

Indications and techniques employed for keratoplasty in the Eastern province of Saudi Arabia: 6 years of experience

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BACKGROUND AND OBJECTIVES: Keratoplasty services in Saudi Arabia have progressed steadily in the past few decades. We sought to identify the leading indications and types of keratoplasty performed in the Eastern Province of Saudi Arabia over a six-year period and to compare these indications with published data.

DESIGN AND SETTING: This was a retrospective descriptive analysis of the records of patients who underwent keratoplasty at four ophthalmology centers in the Eastern Province between 2008 and 2013.

PATIENTS AND METHODS: All keratoplasty procedures were included in the analysis. The primary surgical indication and type of surgery were identified for each case.

RESULTS: Keratoplasties included 570 penetrating keratoplasty, 217 deep lamellar keratoplasty, 80 triple procedures, 24 descemet stripping automated endothelial keratoplasty and 12 Boston keratoprosthesis implantations. The mean age of all patients was 28.8 years (range 14-72 years), and 58.9% of the patient were males. The leading indication for keratoplasty was keratoconus 53.10%, bullous keratopathy 13.80%, corneal scarring 10.7%, regrafts 9.1%, and stromal dystrophies 4.9%.

CONCLUSIONS: In this study, the leading indications for keratoplasty were keratoconus, bullous keratopathy, corneal scarring, regrafts and stromal dystrophies. A significant increasing trend for descemet's stripping automated endothelial keratoplasty surgeries was observed in spite of the number of cases.

Corneal transplantation, also called corneal grafting or keratoplasty, has evolved rapidly during the last few decades from full-thickness corneal grafts (penetrating keratoplasty) to endothelial keratoplasty, where there is selective replacement of diseased corneal endothelium.^{1,2} Recent advancement and refinement in microsurgical techniques has led to the development of unique forms of lamellar keratoplasty, which has enabled replacement of the affected tissue instead of the full thickness corneal graft. With the steady innovative improvements in ocular immunology, ocular pharmacology, corneal storage, and eye banking procedures, keratoplasty has become one of the most widely practiced transplantations in humans.³⁻⁷ Keratoplasty remains the ultimate treatment for an estimated 80-90% of blindness after corneal opacification regardless of various inherent challenges in the developing world.⁷

The major indications for keratoplasty differ across the world, primarily due to the spectrum of corneal

disease in each country and the socioeconomic factors influencing the etiology of corneal blinding diseases. Pseudophakic corneal edema (corneal edema as a result of cataract and intraocular lens surgery), keratoconus (where the cornea progressively loses its uniform oval shape and become conic) and regrafts have been the most common clinical indications for corneal transplantation in the developed world since the 1980s.⁸ However; there has been a gradual change in indications for keratoplasty in the developing world in the past three decades. This change is attributed to several factors including advances in medical and surgical ophthalmic care, improvement in hygiene measures and public awareness.⁶ Accordingly, a tremendous decrease in the incidence and consequences of diseases like trachoma and microbial/ herpetic keratitis has been observed.⁹ Similarly, advancements in cataract surgery have decreased the incidence of pseudophakic or aphakic bullous keratopathy.⁸ Additionally, corneal opacifi-

cation is described as the third leading cause of bilateral blindness after cataract and glaucoma, affecting around 7-9 million people, 90% of whom live in the developing world.⁹ However, Al-Towerki et al, in 2004 described a great decline in the number of procedures performed for corneal scarring in Saudi Arabia.⁹

Keratoplasty services in Saudi Arabia have progressed steadily in parallel with socioeconomic development and population growth in the past few decades.^{9,10} Improvements in the storage media and transport process have allowed for easier importation of corneas from North America that has considerably decreased the gap between demand and supply in the Eastern Province of Saudi Arabia. In this study, we report the indications for keratoplasty and the preferred types of keratoplasty performed in the Eastern Province in the last six years from 2008 to 2013. The main objective is to understand the pattern of corneal transplantation pathology in our region and to compare these indications with those of other publications in different parts of the world.

PATIENTS AND METHODS

A retrospective analysis of records of all cases of keratoplasty performed between January 1, 2008 and December 31, 2013 was conducted. Cases were performed at four ophthalmology centers in the Eastern Province, Saudi Arabia-Dhahran Eye Specialist Hospital (DESH), King Fahd Hospital of the University, Magrabi Eye and Ear Hospital and Kahhal Medical Center. The study was approved by the ethical committee (2013) and the medical research review board and carried out in accordance with the tenets of the Declaration of Helsinki.

