

## Original Article

# Penetrating Keratoplasty – Indications in a tertiary care center in Nepal

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## Abstract

**Introduction:** Penetrating keratoplasty has become one of the most commonly performed transplant procedures where full thickness diseased host corneal tissue is replaced with healthy donor corneal tissue. Aims of penetrating keratoplasty include improvement in visual acuity, removal of infectious load, alleviate pain or even to simply save the anatomy of the eye. Visual improvement and removal of infection is the prime objective of majority of corneal grafts. The objective of the study was to evaluate various current indications of penetrating keratoplasty in central Nepal and its difference from the developed world.

**Material and methods:** A hospital based study of 36 patients who underwent penetrating keratoplasty between January 2014 and June 2015 was carried out at B.P. Koirala Centre for ophthalmic studies. Following clinical examination and investigations, surgical intervention was done when required. The patient data were recorded and followed up. Indication for surgery, investigations and demographic profile were assessed.

**Results:** Mean recipient age was 46.56 years (+/- 16.02 years). The male: female ratio was 1.57:1. The most common indication for penetrating keratoplasty was infectious keratitis (44.44%), followed by corneal opacity or scarring (30.56 %), re-grafts (13.89%), bullous keratopathy (2.78%), keratoconus (2.78%) and others (2.78%)

**Conclusion:** Though corneal diseases and indications for transplant surgery in developing countries are different from those in the western world, penetrating keratoplasty has emerged as one of the most successful way to reduce corneal blindness and to restore vision.

**Key words:** Corneal opacity, Corneal ulcer, Nepal, Penetrating keratoplasty, Trauma.

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## Introduction

Penetrating keratoplasty is a one of the most common transplant procedures in which full thickness diseased host corneal tissue is replaced with healthy donor corneal tissue. Aim of penetrating keratoplasty include improvement of vision, removal of infection load, removal of scarred cornea or sometimes

for tectonic support -to save the eye in Nepal and throughout Asia. But in developed countries like in North America, leading indication of PK is phakic or aphakic bullous keratopathy, in Australia and Europe leading indication is Keratoconus.(Bidaut-Garnier et al., 2016)

Historically, ‘keratoplasty’ has been attributed to Franz Reisinger, who first coined the term in a publication in 1824.(Anwar and Teichmann, 2002; Castroviejo, 1931; Mannis and Mannis, 2018) In 1906, Eduard Zirm was the first to documented successful human corneal transplant .(Anwar and Teichmann, 2002; Armitage et al., 2006; Castroviejo, 1931; Mannis and Mannis, 2018)Despite the fact that several of the fundamental principles of PK were identified by Zirm , it would take almost another half of a century to transform these early methods to the modern techniques of corneal transplantation. Ultimately, it would be the work of Ramon Castroviejo which would have the most profound influence on modern-day keratoplasty.(Castroviejo, 1931)

According to the World Health Organization(WHO), corneal diseases are a significant cause of vision loss and blindness - second only to cataract in overall importance. (“Vision impairment and blindness,” 2019.) Corneal opacities and trachoma constitute 8.7% of causes of global blindness as reported by World Health Organization in 2002. (Resnikoff et al., 2004) Unilateral corneal blindness are usually not included in the WHO data, but based on India’s bilateral-unilateral ratios of 0.1% to 0.56% prevalence.(Dandona and Dandona, 2003), it is estimated to occur in 23 million globally. More startling is the rate of new unilateral corneal blindness cases, with one prospective study in Nepal indicating an annual incidence of corneal ulceration to be 799 per 100,000 people, primarily unilateral ulcerations.(Whitcher et al., 2001) In Nepal, though the prevalence of trachoma reduced by 74%, the causes of corneal scarring and

phthisis, trauma and corneal infections did not reduce because of lack of primary eye care and treatment facilities in more remote rural areas. Relatively this became the more prominent cause of blindness.(“Epidemiology-of-Blindness-Nepal,” 2012.)

Often in our set up, patients present late or are referred after inadequate therapy which might lead to complications such as perforation, opacities, staphyloma or uncontrolled infection. So, timely and correct intervention as penetrating keratoplasty will not only preserve the integrity of the globe but also prevent vision loss. In Nepal, barriers to performing penetrating keratoplasties have gradually been overcome. With the establishment of the Nepal Eye Bank in 1996 and Hospital Cornea Retrieval Programme (HCRP) with recruitment of grief counsellors at Tribhuvan University Teaching Hospital (TUTH) from March 2012, the country has become self-sufficient in donor cornea supply. The availability of high-quality corneas, trained surgeons and staff, and modern facilities have made penetrating keratoplasty available as a therapeutic modality in Nepal.

