COMPARATIVE STUDY OF CONJUNCTIVAL AUTOGRAFT WITH LIMBAL STEM CELLS TRANSPLANTATION FOR PREVENTION OF RECURRENCE OF PTERYGIUM

By

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LIST OF ABBREVIATIONS

AMT - Amniotic membrane transplantation

CAG - Conjunctival autograft

DNA - Deoxyribose Nucleic Acid

FU - Flouro Uracil

LCAT - Limbal Conjunctival autograft

LSCD - Limbal Stem Cell Deficiency

MMC - Mitomycin C

MMP - Matrix Metalloproteinases

PMC - Post Mitotic Cell

SC - Stem Cell

TAC - Transient Amplifying Cells

TDC - Terminal differentiated cells

UV - Ultraviolet

VEGF - Vascular endothelial growth factor

ABSTRACT

BACKGROUND:

Pterygium is a degenerative condition of the subconjunctival tissue which proliferate as vascularised granulation tissue to invade the cornea destroying superficial layers of stroma and Bowman's membrane.Ultraviolet light-induced damage to the limbal stem cell barrier with subsequent conjunctivalisation of cornea is the currently accepted etiology of this condition. The limbus and its stem cells are very important in the pathogenesis of pterygium.

The present study was carried out to compare the results of pterygium excision with conjunctival autograft and limbal stem cell transplantation in treatment of primary pterygium

AIMS AND OBJECTIVES:

1. To study the results and to compare the recurrence rate of Pterygium excision with conjunctival autograft and limbal stem cell transplantation.
2. To evaluate the efficacy of limbal stem cells in treatment of primary pterygium.

METHODS:

It is a hospital based study of patients who were operated for Pterygium in which 50% patients underwent Pterygium excision with limbal stem cell transplantation and 50%patients underwent Pterygium excision with conjunctival autograft. All patients were inpatients of Department of Ophthalmology at B.L.D.E.U's Shri. B.M.Patil Medical College Hospital and Research Centre, Bijapur. Duration of this study was from October 2011 to February 2013.

RESULTS:

Mean age in Group A was 43.2 years and 41.5 years in Group B. In this study it was observed that 21.7% belonged to grade I, 50% to grade II and 28.26% to grade III. Maximum incidence of pterygium (30.43%) was seen in the age group of 31–40 years followed by 41-50 years(26.08%). At Subsequent follow up, recurrence was seen in 03(6.52%) patients in group A and no recurrence was seen in group B.

CONCLUSION:

Both the surgical methods of excision of pterygium that is Conjunctival autograft and Limbal stem cell transplantation were effective in the management of pterygium.

Limbal stem cell transplantation proved to be more effective and safe in prevention of pterygium recurrence and in rapid restoration of normal epithelial morphology

Key words : Pterygium, Limbal, Autograft, Recurrence

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INTRODUCTION

Pterygium is a common degenerative condition specially affecting population in tropical and subtropical areas worldwide. The word 'Pterygium' is a Greek word meaning 'Wings of an insect', which denotes the shape of this condition. Pterygium is a degenerative condition of the subconjunctival tissue which proliferate as vascularised granulation tissue to invade the cornea destroying superficial layers of stroma and Bowman's membrane.[1] The main histopathological change in primary pterygium is elastodysplasia and elastodystrophy of subepithelial connective tissue. It usually originates from the nasal bulbar conjunctiva in the interpalpebral zone, but also occasionally from the temporal conjunctiva.

Multiple factors like Ultraviolet radiation, tear film abnormalities, hot and dry climate, wind and outdoor work play an important role in development of pterygium. The UV type B light in solar radiation has been found to be the most significant environmental factor in pterygium pathogenesis[2,3] Recent studies[4-7] have suggested that p53 and human papillomavirus may also be implicated in pterygium pathogenesis. Matrix metalloproteinases (MMPs) and tissue inhibitors of MMPs (TIMPs) at the advancing pterygium edge may be responsible for the inflammation, tissue remodeling, and angiogenesis that characterize pterygia, as well as the destruction of Bowman's layer and pterygium invasion into the cornea[4-7]. Tseng et al.[8] have also speculated that pterygium may represent an area of localized limbal stem cell deficiency

Symptomatically, patients may experience foreign body sensation, burning, watering of eyes, blurred vision and cosmetic disfigurement. In advanced cases, the pterygium may cause visual loss secondary to loss of corneal transparency within the

visual axis or pterygium induced astigmatism. In some patients with advanced pterygia, ocular motility may be restricted, leading to diplopia in certain fields of gaze Surgical treatment of pterygium is directed at excision, prevention of recurrence, and restoration of ocular surface integrity. A myriad of techniques, some combined with others, have been described for achieving these goals. The main complication of these procedures has been the recurrence rate, which has been estimated as high as 30%-70%.[9] Surgical techniques for pterygium include bare sclera excision, excision with simple conjunctival closure, excision with administration of antimetabolite adjuvants such as mitomycin C (MMC),[10]excision with conjunctival autograft[11,12] and excision followed by amniotic membrane transplantation.[13] Treatments such as radiation therapy, the use of antimetabolites agents have succeeded in diminishing the rate of recurrences from between 5% and 12%[14,15] However, serious complications are associated with these methods of treatment, such as secondary glaucoma, cataracts, uveitis, corneal perforation, and scleral necrosis, resulting in perforation and endophthalmitis.[16,17]

In 1985, Kenyon and collaborators introduced conjunctival autograft as a technique for the treatment of recurrent or advanced pterygium.[11] Although this surgical technique is more time-consuming, it has reduced the number of recurrences with the same efficacy as the previously described treatments without the risk of potentially serious complications. Recently, the importance of limbal stem cells in the pathogenesis of pterygia has been reported,[18] and authors have suggested that a healthy limbus acts as a barrier to conjunctival overgrowth.[19] Conceptually, one could possibly reduce the pterygium recurrence by including healthy limbus in the conjunctival autograft. Besides, moving a limited area of limbus stem cells may not be detrimental to the ocular surface. As the limbal epithelium acts as a junctional

barrier to conjunctival overgrowth and pterygium is considered to represent a “local limbal deficiency”. Also the inclusion of limbal epithelium in conjunctival graft would restore the barrier function of the limbus.

The present study was carried out to compare the results of pterygium excision with conjunctival autograft and limbal stem cell transplantation in treatment of primary pterygium

AIMS AND OBJECTIVES

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REVIEW OF LITERATURE

HISTORICAL REVIEW:

Pterygium has been defined by Duke-Elder as a triangular shaped degenerative and hyperplastic process, occurring medially and laterally in the palpebral aperture, in which the bulbar conjunctiva encroaches onto the cornea.[20]

Sushruta, who lived in 1000 BC, gave an accurate description of a pterygium and its treatment with pulverized salt and stimulation with a palm branch. When the pterygium was inflamed and swollen, he tore it out with forceps and removed any remaining tissue with a flesh-stripping ointment. He also described the ease with which the lesion reappeared.[20]

Hippocrates (469 BC) suggested the use of eye drops containing lead, zinc, copper, iron, bile juices, urine, and maternal milk.[20]

Celso (50 AC) and Galeno (131 AC) also suggested a topical treatment with solutions of white wine, vinegar, euphrasy water, candied sugar, nitrated fennel water and, in the more serious forms, the physical removal. This was done by passing a thread underneath the growth and allowing it to slide over the scleral surface with a to and fro movement as far as the medial canthus: then when the pterygium was detached from the underlying sclera, it was cut with scissors. [20,21,22]

Paolo Egineta (660 AC) and **Arab Asicenna** (1037 AC) who suggested cutting the pterygium with scissors. [23,24]

Amurose Pare (XVI Century) wrote about a pterygium: "You have learned that a pterygium is an illness that always recurs, even when you have done everything in your power to cure it": this concept has remained true to the present day. [20,24,25,26]

In the XVIII century, it was fashionable to treat a pterygium with copper sulfate in the XIX century with silver nitrate and lead acetate, and atropine was added to encourage the healing of the associated corneal ulcers.[20,26,27]

The XIX century saw the advent of surgery of pterygia.

