Original article

Indications for keratoplasty in Nepal: 2005 - 2010

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Abstract

Introduction: Corneal disease, especially infective keratitis, is one of the major causes of visual impairment and blindness in developing countries. **Objective:** To find out the current indications for keratoplasty, how these indications have changed over time as well as how they are different from those in other parts of the world. **Materials and methods:** A retrospective study of a case series of 645 keratoplasty surgeries (589 patients) was conducted at the Tilganga Institute of Ophthalmology from January 2005 to December 2010. **Outcome measures:** The cases were evaluated in terms of demographic parameters, preoperative diagnosis and the type of surgery performed. **Results:** The most common indication for surgery was active infectious keratitis (264 eyes, 40.9 %), followed by corneal opacity (173 eyes, 26.8 %), regraft (73 eyes, 11.2 %), bullous keratopathy (58 eyes, 9.0 %), keratoconus (45 eyes, 7.0 %) and corneal dystrophy (11 eyes, 1.7 %). The mean recipient age was 41.7 ± 19.9 years with over a half of the patients between 15 to 49 years of age. More men (64.1 %) underwent keratoplasty than women (35.8 %). 59.8 % of the eyes with infectious keratitis had a perforated corneal ulcer. 49.7 % of corneal opacities were due to previous infectious keratitis. 72 % of regrafts were for endothelial failure of various causes. In older patients (> 50 years), bullous keratopathy was an important indication, after infectious keratitis. Keratoconus and corneal scar were major causes of keratoplasty in children of 14 years or less. Four percent of the patients had keratoplasty in both the eyes. 17.1 % of the patients who had one eye operated on had a blind fellow eye with a vision of less than 3/60. **Conclusion:** Currently, keratitis, either active or healed, is the major indication for keratoplasty, suggesting that improved primary eye health care is necessary to decrease the prevalence of corneal blindness.

Keywords: keratoplasty, infectious keratitis, developing countries, corneal blindness

Introduction

Corneal diseases are a major cause of visual impairment and blindness in developing countries. Corneal pathology is second only to cataract as an etiology for visual impairment in Nepal (Whitcher et al, 1997). Keratoplasty is frequently the only method of visual restoration for corneal blindness. In Nepal, the first keratoplasty surgery was done in 1967. In the subsequent three decades, few keratoplasty surgeries were performed because corneal tissue had to be imported from abroad.

The establishment of the Nepal Eye Bank in the Tilganga Institute of Ophthalmology (TIO) in 1994 permitted an increase in surgical volume; however, a growing population and an increasing prevalence

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of corneal blindness have made it difficult to keep up with the escalating tissue demands. This study examines the indications for keratoplasty, including demographics and types of surgeries performed in the TIO, a tertiary eye center in Kathmandu, Nepal. The findings of the study are compared with those in the published literature, including that of ours (Tabin et al, 2004).

Materials and methods

Patient records of all consecutive cases of keratoplasty performed in the TIO between January 2005 and December 2010 were retrospectively reviewed. Information collected from the records included: age, sex, the distance the patients had to travel to reach the TIO, preoperative diagnosis, preoperative visual acuity of both eyes, type of surgery (penetrating keratoplasty (PK), deep anterior lamellar keratoplasty (DALK), Descemet's stripping and automated endothelial keratoplasty (DSAEK), patch graft, or others) and the procedures performed in addition to the main surgery. The patients were stratified 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, regrafts, bullous keratopathy, keratoconus, corneal dystrophy, and others. Keratoplasty performed for active bacterial, fungal or viral ulcers were included under infectious keratitis. For patients with corneal opacity and regrafting, the causes for opacification and reasons for the graft failure were noted. The 'others' category included: metabolic corneal disorders, corneal degenerations and tectonic patch grafts for peripheral corneal diseases or scleral thinning.

Results

Demographics

A total of 645 eyes from 589 patients were reviewed for this study. The mean patient age at the time of surgery was 41.7 ± 19.9 years (range 15 months to 87 years). More than 50 % of the patients were 15 to 49 years old (Table 1). 378 (64.2 %) patients were male and 211 (35.8 %) were female.