The purpose of this study was to evaluate various current indications of penetrating keratoplasty in central part of Nepal and its difference from the developed world.

### Materials and methods

This was a hospital based, clinical study carried out at B. P. Koirala Lions Centre for Ophthalmic Studies (BPKLCOS), Tribhuvan University Teaching Hospital (T.U.T.H.), Kathmandu, Nepal. All the patients undergoing penetrating keratoplasty from 1<sup>st</sup> of January 2014 to 30<sup>th</sup> June 2015 (18 months), at BPKLCOS were included in the study. New patients undergoing penetrating keratoplasty were included in the study for a total of one year. These patients were followed up for next six months. Ethical clearance from the institutional review board, Institute Of Medicine (IOM) was obtained.

Informed and written consent was taken from the patients who were willing to take part in the study.

After taking an informed consent, patient's personal details, detailed clinical history, general physical examination and detailed ophthalmological examination were carried out in all the participants as per our study protocol. History of onset of various symptoms like pain, redness, photophobia, watering, discharge and diminution of vision was taken along with history of predisposing factors like corneal trauma, dry eyes, contact lens wear, prolonged use of topical or systemic corticosteroids, topical anti-glaucoma medication or previous ocular surgery. History also included systemic illness like diabetes, chronic debilitating illness especially malnutrition, collagen vascular disease, immunocompromised status, tuberculosis, was taken. Occupational history was also taken in those patients where it was relevant. History of treatment prior to visit to BPKLCO or to TUTH emergency was also noted.

General physical examination was done to rule out anemia, malnutrition and any other evidence of systemic illness. Visual acuity was assessed using the internally illuminated vision-drum with Snellen multiple optotype. For illiterate patients the E-chart was used to record the visual acuity. Visual acuity taken by Snellen's chart was converted to logMAR units for statistical analysis. Slit lamp examination was done using Haag Streit 900 slit lamp biomicroscope in appropriate magnification and illumination. The procedure included detailed examination of the eye starting from eyelids and going inwards systematically. The bulbar conjunctiva, the upper and lower tarsal conjunctiva and the precorneal tear film were examined. Detailed examination of the cornea was done which included the examination of cornea to note the presence of any corneal pathologies like epithelial defect,

ulcer, opacities, leucoma, descemetocoel, perforation, sealed perforation, degenerations or keratopathies. Apart from this if there was any sclera involvement, it was recorded. This was followed by examination of anterior segment, status of lens and vitreous, followed by posterior segment examination wherever possible. B-scan ultrasonography was done in all opaque corneas and hazy media to rule out any possible posterior segment pathology. Intra Ocular Pressure was taken whenever possible by Applanation or non-contact tonometer. Investigation for fitness for general anaesthesia was done wherever necessary.

The patients were divided into three age groups: 0 to 14 years, 15 to 49 years, and 50 years and above. Indications for keratoplasty were divided into seven main diagnostic categories: infectious keratitis, corneal opacity or scarring, re-grafts, bullous keratopathy, keratoconus, corneal dystrophy and degenerations, and others.

As per the indications, optical, therapeutic, tectonic or cosmetic penetrating keratoplasty was performed.

### **Surgical technique:**

With full aseptic precautions, the affected eye was painted and draped. Lids were separated using Barraquer's wire speculum.

- 1) Donor corneal button preparation  
The donor cornea with scleral rim was carefully placed on sterile cloth with the endothelial side up. An appropriate size trephine was used for punching of donor cornea. The donor button was carefully removed and placed in a sterile bowl with Mc-carey Kauffman media. The cut corneo scleral rim was also sent to eye bank if any further infection or adverse reaction was noted in donor cornea after keratoplasty.
- 2) Recipient bed preparation  
The trephine used for the recipient cornea was 0.5mm less than that used for donor

