"ONE YEAR CROSS-SECTIONAL STUDY OF VISUAL OUTCOME AND GRAFT SURVIVAL IN PENETRATING KERATOPLASTY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE,BELAGAVI"

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LIST OF ABBREVIATIONS USED

CF	-	Counting Fingers
D	-	Diopter
DM	-	Descemet's memebrame
HMCF	-	Hand movements close to face
hrs	-	hours
Inj	-	Injection
IOL	-	Intra-ocular lens
K	-	Potassium
M	-	Meters
MK	-	McCarey Kauffman
mm	-	millimeters
Na	-	Sodium
PK	-	Penetrating Keratoplasty
PLK	-	Posterior Lamellar Keratoplasty
pm	-	picometer
WHO	-	World Health Organization
yrs	-	years

ABSTRACT

Background and objectives

Corneal blindness is one of the most challenging public health problems all over the world, especially in developing countries like India, where it is one of the leading cause of visual disability. Penetrating keratoplasty (PK) is the mainstay surgical treatment of corneal blindness and is a well-established fact.

Common causes of corneal opacity are keratitis, trauma, phakic or pseudophakic bullous keratopathy, adherent leucoma, corneal dystrophies and keratoconus.

In patients with both corneal and lenticular opacities, combined cataract extraction/intraocular lens (IOL) insertion with penetrating keratoplasty (PK), which is known as the triple procedure, is one treatment option.

This study is undertaken to elucidate various aspects of keratoplasty, including indications, pre-operative assessment, surgical techniques, post-operative management, complications, anatomical and functional outcome.

Objectives of this study are:

1. To analyze the visual outcome after penetrating keratoplasty.
2. To evaluate the intra-operative and post-operative complications after penetrating keratoplasty.
3. To study factors affecting graft survival after penetrating keratoplasty.

Methodology

The present study is a one year cross-sectional study conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on patients undergoing penetrating keratoplasty during the period between 1st January 2015 – 31st December 2015. This study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belagavi. The patient underwent penetrating keratoplasty/ triple procedure (according to need) to evaluate the visual outcome and graft survival after surgery.

Results

The mean age was 50 $\pm$ 2.3 yrs. Majority of the patients were in the range of 51-60 yrs that is 45%. There was a male preponderance in the study (65%).

The most common indication was corneal scarring due to various causes (70%), followed by keratitis (20%) and corneal dystrophies (10%). Co-relation between enucleation and transplant time was statistical significant using Fisher Exact test with p value <0.001.

The time interval between retrieving the donor cornea and the outcome of graft was statistically significant with p value of 0.039 using Fisher Exact test.

88.88% patients with post-operative complication went into graft failure and 11.11% had graft survival even with complications.

60% of had successful grafts and 40% patients had graft rejection.

Conclusions and interpretation

On conclusion of this study, 60% patients had successful keratoplasty and 40% went in graft failure. The survival of the graft is dependent on various factors like time interval between the enucleation time and transplant, age of the donor cornea, recipient age, intra and post-operative complications and the suturing techniques.

Keywords

Penetrating Keratoplasty, Visual Outcome, Graft Survival

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INTRODUCTION

Though the incidence of blindness worldwide is not accurately documented, but the data released in 2000 by the World Health Organization suggested that there are around 50 million blind population in the world.[1] In addition, nearly 150 million people suffer from low vision (as per the WHO definition of blindness and low vision).[2]

There are 200 million people worldwide who are visually disabled due to various causes which is a disastrous and intolerable situation in both social and economic terms. Furthermore, in the absence of more aggressive interventions, blindness prevalence is presumed to increase by approximately 2 million per year as a result of rising proportion of ageing population and service deliverance not keeping in pace with the incidence.[1] The global data has recognized three crucial reasons for blindness worldwide, namely cataract, trachoma, and glaucoma.[3]

Thus, corneal disease remains the second most important cause for blindness today, following cataract which is almost totally reversible in the present era. Around 6 million population of India is suffering from corneal blindness.

On speculating Indian data, it is concluded that approximately 1.5-2 million people develop corneal ulcer annually in developing countries. The most prevalent sources of corneal blindness according to this survey included keratitis in childhood (36.7%), trauma (28.6%), and keratitis during adulthood (17.7%).[4]

Visual rehabilitation in most of these cases can be achieved with corneal transplantation. However, an analysis of published reports on blindness certainly

exhibits that 80% of visually impaired people belong to the less developed world, countries where persistent economic destitution is aggravated by the added challenge of failing vision. Also, the diseases resulting in blindness vary amongst the developed and the under developed economies; and main causes of corneal blindness in under developed nations are either treatable or preventable.[4] These facts alert personalization of blindness control programs to different areas and appropriate utilization of available resources. Therefore, it is crucial to encourage the part of corneal transplantation in decreasing blindness.

What is the role of corneal transplantation in diminishing blindness?

A substantial population with corneal blindness fall in the economically backward regions of the world where the leading causes include vascularized corneal scar and adherent leucoma resulting from trachoma, keratitis in childhood, trauma, and keratitis in adults and efficient eye banking facilities do not exist. Moreover, there is an additional lack of experienced corneal surgeons in these regions with co-existing financial constraints which limit accessibility to quality surgery as well as long term care. These considerations raise a significant concern regarding the part of keratoplasty in diminishing blindness worldwide. Improving the consequence of comparatively high-risk keratoplasty would need improvement in eye banking quality, high-standard teaching programs in corneal subspecialty and eye banking, improved surgical infrastructure and refinement in postoperative care of corneal grafts. However, until preventive policies become successful and make an outstanding difference, corneal transplantation is the only option for visual rehabilitation of those currently blind from corneal diseases. Thus a complete approach involving both

preventive and therapeutic interventions would be the most effective combat for corneal blindness in both immediate and long-term perspective.

Requirement for Corneal Graft Registry

A corneal graft registry consists of all the important information of tissue and donor details and utilization of cornea. It is maintained by the eye banks. Various countries have developed corneal graft registry for evaluation of keratoplasty services and outcomes. These include

1. Australian Corneal Graft Registry (ACGR)

2. Singapore Corneal Graft Registry (SCTS)

3. UK Corneal Transplant Study (UKTS)

4. Swedish Corneal Transplant Register

However, in a country like India with different disease epidemiology, compliance and follow up, it is necessary to have our own registry to audit and evaluate the available transplant services and utilize this information to improve our outcomes. It will also stimulate and facilitate research on corneal transplantation and will help in establishing our own protocols and standards.

Donor Tracking Protocol

It is a system that helps in collection and collation of statistical information on the practice of corneal transplantation and helps in tracking the donor and other tissue details. It is an indirect means of evaluating both immediate and long term outcomes

of corneal transplantation and helps to provide feedback to contributing eye banks and operating surgeons for the benefit of their patients.

In the corneal diseases, the transparency, smoothness, and regularity of cornea is lost resulting in considerable visual loss. This is the most important factor for widely practicing the corneal transplant nowadays.

In 3rd world nations, blindness due to corneal diseases is one of the leading cause. This is our misfortune that corneal blindness affects mostly the working population resulting in loss of productivity and added burden on our national economy.

Corneal grafting is done to restore the vision of the patients and is a boon for such patients as most of them can be successfully treated by this procedure. The major hurdle in meeting the vast challenge of corneal blindness is the availability of donor cornea for keratoplasty.

To avoid disappointment and to achieve the successful cornea transplant, it is necessary to understand the different factors influencing the graft survival after penetrating keratoplasty. With due consideration to all the above factors, present study was carried out in our tertiary care center.

AIMS AND OBJECTIVES

1. To analyze the visual outcome after penetrating keratoplasty.
2. To evaluate the intra-operative and post-operative complications after penetrating keratoplasty.
3. To study factors affecting graft survival after penetrating keratoplasty.

REVIEW OF LITERATURE

ANATOMY OF CORNEA

The transparent cornea comprises of anterior one sixth of the eyeball.[5] Mechanical strength of the cornea is due to interwoven fibrous collagen, protecting the inner structures of the eye from physical injury and maintaining the ocular contour.[5]

The anterior surface of cornea is protected by the tear film, whereas the posterior surface is in direct contact with the aqueous humor. The highly vascularized limbus, which is thought to contain a reservoir of pluripotent stem cells, is the transition zone between the cornea and sclera. The anterior surface of cornea is convex and aspheric, and it is horizontally oval because of scleralization superiorly and inferiorly.[6]

The adult human cornea measures 11-12 mm transversely and 9-11 mm vertically.[6] Central thickness being approximately 0.5 mm, with the thickness increasing gradually toward the periphery, where it is about 0.7 mm thick.[6] It has total 6 layers with addition of a new layer in 2013 named after the discoverer, Dr. Harminder Singh Dua. The corneal curvature is not constant, being greatest at the center and smallest at the periphery. The radius of curvature is between 7.5 and 8.0 mm at the 3-mm central optical zone of the cornea, where the surface is almost spherical. The refractive power of the cornea is 40 to 44 D, constituting about two-thirds of the total refractive power of the eye.[6]

HISTOLOGY AND BIOCHEMISTRY

The cornea comprises of three different cellular layers and two interfaces: the epithelium, Bowman's layer, the stroma, Dua's layer, Descemet's membrane, and the endothelium. The cell types that constitute the cornea thus include epithelial cells, keratocytes (corneal fibroblasts), and endothelial cells.

Corneal epithelium

The corneal epithelium is made up of non-keratinized, stratified, squamous epithelial cells. An important physiological role of the epithelium is to provide a barrier to the external stimuli. The presence of junctional complexes between neighboring corneal epithelial cells prevents the passage of such agents into the deeper layers of the cornea. As in epithelia in other parts of the body, basal cells of the corneal epithelium are anchored to a basement membrane. The presence of the basement membrane between the basal epithelium and the stroma fixes the polarity of epithelial cells.

Bowman's layer

An acellular, membrane-like zone, is present at the interface between the epithelium and stroma. Given that this structure is not a membrane but rather a random arrangement of collagen fibers and proteoglycans, the term Bowman's layer is preferable. The collagen fibers in Bowman's layer are primarily collagen type I and III and secreted by stromal keratocytes. Bowman's layer is considered to be the anterior part of the corneal stroma. Bowman's layer does not regenerate after injury.[6]

Stroma

The stroma constitutes the largest portion, more than 90%, of the thickness of the cornea. The peripheral portion of the cornea connects to the anterior sclera at the limbus, where the tissue loses its transparency. Many characteristics of the cornea, including its physical strength, stability of shape, and transparency, are largely attributable to the anatomic and biochemical properties of the stroma. The uniform arrangement and continuous slow turnover (production and degradation) of collagen fibers in the stroma are essential for corneal transparency.[6]

Descemet's membrane

Descemet's membrane, the basement membrane of the corneal endothelium, gradually increases in thickness from birth (3 pm) to adulthood (8-10 pm) in humans.[6] DM is composed primarily of collagen types IV and VIII and laminin but also contains fibronectin.[6] Collagen fibrils in the stroma are continuous with those in Bowman's layer but not with those in Descemet's membrane. DM adheres tightly to the posterior surface of the corneal stroma. Rupture of DM by physical stress, such as compression birth injury, results in the penetration of aqueous humor into the corneal stroma and consequent stromal edema. It does not regenerate after endothelial cells re-cover the ruptured area.

Dua's Layer

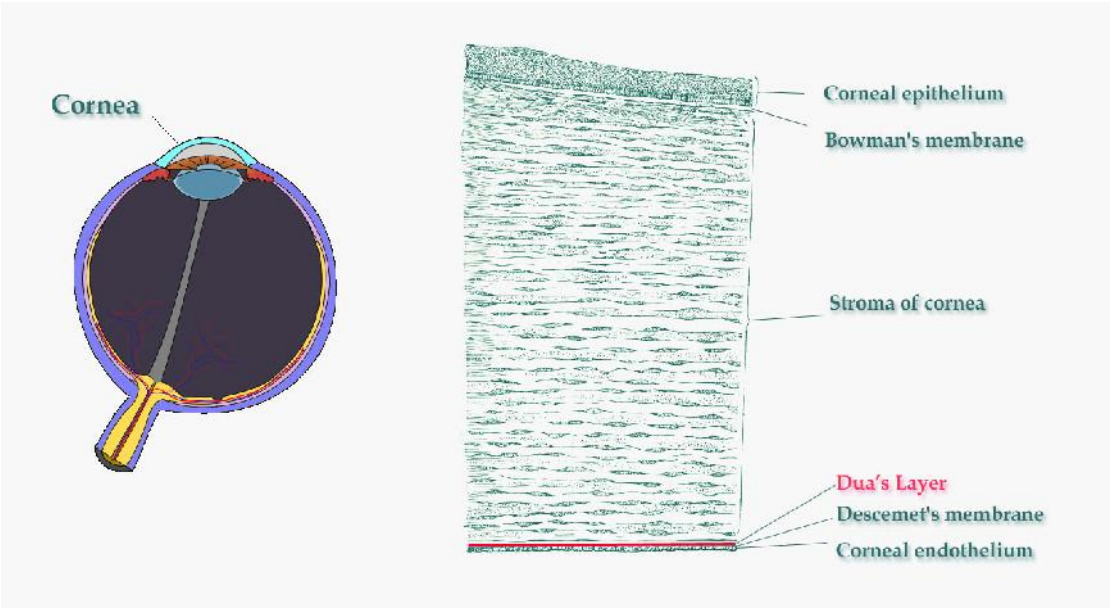
It is a very thin, strong layer - thickness of 15 microns and can withstand 1.5 to 2 bars of pressure. The experimental results were studied by optical and electron microscopy. The images revealed a thin layer of corneal collagen between the corneal

stroma and DM. The findings were published in Ophthalmology in May 2013. The layer was named after the lead author, Harminder Dua.[7]

Endothelium

A single layer of cells covering the posterior surface of Descemet's membrane in a well-arranged pattern. These cells are uniform in size and are hexagonal in shape. Normal cell density in young adults is about 3500 cells/mm^2.[6] Endothelial cells contain a large nucleus and abundant cytoplasmic organelles, including mitochondria, endoplasmic reticulum, free ribosomes, and Golgi apparatus, suggesting that they are metabolically active. These cells interdigitate and contain various junctional complexes, including zonula occludens, macula occludens, and macula adherens. In addition, gap junctions allow the transfer of small molecules and electrolytes between the endothelial cells. The interconnected endothelial cell layer provides a leaky barrier to aqueous humor.[6]

FIGURE NO 1: LAYERS OF CORNEA



CORNEAL TRANSPARENCY

Corneal transparency is most important because any opacity in the cornea will scatter light, degrading the optical image. It's maintained by -

- Anatomical Factors: The uniform, regular and tight arrangement of the corneal epithelium and unusual arrangement of corneal lamellae and avascularity.[8]

- Physiological Factors: Comparative state of corneal dehydration is due to corneal endothelial barrier and pump.[8]

CORNEAL ENDOTHELIAL BARRIER AND PUMP

The corneal endothelium forms a barrier between the aqueous humor and the corneal stroma. Tight junctions are an important component of the endothelial barrier, connecting cells at the apical most part of the lateral membrane. Tight junctions of the corneal endothelium are present around endothelial cells which serve in selective diffusion of extracellular ions and macromolecules. Because the tight junctions of the corneal endothelium are known to be "leaky" the increased permeability is advantageous, because it permits diffusion of nutrients from the aqueous humor into the stroma. Metabolic pumps (Na K-ATPase) are present on the lateral membranes of corneal endothelial cells, which help in transportation of Na ions from the corneal stroma to the aqueous humor. Overall, this dynamic pump—leak system maintains corneal relative dehydration and permits sufficient nutrient delivery into the stroma and epithelium. Disturbance of the corneal endothelial cells usually results in corneal edema, swelling, and opacity.[9]

HISTORY OF CORNEAL TRANSPLANTATION

Penetrating Keratoplasty is considered as the most frequently performed and the most successful organ transplant technique worldwide. In early 19th century, K. Himly of Germany suggested the corneal transplant from one animal to another. It was F. Reisenger who suggested corneal transplant in human eye with animal corneal graft in 1824 and coined the term keratoplasty. [10]

The first successful corneal transplantation was performed by S. Bigger in animals. Henry Power reported his experimental work on animal and human in 1872. He was the first to give importance to proper graft placement, infection free, minimal endothelial damage and use of fresh corneal graft.[10] In 1886 Von Hippel reported the first lamellar corneal grafting.[10] The first penetrating keratoplasty in a human subject was performed by Edward Konrad Zirm on a patient of chemical burn in 1906. In 1908, Plange performed the first autokeratoplasty, where he replaced the scarred cornea of the blind eye with a lamellar graft from the patient's other eye which was blind with normal clear cornea.

V.P. Fillatov, a Russian ophthalmologist is considered as the father of modern eye banking. He worked on the cadaver cornea as the donor material and he highlighted the importance of protecting the intraocular tissue of the host eye while trephining and advocated direct suturing.[10]

In the late 1950s, small fine needles were used for first time for corneal suturing. Although most of the corneal transplant surgeries evolved in the early 90s, the major advancement in corneal grafting took place in the late 90s. The knowledge of the corneal anatomy and physiology, launch of microsurgical techniques, improved

corneal preservation, effective anti-inflammatory and immunosuppressive agents have resulted in a high success rate of grafting.[10]

Corneal graft rejection is the greatest limitation factor in graft survival and Edward Maumenee was the one to recognize this clinical entity.[10]

Ramon Castroviejo performed the world's first successful human corneal transplant. He devised various instruments and pioneered in various surgical techniques in the field of keratoplasty.[10]

Townley Paton was first to set up an eye bank in New York in 1959. Preservation of donor cornea influences the outcome of the transplant. Capella and Kaufman developed the basic method of cryopreservation in 1965. McCarey and Kaufman introduce the MK medium in 1974 which was the major break-through in corneal preservation.[10]

In the last two decades, with the improvement in the surgical techniques and instruments, lamellar keratoplasty underwent a revolution. Introduction of deep and anterior lamellar keratoplasty has improved the sequelae of corneal transplant surgery. In 1974, Anwar described the air bubble technique for dissection of descemet's layer from stroma. In 2002, Anwar and Techmann described the Big Bubble technique for the same. [11]

In 1998, Melles reported the posterior lamellar keratoplasty (PLK) which was an alternative for PK, in which only the endothelium is involved.[12] Terry and Ousley reposted the successful result using the same procedure, also called the Deep Lamellar Endothelial Keratoplasty (DLEK). In 2006, Gorovoy described the Descemet's

Stripping Automated Endothelial Keratoplasty (DSAEK) in which the manual stromal dissection was replaced by the microkeratome dissection.[10]

In 2006, Tappin reported the transplantation of 7.5 mm diameter DM through a 8 mm scleral incision using flat carrier device. Melles described the clinical outcomes of DM transplantation through self sealing corneal incision in the same year known as Descemet's Membrane Endothelial Keratoplasty (DMEK).[10]

Appreciably improved outcomes in recent years have been attributed to the development in anesthesia, asepsis, immunological and anti-inflammatory therapy and improved instruments.

