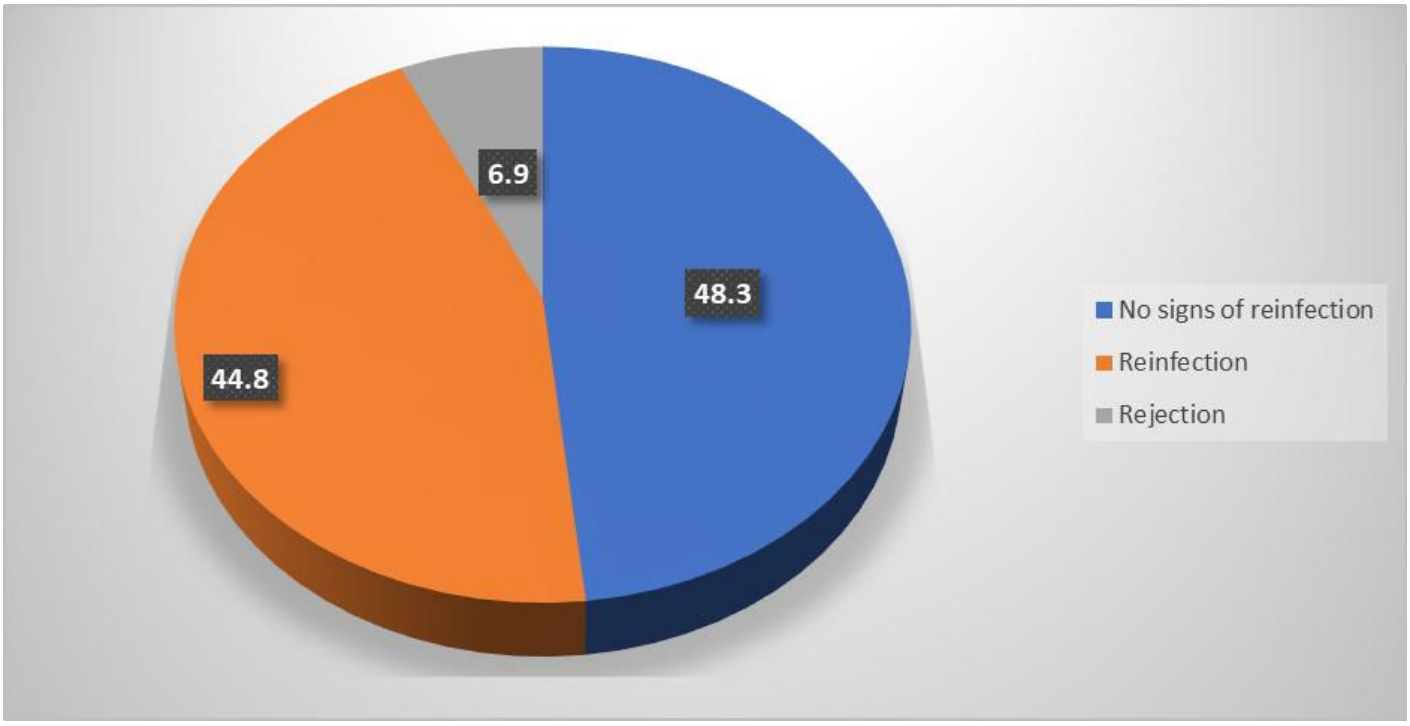


Figure 1: Distribution of patients according to postoperative steroid trial.

