

## Research Article

# Preoperative risk factors and incidence of glaucoma after penetrating keratoplasty

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**Received:** 18 July 2014

**Accepted:** 4 August 2014

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## ABSTRACT

**Background:** Glaucoma following penetrating keratoplasty is one of the serious complications due to its frequency of occurrence, difficulty in diagnosis and management, risk of graft failure and irreversible visual loss due to optic nerve damage. The incidence of glaucoma after keratoplasty varies from 9% to 31% in the early postoperative period and from 18 to 35% in the late postoperative period. The aetiology of this disorder is multifactorial and the clear understanding of the various mechanisms that operate during different time frames following penetrating keratoplasty is essential to chalk out the appropriate management algorithms.

**Methods:** Prospective analysis of 100 consecutive eyes which underwent penetrating keratoplasty during the period from September 2009 to December 2010 at Bangalore West Lions super speciality eye hospital was done. The patients were followed up for a minimum period of 9 months.

**Results:** Out of 100 patients mean age distribution was  $47 \pm 11$  years. Of the 100 patients male 68% and 32 female (32%). Out of 100 eyes 38% of them had vision  $<6/60$ , 36% of them had vision between  $6/36-6/18$  and 26% of them between  $6/18-6/6$ . Raised intraocular pressure was found in 15 out of 100 eyes. Mean raise in intraocular pressure was  $29 \text{ mmHg} \pm 1.5 \text{ mmHg}$ . Out of 15 patients 4 were steroid responders. Mean time of diagnosis of raised intraocular pressure was  $5 \pm 9.5$  months. Pseudophakic Bullous Keratopathy (PBK) in 5 (33.3%) patients, aphakic bullous keratopathy (ABK) in 3 (20%) patients, graft rejection in 2 (13.3%) patients and one each patient (6.7%) of corneal scar, adherent leucoma, chemical injury and congenital hereditary endothelial dystrophy. Aphakic group was at higher risk compared to the other groups and there was not much difference between the phakic and the pseudophakic group.

**Conclusions:** Post penetrating keratoplasty glaucoma continues to be a clinical problem that can be sight threatening in its clinical outcome. It is mandatory that intraocular pressure is monitored on a regular basis. Recognition of the risk factors namely, indications, graft size, lenticular status & associated surgical procedure with penetrating keratoplasty would help in early diagnosis of post penetrating keratoplasty glaucoma. Most of these cases are amenable to medical management.

**Keywords:** Glaucoma, Keratoplasty, Operation

## INTRODUCTION

Numerous noteworthy advancements have been made in the fields of surgical techniques and postoperative care following penetrating keratoplasty. However, in spite of these advancements, complications of corneal grafting surgery have not become rare.<sup>1</sup> Glaucoma following penetrating keratoplasty is one of the serious complications due to its frequency of occurrence, difficulty in diagnosis and management, risk of graft failure and irreversible visual loss due to optic nerve damage.<sup>2,3</sup>

The incidence of glaucoma after keratoplasty varies from 9% to 31% in the early postoperative period and from 18 to 35% in the late postoperative period.<sup>4,5</sup> The aetiology of this disorder is multifactorial and the clear understanding of the various mechanisms that operate during different time frames following penetrating keratoplasty is essential to chalk out the appropriate management algorithms.

Post-penetrating keratoplasty glaucoma is defined as elevation of intraocular pressure >21 mmHg with or without optic nerve head and visual field changes.<sup>1,6</sup>

The risk factors for post penetrating keratoplasty glaucoma are preoperative diagnosis of inflammatory diseases, peripheral anterior synechiae, preoperative glaucoma and additional surgery combined with penetrating keratoplasty.<sup>7</sup> Association between topical steroid use and elevated intraocular pressure is well known. Steroid-induced intraocular pressure elevation is one of the important causes of late-onset post-keratoplasty glaucoma.

Both acute and chronic intraocular pressure elevations after penetrating keratoplasty are at times very difficult to control. Medical therapy is tried first, because every surgical procedure can further endanger the survival of the graft.

Glaucoma certainly is one of the most threatening complications following penetrating keratoplasty. Taking care of possible risk factors, improving the surgical techniques and closely following the patient can significantly increase the overall success rate.

This study addresses the preoperative factors, diagnosis, and management of glaucoma after penetrating keratoplasty.