Table 1: Distribution of surgeries by age group

Age group (years)	Surgical eyes	Patients
<15	40 (6.20%)	34 (5.80%)
15 to 49	356 (55.2%)	323 (54.8%)
50+	249 (38.6%)	232 (39.4%)
Total	645	589

One hundred and forty-four (24.5 %) patients were from the Kathmandu Valley, a 220 square mile area encompassing three urban districts: Kathmandu, Lalitpur and Bhaktapur. Three hundred and eighty-nine (66.0 %) came from the remaining 72 districts of Nepal (Figure 1). Fifty-six patients (9.50 %) were from foreign countries, the majority of them (49 patients, 87.5 %) from India. The others were from Bhutan (4), Cambodia (2) and Tibet (1). Of the patients who underwent keratoplasty for infectious keratitis, 79.8 % were from the districts outside the Kathmandu Valley and 8.9 % were from India.

Pre-operative visual acuity

The majority of the operated eyes (584 of 645, 90.5 %) had a pre-operative vision of < 6/60. Six eyes (< 1 %) had a vision of 6/6 to 6/18, and required keratoplasty for peripheral corneal disease or scleral thinning. Twenty-four patients (4 %) had bilateral keratoplasty done. Of the 565 patients who had only one eye operated on, 97 (17.1 %) had a blind fellow eye (vision < 3/60); 82 (14.5 %) of the fellow eyes were visually impaired with the best corrected vision of < 6/18 and > 3/60.

Indications

The most common indication for keratoplasty was infectious keratitis (40.9 %), followed by corneal opacity (26.8 %), regraft (11.3 %), bullous keratopathy (BK) (9.0 %), keratoconus (7.0 %) and corneal dystrophy (1.7 %) (Table 2 and Figure 2).

Table 2: Indications for keratoplasty

Indications	Surgical eyes
Infective keratitis	264 (40.9%)
Corneal opacity	173 (26.8%)
Regraft	73 (11.3%)
Bullous keratopathy	58 (9.0%)
Keratoconus	45 (7.0%)
Corneal dystrophy*	11 (1.7%)
Other#	21 (3.3%)
Total	645

*The different types of corneal dystrophy include congenital hereditary endothelial dystrophy (CHED) (3 eyes), stromal dystrophy (6 eyes) and Fuchs' dystrophy (2 eyes).s

[#]Scleral thinning, metabolic diseases, corneal degenerations,[+] Mooren's ulcer, limbal dermoid, corneal trauma, squamous cell carcinoma, exposure of glaucoma drainage implant

The types of corneal degeneration included Terrien's marginal degeneration and Salzmann's nodular degeneration. All of the infectious keratitis cases by definition had active infections. One hundred and fifty-six eyes (59.8 %) had perforated corneal ulcers and 106 eyes (40.1 %) had ulcers which were either not responding to treatment or were impending to perforate. The majority of the eyes with corneal opacity (86 eyes, 49.7 %) were due to prior keratitis (fungal, bacterial, or viral), followed by trauma (39 eyes, 22.5 %) (Table 3). The patients associated with past or present Vitamin A deficiency had bilateral corneal lesions and either one or both eyes were operated on. Table 4 shows that 72.6 % of the graft failures were due to endothelial decompensation, followed by infectious keratitis (13.6 %).

Table 3: Causes of corneal opacity

Causes of corneal opacity	Surgical eyes
Infective keratitis	86 (49.7%)
Microbial keratitis	*50(58.1%)*
Viral keratitis	*36 (41.9%)*
Trauma	39 (22.5%)
Unspecified	32 (18.5%)
Vitamin A deficiency	9 (5.20%)
Others*	7 (4.0%)
Total	173

* Unspecified interstitial keratitis, corneal scar of congenital glaucoma, chemical injury

Of the eyes with BK, 40 (68.9 %) had a posterior chamber intraocular lens (PCIOL), 8 (13.7 %) had an anterior chamber intraocular lens (ACIOL), nine (15.5 %) were aphakic and one was phakic (1.72 %). Fity-five eyes (94.8 %) with BK were sequellae of cataract surgery and the remaining were due to corneal trauma.

