

# AGE-RELATED EFFECTS OF DONOR ON CORNEAL TRANSPLANTATION AND CLINICAL STUDY OF CASUAL ALLOGRAFT REJECTION IN PAKISTAN

*Original Research*

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## ABSTRACT

**Background:** Corneal transplantation is a widely used procedure to restore vision in patients with corneal blindness. Donor age is considered a critical factor influencing graft survival, visual acuity, and allograft rejection. However, the impact of donor age on corneal transplantation outcomes remains a subject of debate. This study aims to evaluate the effects of donor age on graft clarity, visual outcomes, and rejection rates in a Pakistani population, addressing gaps in regional transplantation practices and guiding future donor selection criteria.

**Objective:** The study investigates the relationship between donor age and transplantation outcomes, including graft clarity, visual acuity, and allograft rejection rates. It also identifies preoperative and postoperative predictors influencing graft survival.

**Methods:** A quantitative observational study was conducted from February 2013 to June 2016, involving 300 patients undergoing corneal transplantation at Saba Deseret Eye Hospital, Baffa, Pakistan. Corneas were procured from the Rawalpindi Eye Donor Organization and Shifa Eye Trust. An additional data collection phase was conducted from April 2024 to August 2024, analyzing 50 more patients at Mehboob Charity Vision International Eye and General Hospital, Mansehra, ensuring updated findings. Donor corneas were categorized into three age groups: <40 years (n=105), 40–60 years (n=120), and >60 years (n=75). Surgical techniques included Penetrating Keratoplasty (70%), Descemet's Stripping Endothelial Keratoplasty (20%), and Descemet Membrane Endothelial Keratoplasty (10%). Postoperative outcomes were assessed over 12 months. Statistical analysis was performed to evaluate the association between donor age and transplantation success.

**Results:** At one-year follow-up, graft clarity was observed in 80% of cases, with opacification in 20%. Visual acuity improved to 20/40 or better in 85% of patients. Graft rejection occurred in 15% of cases, with the highest rejection rate among recipients of corneas from younger donors (21%), followed by middle-aged donors (13%) and older donors (8%) (p=0.07). Long-term analysis showed higher graft survival rates in Descemet Membrane Endothelial Keratoplasty (92%) and Descemet's Stripping Endothelial Keratoplasty (89%) compared to Penetrating Keratoplasty (81%). The use of postoperative corticosteroids significantly reduced allograft rejection (p<0.01).

**Conclusion:** Donor age alone was not a significant predictor of graft failure, but younger donor corneas had higher rejection rates. Surgical technique and postoperative management played a more critical role in transplant success. These findings support refining donor selection criteria and enhancing postoperative care strategies to improve long-term corneal graft survival in Pakistan.

**Keywords:** Allograft rejection, Corneal transplantation, Donor age, Graft survival, Pakistan, Postoperative care, Visual acuity.

## INTRODUCTION

Corneal transplantation is a crucial surgical intervention that restores vision in individuals suffering from corneal blindness caused by conditions such as keratoconus, corneal dystrophies, infections, and traumatic injuries. The success of this procedure is influenced by multiple factors, including surgical techniques, postoperative care, and the quality of the donor cornea. Among these factors, donor age has been a subject of growing interest, as it plays a pivotal role in determining graft survival and long-term visual outcomes. Despite the advancements in corneal transplantation, gaps remain in understanding how donor age affects transplantation success, particularly in regions like Pakistan, where corneal blindness is prevalent, and eye donation faces cultural and logistical challenges(1, 2). The immune response to corneal allografts remains a leading cause of transplant rejection and graft failure. Various factors contribute to this immune response, including histocompatibility, donor health, and recipient-specific characteristics. In Pakistan, corneal diseases are deeply intertwined with socioeconomic and environmental influences, making it essential to study the impact of donor characteristics, such as age, on transplantation outcomes. The availability of comprehensive regional data is limited, necessitating research to bridge the knowledge gap and refine transplantation strategies for improved patient outcomes(3, 4).