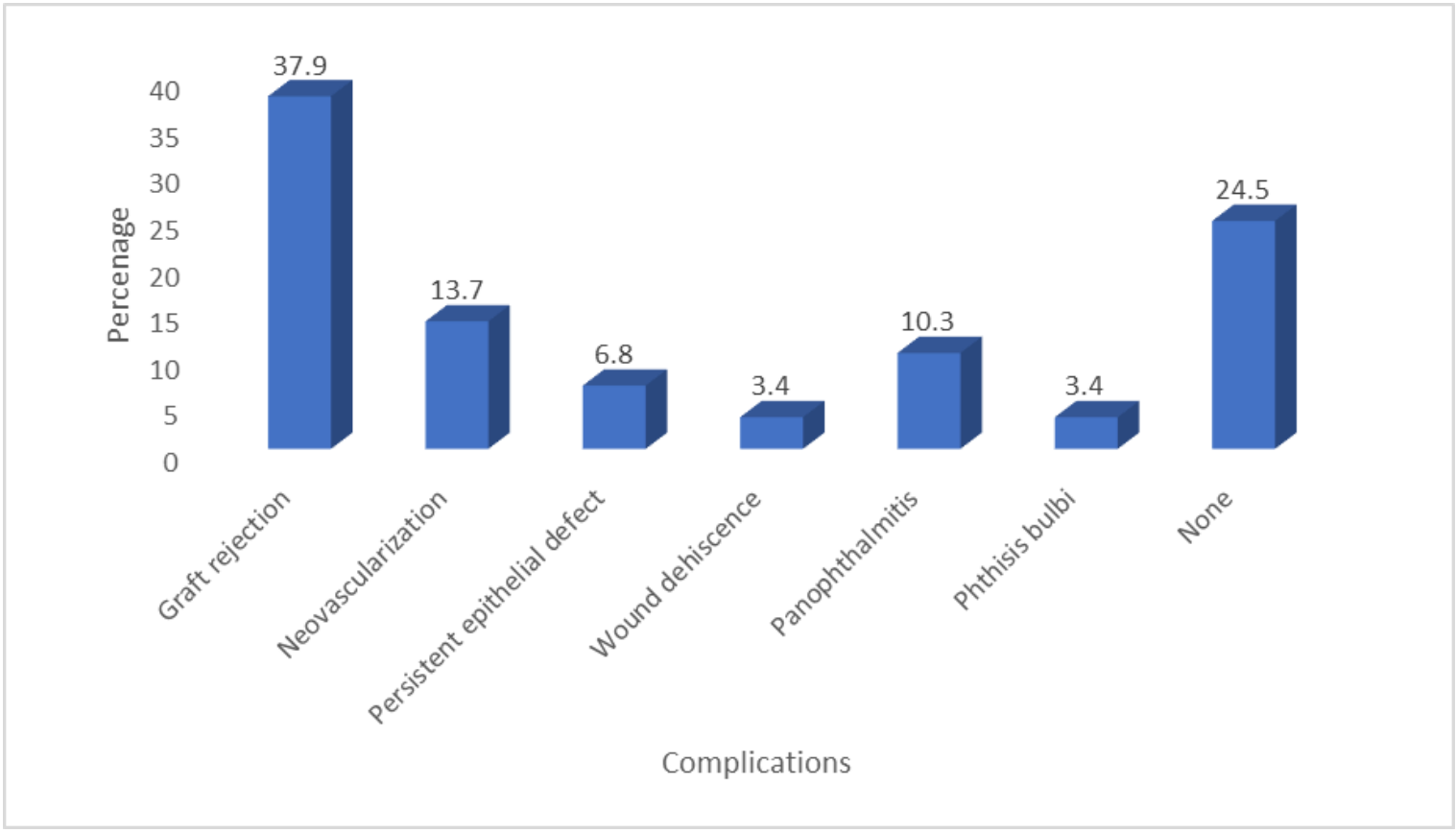
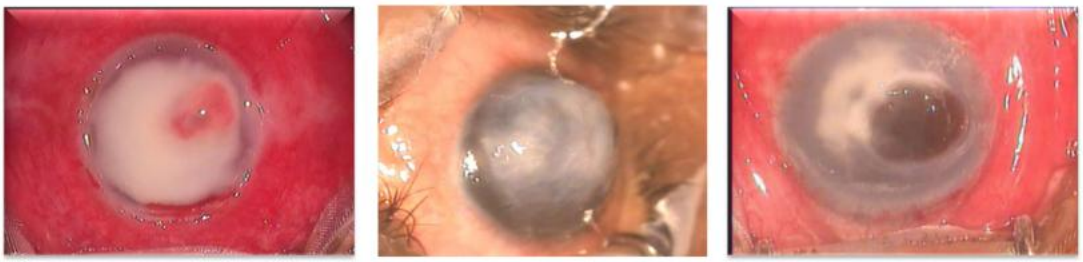
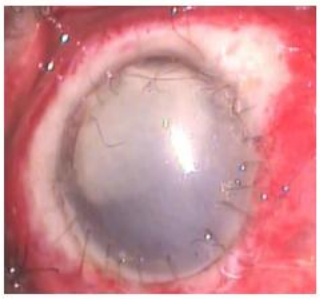


Figure 2: Distribution of patients according to complications.



