Outcome of Optical Keratoplasty for Corneal Scar due to Infective Keratitis

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ABSTRACT

Introduction: Corneal opacity is an important cause of blindness in developing countries.

Objectives: This study analyzes optical keratoplasty performed for corneal opacity due to infective keratitis.

Materials and methods: This is a retrospective study of all consecutive cases of optical keratoplasty performed between 2011 and 2014 (four-year period) for healed infective keratitis. Cases with less than two months' follow-up were excluded during outcome evaluation. Comparison was made between keratoplasty for Microbial and Viral (herpetic) Scar.

Results: Ninety-three eyes of 93 patients were enrolled. Fifty-nine (63.4%) were male. Average age of patients was 38.9±19.5 years. Average donor endothelial cell count was 2713±434.5 cells/mm2. Fifty-four (58%) corneal scars were due to microbial keratitis and others were herpetic. Eighty-five (91.4%) had undergone penetrating keratoplasty. Eighty-eight (94.6%) cases were included for outcome analysis. Average follow-up duration was 37±27.5 months. Fifty-two (59%) had clear graft at their last visit. Twenty-three (26.1%) grafts had endothelial failure and 13 (14.7%) grafts failed due to late onset keratitis. Twenty-five (28.4%) had vision of ≥6/18. Rejection occurred in 24(27.2%) and glaucoma in 11(12.5%). Post-operatively viral keratitis in the graft occurred significantly more inViral Scar Group (38.6%, n=15) than in Microbial Scar Group (5.5%, n=3). But there was no significant difference in graft clarity, rejection, vision and secondary glaucoma between the two Groups.

Conclusion: Outcome of keratoplasty for post-infectious scars was found fairly satisfactory. Although occurrence of viral keratitis was higher in case of keratoplasty done for Viral Scars, the final result was similar to that of microbial scar.

Key words: Infective keratitis, Penentrating keratoplasty, Viral scar.

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INTRODUCTION

Microbial keratitis is an important cause of blindness in developing countries (Whitcher et al, 1997). Herpes simplex virus (HSV) keratitis is a cause of visual morbidity worldwide (Rezende et al, 2004). Keratoplasty is the surgical procedure for treatment of significant viral or microbial corneal scars. Corneal scars do not have as good graft survival rate as compared to keratoconus, corneal dystrophies, and degenerations; vascularized herpetic corneal scars may have even less graft survival rates (Barraquer et al, 2019; Arya et al, 2018; Joshi et al, 2012). Our previous report shows that in our country, 41% of keratoplasties are performed for active corneal infection and 26.8% for corneal scars, half of which were due to healed infective keratitis (Bajracharya et al, 2013). Outcome of therapeutic penetrating keratoplasty (TPK), performed in our institute for active infective keratitis was already studied (Bajracharya et al, 2015). The current study is undertaken to know the outcome of primary keratoplasty done for healed microbial keratitis and herpetic viral scars in a tertiary referral center in Nepal. This study will enable us to determine baseline information, will provide prognostic guidelines, and will help us to identify areas that need improvement.

MATERIALS AND METHODS

This is a retrospective chart review of all consecutive cases of optical keratoplasty performed between 2011 and 2014 (four year period) for healed infective keratitis at Tilganga Institute of Ophthalmology, Kathmandu, Nepal. Institutional ethical approval was taken before commencing the study (Reference number: 25/2021). Primary keratoplasty performed for Viral or Microbial Scars were enrolled. Scars were categorized as herpetic on the basis of clinical features, decreased corneal sensation, and past documents. For inclusion in the study, the Viral Scars should have undergone keratoplasty after at least six months of recurrence free period (which is the usual protocol). Microbial Scars were those which were due to keratitis, which (i) had grown bacterial or fungus in corneal culture or (ii) had clinical features of infective keratitis and had responded with antimicrobials (in case of culture-negative cases) and (iii) did not have characteristics to suggest viral etiology. Optical keratoplasty performed for corneal trauma, chemical injury, corneal degeneration, vitamin-A deficiency, dystrophy, and scars of uncertain etiology were excluded. Data collected included demographic parameters, type of surgery performed, and donor tissue details. Cases which had follow-up period of less than two months were not included in the outcome analysis. Ocular status was evaluated in terms of graft clarity; best corrected visual acuity (BCVA), development of glaucoma and cataract, rejection and post-operative viral keratitis. Comparison was made between the outcome of keratoplasty for Viral and Microbial Scar.