Russian ophthalmologist, Vladimir Filatov's attempts at corneal transplantation started with the first attempt in 1912 and continued, gradually refining until on 6 May 1931, when he successfully grafted a patient using corneal tissue of a deceased person. In 1935, Filatov demonstrated that cadaver cornea was a satisfactory donor material.[13, 14]

The key to successful keratoplasty is healthy endothelium. In 1968, Maurice first reported the specular microscope for viewing the endothelium of intact cornea which was subsequently modified by Laing, Sandstrom and Leibowitz, which provided an excellent means of studying the donor material and transplant endothelium.

After introduction of preservative media for cornea and various other technology, success rates have increased significantly. Though great achievements have been made in corneal transplant surgery, corneal graft rejection is still a big

problem like a black hole in the universe as it constricts the circle of successful penetrating keratoplasties.

Advances in operating microscopes have allowed surgeons to have a more magnified view of the surgical field, while advances in material science enabled them to use sutures thinner than the human hair.

Establishment of eye banks has played an instrumental role in corneal transplants. These are establishments located throughout the world, so as to synchronize the distribution of donated corneas to surgeons, as well as providing eyes for research.

Many advances have been developed in this surgery ranging from preservation of the corneal graft to types of surgery. PK is the most commonly performed surgery in corneal blindness in developing as well as in developed countries.

The key to solving the problems of corneal blindness in developing countries is prevention rather than the cure. However once the damage occur keratoplasty can play a role in relieving visual disability in affected individuals.

INTRODUCTION

Keratoplasty is a surgical procedure in which abnormal host corneal tissue is replaced by healthy donor cornea. Term Keratoplasty was coined by F. Reisnger in 1824.[10]

Types

- Full thickness keratoplasty (Penetrating)
- Partial thickness keratoplasty (Lamellar or Deep Lamellar)

Around 6 million people in India are suffering from corneal blindness. Keratoplasty is the best surgery to treat such type of blindness.

Basically there are 4 types of indications in keratoplasty procedure [10]

1. Optical: Where grafting is done for visual rehabilitation.
2. Tectonic: For restoration of altered corneal structure.
3. Therapeutic: Tissue substitution for infected corneal diseases.
4. Cosmetic: To improve the cosmetic appearance of the eye

INDICATIONS OF KERATOPLASTY:

In our study, we have dealt with optical keratoplasty. Optical keratoplasty is to improve the visual acuity. Common indications of optical penetrating keratoplasty include aphakic bullous keratoplasty, corneal opacities following infectious keratitis, trauma, graft failure, endothelial and stromal corneal dystrophies, corneal degeneration and congenital corneal opacities.[15] While keratoconus, pseudophakic bullous keratopathy and Fuch's dystrophies are the most common indications for optical penetrating keratoplasty in the western world.[16] In developing countries like India, corneal scarring, caused by infection and trauma are the major indications of this surgery.[17,18]

Taben et al[18] studied 408 patients in Nepal to identify the indications and outcome in optical penetrating keratoplasty in developing countries. Corneal scar was the main indication (37.3%) followed by adherent leucoma (35%) and pseudophakic bullous keratopathy (5%).

Shipla A Joshi [19] studied 181 case series in western India and found that the corneal opacities secondary to the keratitis and trauma are the major indications.

INDICATIONS OF PENERTATING KERATOPLASTY IN INDIA

- Corneal scar 40.9%
- Failed graft 15%
- Fuchs dystrophy 9.3
- Ulcerative keratitis 8.3%
- Pseudophakic bullous keratopathy 7.6%
- Keratoconus 5.9%
- Others 21.5%

EXPECTED OUTCOME IN VARIOUS INDICATIONS AFTER PENETRATING KERATOPLSTY

It depends upon initial pathological condition of the recipient cornea apart from other factors such as quality of donor tissue, surgical technique, timing of surgery, post-operative care etc.

The various prognostic groups are follows [20]

- Group 1 - Excellent prognosis
  - Keratoconus
  - Traumatic scar
  - Superficial stromal scar
  - Lattice dystrophies

Best reported rates of keratoplasty success are for Keratoconus. Keates and Falkenstein reported 100% graft success.[21]

Kirkness et al[22] reported 97 % graft clarity in cases of Keratoconus.

- Group 2 - Good prognosis
  - Small vascularized scar
  - Bullous keratopathy
  - Fuchs dystrophies
  - Macular dystrophy
  - Interstitial keratitis

Prognosis in this group is very good with 80-90% success rate.

Olson et al[23] reported 89% clear grafts in this group.

Pineros et al [24] reported clear grafts in Fuch's dystrophy as 89% and visual acuity of 6/12 or better in 64% of cases at 8 year follow-up.

- Group 3 - Fair prognosis
  - Moderately vascularized cornea
  - Congenital hereditary endothelial dystrophies
  - Scar following bacterial corneal ulcer
  - Active keratitis
  - Corneal opacities in pediatric group
  - Chemical injury

Stulting et al[25] reported 60% success in graft for congenital opacities.

Dana et al[26] evaluated the graft survival analysis in pediatric keratoplasty and showed the 80% were clear at the end of 1 year and 67% clear at the end of 2 years.

- Group 4 - Poor prognosis
  - Dry eye - Multiple graft failure
  - Congenital glaucoma epithelial down growth
  - Corneal staphyloma
  - Stevens-Johnson syndrome

Vail A et al[27] reported that increased risk was related with regrafts, patients below 10 years of age, non-optical causes for grafting, endothelial failure and deep corneal vascularization.

DONOR CORNEAL TISSUE EVALUATION

Specular microscopy: Is an important method for evaluation of donor cornea before surgery. It is employed to study the following features of endothelial cells. During our study, specular microscope was not available in our institute. The following features can be examined:

1. Cell density.
2. Cell shape, size, uniformity, pleomorphism, and polymegathism.
3. Presence of corneal guttata.
4. Evidence of any old corneal inflammation and endothelial insult.

CRITERIA TO CONSIDER A CORNEA UNSATISFACTORY[28]

1. Very low endothelial cell count (< 1500 cell/mm^2)
2. Extreme polymegathism and polymorphism.
3. Presence of significant corneal guttata.
4. Presence of inflammatory cells on the endothelium.

GRAFT FAILURE:

Graft failure can be defined as the failure of graft to achieve the stated aim for keratoplasty.[29]

Graft failure is subdivided into two groups [29]

- Early or primary: Failure in the 1st post-operative week or graft never clears.
- Late: Failure beyond 2nd post-operative week.

Filatav[13] described 2 types of opacification of graft, early and late. Maumenne[30] studied the graft failure and divide into three types -

- Early graft failure occurring from first post-operative day to third week
- Intermediate graft failure occurring from third week to two years.
- Late graft failure occurring 3 to 15 years postoperatively.

GRAFT REJECTION:

It is an immune mediated graft failure resulting from allogenic graft rejection.[29]

There are 3 types of graft rejections these are epithelial, endothelial and stromal. Rejection can be directed to any of these layers in isolation or in combination.[29]

FACTORS IN FAVOUR OF GRAFT FAILURE AND REJECTION

1. PRE-EXISTING CORNEAL VASCULARIZATION:

Graft rejection is more likely to occur if there is pre-existing corneal vascularization as it reduces the relative immune privilege of the normally avascular cornea.

Mohan M et al[31] studied 105 penetrating keratoplasties for vascularized corneal opacities. The vascularization was graded from Grade I to V on the basis of quadrant and type of vascularization. Graft clarity of 2+ or more in cases of trachomatous opacity was attained in 93% of cases and that after post infectious opacity in 71.8%. Poor prognosis was seen in cases where deep vascularization was present in more than two quadrants or more than 180 degrees.

2. GRAFT SIZE:

Large grafts are prone to reject as they lie near to the limbus and hence nearer to the limbal vessels and host antigen presenting cells. Small grafts are more likely to go for failure due to insufficient endothelial cells to maintain function. The ideal graft size appears to be 7-8 mm. Graft size more than 8 mm and smaller than 7 mm are significantly associated with failure.

Williams K et al [32] reported that graft size outside the range of 7.0 to 7.9 mm diameter and corneal vascularization are associated with graft failure in the postoperative period.

3. REPEAT GRAFTS:

Repeat grafts have a higher probability of rejection due to sensitization. A similar mechanism applies to blood transfusion.

Cobo et al[33] found 69% graft survival as compared to 50% in re-graft.

4. PRIMARY CORNEAL PATHOLOGY:

Rejection is also influenced by the primary pathology of the cornea requiring grafting, e.g. Keratoconus has a very good prognosis while Herpes Simplex Keratitis has a very poor prognosis.

5. GLAUCOMA MEDICATION: Prolonged glaucoma medication before grafting significantly affects the success of the graft.

6. HLA ANTIGEN MATCHING:

HLA-A and HLA-B antigens are abundantly present in corneal epithelium and they are also found in stromal cells. The studies on effects of HLA matching on graft survival in high risk cases have been carried out.[34]

Beekhies et al[34] studied 107 cases of HLA-A and HLA-B matched corneal transplant and reported 76.3% of graft survival rate at the end of 3 years. Major complication responsible for graft failure may be divided in to the early, intermediate and late.

a. Complications responsible for the early graft failure:

- Primary donor failure or donor tissue inadequacy: Zakov in 1978, suggested that cloudy graft in early postoperative period may be due to poor donor endothelium,

poor apposition of graft to host, surgical trauma to the endothelium and incorrectly stored cornea.

Cobo et al[33] reported 13% incidence of primary donor failure in penetrating keratoplasty.

- Graft infection: Fortunately, purulent infections following corneal transplantation are not more common. Viral, bacterial, fungal or protozoal, all types of infections can lead to graft failure.

  Cobo et al[33] reported 6.7% graft infections in their patients, which were responsible for graft failure in 2%.

  Hassan SS et al[35] concluded that infection is an uncommon but serious complication of corneal transplant as most infected eyes lose vision.

- Wound Dehiscence: It is common and a preventable problem of graft failure.

Binder et al[36] found 5.7% of 369 cases, had wound gape, override or separation. They observed that 27.5% of patients had a wound separation prior to suture removal, 67.5% wound separation occurred immediately after suture removal. They also noted that the highest incidence of wound separation i.e. 47% is with 10-0 interrupted sutures. They also found graft failure in 50% patients with wound gaping.

William et al[37] reported 3% of wound gaping was responsible for 3% of graft failure in their study.

Renucci AM et al [38] reported 21% graft failure after wound dehiscence.

b. Complications responsible for intermediate graft failure :

- Homograft or allograft rejection: In 1931, Maumenee A.E.[30] was the first to produce a graft rejection in vascularized cornea of rabbit by implanting donor skin subcutaneously two weeks after corneal transplantation to increase the amount of allograft antigen, demonstrating individual genetic, and not organ specificity.

Polack FM[39] observed that the earliest endothelial cell layer alteration in the experimental graft rejection occurs at the host graft junction and it is associated with leucocytic infiltration of connective tissue which forms the scar.

In 1973, Jones lined out the diagnosis of allograft rejection as "the diagnosis of allograft rejection can be made when 10 days post penetrating keratoplasty, a previously clear graft in quite eye develops signs of inflammation in anterior segment and when area of edema in the graft moves across the cornea along endothelial line typically starting at and progressing away from a focus of vascularization in the vicinity of graft".

The same Polack FM in 1980 performed penetrating keratoplasty in 100 patients and reported 12% incident of allograft rejection which ultimately leads to graft failure.[40]

Cobo et al[33] reported that allograft rejection is the leading cause of clouded herpetic keratoplasty. In his study, eye undergoing the allograft rejection was the most frequent cause of the clouded graft (64%), which did not respond to the medical treatment. In 13% cases, early graft failure was the second most common cause of graft clouding.

Coster DJ[41] found that the most important cause of graft failure was allograft rejection which occurred in 65% of decompensated graft.

The factors that can predispose or lead to allograft rejection can be summarized as follows:

I. Sub-acute inflammation and inflammatory cells. e.g. herpetic keratitis, iritis, exudates around the exposed sutures.

II. Pre-existing corneal vascularization or that induced by anterior synechiae.

III. Poor apposition of wound.

IV. Repeat grafting.

- Glaucoma: Irvine for the first time recorded the intraocular pressure following the full thickness corneal transplantation. He found the rise in intraocular pressure in 75% cases.[42].

Thoft RA et al [43] observed the prevalence of glaucoma postoperatively without obvious cause in 10% of cases.

Binder PS et al[44] showed that glaucoma occurs more frequently following combined corneal transplant with cataract extraction or in aphakic eyes.

Sihota R[45] did a retrospective study of 747 consecutive penetrating keratoplasties. The occurrence of post-penetrating keratoplasty glaucoma was 10.6%. A high incidence of post-penetrating keratoplasty glaucoma occurs in eyes with adherent leucomas. Anterior vitrectomy and allied surgeries furthermore accentuate

the risk. Anti-glaucoma therapy may not result in optimum visual outcome, despite a clear graft.

Dada et al[46] studied a retrospective review of 747 patients and reported that 19% grafts maintained visual acuity of 6/60 after glaucoma treatment. They concluded that, uncontrolled IOP after PK is one of the major reasons for graft failure and visual loss in this patient population. It is obligatory that the IOP is recorded on a regular basis after corneal transplantation and aggressively treated if found high. Any patient with prior glaucoma must be cautiously examined prior to the corneal transplants. Optimal surveillance and aggressive medical and surgical management can restore both graft and vision in these already compromised eyes.

- Formation of anterior synechiae: It is a hazardous complication as it can produce late edema of graft, local vascularization and perhaps predispose to graft rejection and failure. This explains the great importance of proper anterior chamber formation after keratoplasty.

- Retro corneal membrane: Approximately 2/3rd of cloudy cornea removed by second operation shows histologically, a layer of fibrous tissue on the back of cornea.

- Persistent epithelial defects: These are commonly seen in ocular pemphigoid, exposed eyes and in grafts with poor wound apposition. Persistent epithelial defect can lead to vascularization, ulceration, infection and ultimately to graft failure.

Fong et al [47] found persistent epithelial defects in 15 % of their cases. Persistent epithelial defect can be prevented by using fresh donor material, preoperative correction of lid abnormalities and proper wound appositions.

c. Complication responsible for late graft failure:

- Vitreo-corneal contact: Such a contact can cause the late graft failure in aphakic patients with corneal grafts. Presence of vitreous in anterior chamber leads to delayed wound healing, recurrent ocular inflammation and damage to graft endothelium.

Leibowtz showed that adequate vitrectomy with removal of vitreo-endothelial contact resulted in reversal of graft edema.[48]

Graft failure can be prevented by adequate anterior vitrectomy in required patients.

- Recurrence of host disease in graft :
  - Dendritic ulcer or Herpes Simplex Keratitis: Recurrence of dendritic ulcer or stromal herpes in the graft occurs relatively frequently as compared to failure in these cases from other causes, despite the intensive use of steroids.

Cobo LM et al [33] reported the overall survival rate of keratoplasty for herpes simplex for 2 years was 64% and for 5 years was 62%. The epithelial herpetic recurrence occurred in 32% of eyes undergoing allograft rejection within 4 months of initiation of treatment for rejection. This when compared with otherwise uncomplicated keratoplasty, where the epithelial recurrence was only 6% at 4 months, on high dose corticosteroid therapy without antiviral cover.

Sterk CC et al[49] - In a retrospective study, they evaluated consecutive penetrating keratoplasties for herpes simplex keratitis. Concluded that a recurrence of

a herpetic infection following corneal transplantation is the main cause for graft failure in this group.

Lomholt JA et al[50] found 44% recurrence in his study. The overall one-year survival rate of a clear graft was 84% and the 2-year survival rate was 67%.

- Corneal dystrophies : In a recent survey by Marcon AS et al[51] studied a population comprising of 35 eyes with lattice dystrophy, 17 eyes with corneal dystrophy of Bowman's membrane (CDB), 14 eyes with macular dystrophy, 7 eyes with granular dystrophy, and 4 eyes diagnosed with Schnyder's crystalline dystrophy. There was a simple recurrence in 60% eyes with lattice and in 88% with CDB. The median time to simple recurrence for the first eye transplanted of each patient was 8.4 years for lattice and 2 years for CDB. After 5 years of follow-up, recurrence was respectively 17.1% and 20% in eyes with lattice and 11.8% and 17.6% in eyes with CDB.

- Late donor failure :

It is seen after several years of clear graft. Progressive endothelial cell loss may result in late graft failure. The cell loss appears to be continuous for 10 to 15 years, but the cell count of the central cornea stabilizes. Additional cell loss in the next 10 to 20 years appears to be slow.

COMPLICATIONS OF SURGERY [52]

Significant technological advancements in the last few decades have increased the survival rate of corneal transplant. Numerous advancements have been made in

the field of corneal preservation, surgical techniques and postoperative care. However in spite of these advancements, complications after surgery have not become rare.

The successful management of complications associated with any surgeries requires a combination of recognition and knowledge of important risk factors. Complications of penetrating keratoplasty may be broadly classified into intra-operative and post-operative.

