



## Ophthalmology

## A STUDY TO EVALUATE THE HEALING (RE-EPITHELIALISATION) TIME AND OUTCOMES OF CORNEAL PERFORATION AND DESCEMETOCELE AFTER AMNIOTIC MEMBRANE GRAFTING

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**ABSTRACT** **Background:** Corneal perforation and Descemetocele is a potential disabling complication, caused by diseases like infections, autoimmune diseases, trauma etc. Surgical approaches, such as tissue adhesive, bandage contact lens, AMT (Amniotic Membrane Transplantation), transpositional conjunctival flap, and therapeutic Penetrating Keratoplasty (PK), are available. AMG is one of good alternative for the management of small or impending corneal perforation to reconstruct the surface. AMT can prevent urgent need of penetrating keratoplasty. The aim of present study is to assess the efficacy of AMG in treating corneal perforation  $\leq 2$ mm and descemetocele of any size and to evaluate the time of healing and stability of corneal surface. **Method:** This is a prospective interventional analytical study conducted on all men and women with a diagnosis of corneal perforation  $\leq 2$ mm or descemetocele of any size attending our institute for period of 8 months. All patients were treated with multi-layered amniotic membrane grafting and were followed for 10 months postoperatively. **Results:** We included a total of 59 cases. There were 31 female and 28 male patients. The mean age ( $\pm$ SD) was  $50.93 \pm 17.57$  years. There were 30 cases of corneal perforation and 29 cases of descemetocele. On final follow up, 67.79% patients successfully achieved reepithelization. Epithelial closure was observed within first 4 weeks of grafting in 24 (40.68%) patients, between 5 to 8 weeks in 9 (20.93%) patients and in 7 (16.27%) patients the healing occurred after 8 weeks till 10 months after AMT. No epithelial closure was achieved in the remaining 19 (32.20%) patients. There was no statistically significant difference in relation to age groups and gender when compared to outcome (Success and Failed graft) ( $p=0.869$  and  $0.452$  respectively). Baseline BCVA (Best Corrected Visual Acuity) did not show statistically significant difference between the different subgroups ( $p$ -value= $0.668$ ) and the difference was statistically highly significant postoperatively ( $p<0.0001$ ). BCVA post operatively, on final assessment, was observed statistically significant in the success group ( $p<0.001$ ) with LogMar values of  $1.84 \pm 0.58$  preoperatively to  $0.94 \pm 0.59$  on final follow up. **Conclusion:** In this study, we observed that AMT has good success rate and is a cost effective and non-invasive method in the treatment most cases of various etiologies of small corneal perforations and descemetocele.

### KEYWORDS : AMG, BCVA, PK

#### INTRODUCTION

Corneal perforation and Descemetocele are a potential disabling complication which can cause by Several diseases of eyes including infections, autoimmune diseases, trauma etc. It is an emergency situation which requires prompt intervention, both to restore globe integrity and to minimize the risk of secondary complication including prolonged or recurrent hypotony, phthisis bulbi, endophthalmitis, choroidal hemorrhage and glaucoma. Various management options have been described in the literature, with multi-staged procedures that are often required to facilitate visual rehabilitation. Many surgical approaches, such as tissue adhesive, bandage contact lens, AMT, transpositional conjunctival flap, and therapeutic PK, have been introduced to treat perforated ulcers of the cornea. However, these therapies are associated with variable success rates. In addition, postoperative wound dehiscence, severe vascularization, fibrosis, and corneal melting because of destructive inflammation are all possible outcomes of these procedures.<sup>1</sup> Penetrating keratoplasty for corneal perforations is a definitive treatment but poses technical difficulties in the presence of inflammation. The unavailability of quality donor corneas is also a major constraint in developing countries.<sup>2</sup>

The etiology of Descemetocele and perforation can be classified as traumatic or nontraumatic, with nontraumatic perforation may be further grouped into infectious or non-infectious causes. Infectious etiologies may be secondary to bacterial, fungal, viral, or parasitic infection while non-infectious etiologies include ocular surface diseases like Keratoconjunctivitis Sicca or Sjogren Syndrome or autoimmune disease, Peripheral Ulcerative Keratitis secondary to conditions like, Mooren's ulcer, Wegener's disease, relapsing polychondritis and Rheumatoid Arthritis.