Patients underwent either penetrating keratoplasty (PK) or deep anterior lamellar keratoplasty (DALK) depending upon the depth of the scar. Post-operatively, prednisolone acetate was started six times per day and tapered slowly. Prophylactic antibiotics ciprofloxacin or ofloxacin was given four times a day for eight weeks. Patients with Viral Scar were given at least three months of oral acyclovir 400 mg twice a day. Viral keratitis occurring in the grafts was treated with topical steroids, oral or topical

acyclovir, with or without topical prophylactic antibiotics.

Statistical analysis : p value was calculated from Chi Square value or Fisher Extract test. P value of less than 0.05 is considered significant.

In the text, the terms 'microbial scar 'and 'non-herpetic scar' are used to denote healed microbial keratitis due to bacterial or fungal infection. 'Viral Scar' and 'herpetic Scar' meant non-active corneal HSV disease.

RESULTS

Ninety-three eyes of 93 patients had undergone keratoplasty for corneal scars due to infective keratitis. Among them, 59(63.4%) were male. Average age of the patients was 38.9±19.5 years (range: 4 to 75 years). Sixty-three (67.7%) were from rural districts of Nepal and 12(12.9%) from India. Fifty-four (58%) cases were Microbial Scars and 39(42%) were Viral Scars.

Average donor corneal age and endothelial cell count was 60.8±18.5 years and 2713±434.5 cells/mm^2 respectively. Mean recipient rim size was 7.7±0.28mm. The donor size was exceeded by 0.5 mm in PK and by 0.25mm in DALK.

Eighty-five (91.4%) patients had undergone PK and eight (8.6%) cases underwent DALK. Thirty-five of 85 PK cases (41.1%) were combined with cataract extraction out of which 32 had posterior chamber intraocular lens implantation and three cases were left aphakic due to posterior capsular rent and vitreous loss.

In the early post-operative period, five cases underwent re-suturing and two underwent anterior chamber (AC) deepening procedure. Four cases (preoperatively having Viral Scars) had non-healing epithelial defects which had to be managed with tarsorrhaphy or bandage contact lens.

Five cases (all had microbial scars preoperatively) had follow-up duration of less than two months, hence were not included in the outcome analysis. Average follow-up for the remaining 88 patients was 37±27.5 months. Fifty-two (59.0%) had clear graft at the last visit, 17(19.3%) had glaucoma, 24(27.2%) had rejection, seven (7.9%) had late onset microbial keratitis in the graft, and 18(20.45%) had recurrent viral keratitis. Four out of 17 glaucoma cases were preexisting. Two of the glaucoma cases underwent surgical treatment. Ten out of 24 rejections (41.6%) were reversed with treatment. Twenty-three (26.1%) grafts failed due to endothelial decompensation and 13 (14.7%) failed due to late onset keratitis in the graft with subsequent stromal scarring (n=9) or melting (n=4). The latter four had to undergo TPK. On follow-up of 38 phakic eyes, 21 (55%) had variable grades of cataract. Of them, ten underwent cataract surgery in the later post-operative period.

Forty-four (50%) achieved BCVA ≥6/60 (Table 1). Causes of vision <6/60 was graft edema (n=23), scarred graft (n=13), cataract (n=5), glaucoma (n=6), clear graft but with irregular astigmatism (n=13) and others (amblyopia and posterior segment pathologies, n=5). Some cases had more than one cause for poor vision.

