

## Prevalence and Risk Factors of Corneal Transplant Rejection in Imam Hussain (AS) Hospital during 2009-2013

Dr. Ghazal Norouzi

General Practitioner at Shahid Beheshti Medical School; Shahid Beheshti University of Medical Sciences, Tehran, Iran

[conanp89@yahoo.com](mailto:conanp89@yahoo.com)

**Abstract:** Background: The purpose of this study is to determine the prevalence and risk factors of corneal graft rejection in patients undergoing corneal transplant in Imam Hussain (AS) hospital over the years 2009-2013. Materials and Methods: Patient inclusion criteria were: 1) corneal transplant in Imam Hussain (AS), Tehran, 2) received transplants during 2009-2013, 3) two-year track record in the patient's record. Patient exclusion criteria were: 1) incomplete record, 2) lack of patient follow-up, 3) using systemic immunosuppressive drugs. Information extracted from the records was used for statistical analysis. Results: In this study, a total of 215 cases of corneal transplantation were evaluated in 215 patients; mean age of patients was 49 years. The patients were followed for 24 months. Re-graft ( $P<0.01$ ) and anterior synechiae ( $P=0.009$ ) are a risk factor for graft rejection. No significant relationship was found between irritating sutures ( $P=0.067$ ); corneal vascularization ( $P=0.111$ ); uncontrolled intraocular pressure ( $P=0.120$ ); recurrent herpetic keratitis ( $P=0.134$ ); transplantation accompanied to cataract surgery ( $P=0.186$ ) and recipient age ( $P=0.283$ ) and an increased likelihood of rejection. Conclusion: This study shows that re-graft and anterior synechiae may increase the likelihood of graft rejection. There is no significant relationship between irritating sutures, corneal vascularization, uncontrolled intraocular pressure, recurrent herpetic keratitis, transplantation accompanied to cataract surgery and recipient age and increased likelihood of graft rejection.

[Ghazal Norouzi. **Prevalence and Risk Factors of Corneal Transplant Rejection in Imam Hussain (AS) Hospital during 2009-2013.** *Nat Sci* 2015;13(1):45-48]. (ISSN: 1545-0740). <http://www.sciencepub.net/nature>. 7

**Keywords:** Corneal Transplantation, Penetrating Keratoplasty, Graft Rejection, Risk Factors

### 1. Introduction

Corneal transplant surgery is one of the most common organ transplants surgeries in the world. Due to the vast improvements in the methods and tools used for this surgery, it carries a high chance of success. Currently, the most common cause of late graft failure in corneal graft is rejection by the host immune system [1].

Since corneal transplant requires time and cost and its failure require repeated surgery, risk factors of corneal graft rejection have been the subject of most studies in the field of ophthalmology. Factors such as re-graft, corneal vascularization, anterior synechiae, bilateral transplantation can increase the chance of transplant rejection [2, 3, and 4]. Contribution of these is slightly different; there are sometimes disagreements on their significant effect on increase in graft rejection. For example, the effect of age on the risk of graft rejection which alone is not significantly related to the risk of graft rejection in most studies. However, some others such as Yu Al et al retrospectively examined 377 patients during 2001 and 2011. They found that the risk of corneal graft rejection significantly increased by age of the transplant recipient [12]. A similar difference was found for the effect of cataract surgery associated with corneal graft in an increased risk of graft rejection;

recent studies did not report this relationship [14]. The purpose of this study was to determine the prevalence and risk factors of corneal graft rejection in patients during 2009-2013 in Imam Hussain (AS) hospital.

### Materials and Methods:

This is a retrospective descriptive analytical study. Patients who underwent corneal transplant during 2009-2013 in Imam Hussain (AS) enrolled in the study. The information related to patient follow-up was recorded by two years after transplantation. According to the data from their records, incomplete information available in records so that it interferes the analysis and conclusions of the study, patients avoiding appointed follow-ups and that the patient had been previously treated with immunosuppressive drugs (e.g. in the field of rheumatoid disease) caused his withdrawal from the study. Since this study was retrospective, the number of samples was constant and there was no sample loss as well as the fact that the recorded information was objective, the factor analysis has no effect in this study. In terms of ethical considerations, no cost or financial-mental loss was imposed on patients, health professionals and hospital, and all patient information remained confidential.