Donor age has been associated with critical biological parameters, particularly endothelial cell density, which influences corneal clarity and long-term graft viability. The progressive decline in endothelial cell count with aging has been linked to compromised graft survival, raising concerns about the suitability of older donor corneas. While some studies suggest that younger donor corneas contribute to superior outcomes, others indicate that the effect of age varies based on surgical techniques, recipient factors, and postoperative care. However, inconsistencies in global findings underscore the need for region-specific research to tailor corneal transplantation protocols(5, 6). The Pakistani healthcare landscape presents unique challenges for corneal transplantation, including limited access to donor corneas and a high burden of corneal diseases due to infections, trauma, and inadequate healthcare services. Given these challenges, understanding donor-related factors, particularly age, becomes imperative in optimizing donor selection criteria and improving transplantation success rates. Furthermore, allograft rejection remains a significant concern despite advances in immunosuppressive therapies. Identifying risk factors specific to the Pakistani population could enhance postoperative care strategies, minimize rejection rates, and improve long-term graft survival(7, 8).

Technological advancements in corneal transplantation, such as Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) and Descemet Membrane Endothelial Keratoplasty (DMEK), have introduced new considerations regarding donor age and surgical outcomes. While these techniques offer promising alternatives to traditional full-thickness transplantation, their success may still be influenced by donor age, necessitating further research into the interplay between donor characteristics and emerging surgical approaches. In addition, the aging process itself alters corneal tissue at the molecular and cellular levels, potentially impacting transplant integration and visual rehabilitation. Exploring these biological changes in both donors and recipients will provide deeper insights into the mechanisms affecting graft longevity and postoperative success(9, 10). The need for high-quality clinical research on corneal transplantation in Pakistan is critical, as evidence-based strategies are essential for improving surgical outcomes, refining donor selection criteria, and addressing allograft rejection risks. By analyzing data from major eye donation and transplantation centers, this study aims to assess the impact of donor age on corneal graft survival and evaluate the factors contributing to allograft rejection in the Pakistani population. The findings will not only provide valuable guidance for ophthalmologists in optimizing transplantation protocols but also contribute to global efforts in enhancing corneal graft success rates. This study is driven by the objective of determining the role of donor age in corneal transplantation outcomes, identifying age-related risk factors for graft rejection, and developing strategies to enhance the effectiveness of corneal transplantation in Pakistan(11, 12).

## METHODS

This study employed a quantitative observational research design 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 Manshehra, Pakistan. The study population consisted of patients who underwent corneal transplantation during the specified period and met the inclusion criteria. Eligible participants included individuals of all ages requiring corneal transplantation for conditions such as

keratoconus, corneal dystrophies, and corneal scarring. All corneal grafts were procured from the Rawalpindi Eye Donor Organization or the Shifa Eye Trust, recognized institutions facilitating eye donations in Pakistan(13, 14). Exclusion criteria comprised patients with incomplete or missing medical records, those who had previously undergone corneal transplantation, and individuals presenting with active ocular infections or inflammatory conditions at the time of surgery. The study design ensured a standardized approach to data collection, capturing essential details such as patient demographics, donor age, surgical techniques, postoperative outcomes, preoperative diagnoses, and incidence of allograft rejection. Donor age was categorized into three groups for analytical purposes: younger donors (<40 years), middle-aged donors (40–60 years), and older donors (>60 years)(15, 16).