Scarpa (1802): Removal of the head from the cornea using forceps, section of a portion of the body (3-4 mm) and subsequent concentric excision of the detached tissue as far as the limbus.[28]

Arlt (1850): Excision of the head from the cornea and a diamond shaped portion of the body with conjunctival cross-over plastic surgery.[29,30]

Desmarres (1855): Introduced the technique of deviating the head in an attempt to change the direction of growth and induce it to atrophy. The technique was modified by Terrien who deviated the growth towards the superior fornix as opposed to the inferior fornix suggested by Desmarres.[31]

Knapp (1869): Suggested the technique of transposition. The pterygium is cut longitudinally into two halves that are fixed below the superior and inferior conjuctiva.[29]

Arlt (1872): He performed the first scleral repair following the excision of the pterygium with the addition of autologous or homologous cadaver conjunctiva.[29,30]

Klein (1876): Performed Arlt's technique but he used mucous tissue from other sites.[20]

In the XX century, the techniques of keratoplasty and the physical treatments of pterygium were developed.

In The Twentieth Century

Mc Reynolds (1902): Who presented a modified Desmarres technique which placed the head of the pterygium in a conjunctival pouch.[32]

Gifford (1909): Used a thin epidermal graft to cover the sclera that was exposed following the complete removal of the pterygium.[33]

Morax and Magitot (1911): Used the first artificially- preserved homologous corneal grafts.[29]

Terson (1911): Was the first to use radiation therapy with X-rays.[34]

Fuchs (1911): Presented the first results of autologous penetrating keratoplasty for the treatment of corneal pathologies, and Terson (1913) performed this on pterygia. The technique involved replacing a full-depth corneal disc containing the head of the pterygium with a penetrating disc of the same diameter removed from the superior peripheral cornea. The results were poor due to an opacity developed in discs, and post operative infection.[34]

Magitot (1916): Suggested lamellar autokeratoplasty using a technique which is similar to Terson's but which used lamellar discs removed from the same eye.[29]

Elsching (1926): In order to repair serious conjunctival defects, he performed conjunctival plastic surgery with transposition of a bridge created from the contra-lateral limbus. So Elschnig was the first person to introduce Conjunctival graft for pterygium surgery.[35]

Amorin (1936): Suggested treatment with a diathermy coagulator.[36]

Burnam and Neil (1941): Used a radioactive applicator (Radon).[37]

Kamel (1946): Performed sub-conjunctival cauterization of the pterygium with carbolic acid.[38]

D'Ombrain (1948): Suggested the technique of scleral baring for the first time.[39]

Paufique (1950): Developed a lamellar keratoplasty for the optic and therapeutic treatment of the corneal pathologies; this also included the pterygium which until then considered to be a minor pathology.[40]

Haik (1957): Used topical beta-therapy with strontium 90 (Sr 90).[41]

Meacham (1962): Was the first to use antibiotics to prevent the recurrences.[42]

Panzardi (1964): Used amniotic membrane to repair the conjunctival tissue loss following excision of the pterygium.[43]

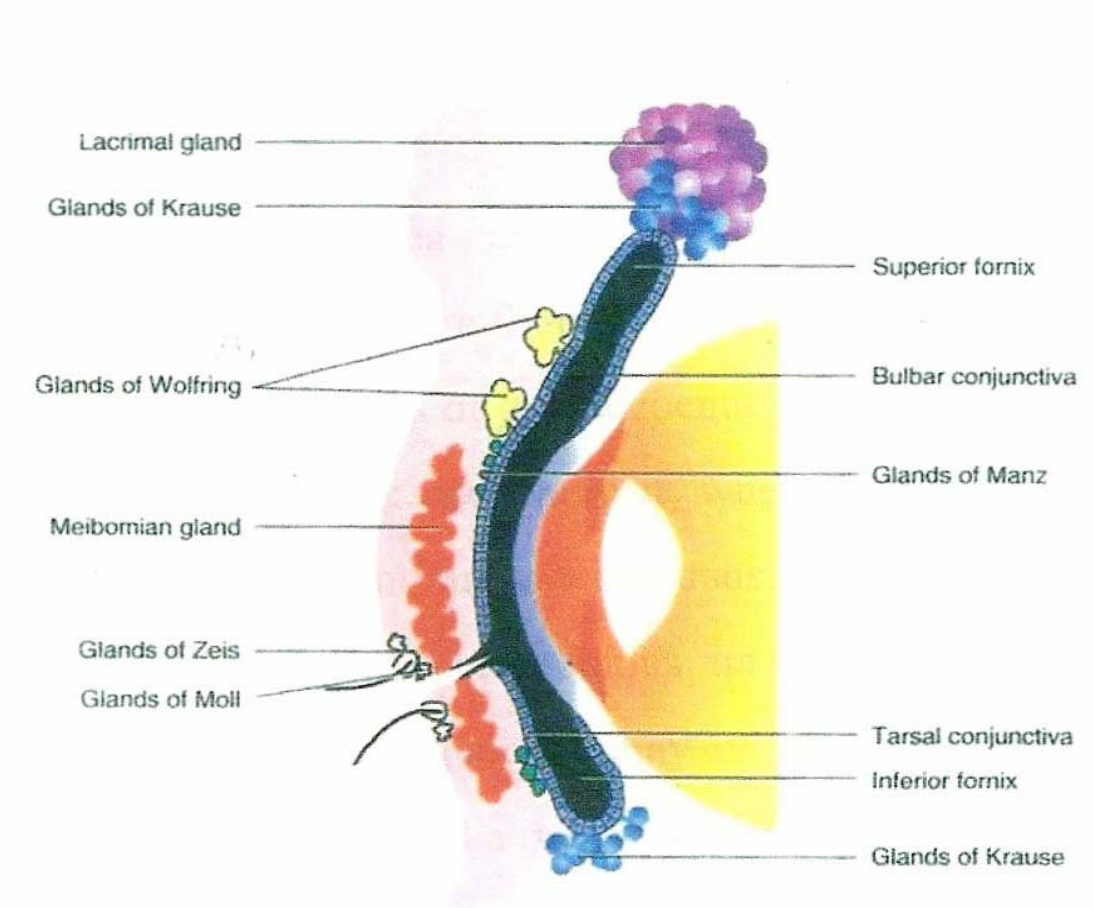
Thoft (1977) described conjunctival autografting for several ocular surface disorders such as unilateral chemical or thermal burns, radiational injury, neoplasms, persistent epithelial defects, fornix reconstruction and degenerative diseases including pterygium.[44]

Kenyon (1985): Reported excellent results in the prevention of recurrences by grafting autologous conjunctiva to the limbus.[11]

Tseng (1990) studied the concept of limbal cell damage, according to which pterygia have been classified under the category of 'corneal stem cell disease'. He suggested that when limbal barrier is broken, conjunctival epithelial cells are allowed to stream on the adjacent cornea. This gave to the concept of Conjunctival limbal autograft.[45]

Maldonado MJ (1995) was first to use intraoperative 5-Fluorouracil as a chemo-adjuvant in the treatment of pterygium.[46]

ANATOMICAL ASPECTS[47]



Anatomy of Conjunctiva

The conjunctiva is a thin, translucent mucous membrane which derives its name from the fact that it attaches the eye ball to the lids. It lines the posterior surface of the lids and is then reflected forwards on to the globe of the eye. The epithelium becomes continuous anteriorly with the epithelium of the cornea. Thus it forms a barrier which prevents ingress to the orbit from outside.

Conjunctiva is divided for purpose of description into three parts

- Palpebral,
- Fornix, and
- Bulbar.

The palpebral part is sub-divided into two zones. The marginal zone extends from the opening of the glands at the lid margin, across the border of the lid as far as the sub-tarsal furrow, which is about 2mm up on the back of the eyelid.

