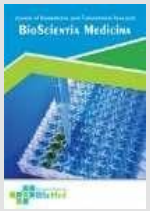
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Surgical Outcome of Amniotic Membrane Transplantation (AMT) in Patients with Corneal Ulcer in Dr. M. Djamil General Hospital, Padang, Indonesia

Rahmi Fatma Sari[1*], Havriza Vitresia[1]

[1]Department of Ophthalmology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia

ARTICLE INFO

Keywords:
Amnion membrane graft transplantation
Corneal ulcer
Surgical outcome

***Corresponding author:**
Rahmi Fatma Sari

E-mail address:
rahmifatmasari22@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v7i6.830

A B S T R A C T

Background: Amniotic Membrane Transplantation or AMT Graft has been known to successfully manage ocular surface diseases, especially corneal ulcers. The amniotic membrane promotes epithelialization and inhibits proteinase activity that is required for wound healing. A corneal ulcer is a potentially sight-threatening condition resulting in permanent corneal opacity. **Methods:** This is a retrospective descriptive study. Subjects were patients diagnosed with corneal ulcers and have been treated with AMT grafts. The data were grouped according to age, gender, severity, cause, visual acuity before and after AMT, and time required for complete epithelialization. **Results:** Fifty-two patients were included in this study, aged 41-50, with a mean age of 43,17. Men were more common than women by 88,5% vs 11,5%. AMT graft was performed for moderate and severe corneal ulcers in this study, and most of them were caused by infection. The visual acuity before AMT was mostly in the second WHO category of blindness and visual impairment. Four weeks after surgery, 34.6% of patients had improved visual acuity. Complete epithelialization was most frequently (59,6%) achieved in 15-28 days. AMT graft was repeated in 3 patients, and other surgical interventions were required for 2 patients. **Conclusion:** The AMT graft has successfully managed corneal ulcer patients, especially in moderate to severe cases, in Dr. M. Djamil General Hospital, Padang, Indonesia.

1. Introduction

A corneal ulcer is a defect in the corneal layer from epithelial to stromal that forms boundaries, walls, and bases that can be caused by infection or non-infection. Corneal ulcers are the fifth most common cause of blindness in the world. The incidence is estimated to be 2.5-799 per 100,000 population/year, in which 5% of cases result in blindness. Corneal ulcers take a long time to heal, even after adequate administration of antibiotics and antifungals. Corneal ulcers often leave corneal scarring and neovascularization leading to decreased visual acuity after healing. If not managed optimally, then corneal ulcers will cause complications such as glaucoma and endophthalmitis. In cases of corneal ulcers that do not respond to medical therapy, surgical intervention is needed, one of which is an Amniotic Membrane Transplantation (AMT) graft.[1-4]

Amniotic membrane (AM) is the innermost layer of the fetal membrane. AM thickness varies between 0.02-0.05 mm and consists of 3 histological layers: epithelial layer, thick basement membrane, and avascular stroma. AM has been shown to have several benefits, namely accelerating epithelialization and having antiangiogenic, anti-scarring, antimicrobial, and anti-inflammatory properties. AM contains growth factors and cytokines that facilitate the proliferation and differentiation of epithelial cells, reduce the inflammatory response by inhibiting protease activity, and reduce the activity of inflammatory cells. Clinical results show that the success rate of corneal ulcer

treatment with single or multilayer AM is about 80%, while for corneal perforation with multilayer AM is 73%.[5-7]

The first use of amniotic membrane transplantation (AMT) in ophthalmology was by De Rotth in 1940, who reported partial success in the management of conjunctival epithelial defects due to symblepharon. Sorsby and Symons, in 1946, found that patients with thermal trauma to the conjunctiva involving the cornea could be treated successfully with AM. In 1995 Kim and Tseng performed AMT for ocular surface reconstruction of severely damaged corneas in a rabbit model. Furthermore, Lee SH et al. 1996, Hanada et al. 2000, Tseng 2001, Solomon et al. 2001, Prabhasawat et al. 2001, Heiligenhaus et al. 2002, Rodriguez-Ares et al. 2003, used single and multilayer AMT for persistent corneal epithelial defects, severe corneal and scleral ulceration, and corneal perforation. Since then, many studies have reported the beneficial effects of human AMT in eye reconstruction.[3,8]

2. Methods

This study is an analytical retrospective study on corneal ulcer patients who underwent an AMT graft at Dr. M. Djamil General Hospital, Padang, from January 2016 - December 2019. The inclusion criteria for this study were patients diagnosed with corneal ulcers who had an AMT graft performed at Dr. M. Djamil General Hospital, Padang, in that period and had complete medical record data. Exclusion criteria were patients who were diagnosed with corneal ulcers and had an AMT graft performed at Dr. M. Djamil General Hospital, Padang, during that period and had incomplete medical record data.