cornea. The trephine was carefully placed over the recipient cornea and partial thickness trephination was done. Side port blade was used to make an entry into the anterior chamber. Viscoelastic material was injected in the anterior chamber to maintain it. Using Castroviejo's corneal scissors, full thickness of the recipient cornea was cut along the already made trephine markings. The recipient cornea was cut in two equal halves and was sent for microbiological and histopathological examination. The donor corneal button was placed carefully on the recipient bed and aligned well. Suturing of the donor cornea to the recipient bed was done with 16 interrupted sutures with 10-0 nylon in all cases. The first suture put at 12'o clock is the most important for the proper alignment of the donor cornea and the second suture put at 6'o clock determined postoperative astigmatism. Rest of the cardinal sutures were put at 3'o clock and 9'o clock making sure that they are not too tight or loose. Rest 12 sutures were put radially around the donor button to the recipient bed. Sutures were buried on the donor side. Anterior chamber was maintained with balanced salt solution and was checked for any leaks. Sub conjunctival injection of gentamycin and dexamethasone or only gentamycin was given depending on whether the case is infectious or non-infectious . Eye speculum removed and the eye was patched till the next day. Additional procedures like synechiolysis, anterior vitrectomy, cataract extraction with PCIOL implantation was done in required cases. Peripheral iridotomy was done in therapeutic penetrating keratoplasty. Intraoperative complications noted were increased vitreous pressure, difficulty in

maintaining the anterior chamber, difficulty in releasing the synechiae and bleeding from iris vessels.

Data was analysed using Microsoft Excel 2010 and SPSS version 22. BCVA were converted from the Snellen units to the logarithm of minimal angle of resolution (logMAR).

## Results

A total of 36 eyes of 36 patients undergoing penetrating keratoplasty meeting the inclusion criteria were enrolled in the study. The mean age of the patients in this study was 46.56 ± 16.02 years. The youngest patient in this study was 5 years old whereas the oldest was 85 years old. 50 % (n=18) of patients belonged to the age group of 50 or more years (Table 1). 61.1% (n=22) of the patients were male and 38.9% (n=14) were female. Male to female ratio was 1.57:1.

**Table 1: Distribution of surgeries by age group**

| Age group (in years) | No. of patients (%) |
|----------------------|---------------------|
| 0-14                 | 2 (5.56)            |
| 15-49                | 16 (44.44)          |
| 50 or more           | 18 (50.00)          |
| Total                | 36 (100)            |

Most of the patients in this study were either farmers (30.5%) or housewives (30.5%). There was nearly equal distribution of patients coming from urban (47.22%, n=17) and rural (52.78%, n= 19) areas. 19 patients (52.8%) underwent surgery in right eye and 17 patients (47.2%) in the left eye. 50 % of the patients (n=18) had a duration of illness of less than one month, while 38.9% (n=14) had a duration of greater than a year (Table 2). 94.4 % (n=34) of eyes had a visual acuity of less than 3/60. Two eyes (5.6%) had a visual acuity in the range of 5/60 - 3/60 at the time of presentation.

**Table 2: Distribution of duration of illness in patients undergoing penetrating keratoplasty**

| Duration of illness | Number of cases n (%) |
|---------------------|-----------------------|
| <1 month            | 18 (50)               |
| < 1 year            | 4 (11.1)              |
| >1 year             | 14 (38.9)             |
| Total               | 36 (100)              |

The most common indication for penetrating keratoplasty was infectious keratitis (44.44%), followed by corneal opacity or scarring (30.56%), re-grafts (13.89%), bullous keratopathy (2.78%), keratoconus (2.78%) and others (2.78%) (Table 3)

**Table 3: Indications for penetrating keratoplasty**

| Indications for penetrating keratoplasty | Number of patients (%) |
|--|------------------------|
| Infective keratitis                      | 16 (44.44)             |
| Corneal opacity or scarring              | 11 (30.56)             |
| Re-grafts                                | 05 (13.89)             |
| Bullous keratopathy                      | 01 (2.78)              |
| Keratoconus                              | 01 (2.78)              |
| Corneal dystrophy and degeneration       | 01 (2.78)              |
| Others                                   | 01 (2.78)              |
| Total                                    | 36 (100)               |

Gram Stain, KOH wet mount preparation and cultures of corneal scraping were obtained for all patients with corneal ulcer (44.4%, n=16).