At this point, the tarsal glands and the lacrimal punctum emerge. The tissues are not smooth and they have minor ridges or elevations. These provide slight depression over the cornea and the tears can run across the depression between the ridges. At the sub-tarsal furrow, perforating vessels pass through the tarsus to reach the conjunctiva.

The tarsal zone is thin, vascular and is light red in colour. It has a good attachment to the underlying tissues and it being transparent, Meibomian glands can be seen from the rear as yellow streaks unlike the upper tarsal conjunctiva which is closely adherent to the tarsus. The orbital zone is loosely attached to the tissues below, lying in a horizontal fold.

The conjunctival fornix is a linear sac folded above, below and laterally and extending along the margin of the orbit. These folds prevents stretching when the eye moves medially. The plica semilunaris has a corresponding function. In order to avoid collapse of the fornix as the globe rotates, there are appropriate connections of the tissues with the superior, inferior and lateral recti. Thus the fornix follows movements of these muscles. The plica semilunaris has corresponding connections with the medial rectus. In it are found the glands of Krause and the unstriped muscle of muller.

By means of this deepening fibrous tissue the levator and recti can act on the fornix deepening it, when they contract. Centrally the fibrous tissue becomes continuous with tarsus.

In the intertendinous interval that is in the diagonal regions of the fornix the conjunctiva may extend to the cornea. The whitish aponeurotic expansion in the fornix from the inferior rectus and inferior oblique is seen through the conjunctiva.

The bulbar conjunctiva is thin and transparent so that white sclera is seen through it. It is attached loosely to the tissues beneath, except around the limbus which is a 3mm wide zone, where it is fastened firmly. The bulbar conjunctiva is at first in contact with the tendons of the recti muscles covered by the tenon's capsule. Thus in exposing these tendons, for instance in tenotomy we must divide the conjunctiva, then the capsule of tenon before they are reached.

In front of the insertion of recti tendons the bulbar conjunctiva lies on the anterior portion of the tenon's capsule, up to a point 3mm from the cornea.

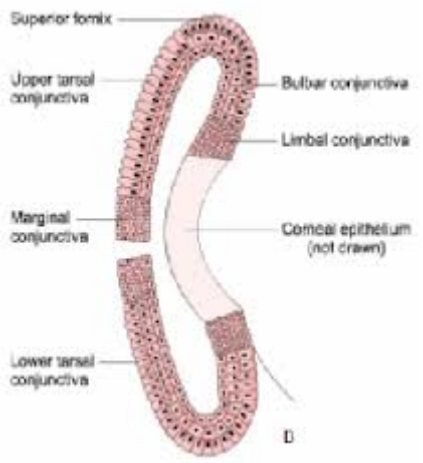
The conjunctiva is separated from the capsule of tenon by loose areolar tissue, in which we find the sub- conjunctival vessels. In between conjunctiva and the sclera, there is the loose episcleral tissue in the anterior portion of the tenon's space. In this space, we find the anterior ciliary arteries which form the pericorneal plexus and the tendons of the insertion of the recti muscles.

At about 3mm from the cornea, the conjunctiva, tenon's capsule and the sclera become much closely united. For this reason, although it is difficult to raise a fold of conjunctiva close to the cornea, a much firmer hold of conjunctiva and episcleral tissues can be obtained here with the forceps than elsewhere.

The palisades of Vogt are found in the limbal conjunctiva as little raised ridges, about 0.55 mm wide and 1 or 2 mm long. They are light elevations, often with pigment in the furrows and are more distant at the lower limbal area.

The main structures are surface epithelium and underlying connective tissue. At the marginal region, there is many layered non-keratinized squamous epithelium resistant to wear and tear. The epithelium extends from its origin near the meibomian gland outlets around the posterior edge of the lid margin up to the subtarsal furrow which lies some 2mm up on the back of the lid.

This furrow is a narrow depression, or fold in the conjunctiva, its length matching the spread of the eye lashes, less than 1 mm deep. It is a trap for materials which would fall on the cornea and assist small specks of debris in the mucus to move nasally with each blink.



Conjunctival epithelium

The epithelium of the tarsal region consists of two or three layers of columnar cells. Because it forms a very thin, uneven layer, with ridges and grooves, it reduces friction, but simultaneously ensures a useful collection area of debris and bacteria.

The epithelium of the fornix consists of 3 or 4 layers of cubical cells, increasing in number from bulbar conjunctiva. Around the limbus a stratified layer appears between 8 and 10 cells thick, with additional squamous epithelium. The surface layer cells of conjunctiva have microvilli similar to those of the cornea.

The stroma consists of the two portions a superficial adenoid layer and a deeper fibrous layer. At the limbus, neither layer passes over the cornea.

The adenoid layer is not present at birth, but is formed first in the region of the fornix 3-4 months after birth. The adenoid layer is thin but most developed in the fornix, being here 50-70μ in thickness. It consists of a fine connective tissue reticulum in the meshes of which the lymphatics lie, it is absent at marginal and tarsal zones.
The fibrous layer is generally thicker than the adenoid, but is almost nonexistent over the tarsus with which it is continuous. In it are found the vessels and nerves to the conjunctiva, the unstriped muscle of muller, and Krauses gland.

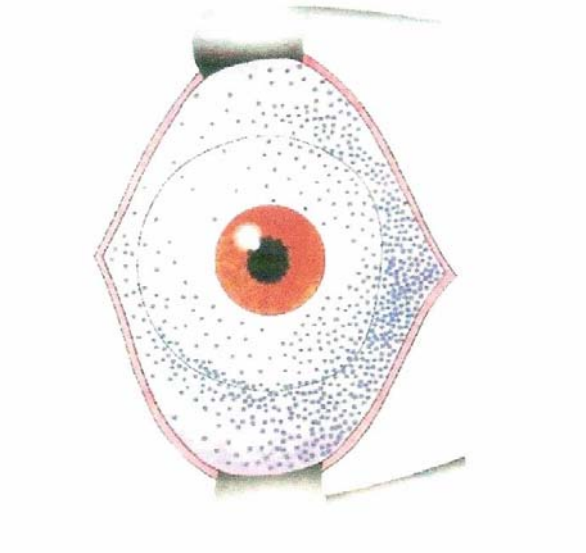
CONJUNCTIVAL BACTERIA

From the first week of life the conjunctiva carries bacteria. The amount is usually equal within both eyes, although this is subject to individual variations.

THE CONJUNCTIVAL GLANDS

Goblet cells are present as monocellular mucus producing glands, which are found in the basal epithelial layer. They rise within the layer to discharge their secretion on the surface although it is uncertain whether, after secreting mucus the cells are able to replenish their supplies. About 1.5 million cells are found in each conjunctival sac, most authorities suggest that the distribution is greatest near

fornices, with fewer in the tarsal conjunctiva. The number from these cells contributes greatly to the content of the tears liquid, which in turn is helpful for moistening and protecting the conjunctiva and cornea so that even extirpation of lacrimal gland becomes innocuous, while on the other hand, xerosis of the conjunctiva involving their destruction leads to desiccation in spite of copious flow of tears.



Distribution of goblet cells

The glands of Krause are accessory lacrimal glands having the same structure as the main glands; they are placed deeply in the subconjunctival connective tissue of the upper fornix between the tarsus and inferior lacrimal glands of which they are offshoots. There are some 42 in superior and 6-8 in the lower fornix, they are thus found largely on the lateral side. Their ducts unite into a rather long duct or sinus which open into the fornix. Similar glands are found in the caruncle.

The glands of Wolfring are also accessory glands, they are larger than the glands of Krause. There are 2-5 in upper lid near the upper region of tarsus, with rather fewer below the lower lid. Since there is no nervous control of these glands,

they maintain a constant level of tear production. Henle's glands are seen in the palpebral conjunctiva between the tarsal plates and the fornices. They are probably not true glands but folds of mucous membrane cut transversely. They resemble lieberkuhns crypts in the large intestine and are lined by epithelium which is like that of the surrounding conjunctiva.