## METHODS

Prospective analysis of 100 consecutive eyes which underwent penetrating keratoplasty during the period from September 2009 to December 2010 was done. The patients were followed up for a minimum period of 9 months. All the patients undergoing optical penetrating keratoplasty at Bangalore West Lions super speciality eye

hospital were included. Patients with pre-existing glaucoma were excluded. Criteria for diagnosis of post-penetrating keratoplasty glaucoma were chronically elevated intraocular pressure of more than 21 mmHg with or without disc and visual field changes. Patients with acute transient elevation of intraocular pressure were not considered as it was attributed to intraoperative use of viscoelastics or pupillary block.

### *Parameters evaluated*

In all patients best corrected visual acuity was recorded and thorough slit lamp examination was done. The anterior segment features noted were the status of cornea, type of intraocular lens present, presence of peripheral anterior synechiae. Intraocular pressure was recorded by Perkin's applanation tonometer or tonopen. Pachymetry was done. Posterior segment was evaluated with indirect ophthalmoscopy in clear media and B scan was used in hazy media.

Postoperative evaluation included best corrected visual acuity, status of the corneal graft, intraocular pressure at 1<sup>st</sup> week, 1 month, 3 months, 6 months and 9 months with pachymetry, gonioscopy, disc evaluation and visual field analysis were done whenever possible.

Postoperatively the patients received predacetate eye drops hourly for the first week, and was tapered to 4 times per day which was maintained for several weeks and gradually tapered to once a day and then for alternate days.

The follow-up information recorded included visual acuity, status of the corneal graft, status of anterior chamber, and the intraocular pressure as measured by Goldmann applanation tonometer or tonopen. Disc evaluation was performed in cases where media was clear and permitted a view of the disc. Visual field analysis could not be done in any patient and therefore, intraocular pressure was the only criterion for assessing the progress or control of glaucoma. In all the patients the first line of management for glaucoma was medical therapy to the maximum tolerated level. When medical therapy failed to control intraocular pressure, surgery was resorted to.<sup>5</sup>

### *Statistical methods*

Results on continuous measurements are presented on Mean  $\pm$  SD (Min-Max) and results on categorical measurements are presented in number or percentage. Significance is assessed at 5% level of significance. Postoperative elevated intraocular pressure was used as the dependent variable. Independent variables included patient demographics, diagnostic categories, and surgical procedures.

The chi-square analyses have been carried out for categorical data. A comparison was termed statistically significant if the P value was <0.05.

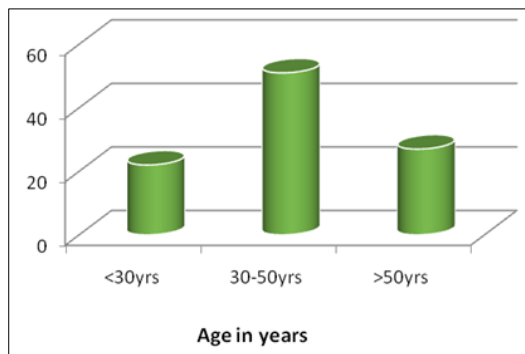
### Statistical software

The statistical software namely SPSS was used for the analyses of the data and Microsoft word, excel have been used to generate tables and graphs.

## RESULTS

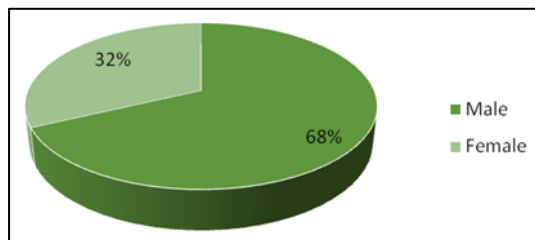
### Preoperative observations

In our study, out of 100 patients 73% were less than 50 years of age and the mean age distribution was  $47 \pm 11$  years (Figure 1).



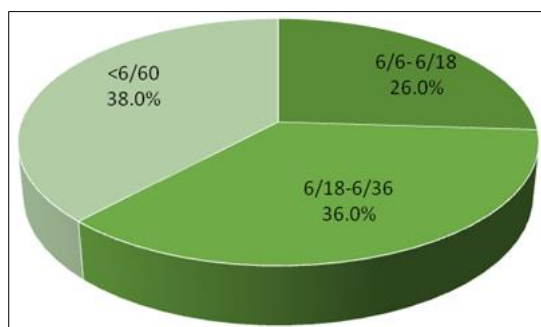
**Figure 1: Age distribution of patients who underwent penetrating keratoplasty.**

Of the 100 eyes of 100 patients who underwent penetrating keratoplasty, 68 were male (68%) and 32 were female (32%) (Figure 2).