Stratifying by age (Table 5), the most common indications for surgery were infectious keratitis and corneal opacity in the 15 to 49 years group, and infectious keratitis and BK in the over 50 years group. Corneal opacity and keratoconus were the most common causes for keratoplasty in children under 15 years of age.

Table 4: Causes of graft failure

Graft pathology	Surgical eyes
Endothelial failure	53 (72.6%)
Endothelial rejection	*16(30.2%)*
Primary failure	*9 (17.0%)*
Glaucoma	*4(7.60%)*
Cataract surgery	*1 (1.90%)*
Other	*23 (43.3%)*
Infective keratitis	10 (13.7%)
Microbial keratitis	*3 (30.0%)*
Viral keratitis	*7 (70.0%)*
Trauma	5 (6.85%)
Others*	5 (6.85%)
Total	73

*Vascularization, astigmatism due to patch graft, recurrence of primary disease

Table 5: Indications for keratoplasty in < 50, ≥50 age group and ≤14 years

Indications		15 to 49 year (Surgical eyes)	≥50 years (Surgical eyes)	≤14 years (Surgical eyes)
Infective keratitis		142 (39.8%)	114 (45.7%)	8 (20.0%)
	Perforated ulcer	*87 (61.3%)*	*66 (57.9%)*	*5 (62.5%)*
	Non healing ulcer	*55 (38.7%)*	*48 (42.1%)*	*3 (37.5%)*
Corneal opacity		113 (31.7%)	47 (18.8%)	13[I] (32.5%)
Regraft		44 (12.3%)	27 (10.8%)	2 (5.00%)
Bullous keratopathy		8 (2.2%)	49 (19.6%)	1 (2.50%)
Keratoconus		31 (8.7%)	1 (0.4%)	13 (32.5%)
Corneal dystrophy		6[II] (1.6%)	2[#] (0.8%)	3[##] (7.50%)
Others*		12 (3.3%)	9 (3.6%)	0 (0%)
Total		356	249	40

*Corneal degeneration, Mooren's ulcer, corneal trauma, limbal dermoid, metabolic disease, sclera thinning, squamous cell carcinoma, exposure of glaucoma drainage implant

[i]Includes scar from congenital glaucoma (2 eyes); healed infective keratitis (4 eyes); vitamin A related (4 eyes); traumatic scar (3 eyes)
[ii]Stromal dystrophy
[#]Fuchs' dystrophy
[##]Congenital hereditary endothelial dystrophy

Table 6: Types of keratoplasties performed

Procedures	Surgical eyes
Penetrating keratoplasty (PK)	560 (86.8%)
Deep anterior lamellar keratoplasty (DALK)	46 (7.1%)
Descemet's stripping automated endothelial keratoplasty (DSAEK)	19 (2.9%)
Patch graft	10 (1.5%)
Others*	10 (1.5%)
Total	645

* Scleral graft, lamellar graft, rotational graft, keratoprosthesis

Table 7: Procedures performed alongside keratoplasty

Keratoplasty	Associated procedure	Surgical eyes
PK	ECCE PCIOL	96 (76.2%)
	Secondary IOL	9 (7.14%)
	ECCE	5 (3.97%)
	Removal of IOL	3 (2.37%)
	Intravitreal injection	3 (2.37%)
	Others*	8 (6.45%)
DSAEK	ECCE PCIOL	2 (1.59%)
Total		124

* Core vitrectomy, intracapsular cataract extraction, exchange of IOL, tarsorrhaphy

