

THERAPEUTIC KERATOPLASTY IN FUNGAL KERATITIS

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HOW TO CITE THIS ARTICLE:

Srinivas, Dakshayani. "Therapeutic Keratoplasty in Fungal Keratitis". Journal of Evidence Based Medicine and Healthcare; Volume 1, Issue 8, October 15, 2014; Page: 1047-1060.

ABSTRACT: BACKGROUND: Fungal keratitis is one of the most difficult form of microbial keratitis for an ophthalmologist to diagnose and treat. It is challenging to treat a case of fungal keratitis and there has been an increase in number of fungal keratitis due to inadvertent use of antibiotics and steroids.¹ **AIMS & OBJECTIVES:** To study and analyze the results of therapeutic keratoplasty in treatment of fungal keratitis. **MATERIALS & METHODS:** This is a hospital-based clinical study of 20 patients with fungal corneal ulcer refractive to medical line of management attending outpatient department and cornea clinic at Regional Institute of Ophthalmology, Minto Ophthalmic Hospital B.M.C. These cases were treated surgically with therapeutic keratoplasty and their results were analyzed with respect to the efficacy of the procedure in curing the disease, maintenance of structural integrity of the globe, visual rehabilitation & usefulness of the procedure as a bed for future optical keratoplasty. **RESULT:** Out of 20 patients underwent TKP for fungal keratitis males predominated among those affected amounting to 12 eyes (60%) incidence, mean age of presenting being 41-50 yrs in 7 cases (35%), 17 of the 20 patients (85%) of them being outdoor workers and related to agricultural occupation, 15 of them (75%) had a positive history with vegetative matter, 16 cases (80%) presented with perforation. The globe integrity was maintained in 18 (90%) of patients, visual outcome poor in the range of PR accuracy in 16 eyes (80%), HM in 2 eyes (10%), PL – in 2 eyes (10%). Complications following the procedure included PED in 13 eyes (65%) which was reversible, secondary glaucoma in 7 eyes (35%) managed medically, iris prolapsed in 2 eyes (10%), wound leak in 9 eyes (45%) of cases due to loose suture that was resutured. One case went for phthisis bulbi. One patient did not come for follow-up. None of the cases showed recurrence. **INTERPRETATIONS & CONCLUSIONS:** Fungal corneal ulcer presents late to the ophthalmologist as the signs are more than symptoms, more common in rural patients, associated with outdoor workers more so those related to agricultural occupation, positively related to injury with vegetative matter. Treatment with TKP in severe fungal keratitis (perforated fungal keratitis and limbal involvement) graft rejection is seen in all the cases with poor visual outcome but with maintenance of structural integration. Hence TKP is a ray of hope for further optical keratoplasty.

KEYWORDS: Optical keratoplasty, phthisis bulbi, therapeutic keratoplasty, fungal keratitis, secondary glaucoma, perforation, vegetative matter, iris prolapsed, cyanoacrylate glues.

INTRODUCTION: Fungal keratitis is one of the most difficult forms of microbial keratitis for an ophthalmologist to diagnose and treat. It is challenging to treat a case of fungal keratitis and there has been an increase in number of fungal keratitis due to inadvertent use of antibiotics and steroids¹. The number of fungal keratitis in developing countries as compared to developed countries is definitely high. Fungal keratitis can be managed by medical line of management using Topical & systemic Anti-fungals, Topical & Systemic Anti-bacterials, to prevent superadded

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bacterial infections & Anti-inflammatory drugs. In case of impending perforations use of cyanoacrylate glues & bandage contact lenses can be used. Ultimately when all these measures fail one has to resort to the final modality that is therapeutic keratoplasty. Hence fungal keratitis is a surgical disease in most parts of the world¹. Studies have shown that approximately one third of them end up being medical treatment failure. or corneal perforations requiring surgical management i.e., Therapeutic Keratoplasty. Corneal blindness accounts for up to 10% of all cases of blindness.² Incidence of fungal keratitis has definitely increased in India and has become a surgical disease because,

1. It is difficult for most of the ophthalmologists to diagnose and treat fungal corneal ulcers.¹
2. Symptoms are less than signs and hence patients often present late to the clinic.³
3. Inappropriate use of antibiotics and steroids can flare up the fungal keratitis.³
4. As the disease is more in rural setup where people are ignorant, they often present with impending perforation or perforated corneal ulcers.⁴

AIMS AND OBJECTIVES OF THE CURRENT STUDY: Corneal blindness accounts for up to 10% of all cases of blindness². As the disease is more in rural setup where people are ignorant, they often present with impending perforation or corneal ulcers. Hence there arises a need to study the efficacy of various surgical procedures in treatment of fungal keratitis.