Data collected included age, gender, severity of corneal ulcer, cause, visual acuity before and after AMT, and time required for complete epithelialization. Corneal ulcer severity was determined based on Harrison's corneal ulcer grading criteria. Causes of corneal ulcers can be infectious and non-infectious. The initial vision was assessed before the AMT graft procedure and visual acuity after AMT was assessed in the second and fourth weeks after surgery. The vision before and after surgery were grouped according to the criteria for blindness according to WHO. Visual acuity is said to have improved if there is an improvement from the previous visual acuity category, permanent if there is no change from the visual acuity category, and worsening if there is a worsening of the previous visual acuity category. AMT graft is said to be successful if there is complete epithelialization and there is no clinical deterioration, such as reduced inflammation, reduced infiltrates, and adequate anterior chamber. AMT graft is said to be unsuccessful (failed) if there is recurrent epithelialization, perforated ulcer, and or repeated procedure.

Data was collected from the patient's medical record. Data was obtained in the form of frequency and percentage. The data were computerized and analyzed statistically using the statistical package for social sciences (SPSS) with the Pearson Chi-Square test analysis for a significant test. The statistical level is significant if $p < 0.05$.

3. Results

Based on inclusion and exclusion criteria, 52 patients were included in this study. The demographic characteristics of patients undergoing this study can be seen in Table 1. It can be seen that the largest age group is the 41–50-year age group (40.4%), with an average age of 43.17. The youngest age is 6 years, and the oldest is 78 years. Meanwhile, based on gender, it was found that the male gender was more dominant (88.5%) than female.

Based on the laterality distribution of corneal ulcers, the left eye was slightly more common (51.9%) than the right eye (48.1%). Based on the severity of corneal ulcers, severe corneal ulcers were the most common (67.3%), followed by moderate corneal ulcers with 32.7%. No mild corneal ulcers were treated with AMT in this study. Based on the etiology of the ulcer, it was found that most corneal ulcers were caused by infection (86.5%), while non-infectious corneal ulcers were only found in 13.5% of cases. In this study, visual changes were assessed before and after AMT grafting and categorized as improvement, persistence, or worsenin

Table 1. Distribution of research subjects based on age and gender.

Subject characteristic		Frequency	
		N	%
Age (year)	≤10	1	1,9
	11-20	3	5,8
	21-30	4	7,7
	31-40	8	15,4
	41-50	21	40,4
	51-60	12	23,1
	>60	3	5,8
Total		52	100,0
Gender	Male	46	88,5
	Female	6	11,5
Total		52	100,0

Table 2. Distribution of corneal ulcers according to laterality.

Laterality	N (eyes)	Percentage (%)
Right	25	48,1
Left	27	51,9
Total	52	100

Table 3. Corneal ulcer severity.

Severity	N	Percentage (%)
Mild	0	0
Moderate	17	32,7
Severe	35	67,3
Total	52	100

Table 4. Etiology of corneal ulcer.

Etiology	N	Percentage (%)
Infectious	45	86,5
Non-infectious	7	13,5
Total	52	100

Table 5. The vision of corneal ulcer patients before AMT graft.

Visual acuity	Category	Total	Percentage (%)
≥6/18	Normal	5	9,6
6/60 - <6/18	Moderate visual impairment	9	17,3
3/60 - <6/60	Severe visual impairment	1	1,9
1/60 - < 3/60	Blindness category I	4	7,7
< 1/60	Blindness category II	33	63,5
NLP	Blindness category III	0	0
Total		52	100

Table 5 shows the visual distribution of corneal ulcer patients before the AMT graft was performed. Based on the distribution of vision, patients with corneal ulcers had the most vision in blindness category II (hand movement/light perception), as much as 63.5% before the AMT graft was performed.