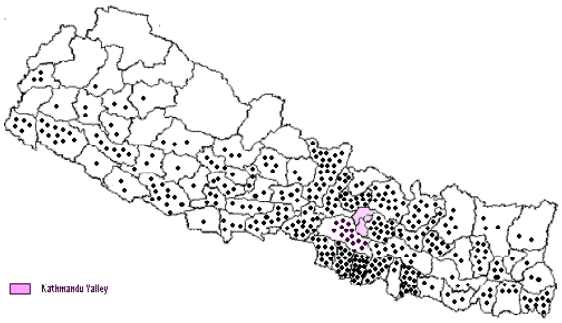

Figure 1: Geographic distribution of the study patients in Nepal

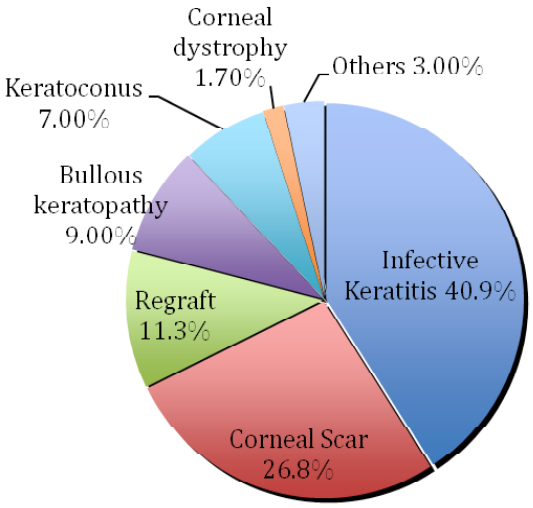

Figure 2: Indications for keratoplasty surgery

Surgical information

The vast majority of the surgeries performed were penetrating keratoplasties (PK) (560 eyes, 86.8 %). There was a much smaller number of DALK (46 eyes, 7.1 %), DSAEK (19 eyes, 2.9 %) and patch grafts (10 eyes, 1.5 %) (Table 6).

124 eyes (19.2 %) had additional procedures performed simultaneously with the main surgery, the majority (76.2 %) being extracapsular cataract extraction (ECCE) with PCIOL implantation (Table 7).

There was a 19.5 % increase in the overall number of keratoplasties performed in this study period, compared to that of our report of the period of 1994 to 1999 (Tabin et al, 2004).

Discussion

Demographics

In this study, the mean age of the patients was similar to that reported from India (Sony et al, 2005; Dandona et al, 1997) and China (Xie et al, 2009), but quite different from that of the UK and the US, where the mean age of the subjects was 54 and 63 years respectively (Yousuf et al, 2004; Ghosheh et al, 2008). The young age of keratoplasty patients in the developing world implies that corneal blindness is more prevalent in the working age population, which could profoundly affect the economic condition of the families and of the nation as a whole.

By gender, more males underwent keratoplasty than females (1.79:1), similar to that in India (Sony et al, 2005; Dandona et al, 1997); but in China, this ratio was even greater (2.7:1) (Xie et al, 2009). The ratio was lower in the UK (1.2:1) (Yousuf et al, 2004), and was seen to be flipped in the USA (0.88:1) (Ghosheh et al, 2008). The observed trends in the developing countries may be explained by two different gender bias theories. Firstly, males frequently have more privileged access to health care and treatment facilities, and thus may have made up more of the surgical population. Secondly, the typical male occupations in the developing world (i.e., agriculture and hard labor) could have made them more prone to work-related trauma, leading to keratitis.

Keratoplasty in patients under the age of 15 years accounted for only 40 eyes (6.2 %), which is similar to the proportion in France (5.2 %) (Legeais et al, 2001) (Tables 1 and 5). As mentioned previously, keratoconus and corneal opacity were the most common indications for surgery in the under 15 years group (32.5 % each), followed by infectious keratitis (20 %) (Table 5). In the USA, a review of 106 pediatric keratoplasties showed congenital corneal opacity and dystrophy as 61 %, while infectious causes accounted for 18.4 % and keratoconus for only 3.3 % (Huang et al, 2009). In India, 43 % of pediatric keratoplasties (out of 168) are reportedly done for healed or active keratitis and 33.9 % for congenital causes but none for keratoconus (Sharma et al, 2007). A small pediatric sample size was the limitation of our study.