INTRAOPERATIVE COMPLICATIONS:

1. Poor anesthesia and positive vitreous pressure

Proper anesthesia and akinesia are prerequisites for keratoplasty. Prior to entry into anterior chamber, the eye must be soft with reduced volume and decreased intraocular pressure.[52] Peribulbar anesthesia may increase orbital volume. Increased pressure may be encountered if adequate measures have not been taken to obtain adequate hypotony.[52]

2. Scleral perforation

Sclera can be perforated while applying suture beneath the superior and inferior recti, resulting in a retinal hole and retinal detachment.[52]

3. Improper Technique of Trephination

Reversed host and donor trephines: Generally donor corneal button is 0.5 mm larger than the recipient bed. Donor button becomes smaller than the recipient if trephine used to cut gets reversed. This results in difficulty in suturing and a water tight wound may not be achieved. Further it also causes rise in intraocular pressure

due to tight sutures, which tends to collapse the trabecular meshwork.[53] This may also cause hyperopia.[54]

- Eccentric host trephination: Improper centration of graft may give rise to high post-operative astigmatism.[54]
- Irregular/oval trephination: This is encountered with blunt and irregular trephines.
- Retained DM.

4. Damaged Donor button

Distilled water should be avoided on trolley so that there is no chance of water getting into the endothelium and damaging it completely. Donor cornea can be damaged during trephination or during placement of the 4 cardinal sutures. [52] Graft loss or graft drop are noted complications during surgeries where patient's own cornea must be replaced and surgery may be rescheduled.

5. Inversion of graft- Occurs rarely**.**

6. Excessive bleeding

This commonly occurs in inflamed or perforated eyes. Severe intraocular hemorrhage may occur during explanting closed looped anterior chamber lens. [52] Bleeding most commonly occurs due to leak from the iris vessels.

7. Injury to iris-lens diaphragm

In patient with iridocorneal scars, injury to iris and lens occurs commonly while performing trephination if special precautions are not taken. [52] Damage to anterior lens capsule that occurs during the trephination should be recognized and extracapsular cataract extraction should be undertaken with placement of IOL.[56]

8. Posterior capsular tear and vitreous prolapse

This occurs during triple procedure i.e. penetrating keratoplasty with cataract extraction. Incidence has been reported to vary from 0 to 16 %.[52]

9. Suture related complication

Broken, loose or tight sutures may occur. Final assessment of suture must be done after the reformation of anterior chamber. [15, 16]

10. Iris incarceration

Iris can be picked up in needle and inadvertently sutured into the wound making pupil eccentric. It may lead to uveitis, wound leak and may enhance the chance of graft rejection.

11. Shallow anterior chamber

12. Wound leak

EARLY COMPLICATIONS:

1. Primary graft failure

It is defined as the irreversible graft edema occurring in the immediate post-operative period. Incidence of primary graft failure is 5%. Irrespective of cause, all cases of the primary graft failure shows donor corneal damage with markedly decreased endothelial cell count.

Factors responsible for primary graft failure are. [57]

a) Selection of donor tissue.

b) Faulty technique of corneo-scleral button excision.

c) Improper corneal preservation.

d) Surgical trauma.

2. Glaucoma

Post keratoplasty glaucoma is described as an acute increase in the intraocular pressure following PK with or without optic nerve and visual field changes. [46]

Incidence is 13 to 38% in phakic eyes and upto 42% in aphakic eyes.

INTERMEDIATE COMPLICATIONS:

1. Graft rejection

Immunological graft rejection is the most common cause of graft failure. Incidence is almost 18 %.[29]

Following are the types of graft rejections[29]

- Epithelial rejection: Appearance of rejection line stain with dye.
- Stromal rejection: These consist of sudden onset of peripheral full thickness haze in previously clear graft associated with circum corneal injection.
- Endothelial rejection: Presents in one of two ways either as keratic precipitates or Khodadoust line.

Potential risk factors for allograft rejection -

- Vascularization
- Previous graft failure
- Intact donor epithelium
- Eccentric graft
- Large graft
- Non HLA matched graft

2. **Graft infection:** is one of the common causes of graft failure

3. **Wound dehiscence:** is common and preventable risk factor of graft failure.

Incidence is high, trauma is important cause of wound dehiscence.

LATE COMPLICATIONS:

1. **Recurrence of disease**

- Dystrophies: Are known but uncommon complication of keratoplasty. Recurrence is noted in Reis Bukler dystrophy, Granular dystrophy, Lattice dystrophy and macular dystrophy.

- Herpes simplex keratitis

2. **Late graft failure of unknown cause**

Occasionally graft remains clear for years and opacifies without any obvious cause. In many cases, late decompensation may be secondary to decrease in endothelial cell density.

3. **Endophthalmitis**

Endophthalmitis is though rare, but sight threatening complication with incidence ranging from 0.1 to 0.7%. The rate of endophthalmitis was 0.2% in 2000-2003 period. 0.45% in the 1990s, 0.376% in the 1980.[5,6]

4. **Late graft rejection**
5. **Infectious crystalline keratopathy**

It is a chronic, progressive corneal infection occurring mostly in anterior lamella of graft without any clinical evidence of stromal inflammation. Commonest organism causing it is Streptococcus viridians.[52]

6. Fibrous in growth

Also known as retro corneal membrane which is a gray white fibrous collagenous tissue invading between DM and endothelial cell layer.[52]

7. Cataract

It is a common cause of decreased visual acuity in patients with successful corneal grafting. The incidence of cataract is varies from 25- 80%. It often occurs following poor surgical technique, altered lens metabolism and toxic effects of corticosteroids and anticholinesterases.[52]

8. Astigmatism

A physical success of graft may fail optically if post-operative astigmatism is too high. Average post keratoplasty astigmatism measures from 4-5 D. Eccentric graft, mal-alignment of graft, faulty suturing techniques are the main causes for high astigmatism. [52]

9. Glaucoma

Tight wound closure can lead to the high intraocular pressure both early and later on post-operatively. Sustained elevation of pressure damages optic nerve as well as the corneal endothelium. Major risk factors responsible for raised pressure are pre-existing glaucoma, aphakic and pseudophakic eye, pigment dispersion syndrome,

prolonged severe inflammation, tight and deep suturing, long term use of steroids, epithelial and fibrous ingrowth. [52]

10. Vitreoretinal problem and maculopathy

Retinal detachment is rare but well known complication. Risk is increased 4 times with vitreous manipulation. Macular edema is a common cause of no improvement in vision in clear graft. Aphakic and pseudophakic bullous keratopathy, trauma predispose to the macular edema. Incidence is also more in combined cataract surgery.[52]

11. Posterior subcapsular cataract formations

It is because of the frequent use of steroids after penetrating keratoplasty. The incidence of posterior subcapsular cataract may be increased.

12. Irreversible mydriasis

Irreversible mydriasis was noted in patient's following penetrating keratoplasty and have been reported.

13. Cystoid macular edema

Olivier Genevois et al [58] reported the incidence of macular edema post keratoplasty to be 9.6%. The surgical technique (penetrating vs lamellar keratoplasty) had no impact on the occurrence of edema ($P > 0.05$), but combined surgery significantly increased the risk of developing edema ($P < 0.05$). Macular edema after keratoplasty seemed to be less frequent than expected (9.6%) and associated mainly with combined surgery.

14. Retinal detachment

Musch DC et al[59] - The time-related risk of retinal detachment during the follow-up of 1146 penetrating keratoplasty procedures was examined, using survival analysis techniques. Twenty-eight retinal detachments were recorded during follow-up. The Kaplan-Meier rate of developing retinal detachment increased from 1.5 % at three months to 2.1% at one year after surgery.

SUTURING TECHNIQUES IN PENETRATING KERATOPLASTY

High astigmatism remains a notable hindrance to prompt visual rehabilitation after successful penetrating keratoplasty. There are four types of suturing techniques

a. Interrupted
b. Combined interrupted and continues sutures
c. Single continuous
d. Doubled continuous

Among the different suturing techniques, single continuous suturing has proved to be better than either interrupted suturing or combined continuous and interrupted suturing in terms of post-operative astigmatism.[60]

DONOR MATERIAL FOR PENETRATING KERATOPASTY

The final goal of clear corneal graft following PK depends on quality of donor cornea.

A. Suitability of potential donor tissue:

1. Age of donor: One of principle criteria used is the age of deceased donors. Foster and Fine in 1971 have presented data indicating that there is no relationship between donor age and outcome of corneal graft.

   The lower age for donor tissue as young as six months and question of upper limit for the donor tissue is left on the surgeon's discretion.

2. Suitability of donor corneal tissue for corneal transplantation: Tissue that may represent a health threatening condition for recipient are subdivided.

I. Absolute contraindications

- HIV
- Death due to unknown cause.
- Rabies
- Creutzfeld-Jakob disease
- Encephalitis
- Death due to infectious course
- Leukemia
- Septicemia
- Intrinsic eye disease

II. Tissue whose use requires cautions

- Multiple sclerosis
- Parkinson's disease
- Diabetes
- Syphilis
- Jaundice

B. Interval between death and enucleation:

This varies according to the circumstances of death in terms of storage of body. 6 hours post-mortem is the maximum recommendation period for enucleation of donor's eyes.

C. Removal of corneal tissue:

The donor eyes are thoroughly irrigated with sterile saline solution, several drops of antibiotics are then instilled in each eye. Eye lids are taped closed and ice packs are placed over closed eyes, to decrease the endothelial metabolism and thus decreasing the endothelium damage. The above measure should be taken till the enucleation procedure starts. There are two methods for enucleation as follow:

1) Total eye enucleation: The enucleation should be performed under sterile conditions after the eye are flushed with topical antibiotics.

- ❖ Wire speculum is placed under the lids and peritomy performed
- ❖ Rectus muscles isolated and cut.
- ❖ Eye ball is raised with enucleation spoon to locate and cut optic nerve with enucleation scissor.
- ❖ After enucleation, each eye is shifted into sterile moist bottles.
- ❖ Eye is immediately transfer to eye bank for refrigeration at 4^{0} C.

Advantages of total eye enucleation are as follows

- ❖ Relatively simple procedure.
- ❖ Dose not require handling of delicate isolated cornea.
- ❖ Protects cornea endothelium.
- ❖ Maintains the intact globe.

2) Excision of cornea in situ: Using sterile condition either with large trephine or with an ab-externo razorblade incision through sclera, 2 mm behind the limbus is made. The incision is continued with small scissors around the entire perilimbal area. Anterior chamber must be maintained to prevent the endothelial loss.

A small forceps is used gently to hold the cornea and separate it from its attachment to ciliary body. The cornea along with its scleral rim is then placed in a sterile vial containing preservative medium for shipping to eye bank.

Advantage of this procedure is -

- ❖ Its a time saving procedure.

Disadvantages

- ❖ Has the potential for contamination.
- ❖ Endothelium damage may occur.
- ❖ Requires more skill than enucleation.

D. Evaluation of corneal tissue:

a) Gross examination: Simple visual examination is performed by directing the light source at cornea from the level of limbus for any transparency, epithelial defects, vascularization etc. This grossly determine the quality of tissue and its use for surgery.

b) Slit lamp examination: Slit lamp biomicroscopy remains the principle means for evaluating the donor tissue. It allows an assessment of the corneal clarity and thickness as well as observation of DM.

c) Specular microscopy: This facility was not available at our institute.

This equipment uses epillumination and applanation cone that allows a direct view of endothelial surface of cornea at 100x magnification. Cell morphology, pattern and density can be observed and assessed. Corneal thickness can be obtained. It permits a far superior view of corneal endothelium than the slit lamp.

Wiffen SJ et al [61] carried out retrospective study of specular microscopic examination of 1,000 consecutive donor corneas conducted at Mayo Clinic Eye Bank from 1986 to 1993. Specular microscopic evaluation excluded 3.4% of donor corneas because of unsatisfactory endothelium. Regardless of evaluation of the endothelium, 6 of 520 transplanted corneas (1.2%) resulted in primary graft failure. Morphologic assessment of donor corneal endothelium by specular microscopy probably lessens, but does not eliminate, the chance of primary donor failure.

d) Culture: Culturing of eye bank donor should be performed routinely. It may be performed either pre-surgically or at the time of surgery.

- Pre-surgical culture: A moist cotton tip dipped in antibiotic drops is rolled over the limbal area. The swab is then placed into the liquid biological media and sent to laboratory.

- Surgical culture: Following excision, the corneal rim should be cultured in media.

Wilhelmus KR et al[62] conducted examination of the discriminatory presentation of donor corneo-scleral rim cultures to predict endophthalmitis after

corneal transplantation. 17,614 corneal grafts were cultured, 2459 (14%) had a positive donor rim culture and 31 (0.2%) developed endophthalmitis.

Culture allows the early identification of the organism in case of immediate postoperative infections thus course of the disease can be altered to prevent the graft failure.

e) Storages and preservation of donor tissue : There are three main methods for the preservation and storage of corneas containing living cells; viz. hypothermia, organ culture and cryopreservation.[63]

a. Short term: Moist chamber technique store at 4^0 C by using hypothermia technique.[63]
b. Intermediate: MK media, Chondroitin sulphate enriched medium, Dexol medium, Optisol medium. Can store up to 1 week at 4^0 C.[63]
c. Long term: Organ culture method can preserve up to 35 days. The most common organ culture medium is Eagle's minimum essential medium (MEM) with 2% fetal bovine serum (FBS), although up to 8% FBS is used by some eye banks.

Cryopreservative method up to indefinite time.[63]

Techniques for corneal cryopreservation were developed in the 1960s and applied clinically. More recently, preservation of endothelial function was noted after ice-free cryopreservation by vitrification of rabbit cornea in a high concentration of propane-1,2-diol. But the problem with cryopreservation and the prospective for damage to the endothelium means that it is rarely used in routine eye banking, except sometimes for clinically urgent transplants where the primary aim is to save the eye.[64]

Some studies with recent evidence suggestive of longer storage times with immunomodulation, may permit better outcomes in high-risk grafts because of the decrease in donor T cells from the donor cornea into the storage media, storage media needs to be optimized for preserving the endothelium for longer periods of time. In addition, because the epithelium is typically unable sustain for longer than 1 week in storage media, research toward preserving the epithelium will also be essential.[65]

MATERIALS AND METHODS

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on patients visiting the outpatient department with corneal opacities, and patients with pre-existing corneal opacities enrolled as recipients in the Department of Ophthalmology.

Study design

One year cross sectional study.

Study period

The present study was conducted from 1stJanuary 2015 to 31st December 2015.

Method of collection of data

Source of Data

All patients visiting the outpatient department with corneal opacities, and patients with pre-existing corneal opacities enrolled as recipients in the Ophthalmology Department at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Sample size

Since it is a hospital based study, all patients undergoing PK in a period of one year were included in the study.

Selection criteria

Inclusion Criteria

Recipient:

1. All patients with leucomatous corneal opacities

Donor cornea:

1. Clear healthy cornea
2. Free of any systemic conditions

Exclusion Criteria

Recipient:

1. Extreme age group (<18 yrs > 70 yrs)
2. Deep vascularization of cornea
3. Posterior segment pathology
4. Uncontrolled glaucoma

Donor cornea:

1. Death of an unknown cause
2. Septicemia
3. Systemic diseases (AIDS, Hepatitis, Pneumonia)

DONOR CORNEAL TISSUE

The donor corneal tissue was obtained from Eye Bank of Department of Ophthalmology at Dr. Prabhakar Kore Hospital and Medical Research Centre and moist chamber method was used for storage and transportation of donor eye.

PRE-OPERATIVE ASSESSMENT:

HISTORY:

Detailed ocular and medical history was taken. Special mention was made about the occupation, history of trauma and previous ocular surgery. History of systemic diseases like Diabetes Mellitus, Hypertension, chronic use of systemic or ocular medications.

OCULAR EXAMINATION:

1. Visual acuity: Both unaided and pin hole vision were recorded by Snellen's chart of both eyes.

2. Anterior segment examination: All patients under went slit lamp biomicroscopy which confirmed the state and nature of the corneal opacity, exclusion of any pre-existing ocular disease and calculation of the graft size to be taken, and other adnexal diseases ruled out like blepharitis, conjunctivitis, lagophthalmos.

3. Posterior segment examination: A detailed dilated fundoscopy was performed. In cases of inadequate view, a B-scan was done to rule out posterior segment pathology.

4. Intra-ocular pressure measurement: IOP was measured by indentation tonometer (Schiotz tonometer)

5. Naso-lacrimal duct patency test was performed in all patients.

6. A-scan biometry performed in cases who underwent triple procedure.

CONSENT:

Written and informed consent was obtained from the patient after explaining the need, complications and prognosis about the visual outcome.

PRE-OPERATIVE PREPARATION:

1. LOCAL TREATMENT: All patients were started on topical broad spectrum antibiotics 8 times/day. In cases of triple procedure, patients were put on Tropicamide (0.8%) and Phenylephrine (5%) combination eye drops every 15 mins prior to the surgery.

2. SYSTEMIC TREATMENT: All patients were started with Intravenous broad spectrum antibiotics.

3. Eyelashes were prepared and Xylocaine (2%) sensitivity was done.

4. 30 minutes prior to surgery Inj Mannitol 100 ml was given.

INSTRUMENTS AND MATERIAL USED:

1. Wire speculum
2. Arruga’s needle holder and muscle hook
3. Conjunctival forceps

4. Eye ball stand
5. Disposable trephines
6. Vannas scissors
7. Iris repositor
8. Collibri forceps
9. 26 gauge needle
10. 10-0 nylon suture
11. Mc Pherson forceps
12. Donor cornea
13. Suture tying forceps
14. Viscoelastic substance

OPERATIVE PROCEDURE:

1. Anesthesia: Local peribulbar block was given to all patients constituting 2% Lignocaine with Adrenaline in 1:100,000.

2. Exposure: Self retaining wire speculum was used to retract the lids. Superior and inferior rectus bridle sutures were taken so as to make globe straight.

3. Preparation of donor cornea: Eyeball was mounted on the stand and with disposable trephine kept perpendicular on the epithelium and rolling movements performed till anterior chamber leak noticed. The donor corneal button was 0.5 mm more than the size of recipient bed. Then the donor cornea was cut with the help of corneoscleral scissors. The donor corneal button was kept in viscoelastic substance with endothelial side up.

4. Preparation of recipient bed: Appropriate size trephine was used to indent the epithelium. A guarded entry into the anterior chamber and 360^0 diseased corneal button was excised with corneoscleral scissors.

