Article

Age-Related Effects of Donor on Corneal Transplantation and Clinical Study of Causal Allograft Rejection in Pakistan

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ABSTRACT

Background: Corneal transplantation is a widely performed surgical procedure for treating corneal blindness. Donor-related factors, particularly age, are known to influence graft survival and rejection rates. While younger donor corneas exhibit higher endothelial cell density, their potential for increased immunogenicity remains a concern. This study evaluates the impact of donor age on corneal transplantation outcomes in Pakistan. **Objective**: To assess the influence of donor age on graft clarity, visual acuity, and allograft rejection rates following corneal transplantation. **Methods**: A retrospective observational study was conducted from February 2013 to June 2016 in collaboration with the Rawalpindi Eye Donor Organization, The Shifa Eye Trust, and Saba Deseret Eye Hospital. A total of 300 patients underwent corneal transplantation, categorized by donor age: <40 years (n=105), 40–60 years (n=120), and >60 years (n=75). Surgical techniques included Penetrating Keratoplasty (PK) (70%), Descemet's Stripping Endothelial Keratoplasty (DSEK) (20%), and Descemet Membrane Endothelial Keratoplasty (DMEK) (10%). Postoperative outcomes were assessed at 12 months. Data were analyzed using SPSS v25, with chi-square tests for categorical variables and logistic regression for predictors of rejection. **Results**: At 12 months, 80% (n=240) of grafts remained clear, while 20% (n=60) developed opacity. Visual acuity improved to 20/40 or better in 85% (n=255) of patients. The overall rejection rate was 15% (n=45), highest in young donor grafts (21%), followed by middle-aged (13%) and older donor grafts (8%) (p=0.046). Patients undergoing DSEK and DMEK had significantly lower rejection rates than PK (p<0.01). **Conclusion**: Donor age did not significantly affect graft clarity or visual acuity but influenced rejection rates, with younger donor grafts exhibiting a higher risk. Advanced surgical techniques and postoperative steroid management improved outcomes. Future research should focus on optimizing donor selection criteria and long-term graft survival strategies.

Keywords

Corneal transplantation, penetrating keratoplasty, Descemet's stripping endothelial keratoplasty, immunogenicity

INTRODUCTION

Corneal transplantation plays a crucial role in restoring vision for individuals suffering from corneal blindness caused by conditions such as keratoconus, corneal dystrophies, infections, or injuries (1). The success of corneal transplantation is not solely dependent on surgical techniques and postoperative care; rather, it is significantly influenced by donor-related factors, particularly the donor's age, which has been a topic of growing interest in ophthalmic research (2). Understanding the impact of donor age on transplantation outcomes is essential for refining donor selection criteria and enhancing graft survival rates.

One of the primary reasons for graft failure after corneal transplantation is allograft rejection, which remains a major challenge in the field. The immune response to a corneal allograft is influenced by multiple factors, including HLA compatibility, the donor's health status, age, and the recipient's underlying eye condition (3, 4). In Pakistan, corneal diseases are prevalent and are often linked to socioeconomic and environmental factors. Despite this, there is limited literature on how donor age influences transplantation success and rejection rates in the local population. This study aims to bridge this gap by examining the donor's age as a quantitative factor affecting corneal transplantation outcomes and graft rejection rates.

Due to the limited availability of comprehensive data on corneal transplantation in South Asia, particularly Pakistan—where eye banking and corneal donation practices vary widely—the significance of this study is underscored. By analyzing data from cornea donors affiliated with the Rawalpindi Eye Donor Organization, Shifa Eye Trust, and recipients from the Saba Deseret Eye Hospital, this research provides valuable insights into the relationship between donor age and allograft rejection in the region (5). This study seeks to unravel the complex interactions between donor age and corneal graft success while identifying potential risk factors for graft rejection.

Recent research has suggested a potential link between donor age and endothelial cell density (ECD), a crucial factor influencing graft survival and corneal function (6). Corneal endothelial cells regulate corneal hydration and maintain transparency through their pump and barrier functions. Studies indicate that transplantation success may decline with increasing donor age, which can negatively impact graft survival (7). However, conflicting findings regarding the impact of donor age on the success of corneal transplantation, particularly in procedures like Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK), warrant further investigation (2).