The glands of manz are saccular or urticular glands found at the limbus.

THE CONJUNCTIVAL BLOOD VESSELS

The arterial supply of conjunctiva comes from three sources:

1. The peripheral arterial arcades
2. Marginal arterial arcades
3. The anterior ciliary arcades

Blood supply of conjunctiva

Of these as far as upper lid is concerned, the peripheral arcade supplies by far the greatest area that is almost the whole of the conjunctival tarsi, the fornix and the bulbar conjunctiva up to 4mm from the cornea.

The peripheral arcade in the upper lid is situated at the upper border of the tarsus between the two portions of the levator. It gives off peripheral perforating branches which pass above the tarsal plate and pierce the palpebral muscle to reach the conjunctiva under which it sends branches upwards and downwards. The descending branches supply nearly the whole of the tarsal conjunctiva. They run perpendicularly to the lid margin and anastomose with the much shorter branches of the marginal artery which have pierced the tarsus at the sub-tarsal fold.

The ascending branches pass upwards to the fornix, then bending round this descends under the bulbar conjunctiva as the posterior conjunctival arteries. They pass

towards the cornea at 4mm from which they anastomose with the anterior conjunctival arteries and branches of the anterior ciliary arteries. The posterior conjunctival vessels are mobile, moving with the bulbar conjunctiva.

The peripheral arcade of lower lid is in front of the inferior palpebral muscle of Muller and generally behaves similar to that of upper lid.

The marginal arcade sends its perforating branches through the tarsus to reach the deep surface of the conjunctiva at the subtarsal fold. These divide into marginal and tarsal twigs. The tarsal conjunctiva is well supplied with blood, hence it is red in colour. The colour diminishes as we pass towards the fornix and the bulbar conjunctiva is colourless except when the vessels are dilated. The anterior ciliary arteries come from the muscular arteries to the recti. Each muscular artery gives off two anterior ciliary arteries except the lateral rectus, which is supplied anteriorly by the ciliary artery which passes forwards at a deeper level than the posterior conjunctival vessels. They do not move with the conjunctiva. They pass forwards and anastomose with each other and form a series of arcades parallel to the corneal margin, anteriorly they form pericorneal plexus, while posteriorly they send twigs which anastomoses with the posterior conjunctival arteries.

The pericorneal plexus is arranged in two layers, a superficial conjunctival and a deep episcleral.

The conjunctival veins accompany and are much more numerous than the corresponding arteries. For the most part i.e. from the conjunctival tarsi, from the fornix and the major portion of the bulbar conjunctiva, they drain into the palpebral veins.

Corresponding to the peripheral arcade of the upper lid, there is an important and well marked venous plexus, which drain into veins of the levator and superior rectus which again drain into the ophthalmic vein.

In the circumcorneal zone supplied by the anterior ciliary arteries, veins are less conspicuous than the arteries. They form a network some 5-6 mm wide, which drain in to the muscular veins.

LYMPHATICS

The conjunctival lymphatics are arranged in two plexus:

A superficial, composed of small vessels, placed just beneath the vascular capillaries and a deep, consisting of larger vessels situated in the fibrous layer of the conjunctiva and receiving the lymph from the superficial plexus. They drain towards commossures, where they join the lymphatics of the lid, to lymph gland, pre-auricular and submandibular.

NERVE SUPPLY OF THE CONJUNCTIVA

Sensory innervation for the bulbar conjunctiva is from the long ciliary nerves which are branches of the nasociliary nerves. The upper fornix and the palpebral conjunctiva are served by the frontal and trochlear divisions of the ophthalmic nerve, while the lacrimal nerve covers the region of the outer canthus. The conjunctiva of the lower eyelid is innervated by the infraorbital nerve. Short ciliary nerves supply the cornea and the circumcorneal zone of conjunctiva.

NERVE ENDINGS:

The nerve may end in

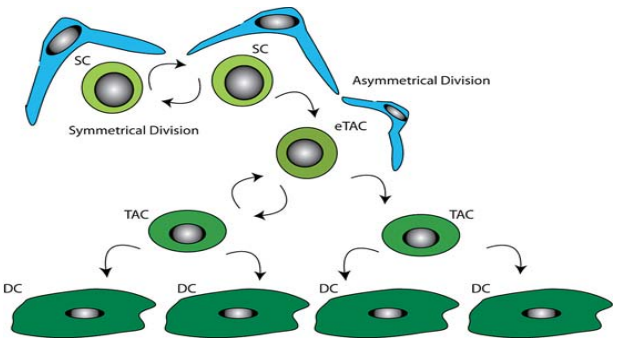
1. Free endings
2. End bulbs of Krause
3. Tufts or
4. Ribbons.

1. **Free endings:** the nerves having lost their myelin sheath, from a subepithelial plexus in the superficial part of substantia propria. From this fibres pass to form an intraepithelial plexus and send free nerve fibrils between these cells.
2. **The end bulbs of Krause** - are round bodies from 0.02 mm to 0.1 mm in length. Each is surrounded by a connective tissue enveloped, continuously with nerve sheath and lines by endothelial cells. It has twisted mass of fibrils one or two nerves enter the envelope, lose their myelin sheath and join the central mass. Nerve endings are numerous in area supplied by the lacrimal nerve but are also numerous around the cornea and the marginal portion of the lids.

ANATOMY OF LIMBUS – It is a zone between cornea, conjunctiva and sclera. It is formed on the corneal side by a line drawn between termination of Bowman's and Descemets membranes and at conjunctival and scleral side by a parallel line approximately 1mm peripherally. This line actively runs outside the schlemns canal. Therefore anatomical limbus includes both Schlemns canal and trabecular meshwork. Commonly limbus is considered to be the outer portion of that zone including only the epithelium and underlying connective tissue down to the corneal scleral collagen

lamellae. The basal cells of the epithelium are the stem cells of the corneal epithelium and the vascular elements which loop into the stromal connective tissue provide nutrients to the avascular cornea. The limbal tissue includes the stratified squamous non keratinized epithelium connecting the cornea and conjunctival epithelium and the vascularized loose connective tissue.

Stem cells are a small subpopulation of specialized undifferentiated self renewing cells, which are capable of indefinite proliferation of large number of differentiated progeny, responsible for the cellular replacement and regeneration in all the self renewing tissues[48]. They have long cell cycle time and long life span under steady state conditions. They have unique property of self renewal. All the cells in a self renewing tissues can be placed into two compartments as Proliferative and Non-proliferative. The cells in the proliferative compartment are capable of DNA synthesis and cell division and whereas cells in the non proliferative compartment differentiate and become mature under the effect of surrounding environment. The cells in the proliferative compartment are the stem cells (SC) and transiently amplifying cells (TAC) that are derived from mitotic division of stem cells. Cells in non proliferative compartment are post mitotic cells (PMC) which are in different stages of maturation by differentiation into the terminally differentiated cells. Thus the cellular hierarchy of these self renewing is comprised of different cell population in the order of SC-TAC-PMC-TDC. Stem cells being the source and hence at highest rank[49] when the limbal epithelium or the limbal stroma is damaged[50], a pathological state termed limbal stem cell deficiency (LSCD) develops in a number of corneal diseases.



Limbal stem cells

Epithelium The limbal epithelium is structurally similar to the corneal epithelium but here the melanocytes or langerhan's cells are found interposed between cells of the limbal epithelium. It has 7 to 10 cell layers and cell to cell junction appear similar to those of cornea. The basal cells of this region appears smaller and less columnar than the basal cells of corneal epithelium and they have more mitochondria.

The Caruncle: It is a small, soft pink ovoid body measuring 5mm x 3mm situated in the sulcus lacrimalis. It is a modified skin. So is covered by a modified stratified squamous epithelium.