Data analyzed included patient age, gender, clinical indications for keratoplasty and type of keratoplasty performed. Whenever two possible clinical diagnoses were identified that previously had a PKP, they were labeled as regrafts despite the presence of any other accompanying condition. Cases in which corneal edema was associated with previous cataract surgery were labeled as corneal decompensation and bullous keratopathy.

The different types of keratopathy included penetrating keratoplasty (PKP), deep anterior lamellar keratoplasty (DALK), Descemet's stripping automated endothelial keratoplasty (DSAEK), triple procedures and Boston keratoprosthesis (KPro). Multiple corneal surgeons performed the keratoplasty procedures.

Terminology

Penetrating keratoplasty is a procedure involving full thickness replacement of corneal tissue. Deep anterior

lamellar keratoplasty is a surgical procedure involving replacement of the corneal stroma down to and sparing the Descemet's membrane. Descemet's stripping automated endothelial keratoplasty is a selective replacement of damaged corneal endothelial cell layer. A triple procedure is keratoplasty procedure combined with cataract extraction and intraocular lens implantation. Boston keratoprosthesis (KPro) is an implantation of an artificial cornea with a collar button design.

The data was amalgamated and de-identified before analysis using SPSS software (version 20).

RESULTS

A total of 920 keratoplasty in 832 patients were performed between January 1, 2008 and December 31, 2013. Sex distribution showed a male predominance with 490 males (58.9%) and 342 females (41.1%). The mean age of all patients was 28.8 years (range 14-72 years).

The most commonly performed keratoplasty procedures included PKP (n=570, 62%), DALK (n=217, 24%), and DSAEK (n=24, 2%). The less frequent types of keratopathy included t-PKP; (n=80, 9%), tectonic PKP (n=8, 1%), triple DSAEK (n=8, 1%), and one case of rotational graft. Boston KPro accounted for 1.30% for total of 12 cases (Figure 1).

Both PKP and DALK procedures showed increasing frequency since the beginning of our study (Figure 2) with keratoconus being the predominant indication. Comparing the surgical techniques, there was a significant increase in the relative frequency of PKP (from 60 cases done on 2008 to 154 cases on 2013) and DALK (from 6 cases done on 2008 to 76 cases on 2012) with a significant drop in frequency in 2013 with 45 cases only.

DSAEK procedures started in 2009 with one case and increased dramatically to 15 cases in 2013. There were few cases per year for Boston KPro in our study in 2008 with one case and the number peaked in 2012 with 4 cases (Figure 2).

Indications for keratoplasty were keratoconus, performed in 488 eyes (53.1%), bullous keratopathy (13.8%), corneal scarring (10.7%), regrafts (9.1%), and stromal dystrophies (4.9%). These five groups accounted for 91.6% of all operations performed. The remaining 8% included less common diseases like Fuchs' endothelial dystrophy (1.9%), microbial keratitis (1.7%), post-LASIK ectasia (1.3%), scarred and vascularized cornea (0.9%), other non-Fuchs' endothelial corneal dystrophies (0.8%), keratoglobus (0.5%), failed keratoprosthesis (0.2%), climatic droplet keratopathy, pellucid marginal degeneration, corneal blood staining, and

sclerocornea (0.1%) each, (Figure 3).

Of the 488 eyes that underwent corneal transplantation for the management of keratoconus, PKP was performed on 280 eyes (57.3%), DALK in 202 eyes (42%), and t-PKP in the remaining 6 eyes (1%). The mean age of the patients at the time of surgery for keratoconus was 27.5 years. The mode for age was 22 years (39 cases) (Figure 4). Keratoconus-associated diseases were noted in only 3% of cases, which included vernal keratoconjunctivitis (VKC) (n=9 eyes), Down syndrome (n=3 eyes of two patients) and retinitis pigmentosa (n=1 eyes). Eight eyes had PKP while 5 eyes with VKC had DALK.

Corneal scars ranked third as an indication for keratoplasty, comprising 10.7%. Unknown causes of the corneal scars were observed in 31.6% of the cases. Corneal scarring secondary to trachoma accounted for 24.5%. Other causes of corneal scarring were old herpetic infection representing 16.3%, microbial infection in 15.3% and traumatic corneal scar in 12.3%.