Here is a hospital based study which analyses the results of therapeutic keratoplasty in fungal keratitis that is refractory to medical line of management.

AIMS & OBJECTIVES: To study and analyze the results of therapeutic keratoplasty in treatment of fungal keratitis.

MATERIALS AND METHODS:

Method of collection of data: This is a hospital-based clinical study of 20 patients with fungal corneal ulcer refractive to medical line of management attending outpatient department and cornea clinic at Regional Institute of Ophthalmology, Minto Ophthalmic Hospital B.M.C. These cases were treated surgically with therapeutic keratoplasty and their results were analyzed with respect to the efficacy of the procedure in curing the disease, maintenance of structural integrity of the globe, visual rehabilitation & usefulness of the procedure as a bed for future optical keratoplasty. A standard case proforma was maintained and study documented under the following important headings – Patient particulars, History, Examination, Clinical diagnosis, Management options which included surgical methods, Follow-up notes & remarks on the follow-up conditions.

Patient particulars: It included patient's name, age, sex, and out-patient/ in-patient number, date of examination, occupation and address.

History: A detailed documentation regarding the complaints, history of injury, duration, progression, associated conditions, relevant history of previous treatment (including ocular surgery), were noted in a chronological order.

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Examination: Ocular examination included recording visual acuity using a Snellen's chart. In patients with visual acuity less than 6/60, acuity was recorded as counting fingers at a particular distance or hand movements or perception of light & projection of rays. Detailed slit-lamp examination with photographs, fundus with indirect ophthalmoscope, and B-scan ultrasonography in cases with hazy media was done and documented Grouping of the fungal keratitis was done in the following manner,

Group I	Ulcer < 6 mm, No hypopyon, no endothelial involvement
Group II	Ulcer > 6 mm with hypopyon & endothelial involvement
Group III	Ulcer with limbal involvement & endothelial involvement
Group IV	Impending perforation
Group V	Perforated ulcers

Table 4.1: Classification of the ulcers

Inclusion criteria:

- Fungal keratitis which have been refractory to medical line of management with no improvement in a period of 4 weeks of initiating medical treatment.
- Impending perforation.
- Perforated fungal corneal ulcers.
- Scleral extension.
- Failure despite of cyanoacrylate glues and bandage contact lenses.

Exclusion criteria:

- Posterior segment involvement.
- Pl -ve eyes.

Investigations: Routine investigations included BP, urine sugar, lacrimal syringing & Hb, bleeding time, clotting time in case of children below 14 years, K.O.H.mount, conjunctival swab for culture, H.P.E. of the corneal button, S.D.A. culture for fungus were done as needed.

Management: Consisted of TKP done on all 20 eyes, with 5 out of 20 graft was sutured to the limbus due to lack of host corneal rim. B grade cornea was used for all the cases. (80%) 16 cases belonged to group E and (20%) 4 cases belonged to group D Donor material was graded based on the state of its tissues. The following table was used to grade the cornea in our institute.

KISHANCHAND CHELLARAM EYE BANK CORNEAL GRADING

Grade	Epithelium	Stroma	Endothelium
A	Clear & intact	Crystal clear	No defects,
B	Bedewing, edema	Striate lines on SLE	Defects +
C	Defects, edema ++	Obvious striae	Defects ++
D	Extensive defects, edema +++, pre-existing disease	Heavy striae, pre-existing disease	Pre-existing diseases

Table 4.2

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All patients were initially treated with topical and systemic anti fungals, atropine eye ointment TID. When there was no improvement with medical line of management TKP was done all these patients.

TKP in our study was done under local anaesthesia (Peribulbar) with facial block. Facial block was first given to prevent the patient squeezing the eye and hence reduce the chances of extrusion of lens and vitreous loss. 100ml mannitol was given pre operatively to reduce the vitreous up thrust intraoperatively. Under all aspectic precautions the part to be operated was painted and draped. Recipient bed was prepared carefully. Psuedocornea and exudative membrane were removed goniosynchiolysis was done. We encountered bleeding from the iris while peeling the exudative membrane which was controlled by mild pressure on the iris.