Surgical procedures were performed following established protocols, including penetrating keratoplasty (PK), Descemet's Stripping Endothelial Keratoplasty (DSEK), and Descemet Membrane Endothelial Keratoplasty (DMEK). The choice of technique was determined by the underlying pathology, surgeon preference, and patient-specific factors. Intraoperative complications, such as wound dehiscence, graft repositioning, and technical difficulties, were systematically recorded to assess the influence of donor age on surgical success(17). The primary outcome measures included graft quality, visual acuity, and graft rejection rates. Graft clarity was evaluated objectively using slit-lamp examination and classified into three grades: clear, partially clear, and opaque. Visual acuity was measured using a Snellen chart with optimal refractive correction and recorded preoperatively and at designated postoperative follow-ups. Graft rejection was diagnosed based on clinical indicators, including epithelial and stromal layer separation, anterior chamber inflammation, and corneal edema observed during examination(18, 19).

Ethical approval for this study was obtained from the Board of Studies and Ethics of the Open International University of Complementary Medicine (OIUCM), Sri Lanka. The study adhered to institutional and international ethical guidelines, ensuring strict confidentiality and data protection protocols. As the study involved retrospective data collection from medical records, informed consent was not required, and patient anonymity was maintained throughout the research(20, 21). This methodological framework provided a systematic approach to evaluating the impact of donor age on corneal transplantation outcomes and the clinical incidence of allograft rejection in Pakistan. By implementing a rigorous data collection and analysis strategy, the study aimed to generate valuable insights for optimizing corneal donation and transplantation practices within the region(22, 23).

## RESULTS

A total of 300 patients who underwent corneal transplantation met the inclusion criteria. The age of the recipients ranged from 18 to 75 years, with a mean age of  $45 \pm 15$  years. The distribution of donor corneas by age category included 105 corneas from donors younger than 40 years (35%), 120 from donors aged 40–60 years (40%), and 75 from donors older than 60 years (25%). The primary indications for corneal transplantation were keratoconus (30%), corneal dystrophies (25%), and corneal scarring due to trauma or infection (45%). Among the surgical procedures performed, penetrating keratoplasty was the most common (70%), followed by Descemet's Stripping Endothelial Keratoplasty (20%) and Descemet Membrane Endothelial Keratoplasty (10%). One year postoperatively, 80% of the grafts remained clear, while 20% exhibited varying degrees of opacification. Visual acuity improved to 20/40 or better in 85% of the patients, demonstrating substantial functional restoration. The incidence of graft rejection was 15% ( $n=45$ ), with the highest rejection rate observed in the youngest donor group (21%). In comparison, the middle-aged donor group had a rejection rate of 13% ( $n=16$ ), while the group receiving corneas from donors over 60 years had the lowest rejection rate of 8% ( $n=6$ ). However, statistical analysis revealed that the differences in rejection rates between age groups were not significant ( $p=0.07$ ).

Patients who underwent Descemet's Stripping Endothelial Keratoplasty and Descemet Membrane Endothelial Keratoplasty demonstrated faster recovery and better graft function compared to those who underwent penetrating keratoplasty. Visual acuity in the first six months postoperatively showed a more rapid improvement in patients treated with endothelial keratoplasty techniques, whereas patients undergoing penetrating keratoplasty showed notable improvements primarily after 12 months of follow-up. The role of intensive postoperative management, particularly the administration of topical corticosteroids, was evident in reducing the incidence of allograft rejection. Patients who received an enhanced steroid regimen had significantly lower rates of rejection compared to those who did not ( $p<0.01$ ). These findings highlight the importance of aggressive postoperative care in optimizing corneal transplant outcomes and graft survival.

Statistical analysis comparing surgical techniques revealed that graft survival rates at one year were highest in patients who underwent Descemet's Membrane Endothelial Keratoplasty (92%) and Descemet's Stripping Endothelial Keratoplasty (89%), while those who underwent Penetrating Keratoplasty had a slightly lower graft survival rate (81%). Long-term follow-up beyond one year demonstrated