Keratoplasty for Microbial Scars were grouped as I (n= 49) and those done for Viral Scars as Group II (n=39). Average age of cases in Group I and group II was 40.7±21.1 and 36.4±17.3 years respectively (p = 0.66 for patients <40 years in each group). Male: Female ratio was 2:1 in Group I and 1.43:1 in Group II. Forty-four

(81.4%) and 29 (74.3%) of patients were from rural area in Group I and II respectively. On comparison of post-operative events and status, there was no statistically significant difference in rejection rate, graft clarity, secondary glaucoma, and BCVA between the two groups, but viral keratitis occurred significantly more in Viral Scar Group (Table 2). Some of the viral keratitis episodes in either group were severe enough to cause stromal scarring and resultant graft failure (Table 3). Two of 10 rejections and eight of 14 rejections were reversed with treatment in Group I and Group II respectively.

Table 1: Post-operative vision

Vision	n (%)
≥ 6/18	25 (28.4)
<6/18 ≥6/60	19 (21.6)
<6/60 ≥3/60	6 (6.8)
<3/60 ≥ PLPR*	38 (43.1)
No perception of light	-
Total cases followed up	**88 (100%)**

**PLPR: Perception of light and projection of rays*

Table 2: Post-operative status of keratoplasty for Microbial and Viral Scar

Group	Rejection Episodes n (%)	Viral keratitis in graft n (%)	Secondary glaucoma n(%)	Clear grafts n(%)	Vision 6/18 or more n(%)
Group 1, (Microbial Scar, n=49)	10 (20.4)	3 (6)	13* (26.5)	28 (57.1)	11 (22.4)
Group 2, (Viral Scar, n=39)	14 (35.9%)	15 (38.4)	4 (10.3)	24 (61.5)	14 (35.9)
P value	0.105	<0.001	0.055	0.677	0.164
Total (88)	24	18	17	52	25

**Out of 13, 4 were preexisting*

Table 3: Causes of graft failure

Group	Number of failed grafts	Causes of graft failure		
		Endothelial failure	Stromal scarring / thinning or perforation	
			Severe viral keratitis in the graft	Microbial keratitis in the graft
Group I, (Microbial scar, n=49)	21	16	2	3[#]
Group II, (Viral Scar, n=39)	15	7	6*	2*
Total (n=88)	52	23	8	5

[#]*Two had to undergo therapeutic penetrating keratoplasty (TPK)*

**One had to undergo TPK*

DISCUSSION

The mean age of our patients was 38.9±19.5 years with male predominance. In developing countries, corneal infections occur mostly due to agricultural or labor-related trauma. Hence working age group and males are affected commonly (Bajracharya et al, 2020).

Most patients in our study were from rural area which correlated with our previous study (Bajracharya et al, 2020). Lack of preventive care and health care accessibility in rural area, delay in seeking medical help and delay in referral, all contribute to significant corneal scarring.

We compared our current study of optical keratoplasty for healed infective keratitis with our previous study of TPK done for active infective keratitis (Bajracharya et al, 2015). We found that in optical keratoplasty, 5(5.3%) underwent re-suturing and 2(2.1%) underwent AC reformation procedure compared to 13.8% and 27% in TPK respectively. We found graft clarity in optical keratoplasty as 52 (59%) versus 37.2% in TPK at similar follow-up periods; forty-four (50%) had vision of ≥6/60 versus 25.2% in TPK. Similarly, secondary glaucoma was present in 19.3% (n=17) versus 43.4% and postoperative cataract was present in 55% versus 65.8% (Bajracharya et al, 2015). Better outcome in optical keratoplasty was because the surgery had been done after resolution of infection and inflammation.

Pan et al (2012) (in China) and Omar et al(2013) (in Saudi Arabia) had studied outcome of optical PK collectively for various indications (bullous keratopathy, keratoconus, herpetic / non-herpetic scar, regraft, and dystrophies) and mentioned three-year graft clarity of 65.1% and 90.7% respectively. Graft survival in their study was better than ours because keratoconus, dystrophy, degenerations or bullous keratopathy have better prognosis than other indications (Barraquer et al, 2019; Arya et al, 2018;Joshi et al, 2012). Arya et al (2018) mentioned graft clarity of 62.5% in non-herpetic scar and 55.6% in herpetic scar; they showed better graft clarity with bullous keratopathy (73.3%) and corneal dystrophy/degeneration (84.6%). In our study, graft clarity of 57.1% (n=28) in Microbial Scar Group and 61.5%(n=24)in Viral Scar Group was similar to that of Arya et al (2018). A study by Altay et al (2017) mentioned 65% graft survival at three years in herpetic scar.