Although the Nepal Eye Bank has been providing a greater number of corneas than previously, there are still barriers to performing a greater number of keratoplasties in Nepal. These include a continued shortage in locally available corneal tissue, an undersupply of corneal surgeons, and, especially in the peripheral hospitals, lack of the surgeon's time for corneal subspecialty care due to the high demand for other ophthalmologic services. The high demand for corneas necessitates criteria for selecting patients for surgery in non-emergency situations. One of the major factors taken into account when projecting graft survival is the likelihood of the patient's follow-up. In Nepal, it is difficult for patients from remote areas to reach a tertiary eye center, so patients need to be selected on the basis of possible follow-up care. Exceptions to this selection criterion include therapeutic keratoplasty and bilaterally blind patients. Both these groups should naturally get priority on the waiting list.

A significant portion of the patients in this study lived in the Kathmandu Valley and the surrounding districts (Figure 1), due to the above selection criteria. However, fewer patients were from the Kathmandu Valley in this study than were in our previous study. Previously, 49.4 % of the keratoplasty patients were from the Kathmandu Valley (Tabin et al, 2004), whereas only 24.5 % of the patients were from the Valley in this study. The reduced proportion of the patients from the Valley is likely because the TIO performs a larger number of emergency eye saving transplants at present, whereas in the past, the majority of the transplants were done for optical purpose (72 %). The majority of the patients (79.8 %) needing keratoplasty for infective keratitis in this study were from outside the Valley.

Infectious keratitis

The leading indication for keratoplasty in this study was active infectious keratitis (40.9 %), which differs from the reports from India, Taiwan and Thailand, where active infections were second (Sony et al, 2005; Dandona et al, 1997), third (Chen et al , 2001) and fourth (Chaidaroon et al, 2003) respectively. Although our findings were more similar to those in other developing countries, where corneal ulceration is considered a silent epidemic (Whitcher et al, 1997), the similarities do not carry over to the developed world. In the UK, for example, only 8.3 % of grafts were done for infective keratitis (Yousuf et al, 2009). The high rates of active infection demand the need for primary eye care services.

Since the TIO is a tertiary referral centre in Nepal for cornea service, many patients with ulcerative

keratitis present at a severe, perforated or intractable stage requiring keratoplasty.

Corneal scar

Corneal scar is the second commonest cause for keratoplasty (26.8%). In this study, the leading cause of corneal opacification was previous infective keratitis, followed by trauma. The proportion of trauma related scars is similar to that reported from India (16.7-21.0%) (Sony et al, 2005; Dandona et al, 1997). Corneal scar is a much less frequent indication for keratoplasty in the developed world, accounting for only 2.5 % of the keratoplasties in France (Legeais et al, 2001) and <2.5 % in the USA (Ghosheh et al, 2008). The majority of the cases with unspecified etiology (18.5%) for corneal scarring in our study are also likely to be attributable to keratitis. In the developing world, keratitis is frequently associated with agriculture related trauma (Whitcher et al, 1997), lack of education, lack of accessibility to eye care facilities and poverty.

Ten years ago, at the time when keratoplasty was started regularly at the TIO, the primary indication was corneal scar (72%) (Tabin et al, 2004). During that time, there had been a large backlog of the patients blind from old infectious keratitis; surgery for active infectious keratitis was less commonly performed. As the awareness of eye diseases in Nepal has improved, the number of patients presenting to the corneal service for active infectious keratitis treatment has increased. This is likely to explain the increased proportion of keratoplasty performed for active infectious keratitis in this report. As Nepal's primary and secondary eye health services expand, it is anticipated that infectious keratitis will be more successfully treated or prevented so that less therapeutic and tectonic keratoplasties will be required.

Regraft

It was the third indication for keratoplasty in our study (11.3%). Graft failure was the most common indication for keratoplasty in the UK (41%) (Ghosheh et al, 2008) and accounted for 22 % of the cases in the USA (Yousuf et al, 2009) versus 5.28 % in Iran (Kanavi et al, 2007). In our study, the majority of graft failures were due to endothelial decompensation (Table 4), whereas in India, ocular surface problems (33 %), allograft rejection and endothelial failure (together 28.2 %) were the major causes (Vanathi et al, 2005). In the UK, 42 % of regrafts were for endothelial failure and 16.5 % for rejection (Yousuf et al, 2009). It is recognized that keratoplasty in the setting of active inflammation decreases the long term survival rates of the corneal graft (Yorston et al, 1996). As the rates of keratoplasty continue to rise in Nepal and surrounding countries, regrafting is likely to make up a larger proportion of the indications for keratoplasty in the near future.