**Figure 2: Sex distribution of patients who underwent penetrating keratoplasty.**

### Postoperative observations



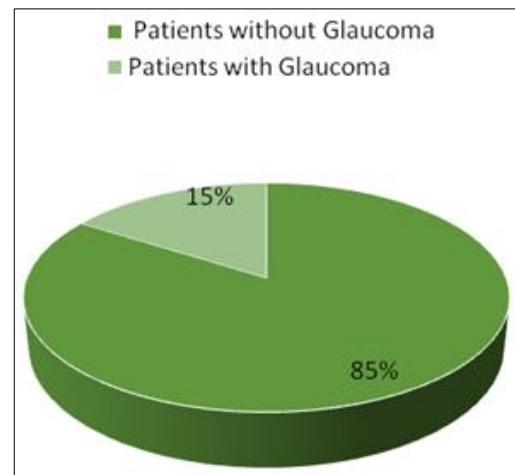
**Figure 3: Distribution of postoperative visual activity.**

Out of 100 eyes 38% of them had vision <6/60, 36% of them had vision between 6//36-6/18 and 26 % of them between 6/18-6/6 (Figure 3).

In our study:

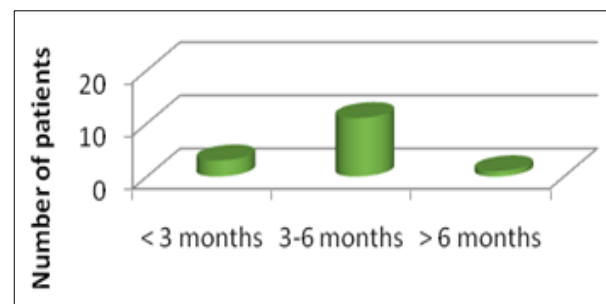
- Raised intraocular pressure was found in 15 out of 100 eyes.
- Mean raise in intraocular pressure was  $29 \text{ mmHg} \pm 1.5 \text{ mmHg}$ .

Out of 15 patients 4 were steroid responders (Figure 4).



**Figure 4: Incidence of post penetrating keratoplasty glaucoma.**

Mean time of diagnosis of raised intraocular pressure was  $5 \pm 9.5$  months (Figure 5).



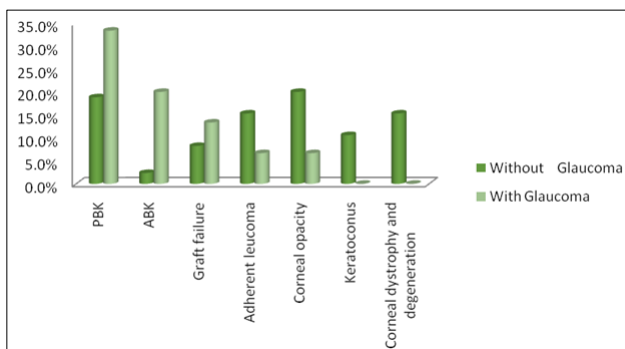
**Figure 5: Time of diagnosis of raised IOP following PK.**

**Table 1: Age distribution of post penetrating keratoplasty glaucoma patients.**

Age	Patients with glaucoma	Percentage
15-25 years	2	13%
25-35 years	3	20%
>35 years	10	66%

**Table 2: Preoperative diagnosis and incidence of glaucoma.**

Preoperative diagnosis	Glaucoma		Total	Relative risk (RR)	95% confidence interval
	No.	Yes			
Pseudophakic bullous keratopathy	16	5 (33.3%)	21	1.7	0.66-4.3
Aphakic bullous keratopathy	2	3 (20%)	5	4.38	1.8-10.5
Graft rejection	7	2 (13.3%)	9	2.33	0.8-6.6
Adherent leucoma	13	1 (6.7%)	14	0.4	1.8-10.5
Corneal opacity	17	1 (6.7%)	18	0.26	0.03-1.9
Chemical injury	1	1 (6.7%)	2	3.26	0.75-14.0
Congenital hereditary endothelial dystrophy	1	1 (6.7)	2	3.26	0.75-14.0
Keratoconus	8	0 (0.0%)	9	-	-
Corneal dystrophy	4	0 (0.0%)	4	-	-
Corneal degeneration	9	0	9	-	-
Fuch's	4	0	4	-	-
Trauma	1	0	1	-	-
Descematocele	0	1 (6.7%)	1	-	-
Endothelitis	1	0	1	-	-