The data was extracted and recorded by interns supervised by ophthalmologist professor. Information

and possible risk factors for corneal graft rejection, such as the type of surgery, the primary cause of transplantation, transplantation results in follow-up surveys and some ecographic characteristics such as age and sex were recorded in these questionnaires. To prevent error in patients who experienced graft rejection and had several concomitant risk factors, the only risk factor recorded as the main cause for corneal graft rejection was considered according to the ophthalmologist. By completing the records for the questionnaires, the database was provided for statistical analysis. The information obtained by statistical tests, chi-square, Fisher's exact test and Mann-Whitney test were evaluated. All the statistical analyses were conducted by SPSS software, version 21. The  $P < 0.05$  was considered as statistically significant. To estimate the incidence of rejection by approximately 95% confidence and a maximum error of 5%, 210 samples were required. Accordingly, 215 cases of corneal transplant performed in Imam Hussain (AS) during 2008-2013 were considered as samples.

#### Results:

A total of 215 patients were enrolled (36.74% females and 63.3% males). The patients were 39.1% aged less than or equal to 40 and 60.9% aged over 40 years. The most common causes of corneal transplant included keratoconus KCN, bullous keratopathy, re-graft, scarring of the cornea, Fuchs endothelial dystrophy, corneal ulcers, fungal keratitis, and stromal dystrophy of cornea, corneal edema, corneal foreign body, old herpetic keratitis and leucoma and iris synechiae.

Totally, 27.9% of patients experienced graft rejection during follow-up. In 30.5% of the patients older than 40 and in 23.8% of the patients less than or

equal to 40 years, rejection was observed. The difference is not statistically significant ( $P=0.283$ ). Out of 11.6% of the patients undergoing re-graft, 64% experienced graft rejection, while 23.2% of the rest 88.4% (without re-graft) suffered rejection, which is statistically significant ( $P < 0.001$ ). vascularization was observed in 24.2% of the patients of which 36.5% experienced graft rejection, while graft rejection occurred in 25.2% of the people who suffered graft rejection; this relationship is not statistically significant ( $P=0.111$ ). In 7.4% of the patients, anterior corneal synechiae was observed, of which 56.3% experienced graft rejection. Graft rejection occurred in 25.6% of the people without anterior corneal synechiae, which suggests the significant relationship between anterior synechiae (iris to cornea) and graft rejection ( $P=0.009$ ). Examining the patients, 86% of the patients suffered irritating suture remains out of which 75% experienced graft rejection, while 27.0% of the patients without irritating suture experienced graft rejection; this difference is not statistically significant ( $P=0.067$ ). In 5.1% of patients, intraocular cataract surgery was done along with corneal transplant, of which 45.5% experienced graft rejection; in 27.0% of the rest, graft rejection occurred. 26.7%; this difference is not significant ( $P=0.186$ ). The uncontrolled intraocular pressure was observed in 4.2% of the patients of which 55.6% experienced graft rejection, while 26.7% of the patients without intraocular pressure experienced graft rejection; The relationship is not statistically significant ( $P=0.120$ ). Post-transplant recurrent herpetic keratitis was observed in 2.3% of patients, of which 60% experienced graft rejection, while 27.1% of the remaining patients experienced graft rejection; this is not statistically significant ( $P=0.134$ ).