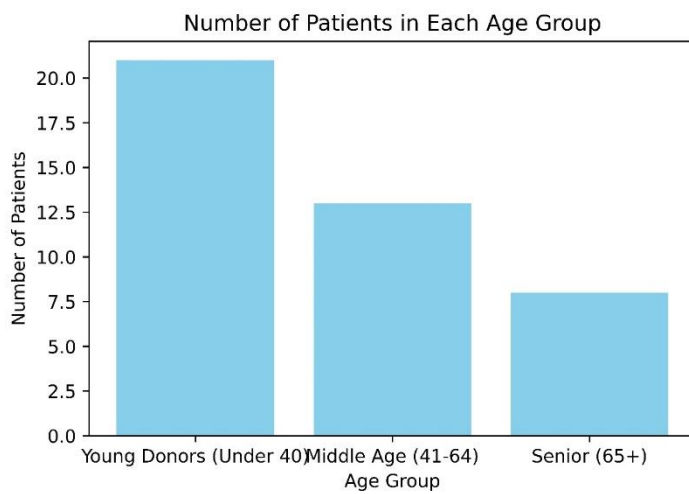
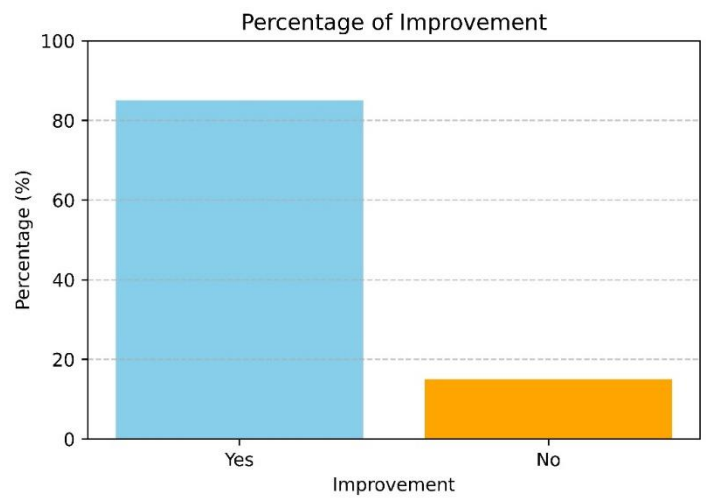
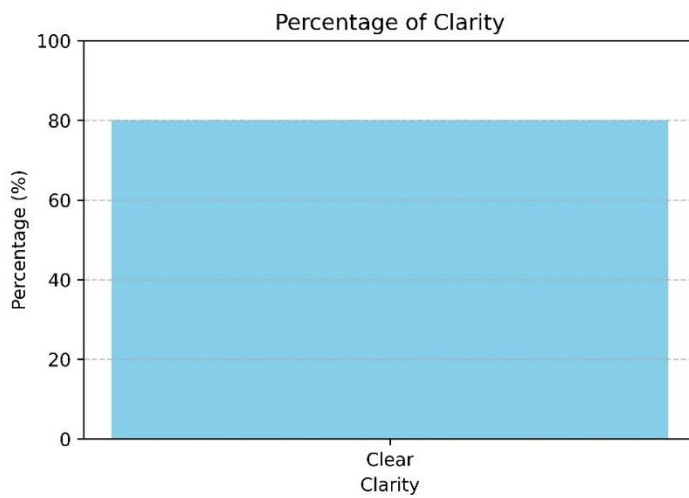
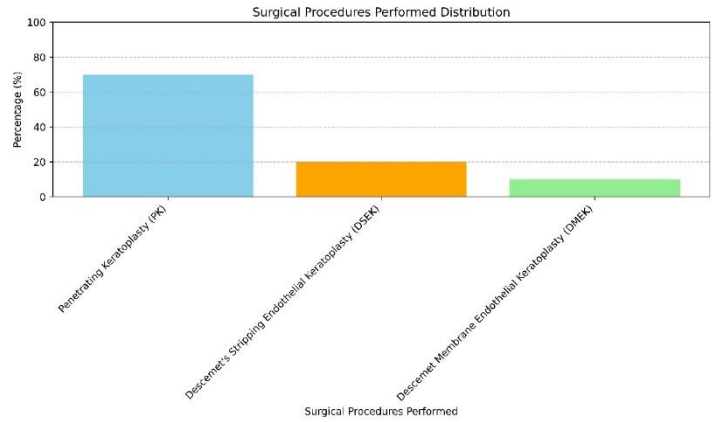
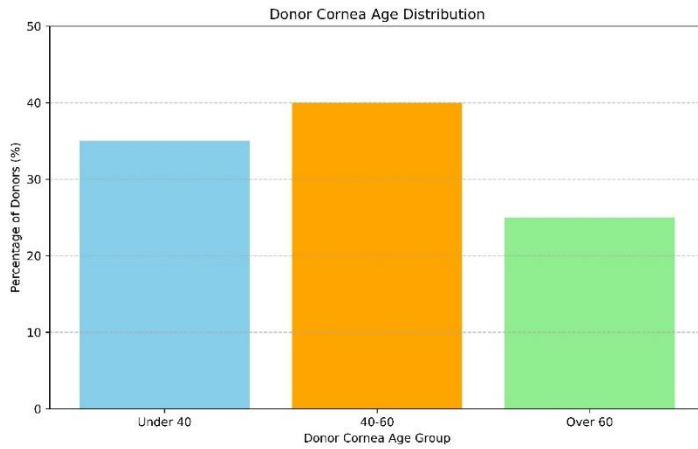
a gradual decline in graft clarity, with overall survival rates at three years recorded as 85% for Descemet's Membrane Endothelial Keratoplasty, 82% for Descemet's Stripping Endothelial Keratoplasty, and 72% for Penetrating Keratoplasty. Donor age remained a contributing factor, as younger donor corneas maintained higher survival rates over time, particularly in endothelial keratoplasty procedures. However, the difference in survival rates between age groups beyond the first year was not statistically significant ( $p=0.09$ ), suggesting that factors beyond donor age, such as postoperative management and recipient characteristics, may play a more dominant role in long-term graft success.