**Figure 6: Preoperative diagnosis vs. incidence of glaucoma.**

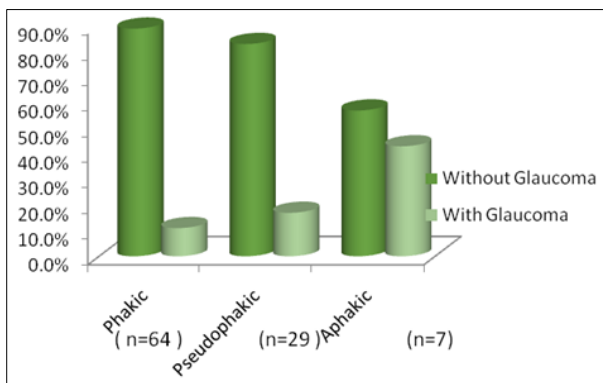
In our study, out of 15 eyes who developed raised intraocular pressure following penetrating keratoplasty the preoperative diagnosis was as follows:

Pseudophakic bullous keratopathy (PBK) in 5 (33.3%) patients, aphakic bullous keratopathy (ABK) in 3 (20%) patients, graft rejection in 2 (13.3%) patients and one each patient (6.7%) of corneal scar, adherent leucoma, chemical injury and congenital hereditary endothelial dystrophy. None of the trauma, keratoconus or corneal dystrophy patients developed glaucoma. The common risk factors for developing glaucoma were aphakic bullous keratopathy with the relative risk of 4.38 and 95% confidence interval being 1.8-10.5, graft rejection with the relative risk of 2.33 and 95% confidence interval being 0.8-6.6 and pseudophakic bullous keratopathy with relative risk of 1.7 and 95% confidence interval being 0.66-4.3.

Statistical significance of relative risks of CHED and chemical injury patients could not be commented because of small sample size.

**Table 3: Preoperative lens status versus incidence of glaucoma.**

Pre op lens status	Without glaucoma	With glaucoma	Total	Significance
Phakic	57 (89.0%)	7 (11.0%)	64 (64.0%)	$\chi^2=5.20$ , df=2, P=0.07415
Pseudophakic	24 (83.0%)	5 (17.0%)	29 (29.0%)	
Aphakic	4 (57.0%)	3 (43.0%)	7 (7.0%)	
<b>Total</b>	85	15	100%	

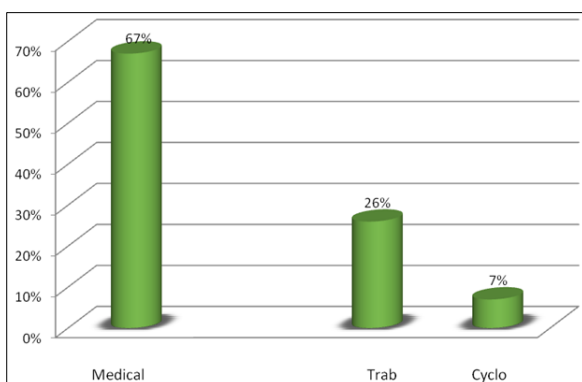


**Figure 7: Preoperative lens status versus incidence of glaucoma.**

On comparing the incidence of post penetrating keratoplasty glaucoma in phakic, pseudophakic and aphakic groups it was found that aphakic group was at higher risk compared to the other groups even though statistical significance could not be achieved as the percentage of aphakic patients in the study group were less ( $P = 0.07$ , near statistical significance) whereas there was not much difference between the phakic and the pseudophakic group.

**Table 4: Management of post penetrating keratoplasty glaucoma cases.**

Treatment	No. of patients
Medically managed	10 (67%)
Surgical management	
Trabeculectomy	2 (13%)
TSCP(Graft failure)	1 (7%)
Awaiting trabeculectomy	2 (13%)



**Figure 8: Management of post penetrating keratoplasty glaucoma cases.**

Among the medically managed patients, one drug was needed in 28% of patients, two drugs in 27% and 3 drugs were needed in 14%.

Topical medications used were:

- Beta blockers (timolol).
- Alpha-2-adrenergic agonists (brimonidine).
- Topical carbonic anhydrase inhibitor (dorzolamide) was the last choice.

The raised intraocular pressure in steroid responders were controlled with 1 or 2 topical anti-glaucoma medication after stopping high dose steroids and were kept on low dose steroids.

## DISCUSSION

Glaucoma is one of the most serious complications after penetrating keratoplasty because of its high incidence and severity and the difficulty associated with its diagnosis and treatment.