Bullous keratopathy

The fourth indication for keratoplasty was BK (9 %). In the USA and New Zealand, it was one of the top two reasons for keratoplasty (Ghosheh et al, 2008; Edwards et al, 2002). In our study, 48 eyes (82.7 %) were pseudophakic (PCIOL [68.9%], ACIOL [13.7%]) and only 15.5 % were aphakic. Since the establishment of the Fred Hollows Intraocular Lens Laboratory in the TIO in 1994, ECCE with PCIOL implantation has been possible to be performed at a lower cost and more widely, making aphakia less common than in the other developing countries, where the prevalence of aphakic BK is higher (Sony et al, 2005; Dandona et al, 1997; Kanavi et al, 2007). The proportion of keratoplasties performed for BK is expected to increase in the near future as more preventable causes of keratoplasty drop and cataract surgery rates increase.

Keratoconus

Keratoconus ranks fifth in our study (7%), and was similar to rates in India (2% to 6%) (Sony et al, 2005; Dandona et al, 1997), but lower than that in New Zealand, France and Iran, where it accounted for 29 % to 45 % of cases (Legeais et al, 2001; Kanavi et al, 2007; Edwards et al, 2002). In the UK and USA, keratoconus was the third common cause for keratoplasty accounting for 15 - 16 %,

whereas in Taiwan, it played a role in only 2.5 % of the cases (Yousuf et al, 2009; Ghosheh et al, 2008; Chen et al, 2001). The low rates of keratoconus in Nepal and India may be due to the greater ethnic diversity than in the European populations (Mamalis et al, 1992).

Dystrophy

The corneal dystrophies were relatively uncommon indications (1.7%) in our study, and Fuchs' dystrophy was negligible. The studies from India have reported slightly higher rates of non-Fuchs' dystrophy (3.8 - 8.4 %), but similar rates of Fuchs' dystrophy (0.74 - 1.2 %) (Sony et al, 2005; Dandona et al, 1997). In the UK and USA, <4 % of keratoplasties were done for non-Fuchs' dystrophy and around 10 % for Fuchs' dystrophy (Yousuf et al, 2009; Ghosheh et al, 2008). The more pressing need for surgery for active or healed infectious keratitis in Nepal may be the reason for the relatively low number of keratoplasties for dystrophy.

Surgical progress

Major advances in corneal surgery have been made in the TIO in the past decade. Improvements in techniques have increased the number of DALKs and DSAEKs performed. The long term benefits of DALK surgery, where endothelial failure and rejection are less of a risk, cannot be overemphasized in a country like Nepal, where people live far from an eye hospital and often cannot come for follow-up visits (Tabin et al, 2004). The first keratoprosthesis surgery was successfully performed at the TIO on a one-eyed patient with recurrent graft failure. Nevertheless, PK remains the most common procedure due to the predominance of infectious etiologies and because corneal leukomas are often of full thickness, necessitating PK (Table 6). The ECCE and PCIOL is the commonest procedure performed along with the keratoplasty because of increased prevalence of complicated cataract associated with keratitis (Table 7). Two eyes with Fuch's dystrophy underwent combined ECCE and PCIOL and DSAEK in the present study.

Conclusion

The inications for kertoplasty in Nepal, in decreasing order of frequency are infective keratitis, corneal opacity, regraft, bullous keratopathy, keratoconus and corneal dystrophy. The importance of reducing corneal blindness is clear by the number of working age patients affected, with probable harmful socioeconomic impacts.

The shift in indications for keratoplasty over the past decade demonstrates that it is possible to expand a keratoplasty program in a developing country over a relatively short period of time and outlines where attention should be focused for future progress.

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