Trephines were used only to create a mark on the host bed as most cases were perforated. In three of the cases free hand grafting had to be done as a round host bed couldn't be prepared. Cataract extraction was done in cases with traumatic cataracts by open sky technique very carefully and the patient was left aphakic. Iridectomy was done as a rule to reduce the incidence of postoperative glaucoma. Open sky anterior vitrectomy was performed when VL was encouraged.

Usually a graft 25-.5 mm diameter greater than the recipient in phakic eyes was used. Where there was no round recipient bed available freehand technique of preparing the graft was followed to suit the defect.

Suturing was done using 10-0 nylon or 9-0 nylon suture with round and tapered continuous sutures can be used and after the suturing is completed the anterior chamber is formed with saline or air. In five cases there was no peripheral corneal rim present as it was destroyed by the disease process and hence had to be sutured to the limbus after doing the Peritomy using 8-0 silk.

Continuation of pre-operative anti-fungal drugs on an average for 7 days post operatively was done. Topical steroids were cautiously used in patients after total ephithelization of the graft. All patients were given topical timolol maleate. 5% BD and Lubricants hourly. Patients with persistant epithelial defect were treated with daily HPMC 2% patching until the defect healed. Cycloplegics like cyclopentolate 1% eye drops tid, homatropine 0.5% eye drops tid or atropine 1% eye ointment 1HS was used.

Follow up: Patients were regularly followed up for a minimum of 6 months and all the pre-operative examination sequences were repeated at follow up to note the improvement / deterioration in the patient's condition. Patients were examined every once a week post operatively for 1 month, once a month there after for 6 months.

RESULTS: A total of 20 eyes with fungal keratitis were studied and treated with TKP. Out of the 20 patients the sex distribution was as shown below:

Sex	Number
Male	12
Female	8

Table 5.1: Sex Distribution

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M.F:12:8, showed that more number of males were affected with the disease probably because they are outdoor workers and are more prone to injuries.

Age distribution was as follows:

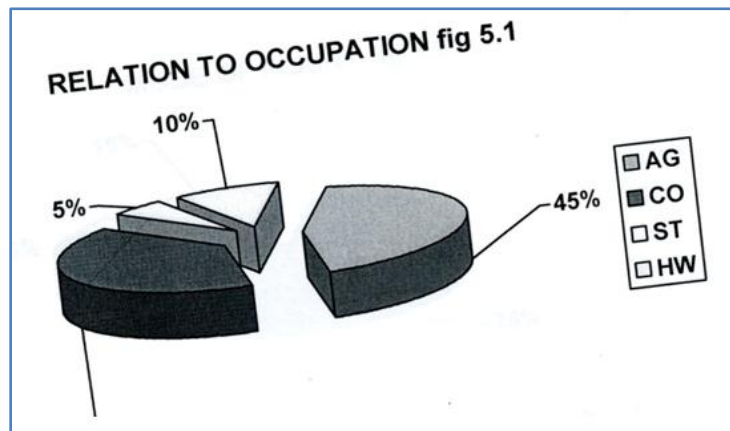
Age	Number
1-10	1
11-20	0
21-30	2
31-40	1
41-50	7
51-60	3
61-70	4
71-80	2

Table 5.2: Age Distribution

Considering the occupation 17 out of 20 were outdoor workers, with 2 being housewives and 1 being a student.

Sex	Number	%
Agriculturist	9	45
Coolie	8	40
Student	1	5
Housewife	2	10

Table 5.3: Relation to occupation



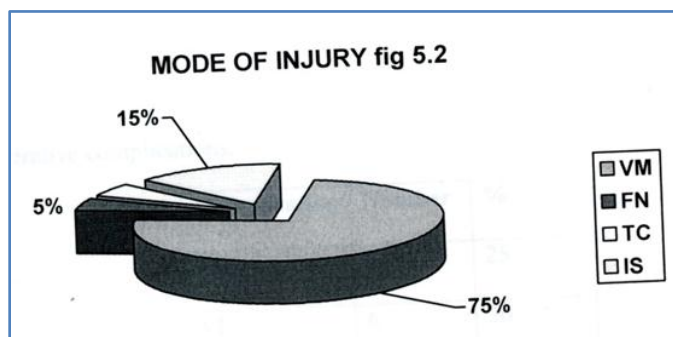
Analysis of the above data gives us an information that fungal corneal ulcers are more common in out door workers and is positively related to the occupation. It is more commonly associated with outdoor workers.