Plica Semilunaris: It is a narrow crescentric fold of conjunctiva lying lateral and partially under the cover of caruncle.

Cornea: It is a transparent structure separated from the sclera by a slight fissure. The cornea is elliptical being 10.6mm in vertical meridian and 11.7mm in horizontal meridian. The cornea forms part of the surface of a sphere but is curved more in vertical meridian than in the horizontal meridian. Thus causing astigmatism with the rule. The anterior and posterior radius of curvature of this central part of cornea are 7.8mm and 6.8mm respectively. Corneal thickness at centre is 0.56mm and at the periphery is 1mm.

Histology of Cornea: 5 Layers of the cornea are:

1) Epithelium
2) Bowman's Membrane (Anterior limiting lamina)
3) Substantia Propria
4) Descemets membrane
5) Endothelium

1. **Epithelium**: It is a layer of nonkeratinised stratified squamous epithelium which is continuous with epithelium of bulbar conjunctiva at the limbus. 50 – 90µ in thickness and has 5 layers of nucleated cells.
2. **Bowman's Membrane**: It is a thin homogenous sheet about 8 – 14mm thick between the basement membrane and substantia propria. This does not regenerate when it has been destroyed. It shows a good deal of resistance to injury or infection. It consists of an acellular mass of condensed collagen fibrils.
3. **Substantia Propria**: It is about 500 mm in thickness. Form 90% of the total thickness of the cornea. Consists of regularly arranged lamellae of collagen bundles embedded in a hydrated matrix of proteoglycan. The lamellae are arranged in layers parallel with each other and with the corneal surfaces.

   The alternate layers of lamellae are at right angles to each other. Among the lamellae are present Keratocytes, wandering macrophages, histiocytes and few lymphocytes.
4. **Descemets Membrane**: It is a thick elastic layer which is covered on its posterior surface by endothelium.
5. **Endothelium**: Single layer of flattened hexagonal cells which are continuous around the angle of the anterior chamber.

Blood Supply: Cornea is an avascular structure. Small loops derived from the anterior ciliary vessels invade its periphery for about 1mm. They are not in the cornea but in the sub-conjunctival tissue which overlaps the cornea.

Nerve supply: Cornea is supplied by anterior ciliary nerves which are branches from the ophthalmic division of the 5th cranial nerve.

PTERYGIUM [51, 52,53,54,55]

a) ANATOMY OF THE PTERYGIUM

i) Macroscopic

A pterygium consists of a head, a cap towards the advancing edge and the body lying limbal to the head.

The head

It is the active part of the pterygium which brings about changes in the cornea anterior to it, forming the cap and activates the subconjunctival connective tissue behind it forming the body. It consists of fibrovascular tissue into which the blood vessels of the body end. It is always raised from the corneal surface to varying extent presenting appearances ranging from fibrous, flat, and a vascular to the fleshy gelatinous type. Owing to its large fibrous tissue content, the head is always firmly adherent to the underlying cornea. [51, 52,53,54]

The body

The body is the part limbal to the head which assumes the characteristic wing shape. It lies mainly over the sclera. As the head pushes on into the cornea the adherent conjunctiva is dragged along and stretched so the folds appear above and below it, sometimes with overhanging edges.

The blood vessels also assume the classical orientation towards the head. There is always some degree of subconjunctival connective tissue hyperplasia.[52,53,54]

The cap

This is the apex of the pterygium anterior to the head. Unlike the head, which is opaque, the cornea of the cap is viewable upto the Descemet's membrane. The transparency is altered possibly due to the biochemical changes induced by the invasion of fibroblasts. It usually extends much anterior to the head of the pterygium and is usually avascular. The apex of the cap is bounded by a line either smooth or dentate, while beyond the margin may be seen peripheral extensions of the cap in the form of greywhite dots, the 'ilots de Fuchs.[55]

The pigment line

This is seen about a millimeter ahead of the cap. It roughly follows the contour of the cap. Its formation is roughly considered to be similar to the formation of the Hudson Stahli line. The thickened layer of tears at the pterygium head and the lacrimal river are thought to be causes. Tears contain lactoferrin, an iron binding protein known to inhibit free radical formation.

This causes iron to be deposited at the advancing edge of the pterygium as the 'Stocker's line. [20,29,30,52,53,54]

ii) Microscopic [47,56]

Histopathologic analysis of the leading edge of the pterygia by Cameron disclosed the following findings:

1. Fibroblastic tissue separating the corneal basal epithelial cells from the Bowman's membrane.
2. Altered orientation of the basal epithelial cells overlying the fibroblastic tissue.
3. Destruction of the Bowman's and superficial stroma beneath the fibroblastic tissue.

4. Normal corneal tissue proximal to the leading edge of the pterygium.

Ocular pterygia and pinguecula have characteristic histologic features:

1. Hyalinization of sub-epithelial connective tissue of the substantia propria which are seen as diffuse or lobular collections of eosinophilic granular material with an associated increase in the number of fibroblasts and other cells.
2. An increased number of thickened and tortuous fibres that stain strongly with elastic stains, immediately adjacent to and beneath the hyalinized region.
3. Connections within the hyalinised and granular areas that may show either eosinophilia or basophilia.[51]

Sub-epithelial hyalinized region:

The hyalinized zone observed by light microscopy immediately beneath the epithelium has an amorphous, slightly eosinophilic or lightly basophilic appearance. It is comparatively acellular. In this region, there are no elastic fibres. Concretions, when present, are frequently seen in this region. Electron micrographs reveal evidence of collagen degeneration with diminished contrast and attendant loss of cross striations and periodicity, with splitting microfilaments at their end. The microfilaments do not show the hollow centers typical of elastic microfibrils. Subsequent clumping of the abnormal collagen fibres results in collection of coarsely granular substances.

There is no evidence of elastogenesis in this area.

Eosinophilic granular material:

Electron microscopic examination demonstrates that the eosinophilic granular material seen by light microscopy represents the earliest phases of elastogenesis, located in the deeper regions of substantia propria and is separated from the epithelium either by the zone of hyalinized material or normal stroma. Elastic staining fibres are sometimes seen within the collections of granular material.

Elastic staining fibres:

Both pinguecula and pterygia, show a large number of elastic staining fibres beneath the hyalinized zone and adjacent to the granular zone. These fibres usually stain intensely with elastic tissue stains, and are eosinophilic in the hematoxylin-eosin stain. These fibres are of refractile nature.

Pseudoelastic nature of Pterygium:

Elastic degeneration in cases of pterygium, as in pingeucula, is characterized by the appearance of vermiform, coiled and knotty fibres, which take up elastic stain, but these so-called elastic fibres, appear to differ from natural elastic tissue because they can only mimic the staining character of the true elastic tissue. They remain unaffected or only partially affected by pancreatic elastase. Various terms have been used to describe them including 'elastotically degenerated,' 'pseudo elastic type,' 'hyperelastosis' and 'elastotic degeneration.'

The most important changes occur in the conjunctival stroma. Most show a hyperplasia of collagen, subconjunctival hyperemia, and neovascularization. The hyperplastic collagen fibres show fragmentation and a little coiling, which is regarded as a pre-degenerative stage. This development of degeneration is an important feature

distinguishing pterygia from pinguecula, in which the degenerative lesion is present from the beginning.

As the collagen ages, or degenerates in pathologic conditions, it loses its natural staining character so that it can take up an elastic tissue stain. Since the staining depends mainly upon the surface chemicals, a degenerative product simulating one of the normal constituents of elastic tissue may perhaps be deposited in the area of degeneration, thus taking up the stain. [47,55,56]

b) DEFINITION AND CLASSIFICATIONS

Definition of pterygium has been advocated in various manners by various authors.