### Age and sex distribution of the study group who underwent penetrating keratoplasty

In our study group, mean age was  $47 \pm 11$  years, 73% of the patients were less than 50yrs of age of which 68% were males and 32% were females. Onur Karadag et al. and Suleyman Kuguet al.<sup>7</sup> reviewed 729 patient with the mean age of  $40.96 \pm 20.4$  years of which 61.9% were male and 38.1% were female.

### Incidence of post penetrating keratoplasty glaucoma

In our series, 15 of 100 consecutive eyes who underwent optical penetrating keratoplasty developed high intraocular pressure, giving an overall incidence of 15% during the mean follow up period of 9 months. Mean time of diagnosis of raised intraocular pressure was  $5 \pm 9.5$  months. Mean raise in intraocular pressure was  $29 \text{ mmHg} \pm 1.5 \text{ mmHg}$ . Foulks et al. and Karesh JW et al.<sup>8,9</sup> reported the incidence of post-penetrating keratoplasty glaucoma varying from 9% to 31% in the early postoperative period and from 18% to 35% in the late postoperative period. In a recently reported series, the incidence of post-penetrating keratoplasty glaucoma was found to be 18%. In another study by Sekharet et al.<sup>10</sup> (1993), of 190 eyes studied 52 developed high intraocular pressure following post-penetrating keratoplasty, giving an overall incidence of 27.4%. Onur Karadag et al. and Suleyman Kuguet al.<sup>7</sup> found the incidence of post penetrating keratoplasty glaucoma to be 16.6% in the late postoperative period. The mean period of time between penetrating keratoplasty and the first occurrence of glaucoma was 5 months.

In our study out of 15 patients who developed raised intraocular pressure 4 patients were steroid responders.

### **Risk factors of post penetrating keratoplasty glaucoma**

The risk of post penetrating keratoplasty intraocular pressure elevation is correlated with the preoperative diagnosis of corneal disease. We found that bullous keratopathy (ABK-33% with the relative risk of 4.38, PBK-20% with the relative risk of 1.7), graft rejection (13.3% with the relative risk of 2.33) adherent leucoma (6.7% with the relative risk of 0.4), were at higher risk of developing raised intraocular pressure whereas as keratoconus (0%) and corneal dystrophy (0%) were at lower risk.

Sekhar GC et al.<sup>10</sup> observed that in conditions such as Aphakic Bullous Keratopathy (ABK), Pseudophakic Bullous Keratopathy (PBK) and vascularized corneal scar the incidence of post-penetrating keratoplasty glaucoma was high (30 to 42%), while in keratoconus and corneal dystrophies it was low (6 and 16%, respectively).

Omur Koradunget al.<sup>7</sup> recently (2010) reported the higher risk of post penetrating keratoplasty glaucoma in bullous keratopathy (RR = 2.59), graft rejection (RR = 2.61), traumatic scar (2.66) and lower risk in patients who underwent penetrating keratoplasty for keratoconus (RR = 0.15) and corneal dystrophy (RR = 0.42).

#### *Preoperative lens status*

We found that preoperative lens status has correlation with post penetrating keratoplasty glaucoma. Pseudophakic (17%) and aphakic (43%) patients were at high risk of developing raised intraocular pressure following penetrating keratoplasty compared to phakic (11%) patients and we also observed that aphakic patients were at higher risk compared to pseudophakics even though it was not statistically significant ( $P = 0.07$ ).

Some, but not all, studies found that aphakic and pseudophakic eyes had a greater tendency for post-penetrating keratoplasty glaucoma as compared to phakic eyes.<sup>11</sup> Onur Karadag et al. and Suleyman Kugu et al.<sup>7</sup> found no difference between aphakic and pseudophakic eyes but a higher incidence of post-penetrating keratoplasty glaucoma was observed in pseudophakic and aphakic eyes compared with the phakics ( $P = 0.001$ ).

Ruthanne B. Simmons et al.<sup>12</sup> showed that postoperative elevated intraocular pressure was significantly more likely in aphakic eyes than in phakic or pseudophakic eyes, with chronic intraocular pressure rise in 46% of aphakic eyes. The results are consistent with reports by Polack<sup>13</sup> and by Goldberg et al.<sup>14</sup> in finding that preoperative glaucoma accounts for the high incidence of elevated intraocular pressure in aphakic eyes postoperatively. Since the advent of disparate graft sizing there has been controversy as to whether aphakia remains an independent risk factor for post-keratoplasty intraocular pressure elevation. These results differ, however, from Foulkset al.<sup>8</sup> who found that aphakia

remained an independent risk factor after controlling for pre-existing glaucoma.