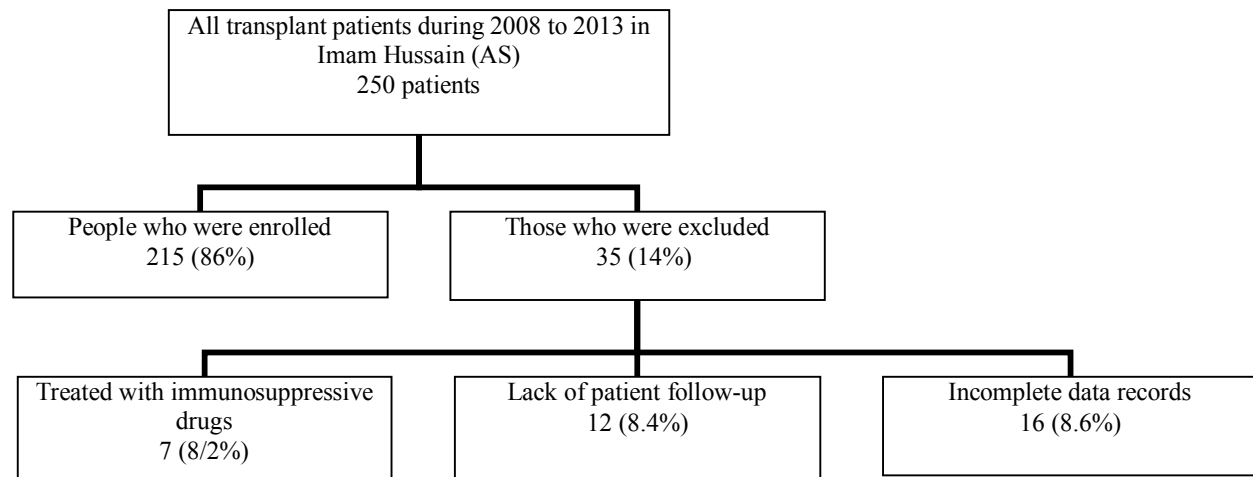


Table 1: Contextual variables

		Number	%
The reason of corneal transplantation	keratoconus KCN	60	27.9%
	bullous keratopathy BKP	45	20.9%
	Failure of the previous graft (Regraft)	25	11.6%
	scarring of the cornea	24	11.2%
	Fuchs endothelial dystrophy	20	9.3%
	corneal ulcers	17	7.9%
	fungal keratitis	9	4.2%
	stromal dystrophy of cornea	9	4.2%
	corneal edema	3	1.4%
	leucoma and iris synechiae	1	.5%
	old herpetic keratitis	1	.5%
	corneal foreign body	1	.5%
Age group	Less than or equal to 40 years	84	39.1%
	Over 40 years	131	60.9%
Gender	Male	136	63.3%
	Female	79	36.7%
Intraocular pressure (uncontrolled glaucoma)	No	206	95.8%
	Yes	9	4.2%
The maintenance of corneal graft	New graft stored in cold wet chamber	118	54.9%
	Maintained in optisol solution	97	45.1%
* Size difference of cornea transplanted to cornea of the recipient	0.5 mm (the recipient less than the donor)	155	72.1%
	0.25 mm	60	27.9%

\* in all cases, the size difference between donor and recipient cornea was ~0.5mm (the recipient 0.5mm less than the donor) except for keratoconus cases, which was ~0.25mm to reduce the myopia after the transplant.

Table 2: The relationship between graft rejection and risk factors

Variable	Category	Graft rejection		P
		Yes	No	
Age	≤40	(23.8) 20	(76.2) 64	0.283*
	>40	(30.5) 40	(69.5) 91	
Regraft	Yes	(64.0) 16	(36.0) 9	<0.001*
	No	(23.2) 44	(76.8) 146	
Vascularization	Yes	(36.5) 19	(63.5) 33	0.111*
	No	(25.2) 41	(74.8) 122	
Anterior corneal synechiae	Yes	(56.3) 9	(43.7) 7	0.009*
	No	(25.6) 51	(74.4) 148	
Irritating suture remains	Yes	(75.0) 3	(25.0) 1	0.067*
	No	(27.0) 57	(73.0) 154	
Simultaneous cataract surgery and corneal transplantation	Yes	(45.5) 5	(54.5) 6	0.186*
	No	(27.0) 55	(73.0) 149	
Intraocular Pressure	High	(55.6) 5	(44.4) 4	0.120*
	Control	(27.6) 55	(73.3) 151	
Recurrent herpetic keratitis	Yes	(60.0) 3	(40.0) 2	0.134*
	No	(27.1) 57	(79.9) 153	

\* Based on Chi-square test. \*\* Based on Fisher's exact test.

### Discussion:

In this study, Regraft increases likely corneal graft rejection, which is consistent with other similar studies ( $P < 0.001$ ) [2, 5, 6]. Examining 377 patients with corneal transplant during 2001-2011, Yu AL et al in Munich, Germany identified regraft as a known risk factor [2].

There was no significant relationship between vascularization and graft rejection ( $P = 0.111$ ), which is different from other studies [7, 2]. Based on CCTS, new vascularization significantly increases in at least

two quarters of the cornea and a minimum depth of 2 mm, while vascularization was not considered in this study. Involvement of individuals with early stages of vascularization without the mentioned criteria and limited 2 years of follow-up can be the cause of this difference [7]. Anterior synechiae increases the risk of corneal transplant rejection, which is consistent with other similar studies ( $P = 0.009$ ). Maguire MG et al supports this [5]. Recurrent herpetic keratitis also showed no significant relationship with transplant rejection ( $P = 0.134$ ). In other studies, the history of