Sir Stewart Duke Elder: True pterygium is a degenerative and hyperplastic process in which the conjunctiva actively invades the cornea. It is essentially a triangular encroachment of the bulbar conjunctiva onto the cornea.[21]

William M. Townsend: Pterygium is a triangular sheet of fibrovascular tissue that appears on the epibulbar conjunctiva.[30]

True pterygium: A true pterygium develops from the bulbar conjunctiva in the interpalpebral area of the eye. It is a degenerative and hyperplastic process, in which conjunctiva actively invades the cornea. [53,54]

Pseudo pterygium: This is a condition in which the conjunctiva becomes attached to a corneal ulcer or an ulcer near the margin. This is the result of an inflammatory process. [53, 54]

True Pterygium[51,52,53,54]**:** The true pterygium arises from the bulbar conjunctiva. It gradually grows towards the limbus in a wedge shaped pattern or triangular pattern. In cases of nasal pterygium it starts from the caruncle, and in cases of temporal

pterygium it starts from the outer canthus. [53,54] There is visible change seen in the normal conjunctiva. The translucency of the conjunctiva is decreased and the conjunctiva is thickened. If the growth is checked then the lesion restricts itself to the conjunctiva without involving the cornea. This true pterygium thus runs backwards from the cornea over the sclera in the form of tightly drawn triangular wing shaped mass. A fully developed pterygium consists of head, neck, and body.

The head directs towards the centre of the cornea and lies over cornea, the neck lies at the limbus, from where extending backwards is the body.The body generally lies over the bulbar conjunctiva and is firmly adherent to the sclera. It has an upper and lower border which shows folds, and a probe cannot be passed for a considerable distance underneath it. The area of adhesion is always smaller than its total breadth, the body of the pterygium ends in a base where these folds merge into the bulbar conjunctiva.

There is considerable amount of tension produced by the pterygium, which can be made out by the straight course of the vessels and the displacement of the plica semilunaris. Sometimes the plica is displaced in such a way that its upper end is pulled out and lies horizontally.

As a result of deep inflammation, fibrous tissue in the form of horizontal bands is laid down in the affected bulbar conjunctiva in cases of pterygium. These fibrous growths attack the cornea and the certain amount of pull exerted either pulls the cornea towards the conjunctiva or the conjunctiva which is more or less mobile. the conjunctiva is dragged towards the cornea, in a triangular pattern.

Different authors have classified pterygium in different ways:

1. William M. Townsend[30] Classified as:

A. Actively growing pterygium.

B. Fleshy or malignant pterygium.

C. Slow growing pterygium.

D. Stationary pterygium.

E. Atrophic pterygium.

2. Doherty Classified[20] pterygia as:

A. Progressive type.

B. Regressive type

3. Fuch's[55] Classified on the basis of vascularity, color, thickness and clinical aggressiveness:

A. Pterygium Crassum.

B. Pterygium Vasculosum.

C. Pterygium Camosum.

D. Pterygium Sarcomatosum.

E. Pterygium Membranosum.

4. Winther[20] (1856) Classified as:

A. True pterygium.

B. Pseudo pterygium.

Pseudo pterygium: When conjunctiva gets adherent to any corneal ulcer, it results in pseudopterygium.

Mechanism of formation of pseudopterygium: in the presence of an inflammation, when a fold of inflamed conjunctiva becomes adherent to a progressive ulcer, near the

corneal margin and is passively drawn across the cornea, a pseudopterygium results. Usually pseudopterygium formation may be seen in conditions like marginal keratitis, burns, membranous conjunctivitis, after excision of new growth, after iris prolapse.[47, 52, 53,54]

Staging of Pterygium[57]

Pterygium formation usually begins at the medial aspect as the tear film tends to be thinnest in this area and there is greater exposure here due to the shape of the eye. In addition, there are more goblet cells in this location, hence more mucin produced and less aqueous available.

Staging of Pterygium

Stage 0: Pinguecula, posterior to the limbus

Stage I: Tissue involvement upto the limbus

Stage II: Tissue just on to the limbus

Stage III: Tissue between the limbus and papillary margin

Stage IV: Tissue central to the papillary zone.

Lucio Burrato's Clinical Classification of Pterygium: [29]

It is based on morphological features of pterygia and involvement of the cornea. There are 3 main clinical types of pterygia according to this classification. They are:

Type I: Small Primary Pterygium:

a. Classical.

b. Fibrous.

c. Pinguecular.

Type II: Advanced primary or recurrent pterygium with no optical zone involvement.

Type III: Advanced primary or recurrent pterygium with optical zone.

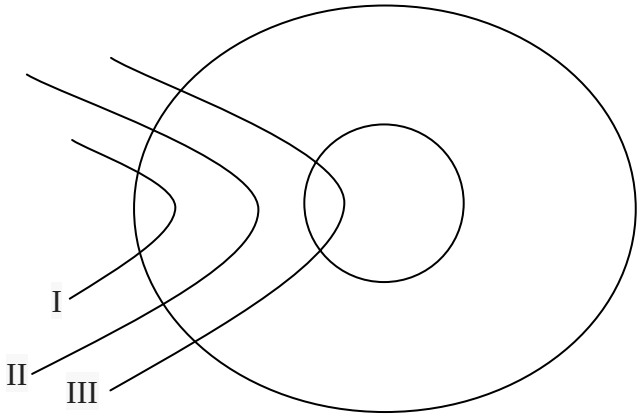
GRADES OF PTERYGIUM:

Tan D.T[58]. has graded it depending on extent of pterygium onto cornea:

Grade I: < 2mm from limbus

Grade II: 2-4mm from limbus

Grade III: >4mm from limbus



c) Prevalence:

The pterygium is one of the commonest ocular surface disorders mostly found in tropical regions with a predisposition to the equatorial belt. Prevalence of pterygium ranges from 0.3% to 37.46% worldwide[2,51]. A true Pterygium is a condition found chiefly in the sunny hot dusty regions of the world, mostly between the Latitude of 37^{o} North and South of the Equator (Poncet, 1881; deTreigny and Coirre, 1933; Anderson, 1954; Cameron, 1962). It is rare in countries such as England or Northern Europe and prevalent in those countries where these conditions are common, as the eastern littoral of the Mediterranean the Northern; Western and Central part of Australia and Texas. High prevalence is seen in “pterygium zone”-i.e. geographical latitude of 37 degree south and north to equator. In India, the prevalence

of pterygium is higher in Maharashtra, Andhra Pradesh, Gujarat and Assam. Most of the data available in India is based on the hospital statistics and fragmentary studied done by different workers.

SYMPTOMS OF PTERYGIUM:

Small pterygium remains asymptomatic. However, patients may experience mild irritation, burning, watering, blurred vision and cosmetic disfigurement. Blurring of vision is because of astigmatism induced by pterygium.[20,29]

In advanced cases, the pterygium by involving the visual axis on the cornea may cause visual loss secondary to loss of transparency within the visual axis.[20]

In some patients with advanced pterygia, ocular motility may be restricted, leading to diplopia in certain direction of gaze.

Site:

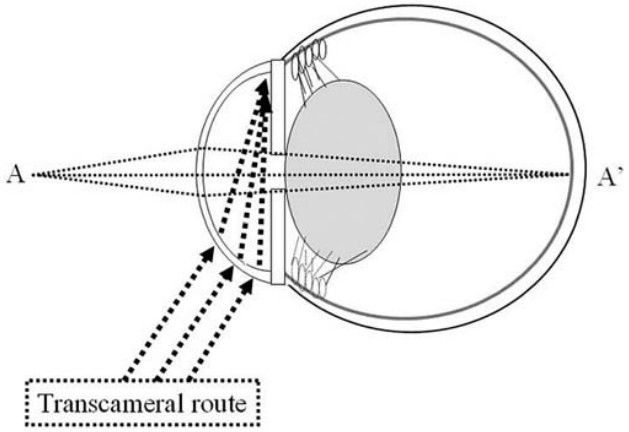
The disease affects mostly the nasal part of the conjunctiva; the temporal part is less commonly affected and the condition is rarely seen on both sides.