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Considering the mode of injury,

Injury with	Number	%
VM	15	75
FN	1	5
TC	1	5
IS	3	15

Table 5.4: Mode of injury



VM – VEGETATIVE MATTER (Stick, Leaf, Bark, Grass etc.,)

FN – Finger nail

TC – Tail of cow

IS – Insignificant history of trauma

It is a known fact that vegetative matter as mentioned earlier is a known source of fungus and fungus inoculation due to injury with these materials is positively associated with fungal corneal ulcers. Hence a history of injury with a vegetative matter should arouse a strong suspicion of the ulcer due to fungus.

K.O.H. Mount showed fungal hyphae in 14 of the cases, with mixed infection being 2 out of 20 and 4 cases were negative for K.O.H.

16 out of 20 cases presented to us with perforation and four of them with total corneal ulcer. 1 patient presented with extrusion of the lens at the initial presentation the lens was not found during the surgery.

KOH +ve	14
MIXED	2
KOH -ve	4

Table 5.5: KOH

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Intra-operative complications,

Complication	Number	%
EOL	5	25
VL	6	30
ID	1	5
EH	0	0

Table 5.6: Intra operative complications

Extrusion of the lens with vitreous loss has been one of the commonest complication that was encountered in our study and was seen in cases with perforation with the lens present at the wound lip.

Post-operative complications,

Complications	Number	%
I P	2	10
P E D	13	65
W L	8	40
S G	7	35

Table 5.7: Post-operative complications

Analyzing the above table, persistent epithelial defect was found in 13 cases (65%) & was managed with HPMC topical application, patching and lubricant eye drops hourly. The next common complication being wound leak in 8 cases (40%) due to loose sutures or sutures giving way in the first few post operative days. These cases were taken up for resuturing and anterior chamber was formed with air. Secondary glaucoma was most commonly associated with vitreous loss and was thought to be because of papillary block, though all cases underwent peripheral iridectomy as a rule secondary glaucoma was still seen and responded to medical management (Timolol.5% BD). Iris prolapsed was seen in 2 case associated with corneal thinning and psuedocornea formation. Out of 20 cases 5 cases underwent grafting where the graft had to be sutured to the limbus because of inadequate corneal rim available and all these grafts opacified earlier when compared to the other grafts that were sutured to the corneal rim.

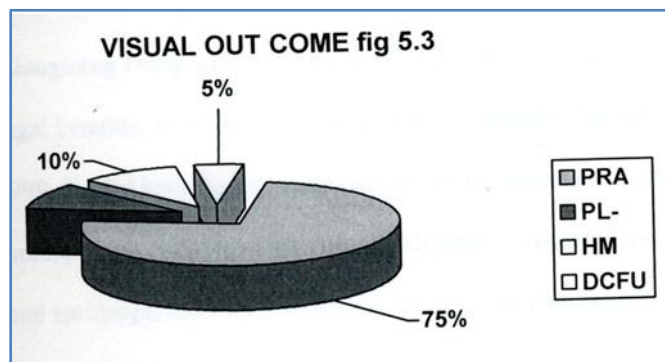
Visual out come:

Vision	Number	%
PL+ PRA	15	75
NFU	1	5
PL-	2	10
HM+	2	10

Table 5.8: Visual out come

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When the visual outcome was analyzed 15 cases (75%) had PR accurate and 2 cases (10%) had HM, but 2 cases (10%) had no perception of light. As already mention earlier restoration of vision was of secondary importance in TKP and preparation of the case for a future optical keratoplasty was one of the main aims. One patient was lost in follow up.



One patient on follow up of 6 months had phthisis bulbi & remaining 18 patients are maintaining the globe architecture. One case is having corneal thinning and awaiting a second graft. On follow up after 6 months all cases were analyzed for presence of secondary glaucoma, presence of retro corneal membrane, graft clarity, vascularization of the graft and visual outcome & 5 of the follow up cases were regarded as potential candidate for a future optical graft in whom there were no vitreous loss and were free of secondary glaucoma.