Management of corneal perforation and Descemetocele depends on multiple factors like the size of the defect, the surgeon's experience, and the etiology of ulcer. The treatment options range from medical

management, use of Amniotic Membrane Graft, bandage corneal patch, and surgical approach like conjunctival flaps or tarsorrhaphy and may also require systemic immunosuppressive treatment etc. Medical treatment alone or along with bandage contact lens, is only effective for small perforations measuring upto 1 mm in diameter. Surgical intervention is required for larger defects ( $>1$ mm in diameter). Surgical intervention may include tissue adhesives, AMG and corneal transplantation.

Tissue adhesives may dislodge and are used as a temporary measure, obviating the need for a PK within a few days. These procedures solve only the tectonic problem, without addressing the inflammatory response going on due to various etiologies or severe deficiency of aqueous tear which is seen in small perforations or descemetoceles associated with neurotrophic keratopathy or autoimmune disorders. Continued tissue degradation in these conditions may result in graft melting or dislodgment of the tissue adhesive.

AMG is one of good alternative for the management of small or impending corneal perforation to reconstruct the surface. Lee and Tseng (1997) were the first to demonstrate the use of Amniotic Membrane for the treatment of corneal epithelial defects by performing a AMT and many studies since then have demonstrated the successful use of AMT in the management of corneal perforations. AM (Amniotic Membrane) is the innermost layer of the placenta and consists of a thick basement membrane and an avascular stroma.<sup>3</sup>

AMT can prevent urgent need of penetrating keratoplasty. Amniotic membrane epithelium contains growth factors including hepatocyte growth factor, keratocyte growth factor and epidermal growth factor. The presence of these trophic factors aids epithelial healing by promoting differentiation and migration of epithelial cells that are in contact with the amniotic membrane. Amniotic membrane also releases inhibitory proteases which induce apoptosis of inflammatory

cells like neutrophils, lymphocytes and plasma cells and further reduces the risk of corneal melt, vascularization, and scarring.<sup>4</sup>

The aim of present study is to assess the efficacy of Amniotic Membrane Grafting in treating corneal perforation  $\leq 2\text{mm}$  and descemetocoele of any size and to evaluate the time of healing and stability of corneal surface.

**MATERIAL AND METHOD**

This is a prospective interventional analytical study.

**Study Group:**

The study included all men and women with a diagnosis of corneal perforation  $\leq 2\text{mm}$  or descemetocoele of any size attending the Upgraded Department of Ophthalmology, SMS Medical College and Hospital, Jaipur, Rajasthan as per the inclusion and exclusion criteria.

**Study Period-**

After IEC approval the study was conducted at SMS Medical College and Hospital, Jaipur from to or till the sample size attained.

**Sample Size-**

Sample size calculated 59 eyes (cases) as per previous studies which showed, after AMG (Amniotic Membrane Grafting) the successful result in 82.3% cases for 80% study power, 0.05  $\alpha$  error and 10% absolute error.

**Inclusion Criteria**

1. Patient with corneal perforation  $\leq 2\text{mm}$  in diameter as assessed by BQ 900 slit-lamp examination with a positive Seidel sign or a descemetocoele of any size with traumatic or non-traumatic cause who attended the ophthalmic casualty or OPD.
2. Patients who give well informed written consent.

**Exclusion Criteria**

1. Non cooperative patients.
2. Other ocular or systemic disorders that could compromise vision and time of reepithelization.
3. Corneal perforation size  $> 2\text{mm}$ .

**METHODOLOGY**

All the 59 patients with corneal perforations upto 2 mm in largest dimension or descemetocoele of any size were treated with AMG. All operations were performed by the same surgeon. All the patients were operated under topical/local /General anesthesia depending on patient's cooperation and age. Firstly, the perforated edges of corneal ulcer were cleaned, and partially necrotic tissue and poorly adherent epithelium was removed with a blunt blade and microsponges. Then a small volume of sodium hyaluronate viscoelastic was used to restore the anterior chamber depth. After cleaning and drying of the ulcer, three to four pieces of the preserved Dry AM (Amniotic Membrane) were trimmed to fit the shape and size of the corneal ulcer and applied one over the other to fill the ulcer bed. A running 10-0 nylon suture or a few interrupted sutures were placed to anchor the AM grafts to the cornea with an attempt to include a few layers in the suture. Finally, a large piece of the AM was applied over the entire cornea as a temporary patch and anchored with a running 10-0 nylon suture to the perilimbal episclera.