Various explanations have been put forward for greater predilection on nasal side.

a. Excess of sub conjunctival tissue.
b. Greater bowing of lateral 2/3rd of upper lid and consequent protection by longer lashes (Cameron, 1965).
c. Greater curvature of nasal fibres of orbicularis causing a greater squeezing effect upon the nasal sub conjunctival tissue (Sugar, 1949).
d. Greater exposure of the nasal interpalpebral conjunctiva to ultra violet radiation (Cameron, 1965).
e. There are two anterior ciliary arteries on nasal side and only one on the temporal side. It is felt that due to this fact any irritant shall lead to greater

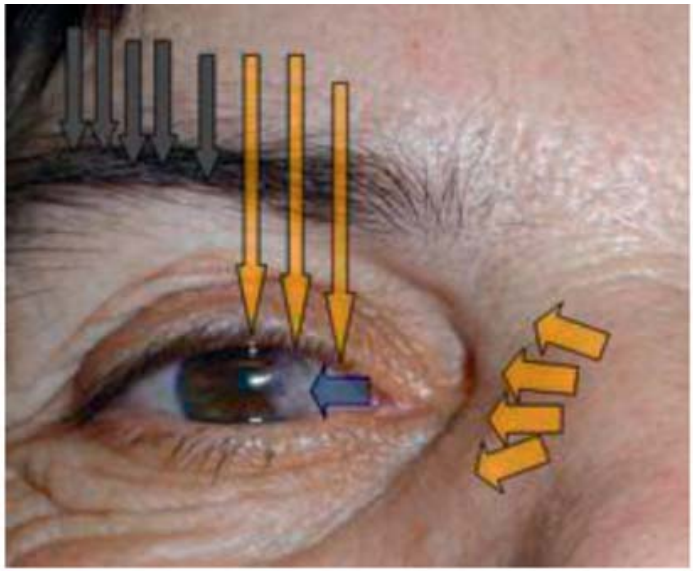
hyperaemia on the nasal side which may be playing an important factor in the development of pterygia on the nasal side (Wolf, 1950).

f. The normal flow of the tears from out inwards towards the puncta and canaliculi, carries with it any dust particles entering the conjunctival sac and accumulates them in the lacus lacrimalis. This, probably, leads to more irritation of the nasal conjunctiva.



Exposure of nasal limbus to UV rays through transcameral route

Transcameral light focusing on the nasal limbus may expose limbal basal stem cells to increased amounts of UVR and be associated with molecular genetic alterations to these cells, eventually leading to pterygium formation.



Causes for nasal pterygium

Light reflected from the lateral aspect of the nose on the corneal limbus as well as incident light falling on nasal limbus due to the short length of brow hair nasally (yellow arrows) may contribute to the formation of pterygium nasally (blue arrow). On the other hand, the temporal limbus is relatively protected from incident light due to the longer length of brow hair temporally (grey arrows) (figure 6).

Age:

The disease affects mostly adults between 25 and 40 years of age. It is rare among children.

Occupation:

The diseases are most common among people whose daily life necessitates a long standing exposure of the eyes to the effects of irritation. Thus, it is common among stone cutters, fishermen in certain localities and farmers (outdoor work with exposure to dust, wind and bright sunlight).

Sex:

The disease is more common in males with a rate of incidence of about 80:20 males to females.

Environmental factors:

This condition is more common in localities where the weather is to the hot side and the sun rays are brilliant. This explains the frequency of the pterygium among stone cutters and among the inhabitants of certain localities.

Heredity and genetics:

Heredity has undoubted influence in the occurrence of pterygia, although its influence is not crucial. The inheritance is dominant with a low penetrance, but it would appear that it is not the actual lesion which is transmitted but rather the tendency of the eye to react in this way to environmental stimuli.

Blood groups:

Duke – Elder (1965) has concluded that there is a definite role of heredity in the aetiology of the pterygium, in the form of dominant inheritance with low penetrance. Beatlie (1947) found same statistical evidence and since blood groups are also determined genetically, we may find some association between blood groups and pterygium. The association or incidence of the pterygium differs amongst the various groups and 'O' is more closely associated than others. Inspite of
statistically significant results the exact role of blood groups, in causation or association needs further elaboration.

d) AETIOLOGY AND PATHOGENESIS OF PTERYGIUM

Pterygium is a condition which affects millions of people living in periequatorial regions, causing much discomfort and disablement and in neglected

cases blindness. It is a condition rarely seen in European ophthalmological centres and is only seen in England in immigrants or in native English who have spent at least three years in periequatorial regions (Cameron, 1965, Youngson, 1970).

Many theories have been developed to explain the etiology of pterygium.

1- The degenerative theory:

The degenerative theory of the etiology of pterygium was claimed by Fuchs[25] (1892). Duke–Elder[20] (1938) mentioned that pinguecula is a precursor for pterygium based on the early signs of hyaline and elastic tissue degeneration in the deeper parts of the tissues in all cases of pingueculae and pterygia and frequent occurrence of pterygium in cases in which a pinguecula is present.

However, Norn[59] (1979) mentioned that pterygium and pinguccula are totally independent degenerations.

Khalil et al.[60] (1982) concluded from his study that degenerative as well as inflammatory changes occurred in cases of pterygium but, it was difficult to confirm which process started before the other or it might be true that both changes started at the same time.

Karai and Hariguchi [61] (1984) claimed that a pinguecula is not necessary for a pterygium.

2- The inflammatory theory:

According to the inflammatory theory, Gerundo[26] (1951) isolated Morax-Axenfeld bacillus from 3 cases out of 25 cases of pterygium.

Kamel[27](1953) suggested that the formation of pterygium is the result of chronic irritative exposure conjunctivitis in the area exposed in the palpebral fissure,

mostly nasal and sometimes temporally. He also added that the degenerative changes that occur in the pterygium are a post-inflammatory degeneration and not a primary degeneration. He based his concept on:-

a. Constant presence of round cell infiltration in the superficial strata of the cornea and conjunctiva of young and progressive pterygia.
b. Marked increase of the Goblet cell of the conjunctiva in cases of pterygia.
c. Deposition of dense fibrous and connective tissue in the submucosa of the conjunctiva and between Bowman`s membrane and epithelium of the cornea.
d. There was no known degenerative condition that starts in a vascular and well nourished area as the limbus, which tends to be self limiting when it progresses towards the non vascular center of the cornea.
e. The vascularity of the pterygium.
f. The periods of more acute inflammatory engorgement that occurred.
g. The occurrence of pterygia in a fixed position which is the most exposed part of the bulbar conjunctiva.

Saif et al.[62] (1967) mentioned that exposure to various extrinsic irritants causes a triple response (congestion duo to capillary dilatation and oedema caused by exudation of fluid from the dilated capillaries and arterioles) that when repeated lead to an inflammatory reaction.

Mortada et al.[63] (1968) claimed that a true pterygium is a chronic non-specific inflammation with subsequent fibrosis of the subepithelial connective tissue of the nasal (rarely temporal) limbus due to the effect of the environmental factors as dust or ultra-violet rays.

3- The neoplastic theory:

Redslob[64] (1933) mentioned that pterygium is a neoplastic polypoid growth of conjunctiva based on the high rate of recurrence.

Kamel[27] (1953) mentioned that the neoplastic theory is not true as there is nothing in the pathology of pterygia that indicates a neoplastic origin.

Khalil et al.[60] (1982) supported the non-neoplastic nature of pterygium as the changes in the epithelium were mainly in the form of alternating regions of thinning and hyperplasia and the layers of the epithelium were always orderly arranged and the basement membrane of the epithelium was always normal with no signs of break or downward invasion of the epithelium.

4- The tear film abnormality (dry eye) theory:

Elliot[22] (1966) and Goldberg and David (1976) claimed that tear film abnormalities would cause local drying of the cornea and conjunctiva predisposing them to these new growths.