Table 6. Vision after AMT graft.

Visual acuity	Category	2 weeks after AMT		4 weeks after AMT	
		n	%	n	%
≥ 6/18	Normal	8	15,4	10	19,2
6/60 - <6/18	Moderate visual acuity	15	28,8	14	26,9
3/60 - <6/60	Severe visual acuity	0	0	0	0
1/60 - < 3/60	Blindness category I	6	11,5	6	11,5
< 1/60	Blindness category II	23	44,2	21	40,4
NLP	Blindness category III	0	0	1	1,9
Total		52	100	52	100

Table 6 shows the visual distribution of corneal ulcer patients after the AMT graft was performed in the second and fourth weeks. When compared with the visual acuity before the AMT procedure, the number of patients in blind category II decreased in the second week (44.2%) and fourth week (40.4%).

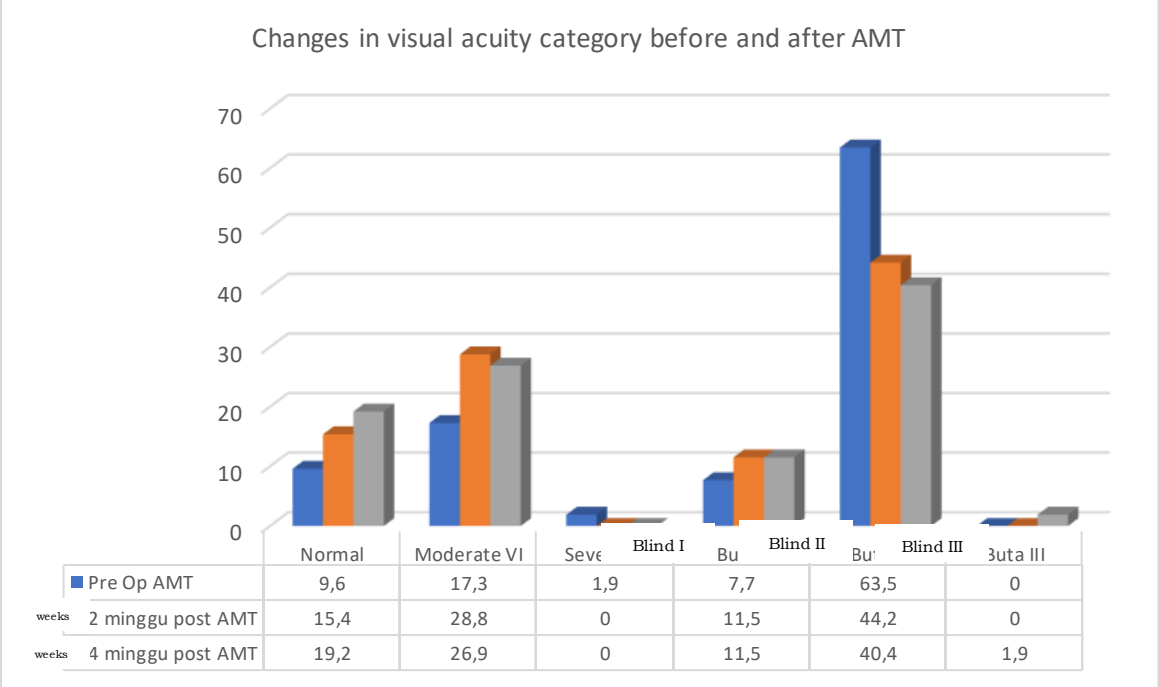


Figure 1. Changes in visual acuity category before and after AMT.

Figure 1 shows the visual changes in each category before the AMT procedure, 2 and 4 weeks after the AMT procedure. There appears to be an increase in the number of cases in the normal category, while in the blind category II, there appears to be a decrease in the number of cases.

Table 7. Changes in visual acuity before and 4 weeks after AMT graft.