5. Additional procedures: Crystalline lens was removed in cases of cataractous lens. Synechiolysis with the help of viscoelastic was performed where needed. In cases with posterior capsular rent, anterior vitrectomy was done.

6. Placement of donor graft on the recipient: The donor cornea was gently placed on the recipient bed with endothelial side down with the help of Collibri forceps.

7. Suturing: With 10-0 nylon, the first suture is put at 12 o' clock position keeping a depth of approximately 90% to avoid wound leak. The suture is tied using an initial triple loop followed by two additional single loops. Viscoelastic substance is placed in the anterior chamber to align the graft in position and maintain anterior chamber depth. The second suture is placed 180^0 away at 6 o' clock position. Subsequently sutures are placed at 3 and 9 o' clock positions. The rest of the graft was sutured by both interrupted and continuous sutures according to surgeon's preference.

POST-OPERATIVE MANAGEMENT:

1. **LOCAL TREATMENT:**
    - Ofloxacin (3mg) with Prednisolone Acetate (10 mg) eye drops hourly.
    - Atropine eye drops 1% TDS.
    - Carboxy Methyl Cellulose eye drops 6 times/day.

2. SYSTEMIC:

- Intravenous broad spectrum antibiotic for 5 days.
- Tab Prednisolone Acetate (dosage according to the weight of patient) in divided doses for 10 days and tapered subsequently.
- Tab Diclofenac 50mg BD.
- Tab Ranitidine 150mg BD.

Introduction

Objectives

Review of Literature

Methodology

Results

Discussion

Conclusion

Summary

Bibliography

Annexure - i

Consent Form

Annexure - ii

Proforma

Annexure - iii
Photographs

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Master Chart

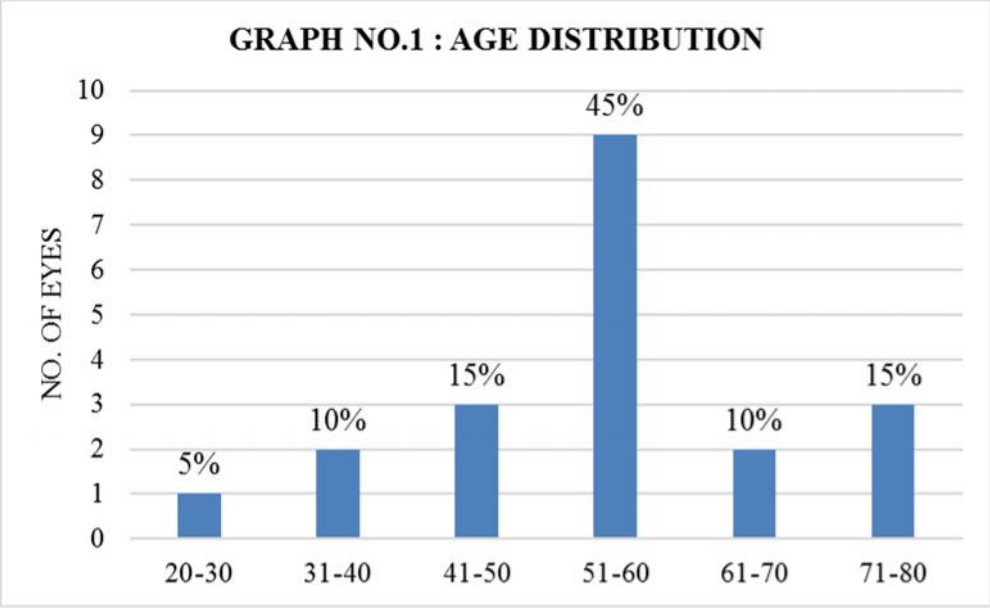
Annexure - v

Key to Master Chart

RESULTS

TABLE NO. 1: AGE DISTRIBUTION

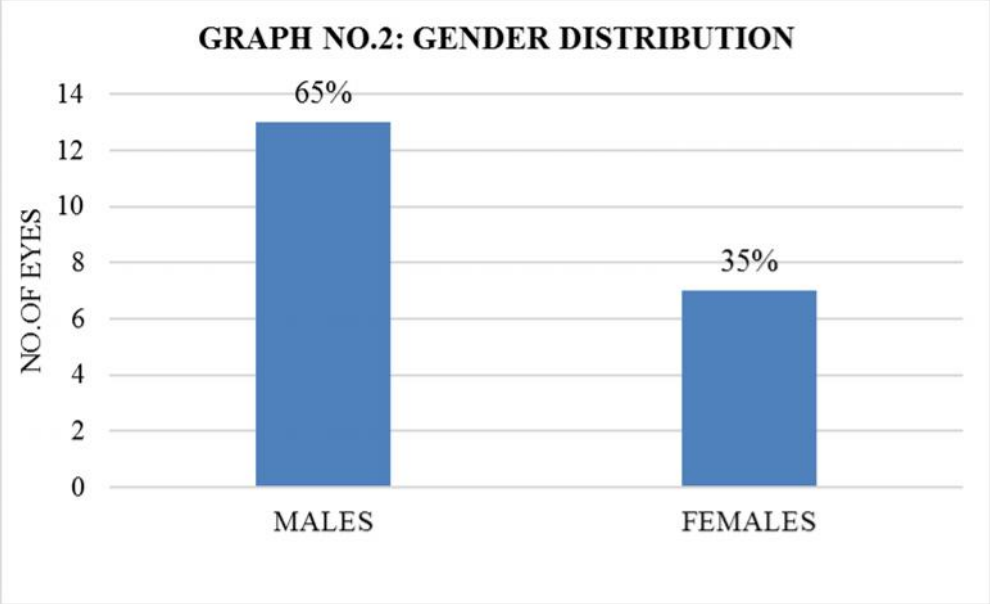
AGE (yrs)	NO. OF EYES	PERCENTAGE (%)
20-30	1	5
31-40	2	10
41-50	3	15
51-60	9	45
61-70	2	10
71-80	3	15
TOTAL	20	100



In the present study, the mean age was 50 $\pm$ 2.3 yrs. Majority of the patients were in the range of 51-60 yrs that is 45%.

TABLE NO.2: GENDER DISTRIBUTION

GENDER	NO. OF EYES	PERCENTAGE (%)
MALES	13	65
FEMALES	7	35
TOTAL	20	100

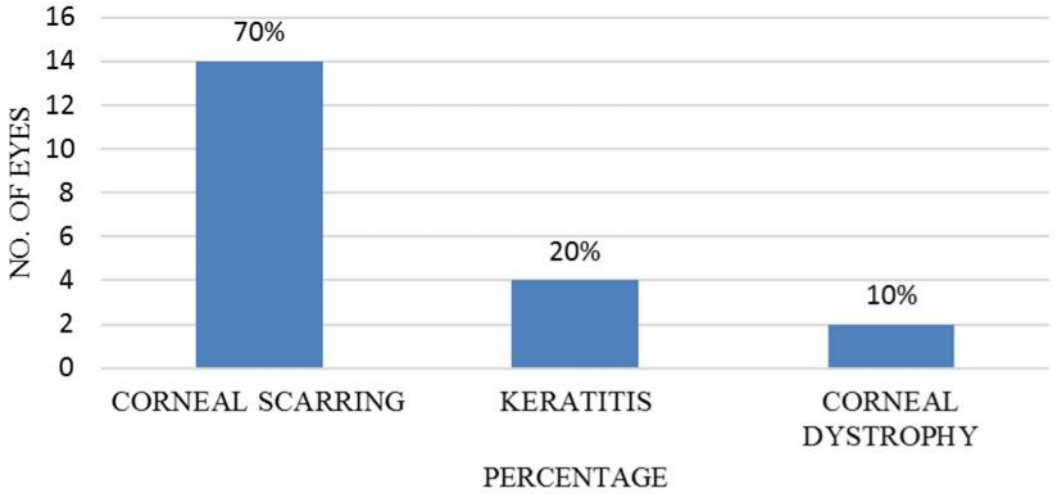


In this study, 65% patients were males and 35% patients were females. Ratio of male : female is 1.8:1

TABLE NO.3: INDICATIONS FOR KERATOPLASTY

INDICATION	NO.OF EYES	PERCENTAGE (%)
CORNEAL SCARRING	14	70
KERATITIS	4	20
CORNEAL DYSTROPHY	2	10
TOTAL	20	100

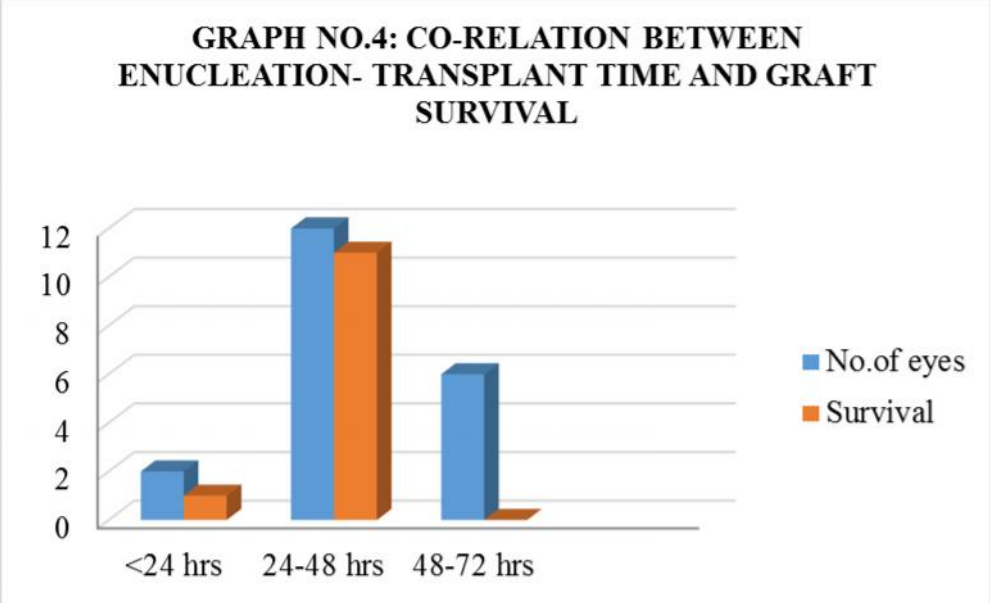
GRAPH NO.3: INDICATIONS FOR KERATOPLASTY



In this study, the most common indication was corneal scarring which was 70% followed by keratitis which was 20% and lastly corneal dystrophies which was 10%.

TABLE NO.4: CO-RELATION BETWEEN ENUCLEATION- TRANSPLANT TIME AND GRAFT SURVIVAL

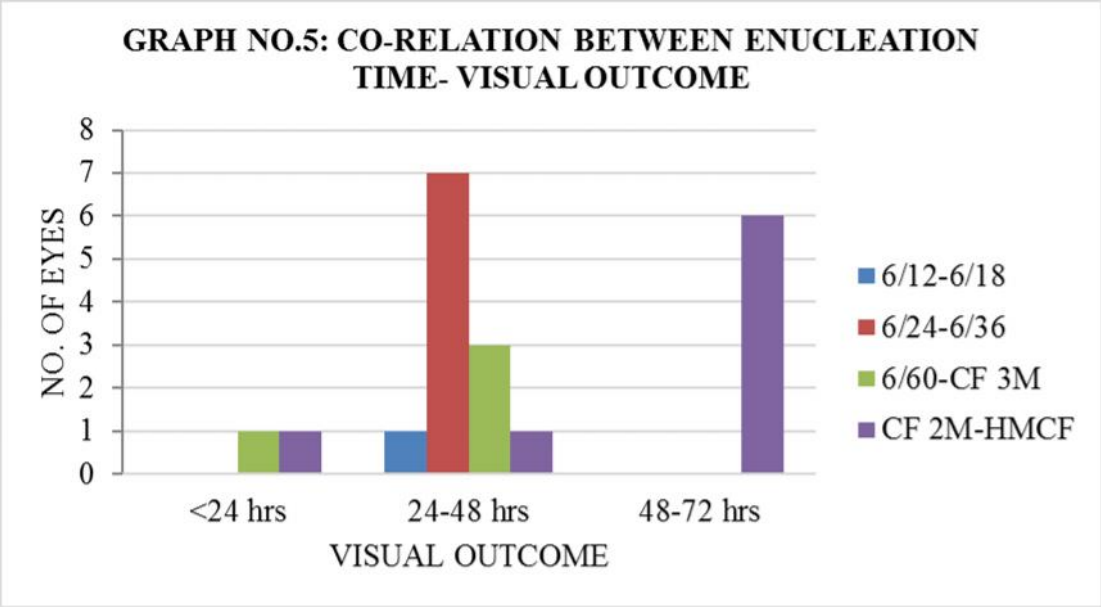
TIME INTERVAL(hrs)	NO. OF EYES	SURVIVAL	REJECTION	CLEAR GRAFT (%)	p value
<24	2	1	1	50	p= <0.001
24-48	12	11	1	91.6	
48-72	6	0	6	0	



In this study, we have divided the cases in three groups according to the time interval between enucleation and transplant. Group 1 underwent PK within 24 hrs of enucleation comprising of 2 eyes with post-operative graft clarity of 50%. Group 2 consisted of PK where enucleation was done between 24-48 hrs comprising of 12 eyes with graft clarity of 91.6%. Group 3 included patients who underwent PK in 48-72 hrs after enucleation comprising of 6 patients with no graft clarity. Corneas more than 72 hrs were not used in our study. Statistical analysis using Fisher Exact Test gave p value of <0.001 which is statistically significant.

TABLE NO.5: CO-RELATION BETWEEN ENUCLEATION TIME - VISUAL OUTCOME

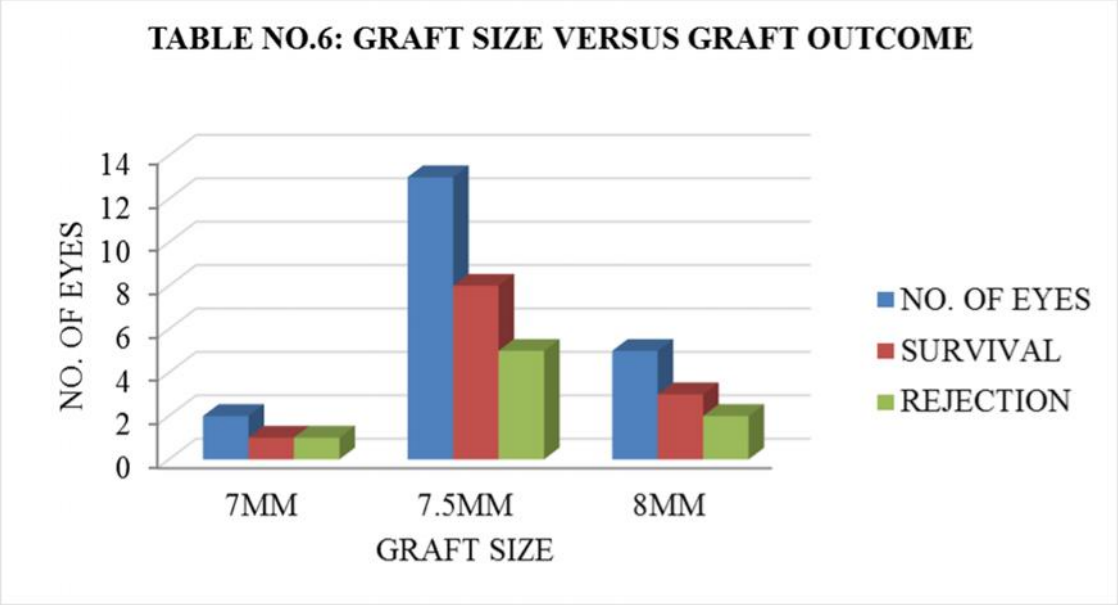
TIME INTERVAL	VISUAL OUTCOME					p value
	6/12-6/18	6/24-6/36	6/60-CF3M	CF2M-HMCF	TOTAL	p = 0.039
<24 HRS	-	-	1	1	2	
24-48 HRS	1	7	3	1	12	
48-72 HRS	-	-	-	6	6	
TOTAL	1	7	4	8	20	



In this study, we have studied the co-relation between the enucleation-transplant time and visual outcome at the end of 6 months. Patients were subdivided into three groups, Group 1 (<24hrs) comprised of 2 patients who attainted vision ranging between 6/60-HMCF. Group 2 (24-48 hrs) had 7 patients who attained vision ranging between 6/24-6/36. Group 3 (48-72 hrs) consisted of 6 patients attaining vision of CF 2M – HMCF. Statistical analysis by Fisher Exact Test gave p= 0.039 which is statistically significant.

TABLE NO.6: GRAFT SIZE VERSUS GRAFT OUTCOME

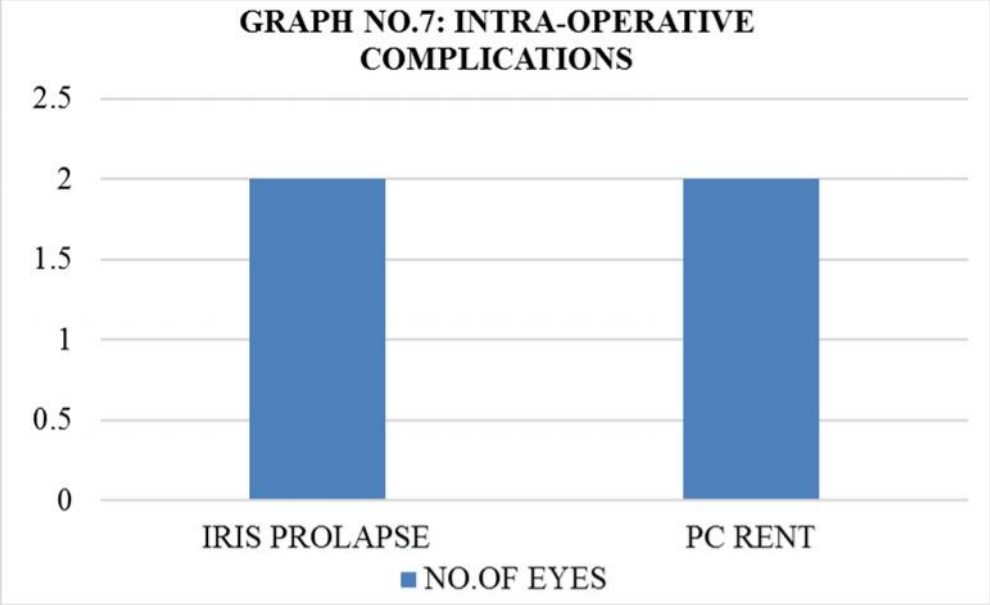
GRAFT SIZE (mm)	NO. OF EYES	SURVIVAL	REJECTION	CLEAR GRAFT (%)	P value
7	2	1	1	50	p= 0.590
7.5	13	8	5	61.5	
8	5	3	2	60	



In this study, we have compared graft size with the graft outcome at the end of 6 months. Graft size of 7 mm used in 2 eyes resulted in graft clarity in 50%. Graft size of 7.5 mm used in 13 eyes with graft clarity of 61.5% and graft size 8 mm used in 5 eyes resulted in clarity in 60%. Statistical analysis done by Fisher Exact Test gave p= 0.590 which is not significant.