Gram staining was positive in 37.5 % (n = 6) specimens whereas KOH wet mount preparation for fungal pathogens was positive in 25% (n=4) of the specimens. Cultures were positive in 50% (n=8) samples.(Table 4, Figure 1)

**Table 4: Laboratory methods used identify the organisms and their results**

| Laboratory Method | Positive (n) (%) | Negative (n) (%) |
|-------------------|------------------|------------------|
| Gram Stain        | 6 (37.5)         | 10 (62.5)        |
| KOH Stain         | 4 (25)           | 12 (75)          |
| Culture           | 8 (50)           | 8 (50)           |

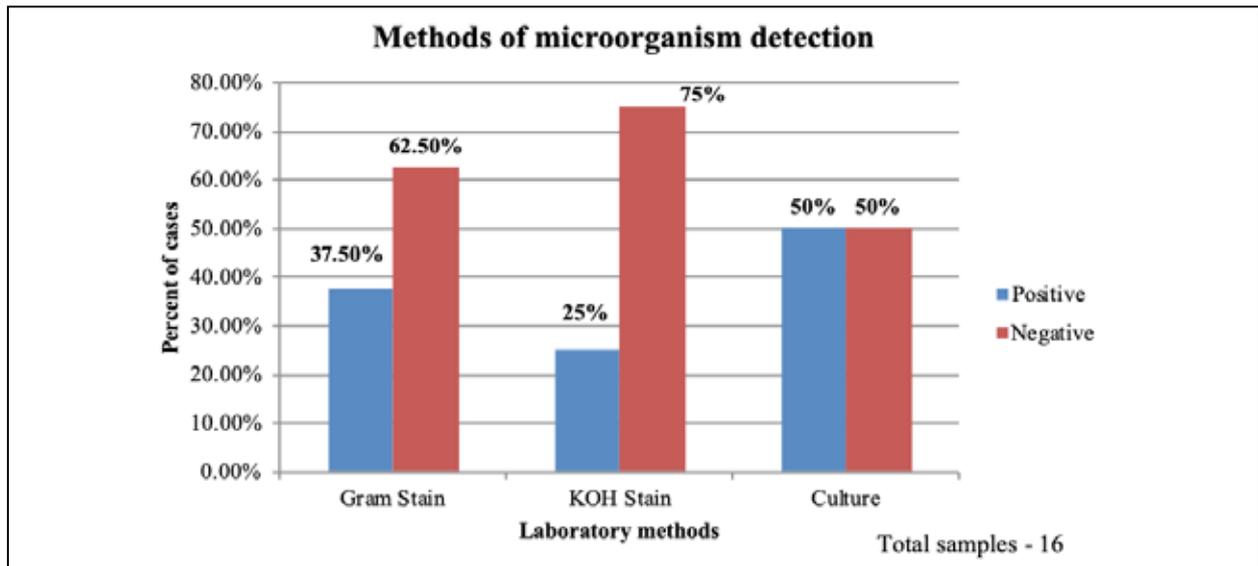
Gram positive bacteria were isolated in 31.25 % (n=5) of the specimens, while mixed Gram positive and negative bacteria were found in one of the specimens (6.25 %).(Figure 2)

Cultures were positive in 8 samples. Out of the 8 samples, streptococcus was isolated in 50 % (n=4).Mixed bacterial growth with staphylococcus and E.Coli was seen in one sample (12.5%). Likewise fungal growth of aspergillus was seen in one specimen.(12.5%) and fusarium was isolated in 25% (n=2). (Table 5)

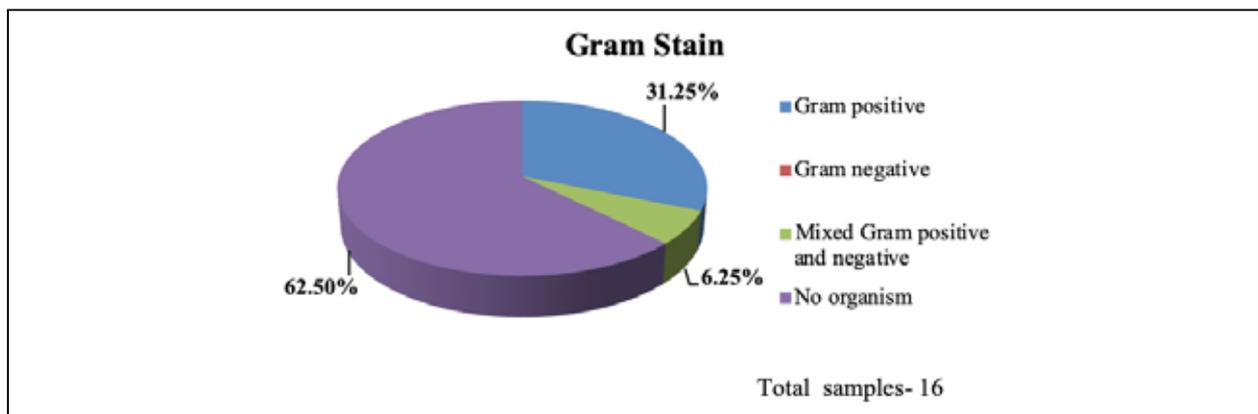
**Table 5: Culture reports from the samples from where the organisms could be isolated**