Visual changes	n	%
Improve	18	34,6
Persist	32	61,5
Decrease	2	3,8

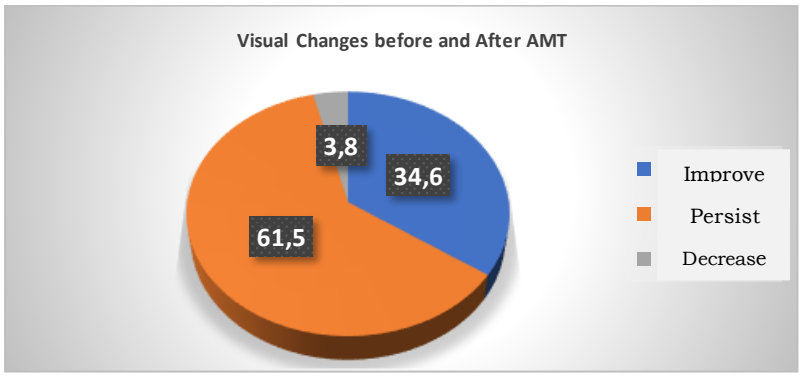


Figure 2. Visual changes before and after AMT.

Table 7 and Figure 2 show changes in the visual category of corneal ulcer patients before the AMT graft and 4 weeks after the AMT graft. It can be seen that visual acuity improved in 34.6% of eyes, while only 2 (3.8%) eyes had visual impairment. In the other 32 eyes (61.5%), the vision was fixed before and after the AMT graft.

In this study, the AMT graft was said to be successful if there was complete epithelization and there was no clinical deterioration, and it was said to be unsuccessful if there was no epithelialization after the procedure or required another surgery after the AMT procedure. It was found that the AMT graft was successful in 46 eyes (88.5%), while the other 6 eyes (11.5%) were unsuccessful.

According to the severity of the ulcers, there was no significant difference in the healing rate after AMT grafting in severe or moderate ulcers, as shown in Table 8.

Table 8. AMT graft success by ulcer severity

The severity of corneal ulcer	**Successful rate N (%)**		**p**
	Success	**Fail**	
Moderate	16 (94,1)	1 (5,9)	0,792
Severe	30 (85,7)	5 (14,3)	
Total	46 (88,5)	6(11,5)	

Of all corneal ulcer patients who underwent AMT graft surgery, the complete epithelialization occurred in the range of days 15-28 postoperatively (59.6%). Two patients (3.8%) had no epithelialization.

Table 9. Distribution of time to complete epithelialization after AMT graft in corneal ulcer patients.

Time to complete epithelialization	**N**	**%**
< 7 days	3	5,8
7-14 days	5	9,6
15-28 days	31	59,6
> 28 days	11	21,1
No epithelialization	2	3,8
Total	52	100

Table 10 shows the number of cases of corneal ulcers requiring another surgery after an AMT graft. There were 5 cases (9.6%) out of 52 cases requiring another surgery, namely repeat AMT graft, paracentesis, or evisceration.

Table 10. The number of cases requiring repeat surgery.

Surgical procedure	N	%
No repeat procedure	47	90,4
Graft AMT	3	5,8
Paracentesis	1	1,9
Evisceration	1	1,9
Total	52	100

4. Discussion

AMT graft was performed on 52 eyes of corneal ulcer patients from January 2016 – December 2019 at the Dr. M. Djamil General Hospital, Padang. Enforcement of the diagnosis of corneal ulcers based on the results of history taking and ophthalmological examination, which includes visual examination with Snellen chart and slit lamp. After the AMT graft, follow-up was performed on days 5, 7, 14, and 28.

The description of the characteristics of the research subjects of corneal ulcer patients who underwent AMT grafting consisted of age and gender. The largest age group in this study was the 41-50 year age group (40.4%). These results are similar to the results of a 2015 study by Uhlig et al. The most common age group for corneal ulcer patients is 40-60 years (63.3%). The study conducted by Casalita et al. at the RSCM in 2019 was slightly different, where the average age of ulcer patients who underwent AMT grafts was 38.1 years. Meanwhile, Chauhan et al. found the mean age of corneal ulcer patients who underwent AMT was 60.4 years.[2,9,10]