TABLE NO.7: INTRA-OPERATIVE COMPLICATIONS

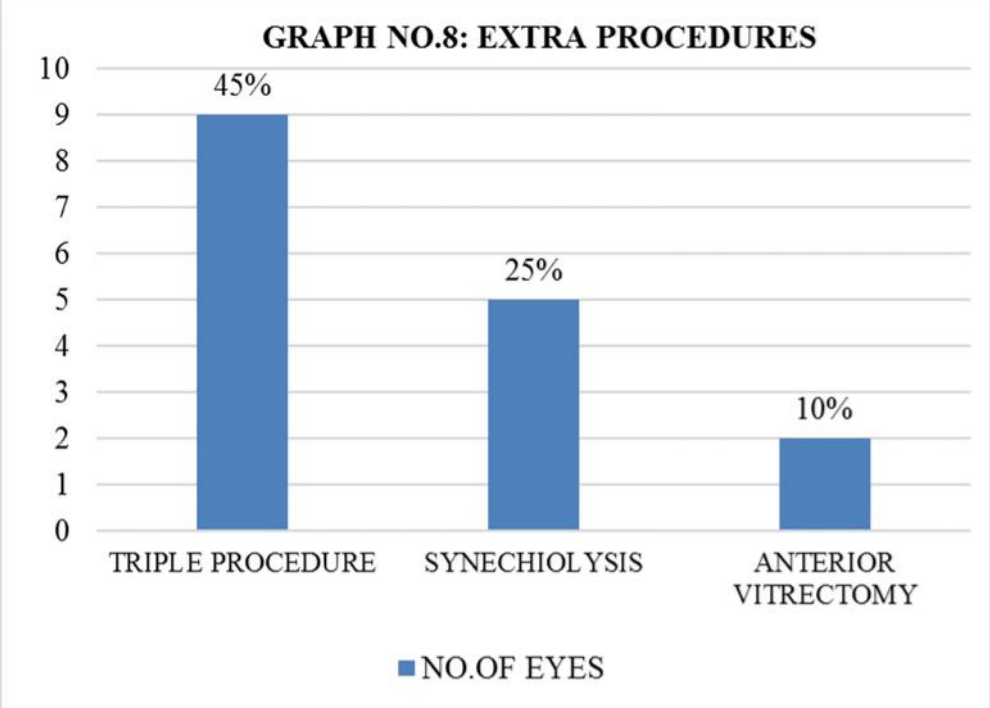
COMPLICATIONS	NO. OF EYES	PERCENTAGE (%)
IRIS PROLAPSE	2	10
POSTERIOR CAPSULAR RENT	2	10



In our study, 20% of the eyes experienced intra-operative complications. 2 intra-operative complications were noticed. 2 patients had iris prolapse and 2 patients had posterior capsular rent.

TABLE NO.8: EXTRA PROCEDURES

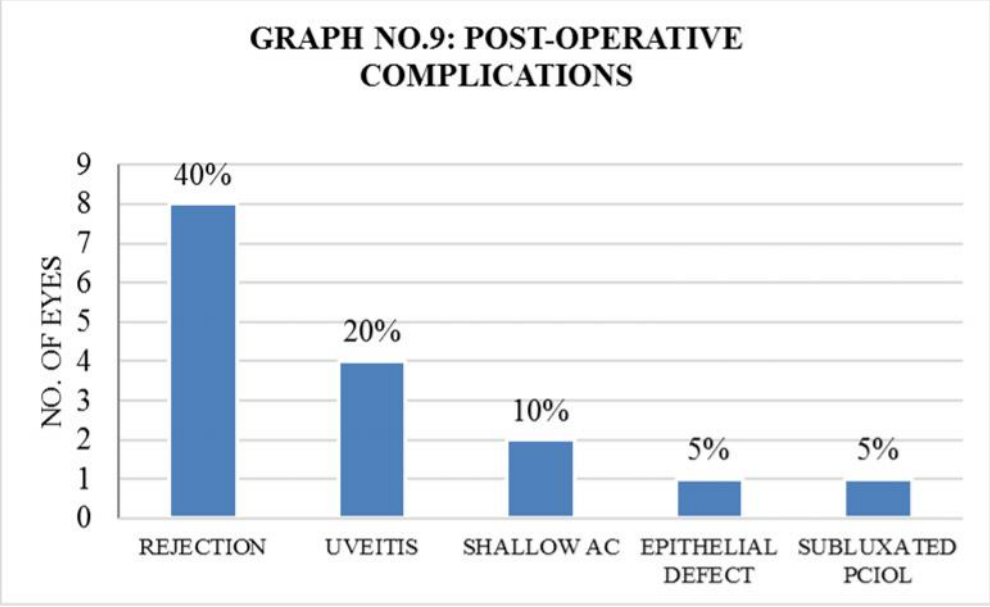
PROCEDURE	NO.OF EYES	PERCENTAGE (%)
TRIPLE PROCEDURE	9	45
SYNECHIOLYSIS	5	25
ANTERIOR VITRECTOMY	2	10



In our study, extra procedures were performed along with PK. Triple procedure was done for 9 eyes (45%), synechiolysis for 5 eyes (25%) and anterior vitrectomy for 2 eyes (10%).

TABLE NO.9: POST-OPERATIVE COMPLICATIONS

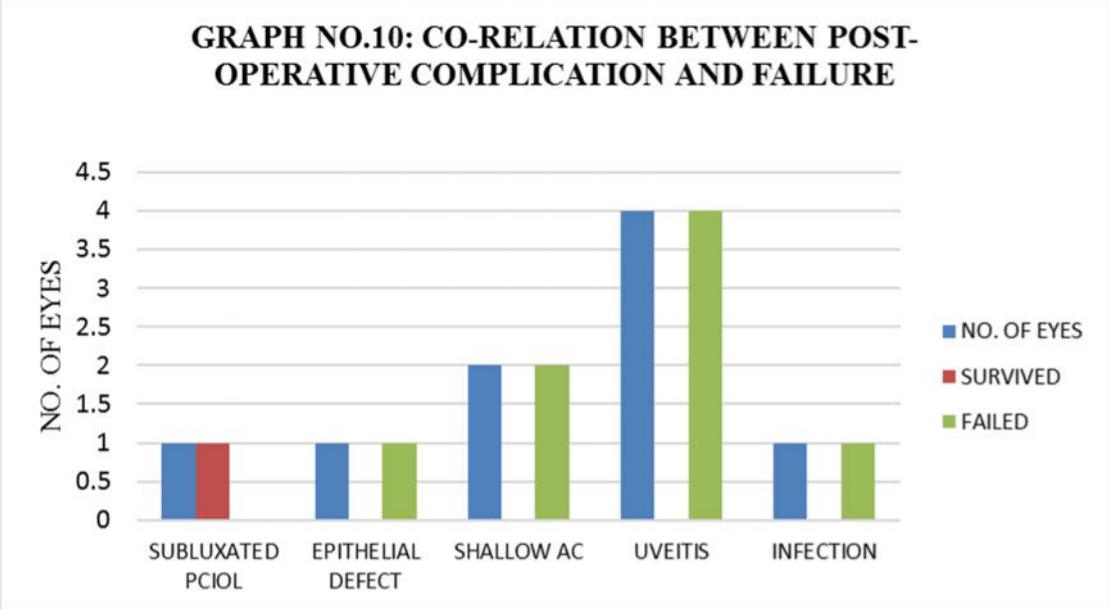
COMPLICATIONS	NO. OF EYES	PERCENTAGE (%)
FAILURE	8	40
UVEITIS	4	20
SHALLOW AC	2	10
EPITHELIAL DEFECT	1	5
SUBLUXATED PCIOL	1	5



In the study, 40% eyes had graft rejection. Second most common complication was post-operative uveitis 20%. Shallow anterior chamber noted in 10% of eyes. 5% eyes had subluxated PCIOL and epithelial defect each.

TABLE NO.10: CO-RELATION BETWEEN POST-OPERATIVE COMPLICATION AND FAILURE

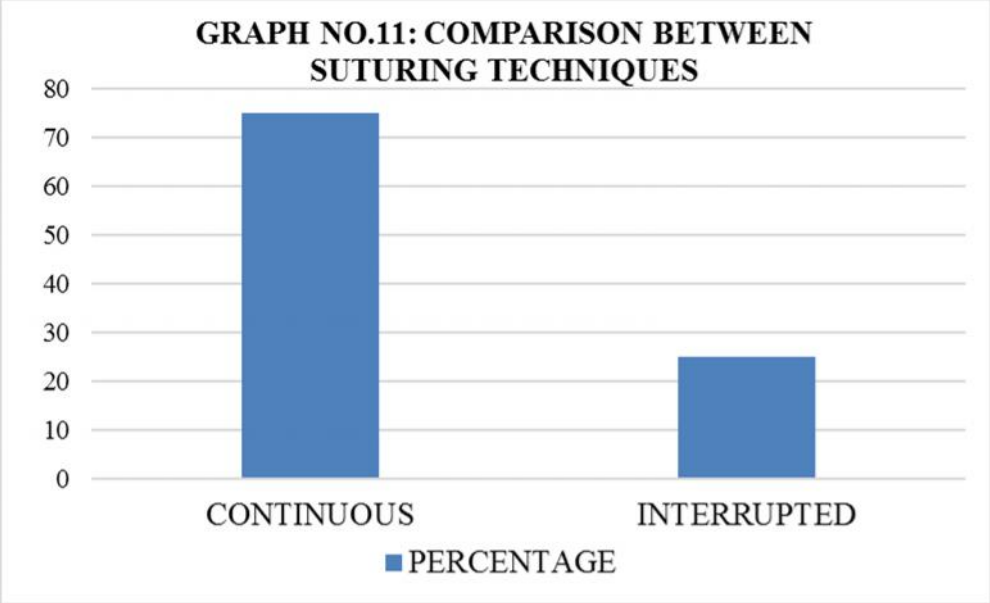
COMPLICATION	NUMBER	SURVIVED	FAILED	%
SUBLUXATED PCIOL	1	1	-	11.11
EPITHELIAL DEFECT	1	-	1	11.11
SHALLOW AC	2	-	2	22.22
UVEITIS	4	-	4	44.44
INFECTION	1	-	1	11.11
TOTAL	9	1	8	100



In this study, 88.88% of patients who had post-operative went into graft failure and 11.11% of patients had graft survival in spite of post-operative complications.

TABLE NO.11: COMPARISON BETWEEN SUTURING TECHNIQUES

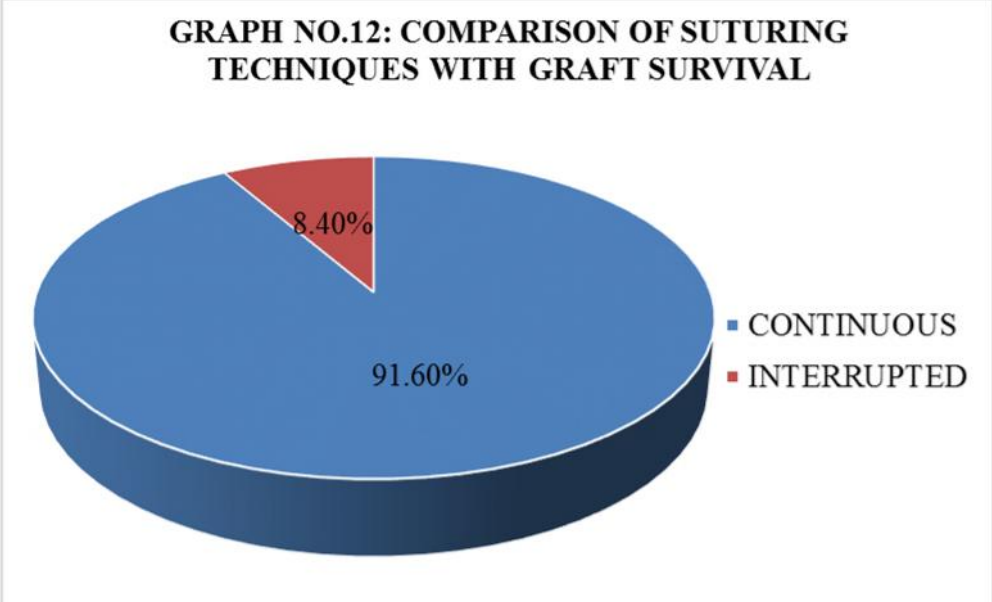
TECHNIQUE	NO.OF EYES	PERCENTAGE
INTERRUPTED WITH CONTINUOUS	15	75
INTERRUPTED	5	25
TOTAL	20	100



In this study, interrupted with continuous suturing technique was employed in 75% of patients whereas remaining 25% patients had interrupted suturing.

TABLE NO.12: COMPARISON OF SUTURING TECHNIQUES WITH GRAFT SURVIVAL

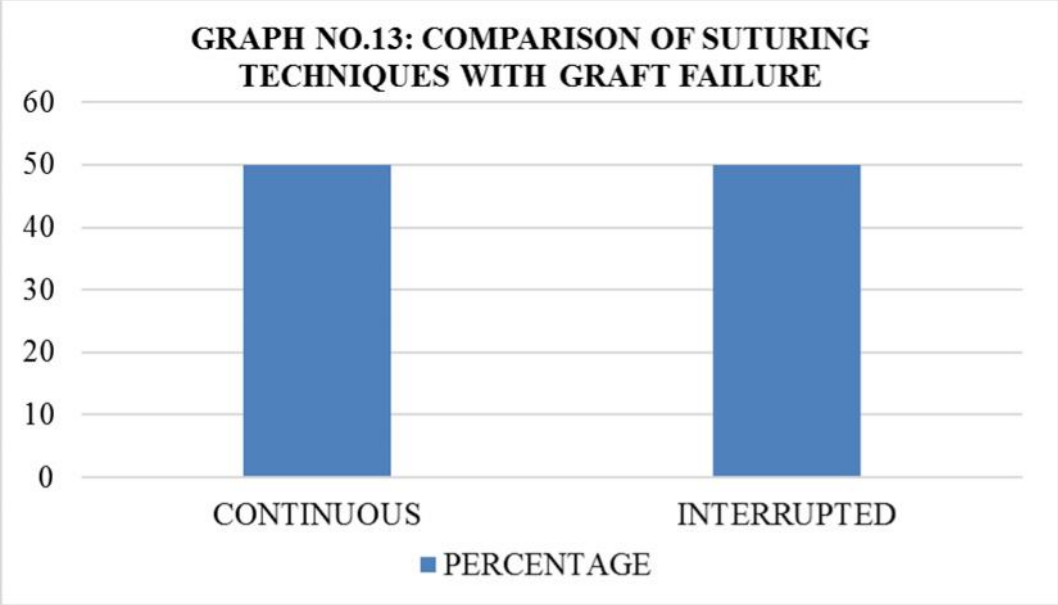
SUTURING TECHNIQUE	NO. OF EYES	PERCENTAGE
INTERRUPTED WITH CONTINUOUS	11	91.6
INTERRUPTED	01	8.4
TOTAL	12	100



In this study, out of the successful cases, 91.6% cases had continuous sutures whereas, 8.4% cases had interrupted sutures.

TABLE NO.13: COMPARISON OF SUTURING TECHNIQUES WITH GRAFT FAILURE

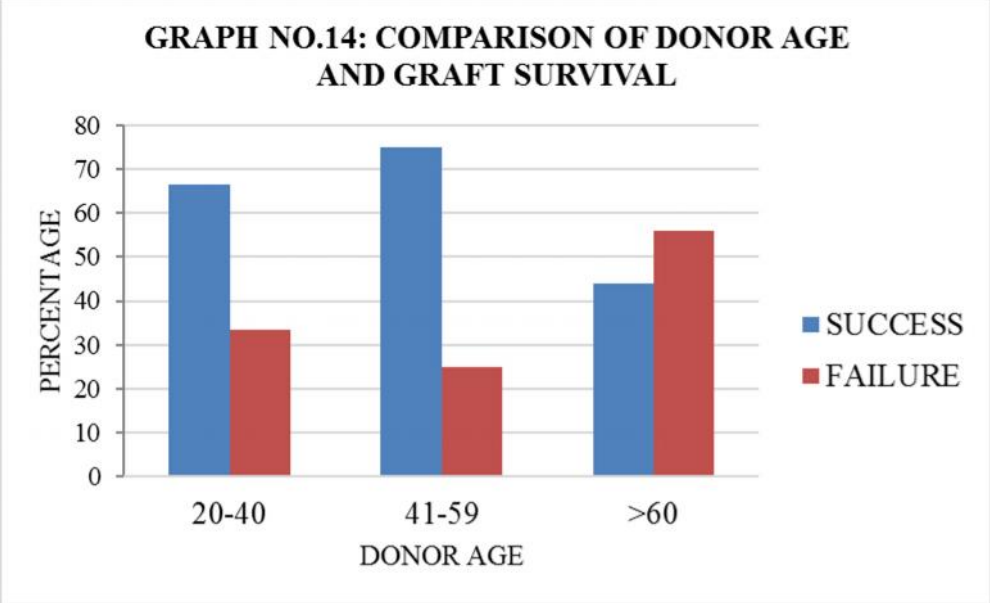
SUTURING TECHNIQUE	NO. OF EYES	PERCENTAGE
INTERRUPTED WITH CONTINUOUS	4	50
INTERRUPTED	4	50
TOTAL	8	100



In this study, out of the patients with graft failure, 50% patients had continuous and 50% patients had interrupted suturing.