Steroid responsiveness was found to be a major risk factor in younger patients in our study.

### **Management**

Medical management (topical drops or systemic) is still the first line of treatment in cases of glaucoma following keratoplasty.<sup>14</sup> In our series, majority (67%) of the patients were managed medically. Surgical intervention was required only when the intraocular pressure was not controlled by maximum tolerant medical therapy. Surgical intervention was required in 33% of patients as compared to the study by Shekar GC et al.<sup>10</sup> where 73% of patients were managed medically and 27% of patients required surgical intervention. Trabeculectomy was the procedure of choice. Cyclocryotherapy was reported in one patient whose graft had failed.<sup>15</sup>

Lin YS et al.<sup>16</sup> studied 28 patients with secondary glaucoma following penetrating keratoplasty who had failed to respond to anti-glaucoma drugs and routine filtering procedures were treated with cyclocryotherapy. The results showed that intraocular pressure was controlled in 89% of the eyes.

Uncontrolled intraocular pressure after penetrating keratoplasty is one of the leading causes of graft failure and visual loss. It is a common complication of penetrating keratoplasty.<sup>17</sup> Knowledge of the risk factors may help to limit the occurrence of glaucoma and to increase the chances of success of the penetrating keratoplasty. Patients undergoing penetrating keratoplasty need more regular postoperative care. Uncontrolled intraocular pressure should be aggressively treated.

### **Summary**

- A prospective analysis of 100 consecutive eyes who underwent penetrating keratoplasty during the period from August 2009 to June 2010 was done. The patients were followed up for a minimum period of 9 months.
- Mean age distribution of the patients in the study group was  $47 \pm 11$  years of which 68 were males (68%) and 32 were females (32%).
- 15 of 100 eyes who underwent penetrating keratoplasty developed high intraocular pressure, giving an overall incidence of 15%, during the mean follow up period of 9 months. Mean time of diagnosis of raised intraocular pressure was  $5 \pm 9.5$  months. Mean raise in intraocular pressure:  $29 \text{ mmHg} \pm 1.5 \text{ mmHg}$ .
- Out of 15 patients who developed raised intraocular pressure 4 patients were steroid responders.
- Bullous keratopathy (ABK-33% RR-4.38, PBK-20% RR-1.7), graft rejection (13.3% RR-2.33), adherent



leucoma (6.7% RR-0.4), were determined as high-risk factors whereas as keratoconus and corneal dystrophy were at lower risk.

- On comparing the graft sizes used with the outcome we have observed that the risk of raised intraocular pressure is high with graft size 8.5mm and above as compared to other groups. This may be due to formation of peripheral anterior synechiae at host graft junction.
- Preoperative lens status has correlation with glaucoma. Pseudophakic and aphakic patients were at higher risk of developing raised intraocular pressure following penetrating keratoplasty as compared to phakic patients and we also observed that aphakic patients were at higher risk as compared to pseudophakics.
- No statistically significant difference among various surgical procedures was observed. However, patients undergoing penetrating keratoplasty with anterior chamber intraocular lens implantation were found to be relatively at higher risk as compared to posterior chamber intraocular lens implantation and the patients undergoing regrant were at higher risk. Distortion of the angle, formation of peripheral anterior synechiae & epithelial down growth were found to be associated in these patients.
- Post penetrating keratoplasty-glaucoma was observed in 11.3% of the eyes with peripheral anterior synechiae and graft host junction synechiae and 5.6% of eyes without peripheral anterior synechiae.
- Steroid responsiveness was found to be a major risk factor in younger patients.
- Medical management (topical drops or systemic) was our first line of treatment in cases of glaucoma following keratoplasty. In our series majority (67%) of the patients were managed medically. Surgical intervention was required only when the intraocular pressure was not controlled by maximum tolerant medical therapy. Surgical intervention was required in 33% of patients. Cyclocryotherapy was reported in 1 patient whose graft had failed.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the institutional ethics committee*

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DOI: 10.5455/2349-3259.ijct20140804

**Cite this article as:** Hemanth Raj MN, Bhanushree G, Hulinaykar RM, Vijayanath V. Preoperative risk factors and incidence of glaucoma after penetrating keratoplasty. *Int J Clin Trials* 2014;1:55-61.