Regrafts accounted for 8.6 % of the indications for keratoplasty. Stromal dystrophies accounted for 4.9 % of the indications for keratoplasty. Macular corneal dystrophy was the most common corneal dystrophy necessitating corneal transplantation in this series (38 of 45 eyes, 84.4%), followed by granular dystrophy (7 of 45 eyes, 15.6%).

DISCUSSION

This study identified indications for keratoplasty in 920 cases at four eye centers in the Eastern province of Saudi Arabia, from 2008 to 2013. Comparing the type of surgical techniques, we noted a significant increase in the relative frequency of PKP (from 60 cases done in 2008 to 154 cases in 2013) and DALK (from 6 cases done in 2008 to 76 cases in 2012 with noticeable reduction in number of cases in 2013 with 45 cases only). The decline in number of DALK procedures could be attributed to the fact that keratoconus cases were the main indication for DALK, which was replaced by other modalities of treatment, like crosslinking and intracorneal rings. Despite this decline in the number of DALK procedures, it was increasingly used for management of keratoconus since 2008 whereas PKP and DSAEK were used for bullous keratopathy. PKP was the dominant technique for infectious corneal ulcers during the study period. PKP remains the main surgical approach for failed grafts and corneal scars.

In our study, the leading indication for keratoplasty was keratoconus, accounting for nearly 53% of all keratopathy procedures over a six years' time span. Likewise, it represented the most common indication

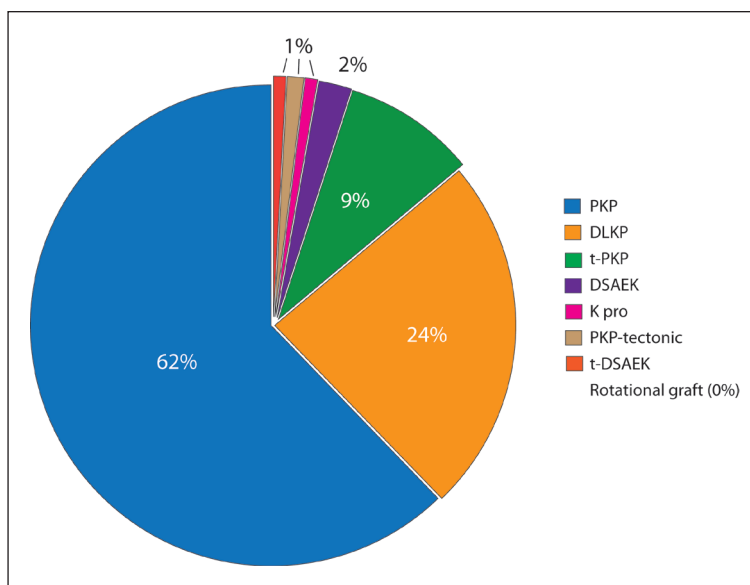


Figure 1. Most common procedures performed in Eastern Province, Saudi Arabia (2008-2013). PKP: Penetrating keratophy; DLKP: Deep lamellar keratophy; t-PKP: Penetrating keratophy with cataract extraction and intraocular lens implantation; DSAEK: Descemet's stripping automated endothelial keratophy; KPro: Boston keratoprothesis and t-DSAEK: DSAEK with cataract extraction and intraocular lens implantation.

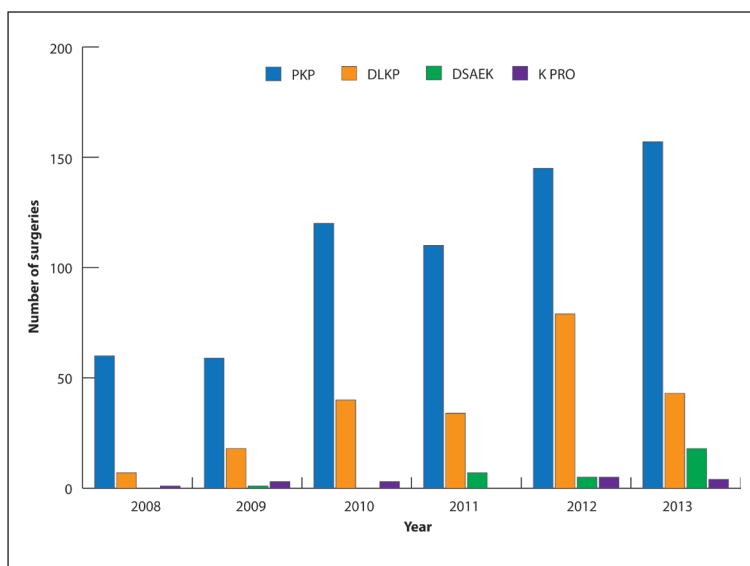


Figure 2. Trends in different keratoplasty techniques in the last six years. PKP: Penetrating keratophy; DLKP: Deep lamellar keratophy; DSAEK: Descemet's stripping automated endothelial keratophy; KPro: Boston keratoprothesis.