TABLE NO.14: COMPARISON OF DONOR AGE AND GRAFT SURVIVAL

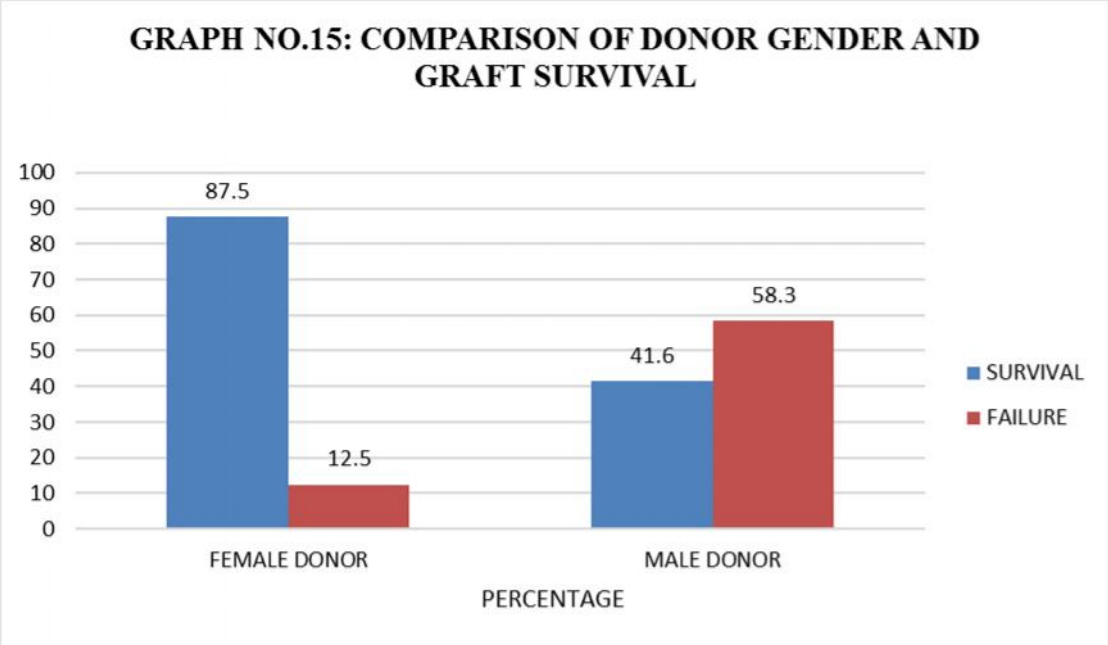
	SURVIVAL		FAILURE		TOTAL	
DONOR AGE	NO. OF EYES	%	NO. OF EYES	%	NO.OF EYES	%
20-40	2	66.66	1	33.33	3	100
41-59	6	75	2	25	8	100
>60	4	44	5	56	9	100



In this study, donor corneas were subdivided into 3 groups. Group 1 with age ranging between 20-40 yrs had a success rate of 66.66% and failure rate of 33.33%. Group 2 with age ranging between 41-59 yrs had a success rate of 75% and failure rate of 25%. Group 3 with age of >60 yrs had a success rate of 44% and failure rate of 56%.

TABLE NO.15: COMPARISON OF DONOR GENDER AND GRAFT SURVIVAL

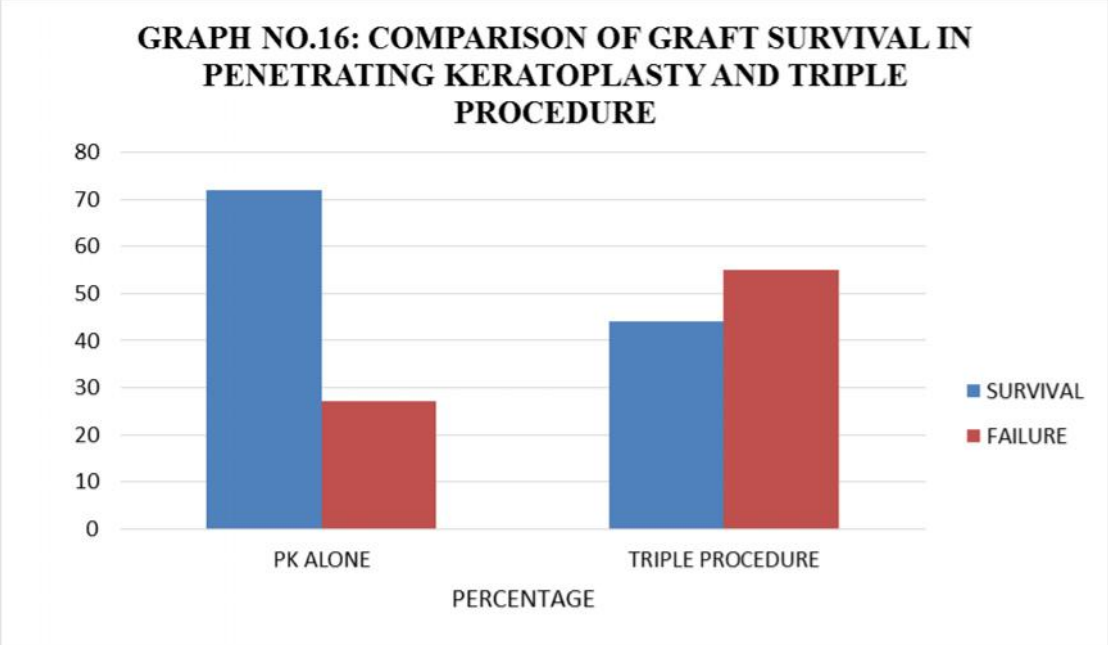
DONOR GENDER	SURVIVAL		FAILURE		TOTAL
	NO. OF EYES	%	NO.OF EYES	%	
FEMALE	7	87.5	1	12.5	8
MALE	5	41.6	7	58.3	12



In this study, female donor group had a survival rate of 87.5% and failure rate of 12.5%. In the male donor group, survival rate was 41.6% and failure rate was 58.3%.

TABLE NO.16: COMPARISON OF GRAFT SURVIVAL IN PENETRATING KERATOPLASTY AND TRIPLE PROCEDURE

PROCEDURE	NO.OF EYES	SURVIVAL	%	FAILURE	%	TOTAL
PK ALONE	11	8	72.72	3	27.27	100
TRIPLE PROCEDURE	9	4	44.44	5	55.55	100



In this study, patients who have undergone PK alone have a higher success rate of 72.72% than patients in triple procedure group where the success rate was 44.44%.

DISCUSSION

Corneal transplantation, nowadays is the most widely used and the most successful transplant, which if technically perfect can overcome the blindness due to the corneal diseases and thus help to split the curtain of darkness and make the entry of "vision", the most beautiful thing in the world.

In the present study, the final outcome in terms of graft clarity and vision were co-related with various factors, and sincere attempts were made to find out the common indications and complications for penetrating keratoplasty.

In the present study, 20 eyes underwent penetrating keratoplasty.

Age and Sex

In the present study, table 1 depicts the mean age to be 50 $\pm$ 2.3 yrs. Majority of the patients (45%) were in the range of 51-60 yrs. In table 2, 65% patients were males and 35% patients were females. Ratio of male : female was 1.8:1. More number of males were affected than females in our study and this trend is seen in most of the other studies. Male preponderance is seen because of various socio economic factors and comparatively easy and accessible health care facilities to them. Males are also more prone to develop trauma and corneal ulcers as compared to the females because of more outdoor work.

According to Thomos et al[66], the age was ranging between 41-67 yrs and 53.3% were males which is comparable with study.

Indications for keratoplasty

In the present study, table 3 depicts, the most common indication was corneal scarring which was 70%, followed by keratitis (20%) and lastly corneal dystrophies (10%). Perhaps most of our patients were from low socio economic strata and from the remote places.

According to Tabin et al[18] corneal scar was the most common indication for PK in 38% followed by adherent leucoma (35%), pseudophakic bullous keratopathy (6%).

Another study done by Shilpa AJ et al [19] also found corneal scar as the main indication for the keratoplasty in 31% followed by pseudophakic bullous keratopathy in 17%.

Our indication was comparable with other studies by Laxman D et al[67] and Dandona L et al [68]. Studies done in India were found to have similar indications due to the similarities in demographic and socio economic status of population.

Co-relation between enucleation- transplant time and graft survival

In the present study, in table 4 we have divided the cases into three groups according to the time interval between enucleation and transplant. First group underwent PK within 24 hrs of enucleation comprising of 2 eyes with post-keratoplasty graft clarity being 50%. Second group had PK done between 24-48 hrs after enucleation comprising of 12 eyes with graft clarity of 91.6%. Third group included patients who underwent PK within 48-72 hrs of enucleation, comprising of 6 patients with no graft clarity. Corneas more than 72 hrs were not used in our study. This comparison was found statistically significant ($p<0.001$) by Fischer Exact test.

Woodford et al [69] reported that death to preservation time longer than 6 hrs predisposes to sloughing of donor epithelium. Hence, donor cornea is compromised.

Co-relation between enucleation time- visual outcome

In the present study, in table 5 we have studied the correlation between the enucleation-transplant time and visual outcome at the end of 6 months. Patients were subdivided into three groups, group 1 (<24hrs) comprised of 2 patients who attainted vision ranging between 6/60-HMCF. Group 2 (24-48 hrs) had 7 patients who attained vision ranging between 6/24-6/36. Group 3 (48-72 hrs) had 6 patients attaining vision of CF 2M – HMCF.

Woodford et al[69] and Wagnor et al[70] noted similar findings and concluded if time interval between death to preservation and transplant is reduced, it can significantly improve the quality of vision.

Graft size versus graft outcome

In the present study, table 6 has compared graft size with the graft outcome at the end of 6 months. Graft size of 7 mm was used in 2 eyes and resulted in graft clarity in 50%; graft size of 7.5 mm was used in 13 eyes with graft clarity of 61.5% and graft size of 8 mm was used in 5 eyes which had clarity in 60%.

Williams K,et al[32] stated that graft size outside the range of 7.0 to 7.9 mm diameter; and corneal vascularization was associated with graft failure in the post-operative period.

Marianne O et al[71] found that an unusually large recipient bed size (>8.5mm) was associated with an increased risk of failure by rejection or ocular surface disease.

Shilpa AJ et al [19] found that graft survival did not differ significantly with graft size, though smaller sized grafts had better results.

Complications

a. Intra-operative complications- In our study, as per table 7, 20% of the patients experienced intra-operative complications, 2 patients had iris prolapse and 2 patients had posterior capsular rent.

b. Post-operative complications- In the study, as per table 9, 40% patients had graft rejection. Second most common complication was post-operative uveitis (20%). Shallow anterior chamber was seen in 10% of patients and 5% patients had subluxated PCIOL and epithelial defect each.

All of the above complications were corresponding with a study conducted by Thomas et al [66] who noted uveitis in 10% of cases, epithelial defects (3%), failure (!3.3%).

Extra procedures

In our study, as shown in table 8 we have seen the extra procedures performed along with keratoplasty. Triple procedure was done for 9 patients, synechiolysis for 5 patients and anterior vitrectomy for 2 patients.

Thomas et al[66] had comparable results as in our study. More manipulation of the intra-ocular tissues predisposes the graft to endothelial and immunologic failure.

Co-relation between post-operative complication and failure

In this study, table 10 depicts that 88.88% of patients who had post-operative went into graft failure and 11.11% of patients had graft survival in spite of post-operative complications.

A study conducted by Wagnor et al[70] reported bacterial keratitis (5.8%), persistent epithelial defects (3.4%) which were similar complications as in our study and the survival of graft also showed comparable results.

Suturing techniques

In this study, as shown in table 11, continuous suturing technique was employed in 75% of patients whereas remaining 25% patients had interrupted sutures put.

In this study, as shown in table 12, out of the successful cases, 91.6% cases had continuous sutures whereas, 8.4% cases had interrupted sutures.

In this study, as shown in table 13, out of the patients with graft failure, 50% patients had continuous and 50% patients had interrupted sutures put.

Dana MR et al [74] studied thirty four patients without pre-operative corneal neovascularization and 41% of the patients had vascularization of cornea secondary to the sutures.

Donor corneal factors

In this study, donor corneas were subdivided into 3 groups. Group 1 with age ranging between 20-40 yrs had a success rate of 66.66% and failure rate of 33.33%.

Group 2 with age ranging between 41-59 yrs had a success rate of 75% and failure rate of 25%. Group 3 with age of >60 yrs had success rate of 44% and failure rate of 56%. (Table 14)

In this study, female donor group had a success rate of 87.5% and failure rate of 12.5%. In the male donor group, success rate was 41.6% and failure rate was 58.3%. (Table 15).

The above results were corresponding to a study by Feizi S et al [72] where they noted that donor age significantly influenced the endothelial cell density (p=0.02).

Procedure factors

In the present study, as shown in table 16, patients who have undergone PKP alone have a higher success rate of 72.72% than the patients in triple procedure group where success rate was 44.44%.

The above results were similar to a study by Inoue K et all[73.]

CONCLUSION

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on all patients visiting the out-patient department with corneal opacities, and patients with pre-existing corneal opacities enrolled in the recipient register of Department of Ophthalmology.

On conclusion of this study, 60% patients had successful keratoplasty and 40% went in graft failure.

Most common indication for PK in our study was corneal scarring due to various causes in the age group between 40-60 years with a male preponderance because they are more prone to develop trauma and corneal ulcers as compared to the females because of more outdoor work.

There are several factors contributing to the survival of the corneal transplantation. Most crucial factor being the time interval between the enucleation time and transplant. Younger donor corneas and younger recipients had a better viability of grafts. Complications faced during and after the surgery resulted in the failure. Technique of suturing the graft had a significant role in the result of the procedure.

The size of the graft taken has not played a significant role in our study.

Even the extra procedures done like cataract extraction, synechiolysis changed the course of graft survival. Patients who underwent combined procedures had a higher rate of failure.

SUMMARY

Corneal blindness is one of the major cause of reversible blindness in the developing countries like India. Reversibility of this type of blindness makes it our duty to eradicate this cause. With the advancement in the surgical techniques and instruments, PK is the mainstay treatment of corneal scarring.

The present study was a one year cross-sectional study conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on patients undergoing PK during the period between 1st January 2015 – 31st December 2015.

Most common indication in this study was corneal scarring among the age group of 40-60 years. Visual outcome and graft survival was noted in 60% of the cases whereas 40% cases went into graft failure.

PK gave a satisfactory visual outcome at our tertiary care centre. A thorough pre-operative evaluation of the donor cornea and recipient eyes is a must to estimate the prognosis of the visual outcome. A meticulous post-operative follow-up is mandatory for these cases to monitor the graft survival.

Lastly, the importance of eye donation calls for a highlight so as to procure donor corneas and their preservation which enables us to fight the noble cause eradication of corneal blindness.

BIBLIOGRAPHY

1. Foster A. Vision 2020 the Right to Sight (editorial). Trop Doct 2003 Oct; 33(4):193-194.

2. Thylefors B, Negrel AD, Pararajasegaram R, Dadzie KY. Global data on blindness. Bull WHO 1995; 73(1): 115 – 121.

3. Congdon NG, Friedman DS, Lietman T. Important causes of visual impairment in the world today. JAMA 2003 Oct 15; 290(15): 2057-2060.

4. Dandona L et al. Blindness in the Indian state of Andhra Pradesh. Invest Ophthalmol Vis Sci 2001 Apr; 42(5): 908-916.

5. Birk DE, Trelstad RL. Extracellular compartments in matrix morphogenesis: collagen fibril, bundle, and lamellar formation by corneal fibroblasts. J Cell Biol 1984 Dec; 99(6):2024-2033.

6. Jay H. Krachmer, Mark J. Mannis, and Edward J. Holland. Cornea 3rd edition.

7. Dua HS, Faraj LA, Said DG, Gray T, Lowe J. Human corneal anatomy redefined: a novel pre-Descemet's layer (Dua's layer). Ophthalmology 2013 Sep; 120 (9): 1778-85.

8. Khurana AK. Anatomy and physiology of eye. 2nd edition 2006; 21-42.

9. Henry F. Edelhauser. The Balance between Corneal Transparency and Edema. The Proctor Lecture. Invest Ophthalmol Vis Sci. 2006 May; 47(5):1754-67.

10. Namrata S, Chandra Shakher, Rasik B Vajpayee. Evolution of corneal Grafting surgery in Corneal Transplantation. 2nd edition 2010; 1-3.

11. Anwar M, Teichmann KD. Bigbubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. J Cataract Refract Surg 2002;28(3):398-403

12. Melles GR et al. A new surgical technique for deep stromal anterior lamellar keratoplasty. Br J Ophthalmol. 1999 Mar; 83(3):327-33.

13. Filtaov VP. Transplantation of the cornea. Arch Ophthalmol. 1935;13: 321-47.

14. Filtaov VP, Bajenova MA. Culture of dried corneal tissue. Arch d'Ophth and Rev. Gen. d'Ophth. 1937;1:385.

15. Hyman L, Wittpenn J, Yang C. Indications and techniques of penetrating keratoplasty 1985-1988. Cornea 1992; 11(6):573-6.

16. Patel NP, Kim T, Rapuano CJ, Cohen EJ, Laibson PR. Indications for penetrating keratoplasty 1989-1995. Ophthalmology. 2000; 107(4):719-24.

17. Urmila Ghatak, Rajesh Sinha, Rasik B Vajpayee. Indication and outcome of penetrating keratoplasty in Corneal Transplantation. 2nd edition 2010; 4-12.

18. Tabin GC et al. Penetrating keratoplasty in Nepal. Cornea. 2004; 23:589-596.

19. Shilpa A Joshi, Seema S Jagdale, Pranav D More, and Madan Deshpande. Outcome of optical penetrating keratoplasty at a tertiary care eye institute in western India. Indian J Ophthalmol. 2012 Jan-Feb; 60(1): 15-21.