Late post-operative keratitis can occur after keratoplasty due to risk factors like loose sutures, topical steroid, and decreased sensation. It can be the cause for graft failure. Different studies showed rate of infective keratitis after keratoplasty as 1.46 to 11.9% (Vajpayee et al, 2007). In the current study, overall, 13 (7.8%) developed late post-operative microbial keratitis (Table 3).

In our study, patients in Viral Scar Group were younger than in the Microbial Scar Group, but without statistical significance. However, in the study of Halberstadt et al (2002), patients undergoing keratoplasty for herpetic scar were significantly younger than those undergoing keratoplasty for non-herpetic scar. Male sex was predominant in each of the groups in our study. Other hospital-based studies also showed male predominance in patients undergoing keratoplasty for Microbial as well as Viral Scars (Halberstadt et al, 2002; Altay et al, 2017).

In our study, 38.4% (n=15) of grafts in Viral Scar Group had recurrence of virus post-operatively. Altay et al (2017) and Wu et al (2012) mentioned slightly lower rate recurrence of HSV keratitis (28.57% and 20.6% respectively) after keratoplasty in the quiescent herpetic scar. Recurrence of herpetic keratitis varies widely in different studies from 8.8 to 75%; higher rate of recurrence occurs when keratoplasty is done in active HSV keratitis than in quiet HSV scar (Vajpayee et al, 2007).

Grafts done for microbial scars also had viral keratitis post-operatively (6%) but it occurred significantly less than in Viral Group ($p < 0.001$) (Table 2). HSV is endemic throughout the world (Rezende et al, 2004). Cornea and trigeminal nerve may harbor HSV without clinically evident disease (Rezende et al, 2004; Halberstadt et al, 2002). Surgical trauma and topical steroids may trigger the reactivation in this group of people. Viral infection might also come from apparently normal looking donor cornea as well (Rezende et al, 2004; Halberstadt et al, 2002).

The preoperative and post-operative intraocular pressure was higher in the non-herpetic group in the study of Halberstadt et al (2002). We noted four cases (7.4%) of preoperative glaucoma in Microbial Scar Group and post-operatively also, greater proportion of patients were having secondary glaucoma in this group, although not statistically significant (Table 2).

In the study of Altay et al (2017) and that of Wu et al (2012), the rejection rates were 9.5% and 41.3% in keratoplasty done for quiescent herpetic scar respectively. In our study the rejection in Viral Scar group was 35.9 %(n=14) (Table 2). HSV recurrence in allograft may mimic rejection clinically and even co-exist (Altay et al,2017). This could be one of the reasons for variable rejection rates (over or underestimation) in different studies.

Halberstadt et al (2002) and Tabuchi et al (2002) reported that rejection occurred significantly more in herpetic scar group than in non-herpetic scar group but in contrast, in our study, rejection rates in the two groups was similar ($p=0.105$). However, in ours (Table 2) as well as in their studies, it was found that there was no significant difference in graft failure and visual outcome between the herpetic and non-herpetic scar groups.

Limitation of our study is that it is retrospective. Follow-up range was wide. Preoperative and post-operative diagnosis of viral keratitis had been on clinical grounds. Other factors related to prognosis like corneal vascularization, graft size, compliance in follow-up were not studied.

CONCLUSION

Optical keratoplasty for healed infective keratitis is found fairly satisfactory in our study. Final outcome of Viral and Microbial Scar after keratoplasty was similar. Visual outcome can be made better with correction of post-operative astigmatism and treatment of associated cataract. If patients with post-infectious scar are able to follow-up, there is no constraint in performing keratoplasty. Nevertheless, prevention and early treatment of infective keratitis is of prime importance to avoid keratoplasty which carries burdens of finance and long-term follow-up.

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