| Organism Isolated       | Number of cases n (%) |
|-------------------------|-----------------------|
| Staphylococcus + E.Coli | 1 (12.5)              |
| Streptococcus           | 4 (50)                |
| Aspergillus             | 1 (12.5)              |
| Fusarium                | 2 (25)                |
| Total                   | 8 (100)               |

The major cause of corneal opacity was adherent leucoma (n=4), followed by post infectious scarring (n=4) and Trauma (n=3). Indications for corneal re-grafts were endothelial graft rejection (n=3) followed by primary graft failure (n=2). There was 1 case of Salzmann's nodular degeneration of cornea. keratoconus and open globe injury each, respectively.



**Figure 1:** Laboratory methods and the detection rates of microorganisms



**Figure 2:** Gram Stain results from the corneal tissues

### Discussion

In our study, the patients who underwent penetrating keratoplasty had a mean age of  $6.56 \pm 16.02$  years. The youngest patient in this study was 5 years old whereas the oldest was 85 years old. The median age was 48.50 years. 50% (n=18). In another study done in Nepal by Tabin G C et al in 2004, the mean age at the time of surgery was 39.2 years ( $\pm 19.7$  years) and maximum number of surgeries were performed in the age group of 20-29 years. (Tabin et al., 2004) Similarly in a study done in India by Thomas M et al in

2015, majority of the cases who underwent penetrating keratoplasty, were in the 41-60 years (50%) age group. (Thomas et al., 2015) In another study conducted in Pakistan by Bhatti M N et al in the year 2009, mean recipient age was 38.1 years (range 14-82). (Bhatti et al., n.d.) However in developed world, the mean age of the recipient group was 56.7 years in a study conducted by Rahman I et al in United Kingdom in 2009. (Rahman et al., 2009) The mean age of surgery was 63 years in Canada and 67 years in the United States in the studies conducted there

respectively.(Maeno et al., 2000; Thompson et al., 2003)

Data obtained from our study is consistent with the results of similar studies done in developing countries where most of the cases that underwent penetrating keratoplasty belonged to the most productive age group socio-economically. This age distribution may also reflect a higher priority placed on eye surgery for younger patients who are more likely to be wage earners than the older ones. However, in developed countries, mean age of people who underwent surgery belonged to older age group owing to the fact that indication for surgery was different as compared to the developing world.

In this study, 61.1% (n=22) of the cases were males and 38.9% (n=14) were females. The male : female ratio was 1.57:1 which was similar to the study done by Tabin GC et al in which 61.3% were male, and 38.7% were female.(Tabin et al., 2004) Similarly, 53.3% were males and 46.7% were females in a study done by Thomas M et al.(Thomas et al., 2015) In Pakistan, in a study conducted by Bhatti MN et al, 73.3% were males and 26.7% females.(Bhatti et al., n.d.) Even though there are significantly more blind women (0.99/100) than blind men (0.68/100) in Nepal,(Brilliant et al., 1985) more men (61.1%) than women (38.9%) underwent keratoplasty. This finding may represent a bias against women receiving equal levels of surgical care in male-dominated family systems. It also might be due to a higher incidence of work-related ocular trauma in men.

Infectious keratitis was the most common indication (n=16, 44.4%) followed by corneal opacity and scarring (n=11, 30.56%) in our group of patients who underwent penetrating keratoplasty. This result was similar to the study done by Tabin GC et al in Nepal, where indication for penetrating keratoplasty included adherent leukoma (35%), corneal scar (37%), and therapeutic grafts for ulcerative keratitis