recurrent herpetic keratitis is significantly associated with increased chance of graft rejection, because there is an increased risk of vascularization and inflammation in the cornea of the patient [8, 9, 10]. About two-thirds of the patients in silent phase of the disease report histologic evidence of vascularization and inflammation of the cornea. In other words, they are at higher risk of graft rejection without a new attack [10], while this study only considers cases of pre-rejection recurrent acute keratitis, which can explain this difference. A loose initiating stitch did not significantly increase the risk of corneal transplant rejection ( $P=0.067$ ), while other studies such as Jonas JB et al found no significant relationship, which can be due to the limited sample size of this study [11]. The age of recipient did not significantly influence the probability of corneal graft rejection ( $P=0.283$ ), which is consistent with majority of the similar studies [1, 2 and 3], while Yu AL et al examining 377 patients retrospectively during 2001-2011 found that old age of the recipient significantly increased the risk of corneal graft rejection [12]. Given that the probability of comorbidities such as glaucoma increases with age, it is slightly difficult to examine the effect of age. For better result, the patients are required to be matched for all other risk factors. There was no significant relationship between uncontrolled intraocular pressure and graft rejection ( $P=0.120$ ). Chodosh J and Haddadin RI identified glaucoma as the most important cause of irreversible blindness after corneal transplant which is in the field of optic nerve damage; however, it clearly adds the likely failure in the transplant [12]. Judgment on control of intraocular pressure in this study was based solely on examinations during follow-up, which may indicate no variation in pressure due to the changes made in the disease and irregular drug use. On the other hand, the effects of intraocular pressure is gradual on the organ, while this study evaluated patients only for two years, which can be a reason for difference. There was no significant relationship between simultaneous intraocular cataract surgery and corneal transplantation and graft rejection ( $P=0.186$ ), which is consistent with findings of most similar studies of the past two years. Although, these association was previously known as a risk factor of graft rejection, the recent studies, including Chaurasia S et al studying 492 corneal transplants during 2010-2012 (out of which 200 were associated with cataract surgery), concluded that this association did not increase the risk of corneal transplant rejection; in contrast, it

reduced the cost and facilitated the improved visibility [14].

### Conclusion:

According to this study, there is a significant relationship between re-graft and the anterior synechiae and increased risk of corneal transplant rejection. No significant relationship was found between irritating suture, vascularization, intraocular pressure, and recipient age, cataract surgery associated with corneal transplantation and recurrent herpetic keratitis and the increased risk of corneal graft rejection.

### References:

1. Kumar V, Kumar A .Immunological aspects of corneal transplant. *Immunol Invest* 2014;43(8):888-901.
2. Yu AL, Kaiser M, Schaumberger M, Messmer E, Kook D, Welge-Lussen U. Perioperative and postoperative risk factors for corneal graft failure. *Clinical Ophthalmology*. 2014 Aug 28;8:1641-7.
3. Bartels MC, Doxiadis II, Colen TP, Beekhuis WH. Long-term outcome in high-risk corneal transplantation and the influence of HLA-A and HLA-B matching. *Cornea*. 2003; 22: 552-6.
4. Price MO, Thompson RW Jr, Price FW Jr. Risk factors for various causes of failure in initial corneal grafts. *Arch Ophthalmol* 2003; 121: 1087-92.
5. Maguire MG, Stark WJ, Gottsch JD, Stulting RD, Sugar A, Fink NE, Schwartz A. Risk factors for corneal graft failure and rejection in the collaborative corneal transplantation studies. Collaborative Corneal Transplantation Studies Research Group. *Ophthalmology*. 1994 ; 101: 1536-47.
6. Trigui A, Smaoui M, Masmoudi J, Mhiri W, Maatoug S, Feki J. Corneal graft rejection: donor and receiver implication. *J Fr Ophtalmol*. 2005; 28: 631-4.
7. Bachmann B, Taylor RS, Cursiefen C. Corneal neovascularization as a risk factor for graft failure and rejection after keratoplasty: an evidence-based meta-analysis. *Ophthalmology*. 2010; 117: 1300-5.
8. Lomholt JA, Baggesen K, Ehlers N. Recurrence and rejection rates following corneal transplantation for herpes simplex keratitis. *Acta Ophthalmol Scand*. 1995; 73: 29-32.
9. Shtein RM, Garcia DD, Musch DC, Elner VM. Herpes simplex virus keratitis: histopathologic inflammation and corneal allograft rejection. *Ophthalmology*. 2009;116:1301-5.
10. Shtein RM, Elner VM. Herpes simplex virus keratitis: histopathology and corneal allograft outcomes. *Expert Rev Ophthalmol*. 2010; 5: 129-34.
11. Jonas JB, Rank RM, BUdde WM. Immunologic graft rejections after allogeneic penetrating keratoplasty. *Am J Ophthalmol* 2002; 133: 437-43.
12. Yu AL, Kaiser M, Schaumberger M, Messmer E, Kook D, Welge-Lussen U. Donor-related risk factors and preoperative recipient-related risk factors for graft failure. *Cornea*. 2014 Nov;33(11):1149-56.
13. Haddadin RI, Chodosh J .Corneal transplantation and glaucoma. *Semin Ophthalmol*. 2014;29(5-6):380-96.
14. Chaurasia S, Price FW Jr, Gunderson L, Price MO. Descemet's membrane endothelial keratoplasty: clinical results of single versus triple procedures (combined with cataract surgery). *Ophthalmology*. 2014 Feb;121(2):454-8.