Then a bandage contact lens was applied in all cases until the epithelial defect is completely healed. Patient received antimicrobial treatment depending upon etiology.

All cases were examined post-operative day 1 then weekly until complete epithelisation occurred and monthly thereafter for 3 months. Outcome of the treatment was measured in terms of vision and maintenance of globe integrity.

**Statistical Analysis:**

Collected data was entered in Microsoft Excel Worksheet. Qualitative data was presented in percentage and proportion form and quantitative data was calculated in mean and standard deviation form. Appropriate statistical tests were applied. A P value less than 0.05 will be considered statistically significant.

**RESULTS**

In our study we included a total of 59 cases as per calculated sample size. All 59 patients were treated with AMT for corneal perforation and descemetocoele. The study was conducted for eight months from September 2021 to April 2022. In our study there were 31 female

patients and 28 male patients. **[Image 1]** The age ranged from 15 years to 82 years with mean age ( $\pm\text{SD}$ ) of  $50.93 \pm 17.57$  years. Maximum patients were in the age group of 51 – 70 years. **[Image 2]**

We observed cases of various etiologies as enumerated in **Table no. 1**, out of which 30 cases were diagnosed as corneal perforation and 29 cases as descemetocoele. Multi-layered amniotic membrane graft was placed in all the patients as per the described method. The patients were followed up for 10 months. On final follow up, 40 (67.79%) patients were successfully treated and achieved reepithelization, whereas 19 (32.2%) patients were marked as failed graft with no signs of reepithelization. **[Image 3]** Tarsorrhaphy was also done as additional procedure in 3 patients, all these patients were successfully treated within 10 weeks' time. Appropriate antibiotics and antifungal were given to the patients. Penetrating keratoplasty was done in 7 cases where the ulcer was not healed with AMT. One case showed recurrence of ulcer after showing signs of healing and finally the AMT was not successful after repeating the grafting.

Among 40 successful patients, epithelial closure was observed within first 4 weeks of grafting in 24 (40.68%) patients, between 5 to 8 weeks in 9 (20.93%) patients and in 7 (16.27%) patients the healing occurred after 8 weeks till final follow up i.e., 10 months after AMT. However, no epithelial closure was achieved in the remaining 19 (32.20%) patients (**Table 2**).

**GENDER WISE DISTRIBUTION OF CASES**

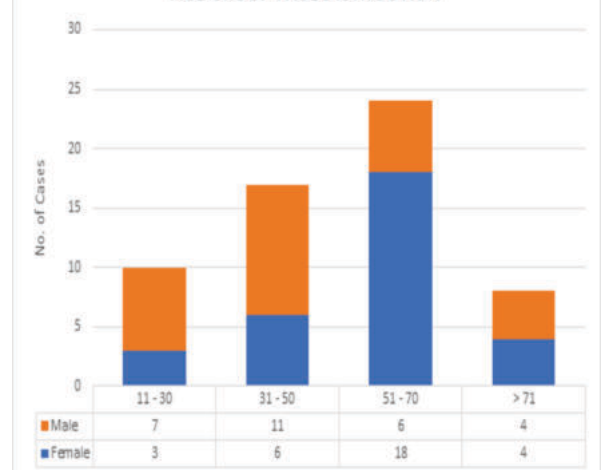


**Image 1:** Sex Wise Distribution Of Cases.

In cases of Mooren's ulcer, Dellen, Neurotropic failed graft, Neurotropic post lid tumor removal, Neurotropic lagophthalmos, and Bullous keratopathy, we observed success in 100% of patients with complete reepithelization. Ulcers in patients with fungal keratitis revealed the lowest closure rates of 33.3%.

Time to epithelial closure was slower in ulcers due to autoimmune (RA), post infectious, whereas significantly fast healing was observed in dellen, neurotropic failed graft and bullous keratopathy cases with 100% cases achieved reepithelization within 1-2 weeks after grafting. (**Table 2**)

**AGE GROUP WISE DISTRIBUTION**



**Image 2:** Age Group Wise Distribution Of Cases.



Image No. 3: Showing Distribution Of Successful And Failed Cases.