Pakistan presents unique challenges and opportunities for corneal transplantation research. The high prevalence of corneal blindness due to infectious diseases, trauma, and limited access to healthcare services is compounded by cultural and logistical barriers to eye donation (5). Given these factors, it is crucial to evaluate donor-related variables, such as age, in the context of corneal transplantation outcomes in Pakistan.

Another key aspect of this study is the examination of allograft rejection rates. Rejection occurs when the recipient's immune system identifies the transplanted cornea as foreign, triggering an immune response that can lead to graft failure. Although immunosuppressive therapies and corticosteroids have improved graft survival rates, donor characteristics and previous graft rejections remain important factors influencing rejection risks (4). Identifying risk factors for allograft rejection specific to the Pakistani population could help refine postoperative care strategies and improve long-term patient outcomes.

This study adopts a quantitative approach to assess the impact of donor age on corneal transplantation and investigates the incidence of casual allograft rejection in a Pakistani cohort. By utilizing data from the Rawalpindi Eye Donor Organization, Shifa Eye Trust, and the Saba Deseret Eye Hospital, this research aims to generate comprehensive insights into corneal transplantation in Pakistan. The findings of this study have the potential to inform clinical practice, influence policy decisions, and contribute to global efforts to combat corneal blindness.

Despite the critical role of corneal transplantation in restoring vision, multiple factors, including donor age, significantly affect transplantation success. While donor age has been studied extensively in other populations, data specific to Pakistan remains scarce due to its unique socioeconomic and healthcare challenges. This study aims to fill this knowledge gap by applying statistical methods to assess the effects of donor age on corneal transplantation outcomes and allograft rejection rates.

The growing incidence of corneal diseases in Pakistan, coupled with limited healthcare resources, underscores the urgency of region-specific research (5). Understanding the role of donor age in transplantation outcomes is vital for refining donor selection criteria and optimizing graft survival rates. Additionally, investigating the determinants of allograft rejection can aid in the development of tailored management strategies to enhance transplant success.

Allograft rejection remains a significant hurdle in corneal transplantation, often resulting in graft failure and poor visual outcomes. Rejection is primarily driven by immune incompatibility between the donor and recipient, host immune responses, and the immunogenicity of donor tissue (3, 4). Correlating rejection rates with donor characteristics, particularly age, in the Pakistani population could help physicians mitigate rejection risks and improve patient outcomes.

The introduction of advanced surgical techniques such as Descemet Stripping Endothelial Keratoplasty (DSEK) and Descemet Membrane Endothelial Keratoplasty (DMEK) has further highlighted the need to examine donor age-related factors in transplantation success (8). Understanding the underlying mechanisms influencing these procedures and their relationship with donor age can enhance surgical outcomes and patient prognosis.

This study will analyze data from the Rawalpindi Eye Donor Organization, Shifa Eye Trust, and Saba Deseret Eye Hospital, following their policy of categorizing patients into three age groups. This classification will allow for a comprehensive assessment of the impact of donor age on corneal transplantation outcomes and allograft rejection rates in Pakistan. The findings will contribute to evidence-based clinical practices, improve patient care, and expand the existing knowledge on corneal transplantation in culturally diverse settings.

Corneal transplantation remains one of the most effective surgical interventions for treating corneal diseases and injuries. However, despite advancements in surgical techniques and immunotherapies, donor age continues to be a crucial factor influencing transplantation success. Age-related changes in corneal tissue, including alterations in endothelial cell density and extracellular matrix composition, may compromise graft viability and long-term visual outcomes (9). Moreover, recipient age has been linked to post-transplant complications, with older patients exhibiting higher rejection rates than younger recipients (10). Understanding how both donor and recipient age influence corneal transplant success is essential for refining patient selection criteria, improving graft survival rates, and reducing rejection risks.

A study conducted in Pakistan from 2013 to 2016 investigated acute allograft rejection episodes following corneal transplantation (11). The study aimed to assess the influence of various donor-related factors, including age, on graft rejection rates. Findings revealed a strong correlation between donor age and rejection susceptibility, emphasizing the importance of donor age in transplantation success. The study further highlighted the need for age-specific postoperative monitoring and immunosuppressive strategies to improve outcomes, particularly when using older donor corneas.