DISCUSSION: Fungal corneal ulcer has been a challenge to most ophthalmologists and hence several studies have been done earlier about fungal keratitis. Similar studies as our study had been undertaken in Shandong Eye Institute and Hospital, Qingdao 266071, PR China by Lixin Xie, Xiaoguang Dong, and Weiyun Shi.¹⁶

Fungal keratitis was diagnosed by KOH staining of corneal scrapings or by confocal microscopic imaging of the cornea. All patients received a combination of topical oral antifungal medicines without steroids as the first course of therapy. Patients whose corneal infection was not cured or in whom the infection progressed during antifungal treatment were given a PKP. After surgery, the patients continued to receive antifungal therapy with gradual tapering of the dose over a 1-2 month period. Cyclosporine was used to prevent graft rejection beginning 2 weeks after PKP. Topical steroid only was administered to the patient whose donor graft was over 8.5mm and with a heavy iris inflammation 2 weeks after PKP.

The surgical specimens were used for microbiological evaluation and examined histopathologically. The patients were followed for 6-24 months after PKP. Graft rejection, clarity of the graft, visual acuity, and surgical complications were recorded. Corneal grafts in 86 eyes (79.6%) remained clear during follow up. There was no recurrence of fungal infection and the visual acuity ranged from 40/200 to 20/20. Complications in some patients included recurrent fungal infection in eight eyes (7.4%), corneal graft rejection in 32 eyes (29.6%), secondary glaucoma in two eyes (1.9%), and five eyes (4.6%) developed cataracts. 98 to 108 of the recipient corneas had PAS positive fungal hyphae in tissue sections; 97 of 108 were culture

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positive for fungus. They concluded that PKP is an effective treatment for fungal keratitis that does not respond to antifungal medication. Early surgical intervention before the disease becomes advanced is recommended.

It is critical that the surgical procedure remove the infected tissue in its entirety in order to effect a cure. Seventy of the 108 patients were male and 38 were female with an age distribution as follows: four patients (3.7%) were less than 20 years old, 52 patients (48.2%) were between 21 and 40 years old, 43 patients (39.8%) were between 41 and 60 years old, and nine patients (8.3%) were older than 60 years. Ninety two patients were farm workers and 16 had other occupations. The patients arrived at our hospital between 5 to 40 days (average of 21.3 days) after the onset of the infection. Fifty three of the patients (49.1%) reported a recent history of injury to the cornea and contact with plant material or soil. Nineteen of the patients (17.6%) had been treated with topical steroids before infection and 36 of the patients (33.3%) were unable to provide a cause for their infection. Fifteen of the eyes (13.9%) had a corneal ulcer less than 6.0 mm in diameter. Thirty nine eyes (36.1%) had ulcers between 6.1 and 8.0 mm in diameter. Fifty four eyes (50%) had ulcers greater than 8.0 mm in diameter. Four of the corneas (3.7%) perforated.

Sex	In our study (%)	Study in China (%)	Study in Chandigarh (%)
Male	60	72.2	74%
Female	40	27.8	26%

Table 6.1: Comparison of sex distribution

Contents	Our study	Study in china	Chandigarh
Mean age of presentation	41-50	21-40	40-50
History of injury with VM	75%	49.1%	55%
Previous treatment with steroids	10%	17.6%	Nil
Presented with perforation	80%	3.7%	25.2%
Recurrence of the disease	0	7.4%	1.5%
Graft failure	100%	29.9%	70%
Pthisis bulbi	5%	Nil	3%
Secondary glaucoma	35%	1.9%	17.7%
Visual acuity	Poor	Good	Poor

Table 6.2: Comparison of the results

In comparison to the study in china, their study included intervention at an early stage and hence their results were encouraging with visual recovery in 79.6% of about 40/200 to 20/20. In our study 80% of the cases were perforated and hence visual out come was of secondary importance. Yet another study done in Chandigarh in 2002 showed overall anatomical success was achieved in 67.3% of patients and complications were more with perforated corneal ulcers than with non perforated corneal ulcers.²² UNICEP (JAN) 2000 study, with cyclosporine A 2% along with PKP post-operatively in fungal keratitis have stated that ocular globe architecture