Table No. 1: Age Group Wise Distribution Of Cases With Mean ± SD

	Etiology	Age Groups				Total	Mean Age	SD
		11 - 30	31 - 50	51 - 70	> 71			
Autoimmune Diseases	AD, Mooren's ulcer	0	0	1	0	1	55	-
	Autoimmune (Rheumatoid Arthritis)	0	3	3	1	7	55	17
	Sjogren disease	0	0	2	0	2	59	1
	Dellen	2	0	0	0	2	23	3
	Stevens-Johnson syndrome	0	1	1	0	2	48	18

Neurotropic Keratitis	Neurotropic (Post HSK)	3	2	7	2	14	52	20
	Neurotropic (Post Infectious)	1	2	4	1	8	52	20
	Neurotropic exposure keratitis	0	1	0	2	3	67	16
	Neurotropic failed graft	0	0	0	1	1	73	-
	Neurotropic post lid tumor removal	0	1	0	0	1	48	-
	Neurotropic, lagophthalmos	0	0	0	1	1	81	-
Infective Etiology	Fungal Keratitis	0	1	2	0	3	56	6
	Infectious Ulcer (Foreign Body)	0	3	1	0	4	47	9
	Spontaneous Bacterial Infection	0	2	0	0	2	42	4
Others	Bullous keratopathy	0	1	1	0	2	50	4
	PED after chemical burn	4	0	0	0	4	25	6
	Traumatic	0	0	2	0	2	58	9
Total		10	17	24	8	59		

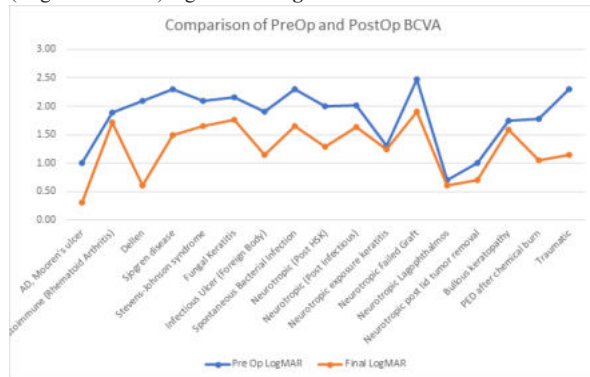
Table no. 2: Showing Distribution Of Cases According To Time To Reepithelization In Different Etiological Groups.

	Time to Reepithelization										
	1-4 Wk		5-8 Wk		>8 Wk		Total Success		FAILED		Total Cases
	No.	%	No.	%	No.	%	No.	%	No.	%	
Autoimmune Diseases											
AD, Mooren's ulcer	1	100.0	0	0.0	0	0.0	1	100	0	0.0	1
Autoimmune (Rheumatoid Arthritis)	0	0.0	1	14.3	2	28.6	3	42.8	4	57.1	7
Dellen	2	100.0	0	0.0	0	0.0	2	100.0	0	0.0	2
Sjogren disease	1	50.0	0	0.0	0	0.0	1	50.0	1	50.0	2
Stevens-Johnson syndrome	0	0.0	1	50.0	0	0.0	1	50.0	1	50.0	2
Infective Etiology											
Fungal Keratitis	1	33.3	0	0.0	0	0.0	1	33.33	2	66.7	3
Infectious Ulcer (Foreign Body)	2	50.0	0	0.0	1	25.0	3	75.00	1	25.0	4
Spontaneous Bacterial Infection	1	50.0	0	0.0	0	0.0	1	50.00	1	50.0	2
Neurotropic Keratitis											
Neurotropic (Post HSK)	6	42.9	3	21.4	2	14.3	11	78.57	3	21.4	14
Neurotropic (Post Infectious)	2	25.0	1	12.5	2	25.0	5	62.50	3	37.5	8
Neurotropic exposure keratitis	2	66.7	0	0.0	0	0.0	2	66.67	1	33.3	3
Neurotropic Failed Graft	1	100.0	0	0.0	0	0.0	1	100.00	0	0.0	1
Neurotropic Lagophthalmos	0	0.0	1	100.0	0	0.0	1	100.00	0	0.0	1
Neurotropic post lid tumour removal	0	0.0	1	100.0	0	0.0	1	100.00	0	0.0	1
Others											
Bullous keratopathy	2	100.0	0	0.0	0	0.0	2	100.00	0	0.0	2
PED after chemical burn	2	50.0	1	25.0	0	0.0	3	75.00	1	25.0	4
Traumatic	1	50.0	0	0.0	0	0.0	1	50.00	1	50.0	2
Total	24		9		7		40		19		59

In the present study there was no statistically significant difference observed in relation to different age groups and gender when compared to outcome (Success and Failed graft) (p=0.869 and 0.452 respectively). Baseline BCVA was checked at the first contact before

surgery, no statistically significant difference in baseline BCVA between the different subgroups of patients was found with p-value of 0.668 Whereas the difference was statistically highly significant postoperatively (p<0.0001).