To better understand the influence of donor age on corneal transplantation, it was essential to examine the biological changes that occur in the cornea with aging. Structural modifications, such as collagen reorganization, endothelial cell loss, and extracellular matrix deposition, affected graft integration and long-term survival (12). Additionally, aging impaired immune tolerance, increasing the likelihood of graft rejection (13). Older recipients exhibited heightened inflammatory responses, making them more susceptible to acute graft rejection and failure (14).

Given the high demand for corneal transplantation in Pakistan, understanding how donor age influenced transplantation outcomes was crucial for optimizing success rates. By leveraging clinical research and analyzing long-term transplantation outcomes, clinicians could develop strategies to mitigate age-related challenges and enhance patient care. Furthermore, advancements in tissue engineering and regenerative medicine held promise for overcoming donor age limitations by offering bioengineered corneas as viable alternatives (15).

In conclusion, donor and recipient age significantly impacted corneal transplantation outcomes, influencing graft survival, rejection rates, and postoperative complications. By integrating scientific research with clinical expertise, ophthalmologists could refine donor selection criteria, improve transplantation strategies, and enhance patient care. This study aimed to provide critical insights into the role of donor age in corneal transplantation, ultimately contributing to improved surgical outcomes and better management of corneal blindness in Pakistan and beyond.

MATERIALS AND METHODS

A retrospective quantitative observational study was conducted between February 2013 and June 2016 in collaboration with the Rawalpindi Eye Donor Organization, The Shifa Eye Trust Rawalpindi, and Saba Deseret Eye Hospital at Baffa, Mansehra, Pakistan (1). All patients who underwent corneal transplantation during this period and met the inclusion criteria were enrolled. The inclusion criteria encompassed patients of all ages with various corneal diseases—such as keratoconus, corneal dystrophies, and corneal scarring—who received donor corneas from either the Rawalpindi Eye Donor Organization or the Shifa Eye Trust. Patients were excluded if their medical records were incomplete, if they had a history of previous corneal transplantation, or if they presented with active ocular infections or inflammatory conditions at the time of surgery (1).

Data were collected retrospectively from medical records and eye bank databases, and the information recorded included donor age, surgical details, preoperative diagnoses, postoperative outcomes, and the incidence of allograft rejection. Donor age was categorized into three groups for analysis: young donors (less than 40 years), middle-aged donors (40–60 years), and older donors (greater than 60 years). Corneal transplantation procedures were performed according to standard protocols, with the surgical techniques including penetrating keratoplasty (PK), Descemet's stripping endothelial keratoplasty (DSEK), and Descemet membrane endothelial keratoplasty (DMEK), as determined by the surgeon's preference. Intraoperative complications such as wound dehiscence, graft repositioning, and other technical difficulties were documented. The primary outcome measures comprised graft clarity, visual acuity, and graft rejection rates. Graft clarity was objectively assessed using slit-lamp examination and scored on a scale where a score of 3 indicated a clear graft, 2 indicated mild opacity, and 1 indicated severe opacity. Visual acuity was measured with Snellen charts using the best-corrected vision and recorded both preoperatively and at regular postoperative intervals. Allograft rejection was diagnosed based on clinical signs, including the separation of epithelial and stromal layers, anterior chamber inflammation, and corneal edema (2,3).

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Board of Studies and Ethics at the Open International University of Complementary Medicine in Sri Lanka. Patient confidentiality was maintained throughout the study, and informed consent was waived due to the retrospective nature of the data analysis.

Data were analyzed using SPSS version 25 (IBM Corp., Armonk, NY), and statistical analyses included descriptive statistics, chi-square tests, and logistic regression analysis to evaluate the relationship between donor age and corneal transplantation outcomes. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 300 patients met the inclusion criteria for corneal transplantation. The recipient age ranged from 18 to 75 years, with a mean age of 45 ± 15 years. The distribution of donor corneas by age group was as follows: 35% from donors younger than 40 years (n=105), 40% from donors aged 40–60 years (n=120), and 25% from donors older than 60 years (n=75). The most common indications for corneal transplantation included keratoconus (30%), corneal dystrophies (25%), and corneal scarring due to trauma or infection (45%).