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was maintained in 80% of patients though visual outcome was poor.²³ Early intervention probably have favourably visual outcome.¹⁶ When patients present to us with perforation a TKP will serve both as treatment as well as tectonic graft and definitely is a ray of hope for a future optical keratoplasty.²²

CONCLUSION:

- Fungal corneal ulcer presents late to the ophthalmologist as the signs are more than symptoms.
- More common in rural patients.
- Males are more affected than females as they work outdoors.
- Associated with outdoor workers more so those related to agricultural occupation.
- Positively related to injury with vegetative matter.
- Treatment with TKP in severe fungal keratitis (perforated fungal keratitis and limbal involvement) graft rejection was seen in all the cases with poor visual outcome but still leaving a bed for future optical PKP.
- Early diagnosis, high degree of suspicions & early intervention gives encouraging results.²⁶
- Secondary glaucoma due to papillary block and persistent epithelial defect were the major complications and could be treated medically.

SUMMARY: This is a hospital-based clinical study & the study consisted of 20 patients with severe fungal keratitis for whom TKP was done on all 20 eyes, with 5 out of 20 graft was sutured to the limbus due to lack of host corneal rim. Continuation of pre-operative anti-fungal drugs on an average of 7 days postoperatively was done. Topical steroids were cautiously used in patients after total epithelization of the graft. All patients were given topical timolol maleate.5% BD and Lubricants hourly. Patients with persistent epithelial defect were treated with daily occlude patching until the defect healed.