of keratoplasty in a previous study in Eastern Province, Saudi Arabia, 10 and in studies from other parts of the world; New Zealand (45.60%),¹¹ Iran (34.51%-42.5%),^{12,13} Australia (29.8%),¹⁴ France (28.80%),¹⁵ UK (28.7%),¹⁶ Zimbabwe (26.80%),¹⁷ and Germany

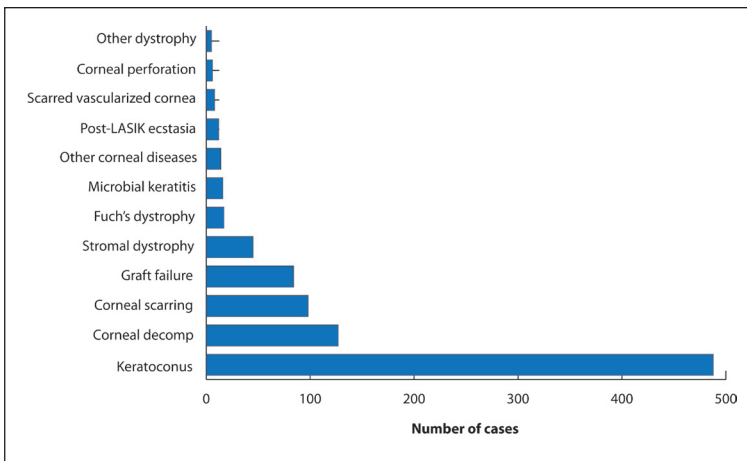


Figure 3. Major indications for keratoplasty. Other non-Fuchs' corneal dystrophies: congenital hereditary endothelial dystrophy, posterior polymorphous dystrophy, basement membrane dystrophy; Other corneal diseases include: Pellucid marginal degeneration, climatic droplet keratopathy, failed keratoprosthesis, corneal blood staining and sclerocornea.

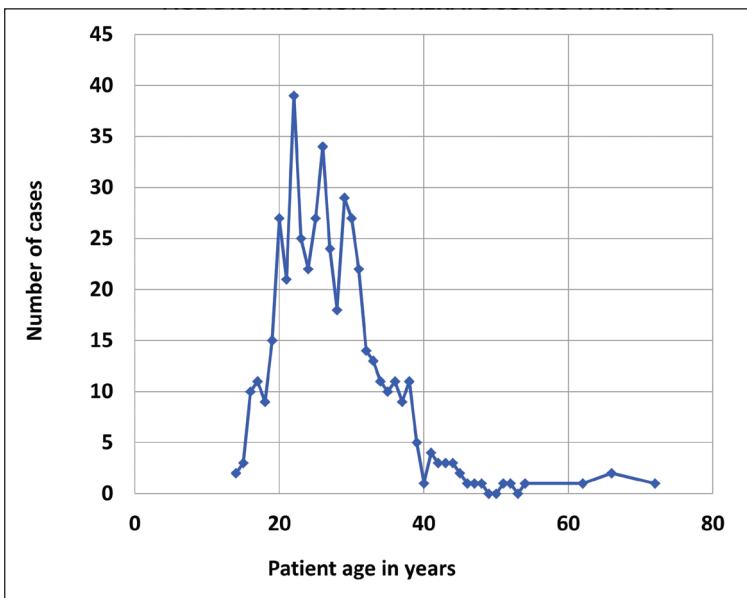


Figure 4. Age distribution of patients with keratoconus who underwent keratoplasty showing peaked frequency in the early 20s.