20. AK bansal, GN rao. Penetrating keratoplasty in LC Dutta modern ophthalmology volume 1; 2013: 257.

21. Keates RH, Falkenstein S. Keratoplasty in keratoconus. Am J Ophthalmol. 1972;74:442-44.

22. Kirkness CM, Ficker LA, Steele AD, Rice NS. The success of keratoplasty for keratoconus. Eye (Lond) 1990;4 (Pt 5): 673-88.

23. Olson RJ, Mattingly TP, Waltman SR, Kuafman HE. Aphakic keratoplasty : visual acuity and optical errors. Ophthalmology. 1880 July;87(7):680-86.

24. Pineros O, Cohen EJ, Rapuano CJ, Liabson PR. Long term results after penetrating keratoplasty for Fuchs' endothelial dystrophy. Arch Ophthalmol. 1996 Jan; 114(1):15-18

25. Stulting RD, Sumers KD, Cavanagh HD, Waring GO 3rd, Gammon JA. Penetrating keratoplasty in children. Ophthalmology 1984;91(10):1222-30

26. Dana MR, Moyes AL, Gomes JA, Rosheim KM, Schaumberg DA, Laibson PR, et al. The indications for and outcome in pediatric keratoplasty. A multicenter study. Ophthalmology 1995;102:1129-38.

27. Vail A, Gore SM, Bradley BA, Easty DL, Rogers CA. Corneal graft survival and visual outcome. A multicenter Study. Corneal Transplant Follow-up Study Collaborators. Ophthalmology. 1994 Jan;101(1):120-7.

28. Rao GN, Shaw EL, Aurther EJ, Aquavella JV. Endothelial cell morphology and corneal deturgescence. Ann Ophthalmol. 1979; 11:885-99.

29. Ben Connell, Michael S Loughnan, Rasik B Vajpayee. Corneal graft rejection in Corneal Transplantation. 2nd edition 2010:122-127.

30. Maumenee AE. The influence of donor recipient sensitization on corneal graft. AM J Ophthalmol 1951;34:142-152.

31. Mohan M, Panda A, Kumar TS. Results of penetrating keratoplasty in vascularized corneas. Ann Ophthalmol. 1990 Jun; 22(6):235-8.

32. Williams KA, Roder D, Esterman A, Muehlberg SM, Coster DJ. Factors predictive of corneal graft survival. Report from the Australian Corneal Graft Registry. Ophthalmology 1992; 99(3):403-414.

33. Cobo LM, Coster DJ, Rice NS, Jones BR. Prognosis and management of corneal transplantation for herpetic keratitis. Arch Ophthalmo1.1980 Oct;98(10):1755-9.

34. Beekhuis WH et al. Corneal graft survival in HLA-A- and HLA-B-matched transplantations in high-risk cases with retrospective review of HLA-DR compatibility. Cornea. 1991 Jan; 10(1):9-12.

35. Hassan SS et al. Infectious disease risk factors of corneal graft donors. Arch Ophthalmol. 2008;126(2):235-239.

36. Binder PS, Abel R Jr, Polack FM, Kaufman HE. Keratoplasty wound separations. Am J Ophthalmol. 1975 Ju1;80(1):109-115.

37. William KA, Swayer MA, White MA, Mahmood MI, Coster DJ. Report from the Australian corneal graft registry. Transplant Proc. 1989 21:3142- 3144.

38. Renucci AM, Marangon FB, Culbertson WW. Wound dehiscence after penetrating keratoplasty: clinical characteristics of 51 cases treated at Bascom Palmer Eye Institute. Cornea. 2006 Jun;25(5):524-9

39. Polack FM, Kanal A. Electron microscopic studies of graft endothelium in corneal graft rejection. Am J Ophthalmol. 1972 May;73(5):711-717.

40. Polack FM. Keratoplasty in aphakic eyes with corneal edema. Ophthalmic surgery.1980 Oct;11(10):701-707.

41. Coster DJ. Factors affecting the outcome of corneal transplantation. Ann R Surg Engl.1981 Mar;63(2):91-7.

42. Irvine AR, Kaufman HE. Intraocular pressure following penetrating keratoplasty. Am J Ophthalmol. 1969 Nov; 68(5):835-844.

43. Thoft RA, Gordon JM, Dohlman CH. Glaucoma following keratoplasty. Trans Am Acad Ophthalmol Otolaryngol. 1974 Mar-Apr; 78(2): OP352-64.

44. Binder PS, Kaufman HE, Abel R Jr. Cyclocryotherapy for glaucoma after penetrating keratoplasty. Am.J.Ophthalmol. 1975 Mar; 79(3):489-92.

45. Sihota R, Sharma N, Panda A, Aggarwal HC, Singh R. Post-penetrating keratoplasty glaucoma: Risk factors, management and visual outcome. Aust N Z J Ophthalmol. 1998 Nov; 26(4): 305-9.

46. Dada T et al. Post-penetrating keratoplasty glaucoma. Indian J Ophthalmol. 2008 Jul-Aug; 56(4): 269-277.

47. Fong LP, Ormerod LD, Kenyon KR, Foster CS. Microbial keratitis complicating penetrating keratoplasty. Ophthalmology 1988; 95(9):1269-75.

48. Leibowitz HM, Laing RA, Chang R, Thoedore J, Oak SS. Corneal edema secondary to vitreocorneal contact. Arch Ophhalmol. 1981 Mar; 99(3): 417-21.

49. C. C. Sterk, Jager MJ, Swart-vd Berg M. Recurrent herpetic keratitis in penetrating keratoplasty. Doc Ophthalmol. 1995; 90(1): 29-33.

50. Lomholt JA, Baggesen K, Ehlers N. Recurrence and rejection rates following corneal transplantation for herpes simplex keratitis. Acta Ophthalmol Scand.1995 Feb;73(1):29-32.

51. Marcon AS, Cohen EJ, Rapuano CJ, Laibson PR. Recurrence of corneal stromal dystrophies after penetrating keratoplasty. Cornea. 2003 Jan:22(1):19-21.

52. Namrata S, Shekhar C, Vajpayee RB. Complication of penetrating keratoplasty in Corneal Transplantation. 2nd edition 2010;95-116.

53. Zimmerman T, Olson R, Waltman S, Kaufman H. Transplant size and elevated intraocular pressure. Postkeratoplasty. Arch Opthalmol 1978;96(12):2231-33

54. Wilsons SE, Bourne WM. Effect of recipient donor trephine disparity on refractive error in keratoconus. Ophthalmology. 1989;96(3):299-305.

55. Wilson SE, Kufman HE. Graft failure after penetrating keratoplasty. Sury Ophthalmol 1990;34(5):325-56.

56. Pucell JJ. Intraoperative complications of penetrating keratoplasty. In: Kerchmer JH, Maninis MJ, cornea: surgery of the cornea and conjunctiva. Vol 3. Mosby St. Louis, 1997;134:1639-44.

57. Buxton JN, Seedor JA, Perry HD, Eagle RC, Pecego JA. Donor failure after corneal transplantation surgery. Cornea 1998; 7(2):89-95.

58. Genevois O, Benzerroug M, Gardea E, Brasseur G, Muraine M. Macular edema after corneal graft: a prospective study by optical coherence tomography. Cornea.2007; 26(6):683-4

59. Musch DC, Meyer RF, Sugar A, Vine AK. Retinal detachment following penetrating keratoplasty. Arch Ophthalmol. 1986 Nov; 104(11): 1617-20.

60. R Vajpayee, V Sharma, N Sharma, A Panda, H Taylor. Evaluation of techniques of single continuous suturing in penetrating keratoplasty. Br J Ophthalmol 2001;85(2):134-138.

61. Wifferi SJ, Nelson LR, Ali AF, Bourne WM. Morphologic assessment of corneal endothelium by specular microscopy in evaluation of donor corneas for transplantation. Cornea. 1995 Nov;14(6):554-61

62. Wilhelmus KR, Hassan SS. The prognostic role of donor corneoscleral rim cultures in corneal transplantation. Ophthalmology. 2007 Mar; 114(3):440-5.

63. Basu PK, Hasany SM. Autolysis of the cornea of stored human donor eyes. Can J Ophthalmol 1974; 9(2):229-35.

64. Armitage WJ. Preservation of human cornea. Transfus Med Hemother.2011; 38(2):143-147.

65. Jeng BH. Preserving the cornea: corneal storage media. Curr Opin Ophthalmol. 2006 Aug;17(4):332-7.

66. Thomas M, Amin H, Pai V, Shetty J. A clinical study on visual outcome and complications of penetrating keratoplasty. IOSR- JDMS. 2015 June; 14(6): 49-60.

67. Laxman D, Chaitra P, Kanwarpal Singh Gill, Madhuri P, Mallikarjun S. Indications of penetrating Keratoplasty in southern India. J clindiagn res. 2013 Nov; 7(11): 2505-07.

68. Dandona L, Ragu K, Janarthanan M, Naduvilath T J, Shenoy R, Rao G N. Indications for penetrating keratoplasty in India. Indian J Ophthalmol. 1997; 45: 163-8.

69. Van Meter WS, Katz DG, White H, Gayheart R. Effects of death to preservation time on donor corneal epithelium. Trans Am Ophthalmol Soc. 2005;103: 209-224.

70. Wagoner MD, Ba-Abbad R, Al-Mohaimeed M, Al-Swailem S, Zimmerman MB. Postoperative Complications After Primary Adult Optical Penetrating Keratoplasty: Prevalence and Impact on Graft Survival. Cornea. 2009;28(4):385-394.

71. Price MO, Thompson RW Jr, Price FW Jr. Risk factors for various causes of failure in initial corneal grafts. Arch Ophthalmol. 2003;121(8):1087-1092.

72. Feizi S, Javasi MA, Ghasemi H, Javadi F. Effect of donor graft quality on clinical outcomes after penetrating keratoplasty for keratoconus. J Ophthalmic Vis Res. 2015 Oct-Dec; 10(4): 364-9.

73. Inoue K, Amano S, Oshika T, Sawa M, Tsuru T. A 10 year review of penetrating keratoplasty. Jpn J Ophthalmol. 2000 Mar-Apr; 44(2): 139-45.

74. Dana MR, Schaumberg DA, Kowal VO, Goren MB, Rapuano CJ, Cohen EJ. Corneal neovascularization after penetrating keratoplasty. Cornea. 1995 Nov; 14(6) : 604-9.

ANNEXURE-I

CONSENT FORM

ID NO.

Mr/Mrs/Ms_____

You are invited to participate in our research study titled **"ONE YEAR CROSS-SECTIONAL STUDY OF THE VISUAL OUTCOME AND GRAFT SURVIVAL IN PENETRATING KERATOPLASTY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI"** conducted by

Respected Sir/Madam we request you to enroll yourself to participate in our study as you are eligible for doing so. Your participation in the study is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to participate you are free to withdraw at any time.

Purpose of the study:-The purpose of the research is to find the visual outcome after penetrating keratoplasty, its intra operative and post-operative complications and to study factors affecting graft survival. This procedure is taken up to reduce the blindness accused by the corneal disorders.

Procedure Involved:- If you agree to enroll yourself in this study, you will be asked to give detailed history. Then you will be clinically examined in detail by slit-lamp examination, fundoscopy, tonometry for measurement of intraocular pressure. Syringing for patency of the lacrimal sac, keratometry and A-scan ultrasonography and investigations like Blood Pressure measurement, Random Blood sugar will be done. Then you will be undergoing keratoplasty where the diseased cornea is removed by measuring via trephine and replaced with healthy donor cornea.

Risks and Benefits:- Rare complications of keratoplasty include graft rejection, graft failure, endophthalmitis, vitreous loss, retro bulbar haemorrhage, for which all necessary precautions will be taken.

Your participation may benefit you and others and others suffering from same ailment in future, by helping us learn more about the disease process and better treatment modalities.

Alternatives:- If you are not willing to participate you will be treated according to the existing protocol & it will not affect your relationship with this hospital.

Costs for participating in this research:- There will not be any extra cost incurred by the participant. The participant will however have to pay for the investigations which are the part of the existing management protocol for this ailment. There is no commitment for any reimbursement or any other compensation for the participant.

Privacy and Confidentiality:- The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to others without your written permission.

Authorization to Publish Results:- When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Compensation:- In the event of injury related to the study, treatment will be made available through KLES Dr. Prabhakar Kore Hospital & MRC, Belagavi. There is no

compensation or payment for such medical treatment by law. The doctors and the staff will provide facilities and medical attention to you.

Questions:- If you have any questions about the research you may please contact:

1. Dr. Ganga S. Pilli, Chairperson, JNMC, Belagavi and chairman of Institutional Ethics Committee. Contact No. 08312471350

Consent for participation in Research Trial

I, Mr./Ms./Mrs _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Name of the participant:_____

Signature or the Left Thumb Print of Subject: _____

Witness Name: _____

Signature of Witness: _____

Name of the investigator:_____

Signature of the investigator:_____

Date: _____

Place: _____

ANNEXURE-II

KERATOPLASTY PROFORMA

PATIENTS ID NO: ☐☐☐

NAME: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

AGE: ☐☐ Years

SEX: ☐ (1-Male; 2-Female)

ADDRESS:_____

CONTACT NUMBER :- ☐☐☐☐☐☐☐☐☐☐

IS THE PATIENT ELIGIBLE FOR STUDY? (1-YES; 2-NO) ☐

HAS INFORMED CONSENT BEEN GIVEN? (1-YES; 2-NO) ☐

CHIEF COMPLAINTS:

DIMINUTION OF VISION RE ☐

Duration:_____ days/ months/years

LE ☐

Duration: _____ days/ months/years

HISTORY OF PRESENT ILLNESS:

1.DIMINUTION OF VISION

1-Gradual; 2-Sudden ☐

1-Progressive ; 2-Static ☐

1- Painless; 2- Painful ☐

1- For distance; 2- For near ☐

2. PHOTOPHOBIA 1- Present; 2- Absent ☐

3. COLOURED HALOS 1- Present; 2- Absent ☐

4. BLACK SPOTS BEFORE THE EYES 1- Present; 2- Absent ☐

5. WATERING 1- Present; 2- Absent ☐

6. REDNESS 1- Present; 2- Absent

7. DISCHARGE 1- Present; 2 - Absent ☐

8. H/O WEARING GLASSES (1-Distance; 2-Near; 3-Both) ☐

Duration: ☐☐ months/years

PAST HISTORY:

1.TRAUMA TO THE EYE: 1- Present; 2- Absent ☐

2.OCULAR SURGERY: 1- Present; 2- Absent ☐

Type of surgery: _____

Duration: ☐☐ months/years

3. OTHER CORNEAL DISEASES:

CORNEAL DEGENERATIONS 1-Present; 2-Absent ☐

CORNEAL DYSTROPHY 1-Present; 2-Absent ☐

MEDICAL HISTORY:

DIABETES: 1- Present; 2- Absent ☐

Duration: ☐☐ months/years

HYPERTENSION: 1- Present; 2- Absent ☐

Duration: ☐☐ months/years

ANY OTHER MEDICAL DISORDERS: _____

SYSTEMIC EXAMINATION:

CVS: 1- Normal 2- Abnormal ☐
if 2, specify :_____

RS: 1- Normal 2- Abnormal ☐
if 2, specify:_____

☐

CNS: 1- Normal 2- Abnormal
if 2, specify :_____

Per Abdomen:1- Normal 2- Abnormal ☐
if 2, specify :_____

EXAMINATION FINDINGS

Visual Acuity:

	OD	OS
DISTANT		
PINHOLE		
AIDED		

Adnexa (1- Normal; 2-Abnormal-specify)	☐	☐
3. Sclera (1- Normal; 2- Congested)	☐	☐
4. Conjunctiva (1-normal; 2-conjunctival congestion; 3-ciliary congestion; 4-chemosis)	☐	☐
5. Cornea (1- normal; 2-opacity; 3-vascularisation-S/F3a, DEEP3b) CORNEAL SENSATION- Present-1; Absent-2 Pre corneal Tear film-Normal-1; Abnormal-2	☐ ☐ ☐	☐ ☐ ☐
6. Anterior chamber (1- normal depth; 2-shallow; 3-deep;4-adherant leucoma)	☐	☐
7. Iris (1-normal colour& pattern; 2-Abnormal)	☐	☐

8. Pupil: Size- ____ in mm Shape:1- Round & Regular; 2-Abnormal;3-Details not made out Reaction: Direct (1. Present, 2. Absent) Indirect (1. Present, 2. Absent) Near reflex (1. Present, 2. Absent)	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
9. Lens Clarity- 1. Clear, 2. Opaque, 3. Details not made out Cataract - (1) , PCIOL - (2) Cataract if present- 1.immature 2.mature 3. hyper mature A) CORTICAL- (1.Present, 2. Absent)	☐ ☐ ☐ ☐	☐ ☐ ☐ ☐
B) NUCLEAR SCLEROSIS- 1. PRESENT, 2-ABSENT,3-details not made out If present- 1. Grade-1 2. Grade-2 3.Grade-3 4. Grade-4	☐ ☐	☐ ☐
(C) POSTERIOR SUBCAPSULAR CATARACT 1. PRESENT, 2. ABSENT,3.details not made out	☐	☐

FUNDUS	OD	OS
GLOW		
MEDIA		
DISC		
C: D RATIO		
BLOODVESSELS		
BACKGROUND		
MACULA		

INVESTIGATIONS:

A) Lacrimal patency

(1-PATENT; 2- regurgitation: 2A- Clear fluid, 2B- Mucopurulent; 3- BLOCKED)

OD ☐

OS ☐

B) IOP:

OD: ☐ mm of hg

OS: ☐ mm of Hg

C) A-SCAN BIOMETRY : SRK II FORMULA

EYE: ☐ (1-Right eye; 2- Left eye)

	OD	OS
K1		
K2		
AXL		
AC DEPTH		
PCIOL		

D) B-SCAN

- RETINAL DETACHMENT 1-Present; 2-Absent ☐
- VITREOUS DETACHMENT 1-Present; 2-Absent ☐
- VITREOUS DEGERATION 1-Present; 2-Absent ☐
- OTHERS 1-Present; 2-Absent ☐