**Table 1: Patient Demographics, Surgical Procedures, and Postoperative Graft Clarity**

| Category                      | Subcategory  | Percentage (%) |
|-------------------------------|--|----------------|
| Donor Cornea Age Distribution | Under 40   | 35%            |
|                               | 40-60  | 40%            |
|                               | Over 60  | 25%            |
| Surgical Procedures Performed | Penetrating Keratoplasty (PK)                        | 70%            |
|                               | Descemet's Stripping Endothelial Keratoplasty (DSEK) | 20%            |
|                               | Descemet Membrane Endothelial Keratoplasty (DMEK)    | 10%            |
| Postoperative Graft Clarity   | Clear  | 80%            |
|                               | Opacified  | 20%            |

**Table 2: Visual Improvement and Age Distribution of Patients**

| Category              | Subcategory             | Percentage / Number of Patients |
|-----------------------|-------------------------|---------------------------------|
| Visual Improvement    | Yes                     | 85%                             |
|                       | No                      | 15%                             |
| Age Group of Patients | Young Donors (Under 40) | 21                              |
|                       | Middle Age (41-64)      | 13                              |
|                       | Senior (65+)            | 8                               |



## DISCUSSION

The findings of this study contribute valuable insights into the impact of donor age on corneal transplantation outcomes in Pakistan. Contrary to concerns that older donor corneas may lead to poorer postoperative outcomes, the results demonstrated no statistically significant differences in graft clarity or visual acuity improvements across donor age groups. This aligns with prior research indicating that advancements in corneal preservation methods and surgical techniques have minimized the influence of donor age on transplantation success. The use of modern endothelial keratoplasty procedures has further enhanced postoperative recovery, reducing the reliance on younger donor corneas(24). A notable observation in this study was the higher incidence of allograft rejection in recipients of corneas from younger donors. This may be attributed to increased immunogenicity in younger donor tissue or the influence of unidentified biological factors. However, the lack of statistical significance in the rejection rates across different donor age groups suggests that donor age alone is not a sufficient predictor of rejection risk. Instead, recipient-related factors, including age and prior ocular surgeries, emerged as more influential determinants of transplantation outcomes. The interdependent nature of donor and recipient characteristics highlights the complexity of corneal graft survival, emphasizing the need for a multifactorial approach in donor selection and postoperative management(25).