(20.90%-25.5%).^{18,19} However, this is inconsistent with other regions where the percentage of keratoconus cases that require keratoplasty showed lower rates in reports from Brazil (13.10%),²⁰ China (13%),²¹ Canada (12%-15.5%),²²⁻²⁴ and the US (11.40%)^{2,3} (Figure 5 shows the percentage of keratoconus cases that were finally treated by keratoplasty in different countries). The 2013 Eye Banking Statistical Report from the Eye Bank Association of America (EBAA) that included in-

formation on all 76 U.S. and 10 international member eye banks showed that Fuchs' dystrophy was the most common indication for keratoplasty in 2013 (21.3%). Post-cataract surgery edema was second (12.4%) and keratoconus (10.4%) was third, while regrant ranked as the fourth indication (9.9%).⁴

The variance in percentage of keratoconus cases requiring keratoplasty surgery could be rationalized by the variance in the reported prevalence of keratoconus, which varies widely depending upon the genetic factors, geographic location, and diagnostic criteria. Environmental factors such as sunshine and hot weather with excessive ultra-violet exposure have been implicated as a contributing factor in the increased prevalence in the Middle East and India.^{25,26} The incidence and severity of keratoconus in Asir Province in Saudi Arabia has been reported to be high with an early onset and rapid progression.²⁵ The results of our study may imply a relative increased frequency of keratoconus in the Eastern Province in the Saudi population; however, these findings cannot be extrapolated to the general population.

The majority of the patients who underwent keratoplasty in this study were less than 40 years with a mean age of 27.5 years, which is much lower than the mean age of 40.6 years reported by Cosar et al. from the Wills Eye Hospital in the United States.²³ The tendency towards younger age in the current study is due to the fact that keratoconus affects a younger population. The second contributing factor is the patient selection criteria at our centers, where younger patients with bilateral disease are given priority for keratoplasty over older patients with unilateral disease. Probably, the dry and dusty climate in our region triggered contact lens intolerance and consequently a need for earlier surgical intervention. Furthermore, diseases associated with keratoconus were treated with keratoplasty. However, pure keratoconus accounted for 97.3% (475/488), and nine cases associated with VKC and only 2 cases of Down syndrome and one case of retinitis pigmentosa (RP). Patients with keratoconus and co-existing vernal keratoconjunctivitis (VKC) are prone to have faster progression secondary to the increased tendency for eye rubbing due to chronic itchiness.²⁷

The second most common indication for keratoplasty in our study was corneal decompensation and bullous keratopathy. These results compare favorably with the results reported by Al-Towerki et al.⁹ However, in the later period between 1998 and 2002 bullous keratopathy showed a relative decline in frequency.⁹ Bullous keratopathy was the leading indication for keratoplasty in several studies in the USA,^{6,28} Canada,^{29,30} Japan,³¹

and Thailand.³² Interestingly, despite improvement in cataract instrumentation and techniques, iatrogenic bullous keratopathy remains one of the most frequent surgical indications for keratoplasty worldwide. This can be attributed to the increasing frequency of performing cataract surgery at early phases of cataract development with relatively high number of cases in developed countries compared with developing countries. Additionally, in the 1970s, a large number of iris-plane and closed-loop anterior chamber intraocular lenses (AC IOLs) were implanted in the developed countries. This resulted in a subsequent spike in cases of aphakic and pseudophakic corneal edema requiring keratoplasty, which continued to be the leading indication for keratoplasty since early 1980s.³³ Prior to 1983, cataract surgery was not frequently performed in Saudi Arabia, thereby resulting in far fewer iris-plane and closed-loop AC IOLs being implanted compared to the rest of the world.⁹ However, the use of unsatisfactory intraocular lens designs as well as variability in the ophthalmic training and skills of surgeons in Saudi Arabia at that time, created a slight accumulation of cases with post-operative corneal decompensation.⁹

Corneal scars ranked as the third indication for keratoplasty in our region comprising 10.66%. This finding reflects the marked reduction in the incidence of corneal scars that was consistent with the observation of Al-Towerki et al.⁹ who described a change in the occurrence of corneal scarring that decreased from 52% in the 1983 - 1987 to 19.8% in 1998-2002. The significant decline in the number of corneal scarring secondary to trachoma, which was the chief indication for keratoplasty between 1983 and 1987, is likely due to changing socioeconomic conditions that have virtually eliminated active trachoma.⁹ Corneal scarring of unknown causes accounted for 3.4% of total cases in the current study. This observation contrasts with findings in other developing countries like India (28.1%-60.7%), and Taiwan (27.9%), where corneal scarring was the leading indication for keratoplasty.^{34,35}

Our study found that secondary keratopathy or re-grafts were the fourth leading indication for keratoplasty, which is not different from most developed countries like the USA.² However re-grafts are becoming an increasing indication for keratoplasty.²³ One of the possible factors affecting the rate of re-graft is the initial indication for keratoplasty and its potential failure risk.³⁶ Wagoner et al³⁶ reported the prognosis for the graft survival to be excellent for eyes with keratoconus and stromal dystrophy, good for stromal scarring, and poor for eyes with corneal edema. Keratoconus accounted for 53% of keratoplasty indications in our region that had