E) MRI

OPERATIVE PROCEDURE:

1-KERATOPLASTY ALONE. ☐

2-KERATOPLASTY WITH PCIOL IMPLANTATION ☐

3-KERATOPLASTY WITH PCIOL WITH TRABECULECTOMY ☐

DIAGNOSIS:

IMPRESSION:

DATE: _____/_____/_____

OPERATING EYE: _____

ANAESTHESIA:

1-PERIBULBAR BLOCK ☐

2- GENERAL ANAESTHESIA ☐

COMPLICATIONS:

A) Operative 1. Present, 2. Absent ☐

If present- specify

B) Post- operative complications:

1. Present, 2. Absent ☐

If present- specify

TIME INTERVAL BETWEEN ENUCLEATION AND KERATOPLASTY

FOLLOW UP PLAN:

PARAMETERS	DAY 1	1 WEEK	1MONTH	3MONTHS	6MONTHS
V/A UNCORRECTED BEST CORRECTED					
GRAFT CLARITY • Rejection • Vascularization • Failure					
ASSOCIATED COMPLICATIONS					

SURGEON'S SIGNATURE GUIDE'S REMARKS AND SIGNATURE

ANNEXURE III – PHOTOGRAPHS

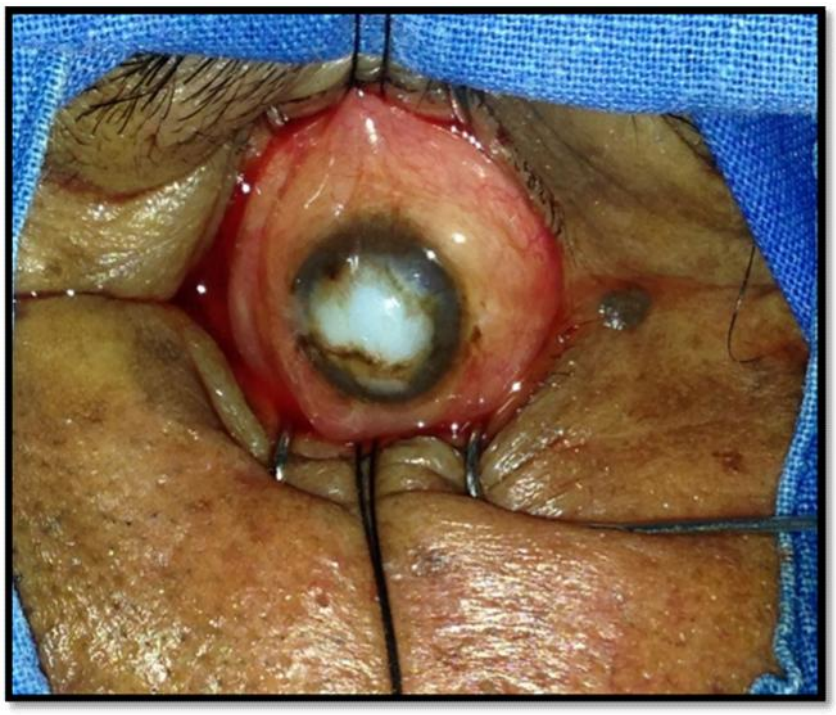


Photo 1- Traumatic corneal opacity

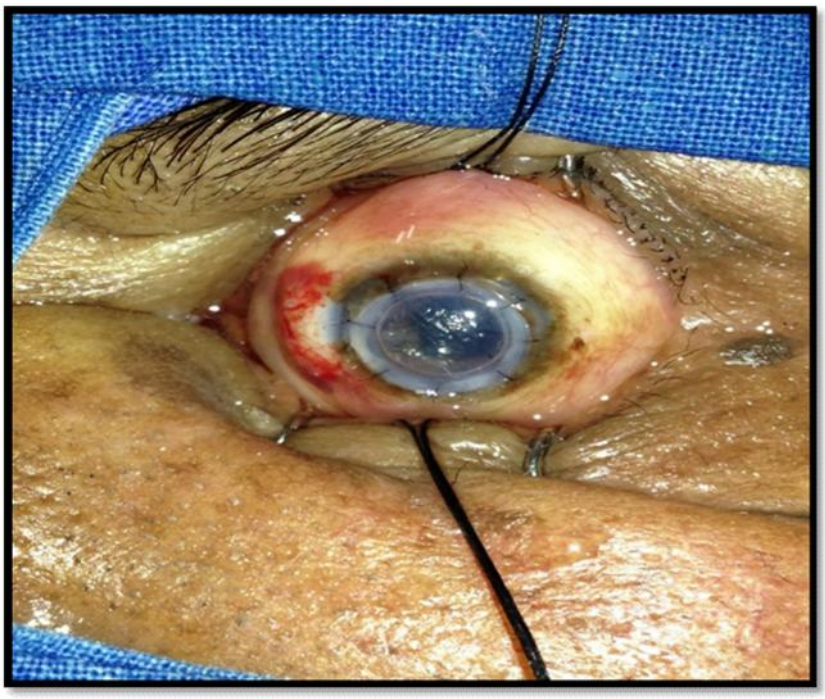


Photo 2- post-operative

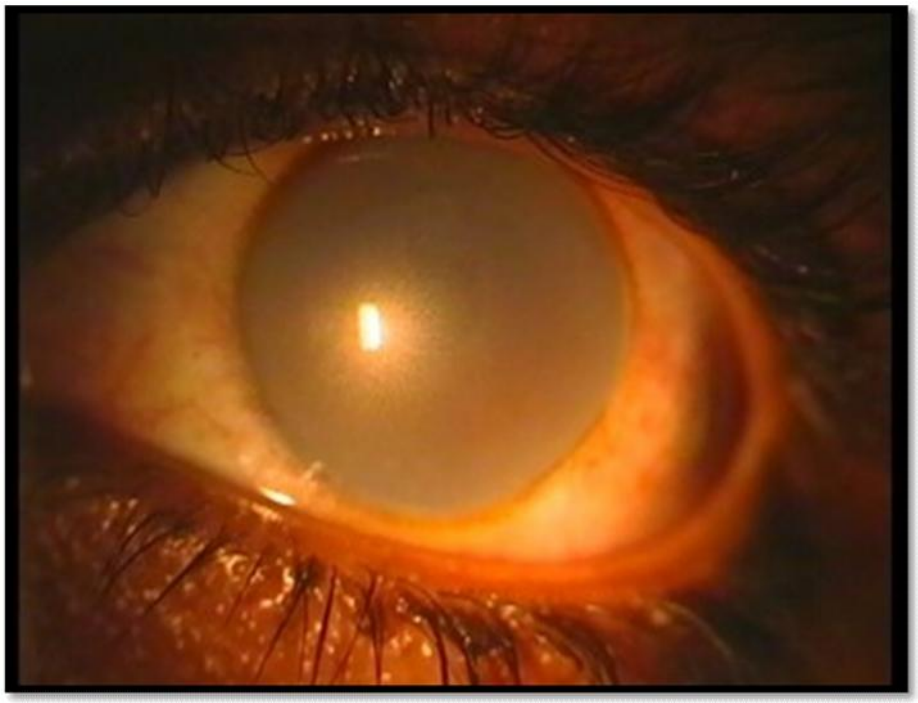


Photo 3 - Hereditary stromal dystrophy

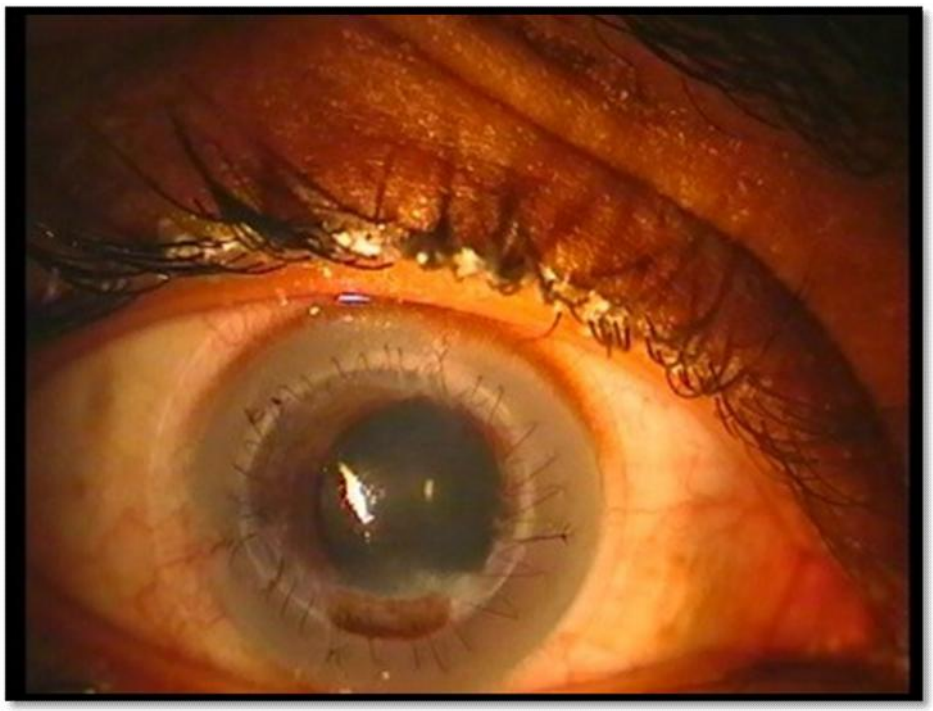


Photo 4 – Post operative

Photo 5 - Stromal dystrophy

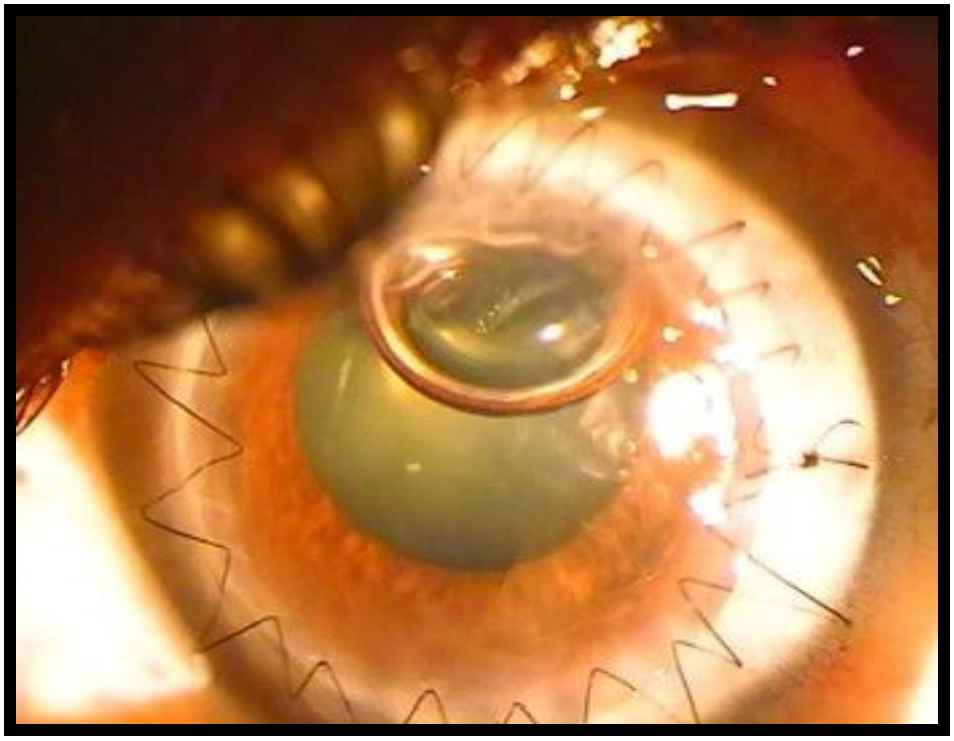


Photo 6 - Post operative

Photo 7 - Disposable trephines

Photo 8 - Keratoplasty set

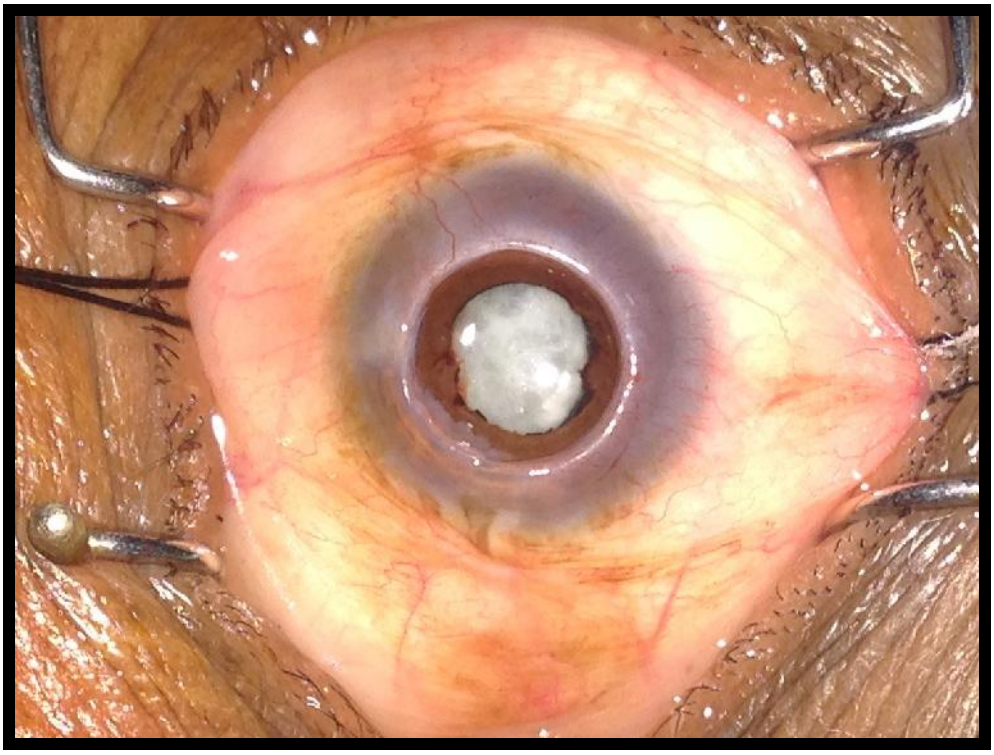


Photo 9 – Preparation of recipient bed and cataract extraction

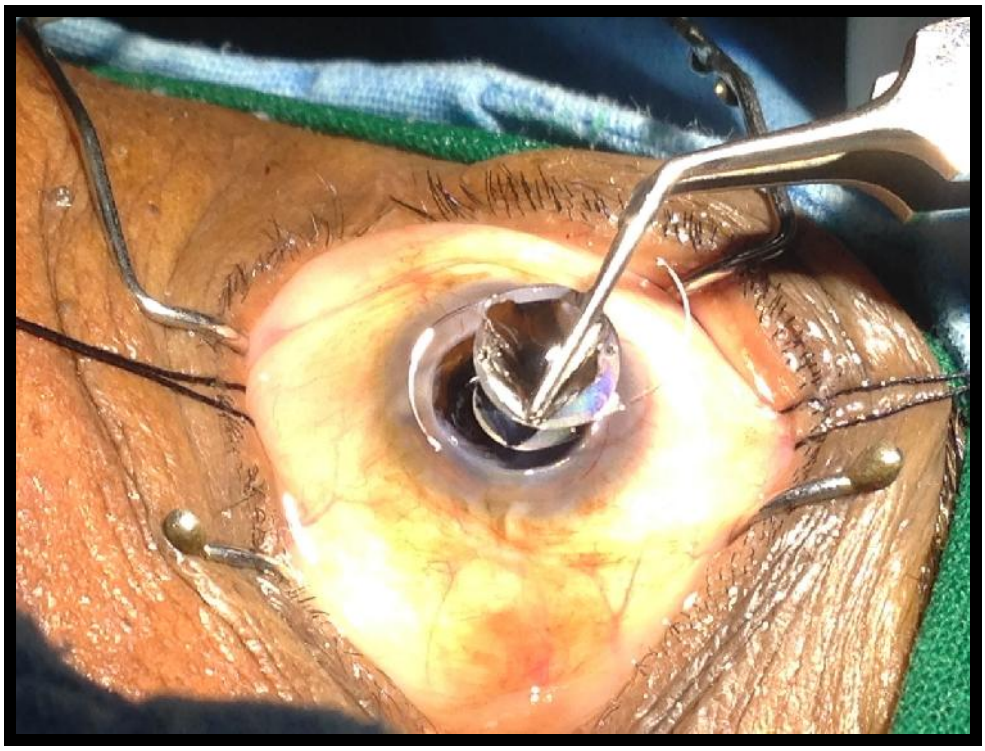


Photo 10 – Placement of posterior chamber intraocular lens

Photo 11 – Placement of cardinal sutures

Photo 12 – Team of surgeons

KEY TO MASTER CHART

+	-	Present
AC	-	Anterior chamber
Acc	-	Accurate
AL	-	Adherent leucoma
AV	-	Anterior vitrectomy
C	-	Continuous
C. VAS	-	Corneal vascularization
CF	-	Counting fingers
CL	-	Clear
D.AGE	-	Donor age
DES	-	Descemetocele
EX. PRO	-	Extra procedure
F	-	Female
f	-	Failure
H	-	Hereditary
H	-	Hazy
HMCF	-	Hand movements close to face
HRS	-	Hours
I	-	Interrupted
Inacc	-	Inaccurate
IP	-	Iris prolapse
IP.NO.	-	Inpatient number
K	-	Keratitis

LCO	-	Leucomatous Corneal Opacity
LE	-	Left Eye
m	-	Meters
M	-	Male
MCO	-	Macular Corneal Opacity
MM	-	millimeters
OP	-	Operative
PCIOL	-	Posterior chamber intra ocular lens
PCR	-	Posterior capsular rent
PL	-	Perception of light
PR	-	Projection of rays
RE	-	Right Eye
S	-	Successful
S.NO.	-	Serial number
SA	-	Stromal Abscess
SD	-	Stromal Dystrophy
SUBLUX	-	Subluxated
SY	-	Synechiolysis
T	-	Trauma
TP	-	Triple procedure
U	-	Uveitis
VA	-	Visual Acuity