The gender of most corneal ulcer patients was male (88.46%). This is in accordance with the results of research by Kim et al. in 2001, where male patients (71.4%) more commonly underwent AMT grafts in corneal ulcer patients. Chauhan et al. found that there was no significant difference between male (54%) and female (46%) genders for corneal ulcer patients who underwent AMT. Different results were obtained by Casalita et al., where the percentage of men was 44%. [2,9,11]

Based on the lateralization, there was no significant difference between the left and right eyes, and distribution was almost the same, namely the left eye in 51.9% of cases and the right eye in 48.1%. Based on the etiology of the ulcer, most corneal ulcers were caused by infection (86.5%) cases, while non-infectious corneal ulcers were only found in 13.5% of cases. In this study, 3 cases of non-infectious corneal ulcers were caused by Mooren's ulcer, 2 cases with vernal keratoconjunctivitis, 1 case due to lagophthalmos associated with Graves' Ophthalmopathy, and 1 case with a diagnosis of peripheral ulcerative conjunctivitis. In this study, the severity of corneal ulcers used the Harrison criteria. Based on the distribution of the severity of corneal ulcers, the most severe corneal ulcers (67.3%) were followed by moderate corneal ulcers with 32.7%. No mild-grade corneal ulcers were treated with AMT in this study.

Before the AMT graft was performed, the patient's visual acuity was mostly in the blind category II (hand movement/light perception), as much as 63.5%. In the second week, most patients' visual acuity was blindness category II (44.2%), which is almost the same as the visual acuity in the fourth week, which is 40.4%. It can be seen that visual acuity improved in 34.6% of eyes while only 2 (3.8%) eyes had visual acuity worsening. In the other 32 eyes (61.5%), the vision was persis before and after the AMT graft. Similar results were obtained in the study by Chauhan et al., where the average visual acuity before the AMT procedure was hand movement, and at the end of the follow-up, there was an improvement in visual acuity in 52.2% of cases. Schuerch et al. obtained an improvement in visual acuity from a mean of 1.8 ± 0.6 LogMar to 1.6 ± 0.8 1 month after the AMT graft. Although AMT causes corneal opacification in the early phase, it will dissolve in the weeks following the procedure, and vision will improve as a result of the restoration of the corneal surface.[2,12]

In this study, there was a high success rate, where 46 of 52 eyes (88.5%) received AMT grafts in eyes with

corneal ulcers, either moderate or severe corneal ulcers. There was no significant difference in the success rate for moderate or severe ulcers (p = 0792). This is similar to the study conducted by Casalita et al., where the success rate was 90%, both in moderate and severe ulcers (p = 0.27).[9]

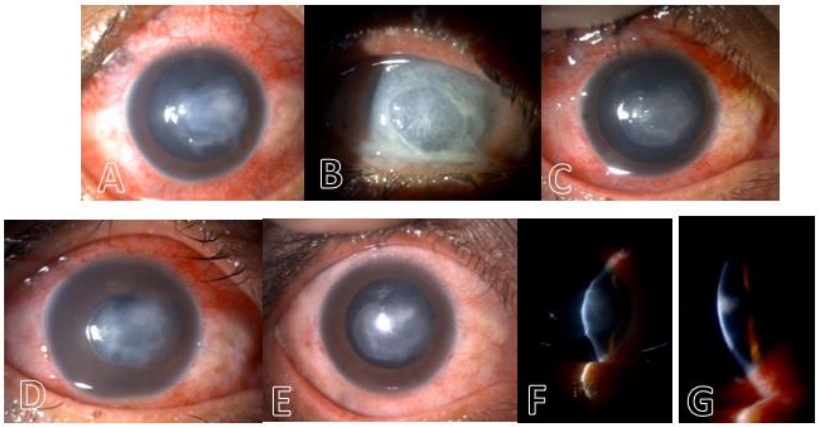


Figure 3. Patient no. 51 with a diagnosis of corneal ulcer OD ec *Staphylococcus aureus* bacteria. A. Prior to the AMT Graft. B. 5 days post-op, C. 7 days post-op, D. 14 days post-op, E. 1 month post-op, F. slit photo before AMT, G. slit photo 1 month after AMT graft.