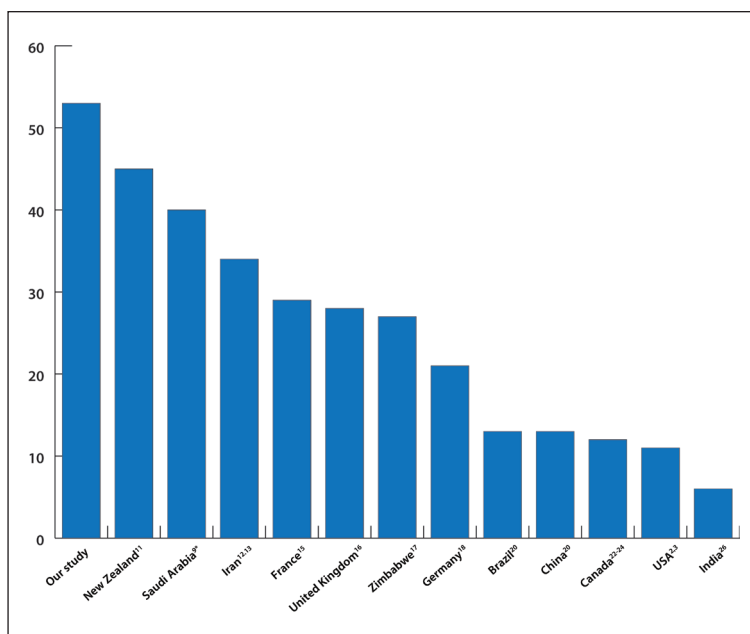


Figure 5. Percentage of keratoconus cases finally treated with keratoplasty in different countries compared with our study.

a low risk of graft failure and that may explain the low rate of re-grafts.³⁶

Stromal dystrophies accounted for 4.9% of the indications for keratoplasty in our study, with macular corneal dystrophy representing 84.4% of these cases. This finding is in line with previously reported rates in Saudi Arabia.^{9,36,37} Recently Alzuhairy et al,³⁷ have shown that the corneal stromal dystrophy distribution in Saudi Arabia included macular corneal dystrophy in 93.26%, granular corneal dystrophy in 4.66% and lattice corneal dystrophy in 2.07%.

Keratoplasty for phakic corneal edema was much less common in Saudi Arabia, primarily because of a much lower prevalence of Fuchs' endothelial dystrophy. Only 1.85% of the eyes had Fuchs' endothelial dystrophy in our series compared to 21.3% in the USA,³ 22.3% in the UK,³⁸ 15% in Australia,¹⁴ in France (9.4%),¹⁵ and Taiwan (4.5%).³⁵ The relatively lower rate of Fuchs' dystrophy in our region compares positively with other studies throughout the world; Japan (1.3%),³⁹ and India (0.8%).⁴⁰ Genetic factors were the presumed explanation for the rare incidence of Fuchs' dystrophy in Japan compared with the western population.³⁹

The apparent diversity in keratoplasty indications among different countries is remarkable. It is interesting to note that the trend demonstrated by Al-Towerki et al⁹ from 1983 to 2002 and Wagoner et al,³⁶ in 2009 continued until 2013. Keratoconus remained the leading indication for keratoplasty in the Eastern Province

as well. **Table 1** shows the worldwide variability in indications for penetrating keratoplasty. Several factors may contribute to this variability including the environment, geographical location, prevalence of corneal disorders, availability of ophthalmic care, and genetic predisposition.

This study has shown that PKP was the major procedure performed in our region. However, we believe that the rates of DALK and DSAEK are likely to grow in coming years due to their higher potential success and the increasing availability of essential surgical infrastructure and skills.

In conclusion, in this study, keratoconus is the leading indication for keratoplasty in the Eastern Province of Saudi Arabia, followed by bullous keratopathy, corneal scarring, re-grafts and stromal dystrophies. Both penetrating keratopathy and deep la-

mellar keratopathy appeared to be an emerging trend as the procedures of choice for dealing with corneal pathologies. Even though the number of Descemet's stripping automated endothelial keratoplasty surgeries was small, there was a significant increasing trend. We hope this study sheds light on the magnitude of corneal disorders requiring keratoplasty in our region and the need for further research for detection, prevention and early intervention.

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