A case of reinfection



Graft rejections

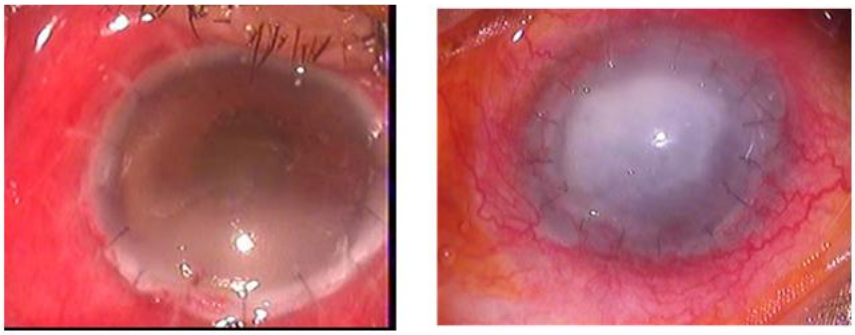


Image showing optical results in Postoperative patient

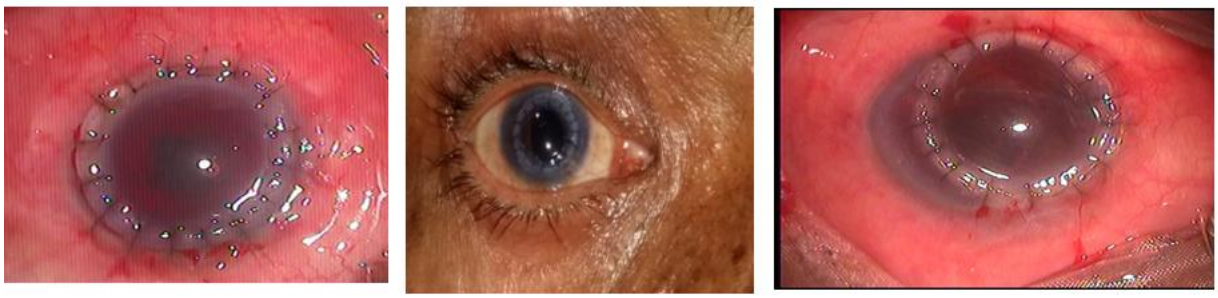


Figure 3: Corneal ulcers at the time of presentation.

Discussion

Large-Diameter Penetrating Keratoplasty (LDPK) plays an important role in surgical management of advanced fungal keratitis. When the diagnosis of fungal keratitis is delayed, extensive corneal tissue destruction often occurs, rendering medical management alone insufficient. Such advanced cases commonly progress to refractory keratitis, ultimately requiring surgical intervention through therapeutic or tectonic keratoplasty to restore ocular integrity and prevent severe complications [10,11].

This study assessed the clinical outcomes of Large-Diameter Penetrating Keratoplasty (LDKP) in 29 patients with microbiologically confirmed fungal keratitis. Large-diameter grafts were utilized with the aim of achieving complete excision of the infected corneal tissue and reinforcing the structural stability of the globe. Despite the benefits of this approach, the

management of fungal keratitis remains inherently challenging due to the frequent occurrence of complications such as suture-related issues, corneal neovascularization and the persistent risk of reinfection [1]. In our cohort, *Fusarium* was isolated in 44.8% cases, with lower incidences of *Aspergillus* and *Candida*. Mixed fungal infections were present in 20.7% of patients. Our microbiological findings are consistent with previous studies from northeastern India, including those by Xie, et al., which identified *Fusarium* and *Aspergillus* species as the predominant fungal pathogens [5]. The most common predisposing factor was trauma involving vegetative matter in our study, which was in agreement with earlier studies [1,3].