The improvement in visual acuity in failed graft group was observed from LogMAR of  $2.12 \pm 0.37$  preoperatively to LogMAR of  $2.25 \pm 0.18$  which was statistically not significant ( $p=0.044$ ). Whereas the improvement in BCVA post operatively on final assessment, was observed statistically significant in the success group ( $p<0.001$ ) with LogMar values of  $1.84 \pm 0.58$  preoperatively to  $0.94 \pm 0.59$  on final follow up. Etiology wise comparison of preoperative and final BCVA (LogMAR values) is given in **Image no. 4**.



**Image no. 4:** Showing Comparison Of Preoperative And Postoperative BCVA (mean LogMAR values) Between Different Etiological Groups.

## DISCUSSION

The effectiveness of AM in treatment of corneal ulcer has been verified. But for treatment of descemetocoele and corneal perforation single layer or multiple layer AMT is not successful because it can't plug the defective zone. In our study, we used pieces of amniotic membrane to plug the defect and a large piece of amniotic membrane to overlay the whole cornea. As a result, this not only generated enough force to prevent the aqueous leak but also provided a basement membrane for rapid epithelization and healing.

In our study we studied the effectiveness of AMT in patients with corneal perforation less than equal to 2 mm in diameter and descemetocoele of any size. The results reveal an overall amniotic membrane grafting success rate of 67.79%. In other similar studies done by Kaspar Schuerch et al<sup>8</sup> and Sandrine Hick et al<sup>6</sup>. They reported 70% and 82% success rate with AMT which is concordant with our study. The mean age of our study group is  $50.93 \pm 17.57$  years which is slightly younger as compared to similar study done by Kaspar Schuerch et al<sup>8</sup>. In most patients ( $n=24$ , 40.68%), epithelial closure was achieved within the first 4 weeks after AMT graft in our study which is faster as compared to mean time to closure in study done by Kaspar Schuerch et al<sup>8</sup> this may be due to comparatively younger population in our study and other contributing factors like comorbidities, and geographical factors.

The patients with neurotropic ulcers post HSK, and infective ulcer due to foreign body, achieved reepithelization much quicker in our study with majority of patients achieved reepithelization within first 4 weeks of grafting. Whereas fungal ulcers, rheumatoid arthritis and neurotropic post infectious ulcer patients the failure rate was higher with 67%, 57.1% and 37.5% patients failed to achieve reepithelization. In the study done by Kaspar Schuerch et al<sup>8</sup> herpetic ulcers and neurotropic ulcers showed highest success rates whereas, ulcers associated with rheumatic disease or due to wound-healing problems after corneal surgery, epithelial closure was not achieved with AMT. These subgroups also revealed a lower epithelial healing rate than those with herpetic ulcers. Solomon et al<sup>3</sup> also reported poor healing and higher failure rate in cases of rheumatoid arthritis and neurotropic ulcers. These results from different studies are in agreement with our study. The small variation in percentage and time to reepithelization observed, may be due to difference in age group and geographical and socio-economic factors.

Our results show that there is statistically significant improvement in visual acuity of patients who achieved successful reepithelization on final follow up. In previous studies, BCVA did not reveal any significant improvement or worsening in the mid/long term.<sup>9,10</sup> AMT may lead to an improvement of visual acuity through corneal surface restoration. In addition, in our study, such an improvement was seen, when analyzing the whole cohort of patients.

There are certain limitations in our study because of lack of a control group and a small sample size that does not represent the target population. Few etiological subgroups had only 1-2 cases so the result of treatment may not be implemented on whole population. Further studies are required in this direction.

## CONCLUSION:

In this prospective interventional study, we observed that AMT can be used effectively in the treatment of small corneal perforations and descemetocoele. It has good success rate and is a cost effective and non-invasive method in most cases of various etiologies of corneal ulceration.

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