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ETIOLOGICAL FACTORS ASSOCIATED WITH CORNEAL GRAFT REJECTION IN INDIA: A DECADE IN REVIEW (2014–2024)

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Abstract This literature review explores the causes of corneal graft rejection reported in Indian clinical studies from 2014 to 2024. A search was conducted across PubMed and Indian journals, identifying studies focused on outcomes of therapeutic and optical keratoplasty. The most commonly reported causes of rejection include pre-existing corneal neovascularization, active microbial keratitis, large graft size, and poor postoperative follow-up or immunosuppression adherence. Lamellar techniques are underreported in Indian settings, while penetrating keratoplasty remains the primary intervention. The review emphasizes ocular surface optimization and postoperative compliance as key to improving graft survival in high-risk Indian populations.

Keywords: Corneal graft rejection, India, therapeutic keratoplasty, penetrating keratoplasty, risk factors, ocular surface, immunological rejection

Introduction Corneal transplantation remains a vital strategy for visual rehabilitation in cases of advanced corneal pathology. In India, microbial keratitis accounts for the majority of penetrating keratoplasties, particularly therapeutic PKP, where rejection and failure are common **[1,2,5]**. The immune-privileged nature of the cornea may be compromised by inflammation, infection, and vascularization, especially in emergency or high-risk graft settings **[4,5]**. Dandona et al. previously noted that therapeutic keratoplasty for infectious keratitis constitutes a significant proportion of indications in Indian settings **[6]**. This review focuses on real-world Indian studies to identify contributing factors to graft rejection over the last decade.

Methods Relevant literature was selected from PubMed and Indian journals, focusing on original Indian studies published between 2014 and 2024. Inclusion criteria were:

- Clinical studies with ≥10 grafts
- Explicit documentation of rejection, failure, or related complications
- Indian patient population

Studies were excluded if they were reviews without data, animal studies, or lacked rejection-related outcomes.

Results

Sharma et al. (2014) reported outcomes of therapeutic PKP for infectious keratitis in 114 eyes. Graft rejection and failure were more common in eyes with prior vascularization and delayed presentation. Larger graft diameters (>8.5 mm) were associated with increased immunological rejection [5].

Raj et al. (2018) studied advanced infectious keratitis managed by therapeutic PKP. They found that rejection and graft melt were common in bacterial and mixed infections. Delayed surgical intervention worsened outcomes [7].

Roy et al. (2021) examined 73 eyes that underwent therapeutic PKP using glycerol-preserved corneas during the COVID-19 pandemic. Although tectonic integrity was maintained, graft clarity was achieved in only 30%, with increased risk of failure due to primary disease severity and delayed surgical access [8].

Victor et al. (2018) analyzed 48 therapeutic PKPs in Eastern India. The study emphasized the role of active microbial infection, especially fungal, as a key factor in postoperative graft rejection and failure. Follow-up challenges and poor ocular surface were also linked to poor outcomes [10].

Khan et al. (2021) presented demographic trends in PKP from northwest Rajasthan, highlighting that therapeutic indications comprised 45% of cases. Rejection was primarily associated with infectious etiology and lack of postoperative follow-up [9].

Summary Table: Key Findings from Indian Studies on Graft Rejection (2014–2024)

Study (Year)	Location	Sample Size	Main Indication	Key Risk Factors for Rejection	Notable Findings
Sharma et al. (2014)	Northern India	114	Infectious keratitis	Neovascularization, large graft size, delayed surgery	Higher rejection with >8.5 mm grafts
Raj et al. (2018)	Uttarakhand	36	Advanced microbial keratitis	Mixed infections, delayed intervention	Higher rejection and graft melt rates
Roy et al. (2021)	South India	73	Severe microbial keratitis	COVID-related delays, glycerol-preserved tissue	Only 30% achieved graft clarity
Victor et al. (2018)	Eastern India	48	Fungal keratitis	Active infection, poor ocular surface, poor follow-up	Fungal infections linked to poor outcomes
Khan et al. (2021)	Rajasthan	100+	Mixed (therapeutic/optical)	Infectious etiology, limited access to care	Therapeutic grafts 45% of total

Discussion Across Indian clinical studies, immunological rejection is closely linked with pre-existing inflammation, corneal neovascularization, and microbial etiology **[5,7,10]**. High-risk grafts such as therapeutic PKP inherently carry poor prognosis due to compromised host beds and the presence of active infection **[5,7,8]**.

The use of large grafts in such settings, though necessary for complete excision, further increases rejection likelihood **[5]**. Additionally, the lack of adherence to corticosteroid therapy, often due to socioeconomic constraints or limited access to ophthalmic follow-up, further compounds the risk **[9,10]**.

Studies using glycerol-preserved corneas (e.g., during the COVID-19 pandemic) revealed higher failure rates, likely due to reduced endothelial viability **[8]**. Poor ocular surface status, particularly in fungal infections, further predisposes to complications **[10]**.

Despite these challenges, these Indian studies highlight that early surgical intervention, smaller graft size when feasible, and rigorous postoperative care can reduce rejection incidence **[5,7,9]**. Emphasis on patient education and improved rural follow-up access are crucial **[9]**.

Despite these challenges, these Indian studies highlight that early surgical intervention, smaller graft size when feasible, and rigorous postoperative care can reduce rejection incidence. Emphasis on patient education and improved rural follow-up access are crucial.

Conclusion Graft rejection in India is predominantly driven by infectious keratitis, vascularized recipient beds, large graft sizes, and poor compliance with postoperative care. Most data pertain to therapeutic PKP, with limited documentation on lamellar graft outcomes. Improving ocular surface health, timely intervention, and postoperative immunosuppression adherence are key to improving graft survival in Indian settings.

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