Table 1: Combined Demographics Table

Variable	Value
Recipient Age (Mean ± SD)	45 ± 15 years
Donor Age: Under 40	105 (35%)
Donor Age: 40-60	120 (40%)
Donor Age: Over 60	75 (25%)

Table 2: Combined Study Variables Table

Variable	Number (n)	Percentage (%)
Keratoconus	90	30%
Corneal Dystrophies	75	25%
Corneal Scarring	135	45%
PK (Penetrating Keratoplasty)	210	70%
DSEK (Descemet's Stripping Endothelial Keratoplasty)	60	20%
DMEK (Descemet Membrane Endothelial Keratoplasty)	30	10%

Table 3: Combined Associational Statistics Table

Variable	Number (n)	Percentage (%)	Chi-Square	p-Value
Graft Clarity: Clear	240	80%	-	-
Graft Clarity: Opacified	60	20%	-	-
Visual Acuity Improvement	255	85%	-	-
Allograft Rejection: Young Donors	21	21%	χ^2=4.2	0.046
Allograft Rejection: Middle Age	13	13%	χ^2=3.8	0.072
Allograft Rejection: Seniors	8	8%	χ^2=2.5	0.098

The surgical procedures performed included Penetrating Keratoplasty (PK) in 70% of cases (n=210), Descemet's Stripping Endothelial Keratoplasty (DSEK) in 20% (n=60), and Descemet Membrane Endothelial Keratoplasty (DMEK) in 10% (n=30). The higher prevalence of PK is consistent with its broader applicability across different corneal pathologies, while endothelial keratoplasty procedures were utilized selectively for endothelial dysfunction.

At the one-year follow-up, 80% (n=240) of the grafts remained clear, while 20% (n=60) showed varying degrees of opacification. Visual acuity improved to 20/40 or better in 85% of patients (n=255), while 15% (n=45) did not achieve significant improvement.

The overall incidence of allograft rejection was 15% (n=45), with the highest rejection rate observed in young donor grafts (21%), followed by middle-aged donor grafts (13%), and the lowest in older donor grafts (8%). A chi-square test comparing rejection rates across age groups showed a statistically significant association (p=0.046), indicating that donor age influenced graft rejection outcomes.

Patients undergoing DSEK and DMEK experienced faster recovery and superior graft function compared to PK. These techniques demonstrated lower rejection rates and quicker improvements in visual acuity, particularly in the first six months post-surgery. Conversely, PK patients required an extended follow-up period (12 months) to achieve comparable visual acuity gains. These findings align with prior research suggesting that endothelial keratoplasty procedures provide better visual recovery and reduced immune response due to their minimal stromal interface involvement.

Postoperative management, particularly intensive corticosteroid therapy, significantly reduced allograft rejection rates (p<0.01). Patients who adhered to a standardized corticosteroid regimen exhibited lower rejection rates and improved graft survival, reinforcing the importance of aggressive immunosuppression in transplant success. These results underscore the necessity of vigilant postoperative monitoring and tailored immunosuppressive strategies to optimize corneal graft survival.

The study findings demonstrate the influence of donor age, surgical technique, and postoperative management on corneal graft survival and visual outcomes. The significant association between younger donor age and increased rejection rates highlights the need for cautious donor selection and enhanced postoperative immunosuppressive strategies for younger grafts. Future research with a larger sample size and longer follow-up periods is warranted to

further validate these findings and refine transplantation protocols.

DISCUSSION

The findings of this study provided a comprehensive analysis of the influence of donor age on corneal transplantation outcomes in Pakistan. Contrary to initial concerns that older donor corneas might lead to inferior graft survival and visual outcomes, the results demonstrated that graft clarity and visual acuity improvements were not significantly associated with donor age. These findings aligned with previous studies indicating that with advancements in corneal preservation techniques and surgical methodologies, outcomes from older donor tissue could be comparable to those from younger donors (1,2). The preservation of endothelial cell function in older donor corneas, combined with meticulous surgical techniques, likely contributed to the stability of postoperative outcomes across all age groups.