Corneal ulcers in this study ranged from 9 mm to 11 mm in diameter, requiring correspondingly large grafts ranging from 10 mm to 12 mm. Nonetheless, the use of large grafts in our cohort was accompanied by notable postoperative complications, including graft rejection in 37.9% of patients, whereas graft reinfection was observed in 13.7% cases, of which, 10.3% cases developed panophthalmitis and 3.4% cases developed phthisis bulbi. Other complications included wound dehiscence (3.4%), persistent epithelial defects (6.9%), corneal neovascularization (13.7%). Thus, graft rejection was the most frequently observed complication, while panophthalmitis represented a serious consequence, often necessitating evisceration. These findings highlight the inherent complexity and risk of managing severe fungal keratitis with large-diameter grafts. Nonetheless, the relatively high rate of clear grafts achieved underscores the potential of LDPK when combined with timely diagnosis and appropriate surgical planning. This finding aligns with findings from Li, et al., who noted that grafts ≥8 mm were associated with a higher recurrence rate of fungal infection [12]. However, the rate of globe preservation remained high at 96.88%. By contrast, smaller grafts (<8 mm) demonstrated marginally lower recurrence rates with similar globe preservation outcomes (96.15%). Despite the elevated risk profile associated with larger grafts, both our findings and those of Li, et al., affirm their therapeutic value in managing advanced fungal keratitis, with 65.5% of our patients achieving clear grafts postoperatively [12]. Our results are further supported by the observations of Song, et al., who reported graft clarity rates ranging from 23% to 81% in cases of infectious keratitis following keratoplasty [13].

Topical corticosteroids were introduced 15 days postoperatively in this study, as a precautionary measure to minimize the risk of fungal reactivation. Despite this delayed initiation, 11 patients experienced complications such as corneal vascularization and Descemet's membrane folds. These findings are in agreement with the work of Xie, et al., who demonstrated that early postoperative corticosteroid use in fungal keratitis is associated with increased rates of reinfection, rejection and graft failure due to immunosuppression-facilitated fungal proliferation [14]. Although the delayed corticosteroid regimen in our series aimed to reduce this risk, complications still occurred, suggesting that fungal clearance was not complete at the time of administration. This could be attributed to delayed fungal reactivation [15]. Even after apparent clinical resolution following 2-3 weeks of antifungal therapy, residual fungal elements may persist in the corneal tissue. The initiation of corticosteroids under these circumstances may suppress host immune responses, facilitating reactivation and recurrence. This mechanism likely contributed to the complications observed in our cohort, underscoring the importance of cautious clinical evaluation prior to steroid initiation.

The primary objective of surgical intervention in our study was the preservation of the globe and restoration of ocular function. Encouragingly, 65.5% of patients achieved optical outcomes and an additional 20.6% demonstrated tectonic success. These findings are consistent with existing literature on large-diameter PK, which has reported similarly favourable outcomes in terms of graft clarity and anatomical integrity [12-15]. However, the occurrence of evisceration in 10.3% of patients and phthisis bulbi in 3.44% reflects the significant risk of adverse outcomes in advanced disease. As supported by previous studies, severe infections and delays in surgical intervention are major contributors to these poor prognoses. Our study had certain limitations, which include small sample size and limited follow-up for long-term graft survival. Also, comparisons with larger cohorts are tempered by potential differences in microbiological profiles, donor tissue quality and surgical timing.

Conclusion

LDPK represents a valuable surgical option for severe fungal keratitis refractory to medical treatment, primarily by facilitating globe preservation and potential visual restoration. However, the approach is not without risks; graft rejection and other postoperative complications remain significant challenges. Optimal outcomes hinge on early surgical intervention, precision in operative technique and a carefully individualized postoperative regimen that balances antifungal control with immune modulation. Future advances in surgical methods, donor tissue preparation and adjunctive therapies may further enhance the efficacy and safety of LDPK in managing this complex condition.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Ethical Approval

The study was approved by the Institutional Ethics Committee.

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