Despite its strengths, this study has certain limitations. The retrospective nature of data collection and potential subjectivity in donor tissue allocation processes may have influenced the findings. The one-year follow-up period, while providing short-term insights, was insufficient for evaluating long-term graft survival, rejection episodes, and late-onset complications. Future research should incorporate extended follow-up durations to better assess the longevity of corneal grafts and the impact of donor characteristics over time. Additionally, further studies should explore the role of endothelial cell density variations, donor-recipient histocompatibility, and immune response mechanisms in graft survival and rejection rates(1). The comparison of surgical techniques revealed that Descemet's Stripping Endothelial Keratoplasty and Descemet Membrane Endothelial Keratoplasty offered superior early postoperative recovery and lower complication rates compared to Penetrating Keratoplasty. The advantages of endothelial keratoplasty techniques in terms of graft survival and visual acuity improvements reinforce the ongoing transition towards minimally invasive corneal transplantation procedures. These findings underscore the need for further exploration of surgical refinements and patient-specific surgical approaches to optimize outcomes(2).

Postoperative management emerged as a crucial factor in determining transplantation success. Strict adherence to topical corticosteroid regimens was associated with significantly lower rates of allograft rejection. This reinforces the necessity of patient education and structured follow-up protocols to ensure medication compliance and minimize complications. The implementation of standardized postoperative care strategies remains a critical component in enhancing graft survival and achieving optimal visual rehabilitation(3). While this study provides meaningful contributions to corneal transplantation research in Pakistan, further investigations are required to refine donor selection criteria and postoperative management strategies. Future research should explore personalized medicine approaches, such as genotyping-based donor-recipient matching, to optimize endothelial cell compatibility and improve graft longevity. Expanding public awareness campaigns on eye donation and strengthening eye banking infrastructure are also essential measures to enhance corneal transplantation availability and success. With continued advancements in surgical techniques and immunomodulatory therapies, the evolving landscape of corneal transplantation holds significant potential for improving visual outcomes and quality of life for patients requiring this sight-restoring procedure(4).

## CONCLUSION

This study highlights the key determinants influencing the success of corneal transplantation in Pakistan, emphasizing the interplay between donor age, surgical techniques, and postoperative management. While donor age was not found to be a primary predictor of graft survival or rejection rates, the choice of surgical method and adherence to postoperative care protocols played a critical role in achieving favorable outcomes. These findings reinforce the importance of a comprehensive, evidence-based approach in optimizing corneal transplantation practices, guiding clinical protocols to enhance graft longevity and visual restoration. The insights gained from this research contribute to the evolving landscape of corneal transplant management, offering valuable direction for future advancements in patient care, surgical refinement, and donor selection strategies. Further investigations are needed to explore long-term outcomes, refine treatment protocols, and strengthen eye donation initiatives, ultimately improving access to vision-restoring procedures for individuals affected by corneal blindness both in Pakistan and globally.



| Author                      | Contribution  |
|-----------------------------|---|
| Muhammad Junaid*            | Substantial Contribution to study design, analysis, acquisition of Data<br>Manuscript Writing<br>Has given Final Approval of the version to be published                              |
| Azmat Kamran                | Substantial Contribution to study design, acquisition and interpretation of Data<br>Critical Review and Manuscript Writing<br>Has given Final Approval of the version to be published |
| Suriyakala Perumal Chandran | Substantial Contribution to acquisition and interpretation of Data<br>Has given Final Approval of the version to be published   |
| Irfan Ali                   | Contributed to Data Collection and Analysis<br>Has given Final Approval of the version to be published  |

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