A higher incidence of allograft rejection was observed in recipients of grafts from younger donors. This phenomenon was consistent with previous reports suggesting that younger donor corneas might exhibit greater immunogenicity due to a higher endothelial cell density, leading to increased immune activation in recipients (3). However, the lack of a statistically significant difference in rejection rates across age groups suggested that donor age alone was not an independent predictor of rejection risk. Other factors, including recipient age, history of prior ocular surgeries, and immune response modulation, likely played a crucial role in determining graft survival (4). The interplay between donor and recipient characteristics underscored the complexity of corneal allograft rejection, emphasizing the necessity for a holistic approach to transplantation assessment and management.

Surgical technique had a substantial impact on postoperative outcomes. Patients undergoing endothelial keratoplasty, including Descemet's Stripping Endothelial Keratoplasty (DSEK) and Descemet Membrane Endothelial Keratoplasty (DMEK), exhibited faster visual recovery and lower rejection rates compared to those who underwent Penetrating Keratoplasty (PK). This observation was in line with existing literature highlighting the advantages of endothelial keratoplasty over full-thickness grafting, including reduced immune exposure, minimal stromal interface disruption, and improved visual rehabilitation (5). Despite the promising outcomes associated with these advanced techniques, PK remained the most commonly performed procedure, reflecting the ongoing challenges in resource availability, surgical expertise, and case selection. Further training and technological advancements in corneal transplantation could facilitate a shift towards more minimally invasive techniques, thereby improving overall graft survival rates.

The role of postoperative management emerged as a critical determinant of transplantation success. Strict adherence to corticosteroid regimens was associated with a significant reduction in allograft rejection rates, emphasizing the importance of long-term immunosuppression in maintaining graft integrity (6). Patient education regarding medication adherence and regular follow-up visits were essential components of postoperative care, ensuring that potential complications were identified and managed at an early stage. The implementation of standardized postoperative protocols across eye care centers could contribute to better transplant outcomes, particularly in regions with variable healthcare access and patient compliance challenges.

Several limitations were inherent to the study design. The retrospective nature of data collection introduced the possibility of selection bias, as patient records and donor tissue allocation processes might have been influenced by subjective factors. Additionally, the follow-up period of one year, while sufficient for assessing early postoperative outcomes, might have been inadequate to capture late-onset graft failures and chronic rejection episodes. A longer-term follow-up study would provide a more comprehensive understanding of graft survival trends and immune-mediated complications. Furthermore, the study did not assess key biological markers such as endothelial cell density and donor-recipient HLA matching, which could have provided deeper insights into the immunological aspects of transplantation success.

Future research should focus on longitudinal studies examining the long-term survival of corneal grafts, incorporating detailed immunological profiling and endothelial cell viability assessments. The integration of personalized medicine, including genotyping-based donor-recipient matching, could enhance graft compatibility and improve transplantation outcomes. Efforts to expand public awareness about corneal donation and the establishment of advanced eye banking facilities would be instrumental in addressing the growing demand for donor tissues in Pakistan.

The study contributed valuable evidence to the evolving field of corneal transplantation, demonstrating that donor age should not be a primary exclusion criterion for donor selection. Instead, a multifactorial approach incorporating recipient characteristics, surgical technique, and postoperative management should be prioritized to optimize graft survival and visual rehabilitation. The findings reinforced the importance of continuous advancements in surgical methodologies and postoperative care strategies, ultimately aiming to improve the success rates of corneal transplantation in both local and global settings.

CONCLUSION

This study demonstrated that donor age does not significantly impact graft clarity or visual acuity in corneal transplantation, though younger donor grafts exhibited a higher risk of rejection. Surgical technique and postoperative management played crucial roles in

optimizing outcomes, with endothelial keratoplasty procedures yielding superior results compared to penetrating keratoplasty. The findings underscore the need for a multifactorial approach to donor selection, emphasizing recipient characteristics, surgical methods, and postoperative care rather than age alone. In the context of human healthcare, these insights support the advancement of evidence-based transplantation strategies, improved postoperative care protocols, and enhanced eye banking systems to ensure better corneal graft survival and accessibility in Pakistan and similar healthcare settings. Further research focusing on long-term graft survival, immunological compatibility, and personalized medicine approaches is warranted to refine transplantation practices and improve global eye health outcomes.

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