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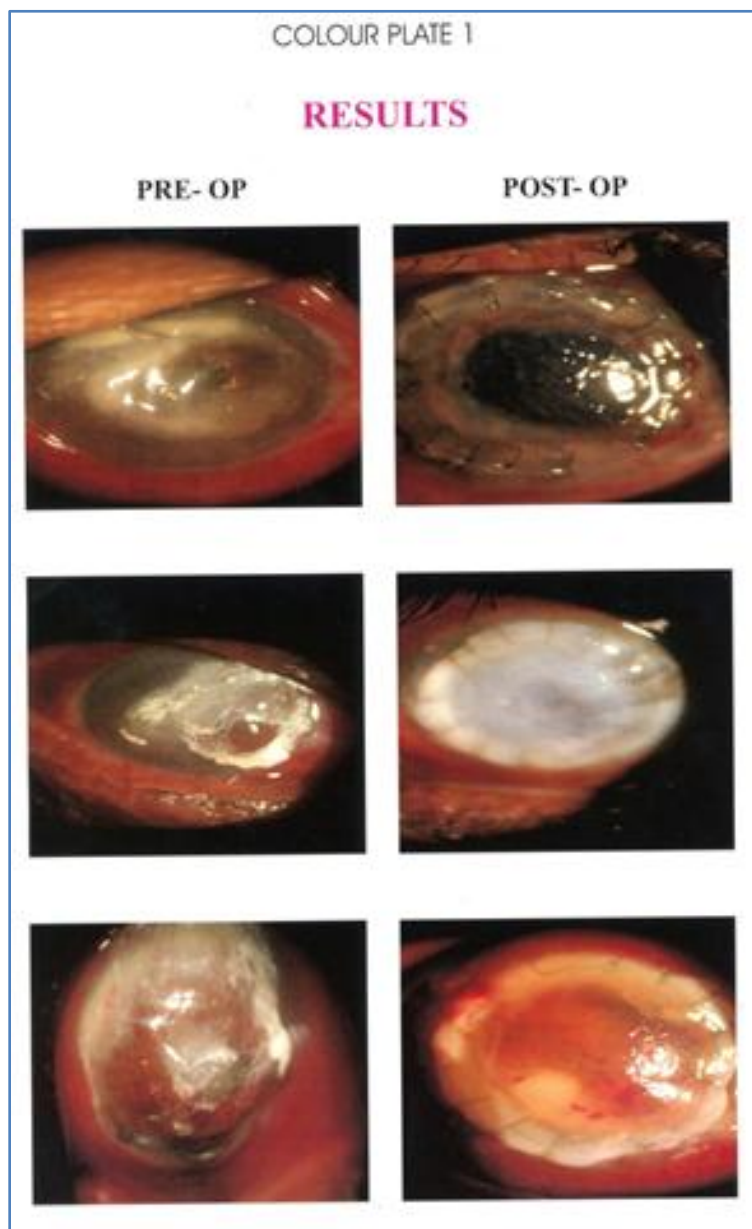
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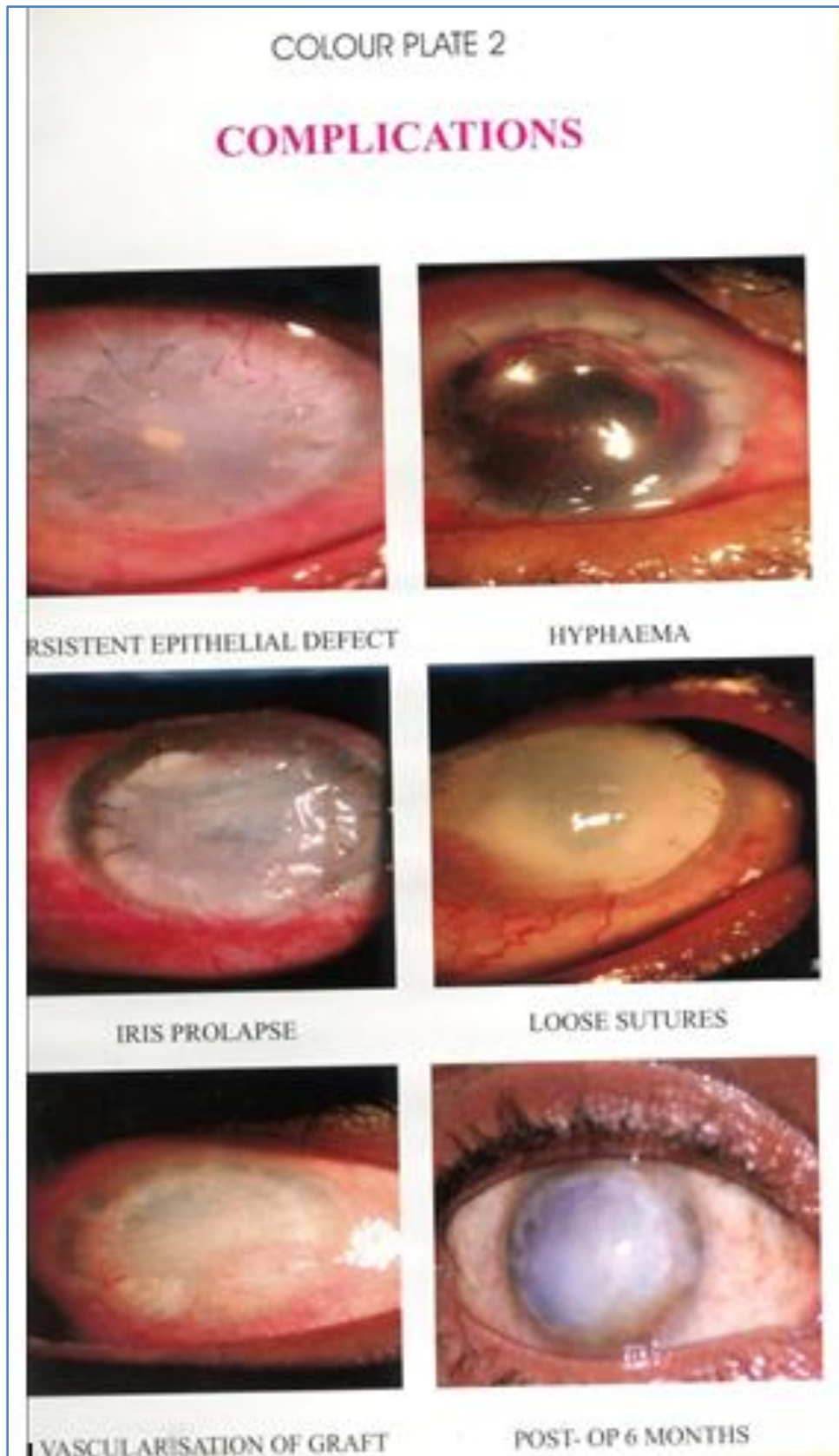
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Date of Submission: 05/10/2014.

Date of Peer Review: 06/10/2014.

Date of Acceptance: 07/10/2014.

Date of Publishing: 10/10/2014.