Of the 52 total corneal ulcer patients who underwent AMT graft surgery, 5 (9.6.5%) required another surgery: repeated AMT procedures in 3 patients, paracentesis in one patient, and evisceration in one patient. The patient who underwent evisceration surgery was a 62-year-old male patient with a diagnosis of impending perforation corneal ulcer of the left eye due to a fungal infection. After 14 days of AMT transplantation, there was no epithelialization at all, and 4 mm hypopyon appeared on the anterior chamber. At one month follow-up, the visual acuity decreased to only light perception. Based on an ophthalmology examination, endophthalmitis was diagnosed in this patient, and so evisceration was performed. One other patient who underwent repeated AMT graft was a patient with Mooren's ulcer, in which the ulcer recurred after the AMT graft. Schallenber et al. in their study found that AMT transplantation was not effective in treating severe Mooren's ulcers because the disease was based on immunological abnormalities. However, AMT plays a role in immunosuppressive therapy in acute conditions such as corneal thinning and persistent epithelial defects. The other 2 patients with repeat AMT grafts were patients with complications of impending perforation after the AMT graft. In 1 patient, paracentesis was performed due to the appearance of a hypopyon as high as 5 mm at 1-month post AMT graft. In one other failed patient, a repeat operation was not performed but was managed medically due to a persistent epithelial defect.[13]

5. Conclusion

The AMT graft has successfully managed corneal ulcer patients, especially in moderate to severe cases, in our hospital.

6. References

1. Ting DSJ, Henein C, Said DG, Dua HS. Amniotic membrane transplantation for infectious keratitis: a systematic review and meta-analysis. Sci Rep. 2021; 11(1): 1–15.
2. Chauhan RS, Chhikara C, Rathi A, Chugh JP, Goel A, Sumpi C. Role of amniotic membrane transplantation in corneal ulcers. Saudi Journal of Medical and Pharmaceutical Sciences. 2021; 7(2): 114–25.

3. Byrd L, Martin N. Corneal Ulcer. StatPearl Publishing. 2021.
4. Thatte S. Efficacy of Amniotic Membrane Transplantation in Refractory Infective Keratitis Leading to Stromal Thinning, Descematocele and Perforations. JOJ Ophthalmol. 2017; 3(3): 1–6.
5. Mamede AC, Carvalho MJ, Abrantes AM, Laranjo M, Maia CJ, Botelho MF. Amniotic membrane: From structure and functions to clinical applications. Cell and Tissue Research. Springer Verlag. 2012; 349: 447–58.
6. Cirman T, Beltram M, Schollmayer P, Rožman P, Kreft ME. Amniotic membrane properties and current practice of amniotic membrane use in ophthalmology in Slovenia. Cell Tissue Bank. 2014; 15(2): 177–92.
7. Fan J, Wang M, Zhong F. Improvement of amniotic membrane method for the treatment of corneal perforation. Biomed Res Int. 2016; 2016: 1–9.
8. Letko E, Foster CS. Amniotic membrane transplantation. In: Foster CS, Azar DT, Dohlman CH, editors. Smolin and Thoft's the cornea scientific foundations and clinical practice. 4th ed. Philadelphia: Lippincott William & Wilkins. 2005; 980–90.
9. Casalita V, Nora RLD, Edwar L, Susiyanti M, Sitompul R. Amniotic membrane transplantation for infectious corneal ulcer treatment: A cohort retrospective study. Medical Journal of Indonesia. 2020; 29(4): 379–85.
10. Uhlig CE, Frings C, Rohloff N, Harmsen-Aasman C, Schmitz R, Kiesel L, et al. Long-term efficacy of glycerine-processed amniotic membrane transplantation in patients with corneal ulcer. Acta Ophthalmol. 2015; 93(6): e481–7.
11. Kim JS, Kim JC, Hahn TW, Park WC. Amniotic membrane transplantation in infectious corneal ulcer. Cornea. 2001; 20(7): 720–6.
12. Schuerch K, Baeriswyl A, Frueh BE, Tappeiner C. Efficacy of amniotic membrane transplantation for the treatment of corneal ulcers. Cornea. 2019; 00(00): 1–5.
13. Schallenberg M, Westekemper H, Steuhl KP, Meller D. Amniotic membrane transplantation ineffective as additional therapy in patients with aggressive Mooren's ulcer. BMC Ophthalmol. 2013; 13(81): 1–6.