(9%), pseudophakic bullous keratopathy (PBK, 6%), keratoconus (4%), and aphakic bullous keratopathy (ABK,3%).(Tabin et al., 2004) Similarly Thomas M et al concluded that, in India most common indication for Penetrating keratoplasty was corneal opacity 36.7%.(Thomas et al., 2015) In another study done in India by Dadona L et al in 1997, the indications for PK were corneal scarring in 28.1% including adherent leukoma in 7.5%, regrafts in 17.1%, active infectious keratitis in 12.2%, aphakic bullous keratopathy in 11.8%, pseudophakic bullous keratopathy in 10.6%, corneal dystrophies in 8.4% including Fuchs' dystrophy in 1.2%, keratoconus in 6% and miscellaneous in 5.9%.(Dandona et al., 1997) Similarly in Northern India, indication for penetrating keratoplasty included corneal scarring (38.03%) followed by acute infectious keratitis (28.38%), regrafting (11.5%), aphakic bullous keratopathy (7.27%), pseudophakic bullous keratopathy (6.18%), and corneal dystrophy (3.85%).(Sony et al., 2005) In a study done in Pakistan by Bhatti M N et al, the leading indication was corneal scar (46.7%).(Bhatti et al., n.d.) This pattern is very different from that found in the developed world, where corneal scarring and ulcerations account for only 8.4% of cases performed in the United States.(Thompson et al., 2003) In contrast, PBK was the leading indication for surgery in two large American series accounting for 32% of cases in each study (1982-1996 (Thompson et al., 2003) and 1996-2000(Cosar et al., 2002)). Studies from Australia, France, Germany, and Sweden all found keratoconus to be the most common indication for penetrating keratoplasty, accounting for 29-31% of all cases.(Claesson et al., 2002; Jonas et al., 2002; Legeais et al., 2001) Fuchs dystrophy accounted for 9-23% of transplants in the developed world.(Claesson et al., 2002; Cosar et al., 2002; Dobbins et al., 2000; Jonas et al., 2002; Legeais et al., 2001) The indications for surgery in Nepal are consistent with findings

from other developing countries. In our study, infection was documented in 44.4% of all cases. Corneal scar and adherent leukoma together comprised 30.5% of all cases. Trauma was a risk factor in 58.3% of all cases. This figure may be underestimated because many corneal scars of unknown etiology are likely to be due to minor trauma and undiagnosed infections in early childhood. Our study population was at high risk for trauma because large percentages of patients were farmers, and many reported a history of injury by maize leaf or other agricultural products. As a whole, these findings support the high prevalence of ocular trauma in Nepal reported by the Bhaktapur Eye Study (Upadhyay et al., 2001) and suggest that even minor inciting events can progress to end-stage corneal disease.

However, our study data varies in indications of penetrating keratoplasty compared to the developed world. There was only one case of pseudophakic bullous keratopathy in our study. Similarly Fuch's endothelial dystrophy is a rare occurrence in our part of the world and requires investigations like specular microscopy for diagnosis. Our study had no cases of this type of dystrophy. However, there was a case of Salzmann's nodular degeneration and keratoconus each of which underwent penetrating keratoplasty in our study.

Eighteen patients (50%) had a duration of illness of less than one month, while 38.9% (n=14) had a duration of greater than a year in our study. 83.33 % (n=15) of eyes who presented within one month of illness were of corneal ulcer. Eyes with early presentation were the cases with corneal ulcer who had painful red eye and required early intervention. However, corneal opacities due to previous corneal insult or adherent leucomas are painless and hence even though present for a long time; delayed presentation can also be due to lack of awareness about treatment and unavailability of tissue.

## Conclusion

The most common indication of penetrating keratoplasty in our study was infectious keratitis, followed by corneal opacity and scarring and regrafts. On the basis of results of this study, it can be concluded that there is a definite place for penetrating keratoplasty as an emergency and for therapeutic benefits in the management of corneal blindness in a setup like ours. Patients are highly motivated to seek treatment once they are aware that surgical options are available. Indications for penetrating keratoplasty have changed in time because of the invention of lamellar surgeries and endothelial keratoplasty in India and other developed countries. However, in developing countries like Nepal and Bangladesh, most of the keratoplasty procedures performed are conventional full thickness penetrating keratoplasty. In western world, indications for penetrating keratoplasty have changed over time due to newer innovations. For instance, newer treatment options for keratoconus such as collagen cross linking, scleral contact lenses, Intacs rings and Bowman's membrane transplant has taken over a major portion of cases who might have undergone penetrating keratoplasty otherwise. In a developing country like Nepal, where corneal pathologies are emerging cause of blindness, penetrating keratoplasty can be a surgery which restores functional vision, resulting in recovered productivity and improved quality of life. Judicious patient selection, careful planning of surgical techniques, appropriate follow up care can enhance the chance of successful outcome.

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