Paton[65] (1975) postulated that exposure to dryness, hot weather, ultra-violet rays, glare and reflections of strong light cause the primary thickening of a limbal mass leading to limbal elevation, which in turn create an exposure problem to the cornea due to poor lid apposition on it.

Taylor[3] (1980) stated that dryness of the cornea and conjunctiva that occurs due to disruption of the tear film, as a result of either evaporation or micro-trauma from micro-patches of dust, to be a primary factor in pterygium development. He also mentioned that drying of the inter-palpebral tear film occurs most readily in the medial third of the inter-palpebral fissure as this part of the conjunctiva is farthest

from the lacrimal gland and nearest to puncta, also, as the eyes when partially closed against glare or wind, the medial third of the conjunctiva remains relatively more exposed than the lateral third.

Caldwell[66] (1985) stated that drying and exposure may produce an anoxic condition of the cornea, similar to that occurring in the periphery of the retina in case of diabetes. This anoxia probably produces an angiogenic factor which in turn would lead to neovascularization of the dellen area leading to fibro-vascular ingrowths onto the cornea.

Coroneo[19] (1999) mentioned that drying of the tear film by wind devitalizes tissues of the medial third of the palpebral aperture and this allows actinic radiation to damage the conjunctival and corneal epithelium and Bowman`s membrane.

5- The immunological theory:

Pinkerton et al.[67] (1984) mentioned that the presence of lymphocytes and plasma cells in the stroma of the pterygial tissues indicates that an immunological process may be involved in the pathogenesis of pterygium. He also added that the localization of Ig G and Ig E indicates an immunological mechanism and the presence of Ig E suggests a possible involvement of type (1) hypersensitivity.

Ibrahim et al.[68] (1991) mentioned four points in support of immunological theory:

1) The demonstration, in the pterygial tissue of immunoglobulins and complement suggests that an immune complex mediated type (III) hypersensitivity.
2) The presence of immunoglobulins along the walls of the epithelium may be suggestive of a type (II) hypersensitivity.

3) Deposition of fibrinogen may be attributed to vascular injury mediated by immune complexes.
4) The fibrinogen detected in the inflammatory cells may represent phagocytosed fibrinoid material derived from the necrosis resulting from local antigen antibody interaction.

Nakagami et al.[69] (1999) showed that the mean number of most cells in the pterygia specimens was twice as high as that in the normal conjunctival tissues.

6- The mechanical theory:

Wong[70] (1978) suggested that a pterygium angiogenesis factor may exist which develops following repeated irritation at the limbus. This factor produces vessel ingrowth and the formation of pterygium.

Barraquer et al.[71] (1980) postulated that chronic irritation may result in repeated attacks of conjunctival inflammation and punctate conjunctival ulcerations, leading to a cicatricial reaction in the subconjunctival tissue which undergoes a retraction process, moving towards the limbus, forming a tiny roundlet that is higher than the limbus. Once the limbic elevation has been formed, the lids no longer touch the cornea in front of the elevation, leading to discontinuity of the precorneal tear film, desiccation, dellen formation and then ulceration of the limbic elevation. Healing of the ulceration attracts the conjunctiva forming a pterygium. Repetition of these corneal ulcerations result in migration of the ptergium towards the center of the cornea.

Aziz[72](1986) claimed that environmental factors as excessive dust, fumes, draughts of air might act as irritating agents which would lead to congestion of the eye and help in pterygium formation.

Coroneo[19] (1999) mechanical irritation by dust particles enhanced by the tear flow from lateral to nasal side of conjunctiva has been proposed as a mechanism. However, pterygia accour in dust- free areas for example at sea, in sailors.

7- The hereditary theory:

Duck-Elder[20](1965) stated that heredity has undoubted influence on the occurrence of pterygia.

Hilgers[73] (1960) mentioned that some pedigrees have showed an apparent transmission through several generations suggesting an autosomal dominant mode of inheritance.

Mortada et al.[63] (1968) and Coroneo (1993) did not believe in the hereditary theory because they thought that this might simply reflect common environmental factors or occupations or an inherited anterior segment shape factor.

8- The ultra-violet rays theory:

Blum[20](1959) stated that UV rays at least in the skin are the most important nuclear damaging agent, as he observed by his experimental study the occurrence of epithelial hyperplasia, degeneration of the Bowman`s membrane and vascularization of the corneal stroma in a mice by the action of large doses of UV rays.

Moran and Hollow[2] (1984) mentioned that the ultra-violet theory of pterygium causation is supported by studies on rural Australian and Japanese Welders. In the Australian study, a strong positive correlation between climatic ultra-violet radiation and pterygium prevalence was demonstrated. Also, there was a comparable prevalence in male and female aborigines and the rates were higher than for non-aborigines. This was thought to be due to the fact that non-aboriginal women in rural

Australia generally spend less time out of door than men and are well housed and able to escape from solar radiation, either direct or scattered.

Taylor et al.[3] (1989 & 1992) mentioned that the ultra-violet radiation is divided into three bands : UV-A (400- 320nm), UV-B (320-290nm), and UV-C (290- 100nm) , based on its biologic activity. The ultra-violet C does not naturally penetrate to the earth`s surface, but the cornea would absorb almost 100% of this radiation below 290nm.

Coroneo (1993) has explained the occurrence of the pterygium most commonly at the side of conjunctiva. He proposed that the anterior eye acts as side on lens, focusing light from the side of the cornea, then light proceeds across the anterior eye via transcorneal pathways to the other side. The degree of limbal focusing is determined by corneal shape and anterior chamber depth, and this may explain why particular individuals in a common environment are affected by these conditions. As these factors are quantifiable, it may be possible to identify at risk individuals by using puter assisted optical ray tracing techniques, Coroneo (1993) stated that the peak light intensity at the nasal limbus is approximately 20 time that of the incident light intensity. This irradiation may be particularly injurious as the corneal epithelial stem cells are struck from behind and are not protected by the more superficial layers of the epithelium.

9- The limbal stem cell dysfunction theory:

Recently, it has been proposed that pterygium may be due to limbal stem cell dysfunction. Chen and Tseng[8] (1990) stated that the corneal epithelial stem cells which are located in the basal limbal epithelium, play a role in maintaining the junction between cornea and conjunctival epithelia.

It has been reported that the primary abnormality in the pathogenesis of pterygium is the abnormal stem cells. This is evidenced, recently, by the immuno-chemical techniques that showed altered limbal epithelial stem cells at the leading edge of pterygia along the normal corneal epithelial membrane.

Based on these data, Dushku & Reid[74] (1994) proposed that the pathogenesis of pterygia is due to altered limbal epithelial basal cells giving rise to a zone of motile daughter cells, the pterygium cells, which leave the limbal region and migrate centripetally along the corneal basement membrane dissolving Bowman`s layer. Since these altered limbal basal cells are found at the microscopic advancing edge over Bowman`s layer with no fibroblast mass under them, the pterygium cell apparently precedes the rapid growth of the fibroblasts from the stroma.

Grimmett and Holland[75] (1997) stated that a healthy limbal stem cell population provides a stable junctional barrier that prevents conjunctivalization of the cornea. So, pterygium formation may ultimately represent a focal limbal stem cell dysfunction state.

A) **Based on the underlying etiology, corneal diseases manifesting LSCD can be subdivided into two major categories[76]**

In the first category, limbal epithelial stem cells are destroyed by known or recognizable offenders such as chemical or thermal burn, Stevens- Johnson syndrome/ toxic epidermal necrolysis, multiple surgeries or cryotherapies or medications (iatrogenic), contact lens, severe microbial infection, radiation, and anti-metabolites including 5-fluorouracil and mitomycin C.[77]

A second category is characterized by a gradual loss of the stem cell population without known or identifiable precipitating factors. In this situation, the limbal stromal niche is presumably affected and progressively deteriorates by a variety of etiologies that include aniridia and coloboma, neoplasia, multiple hormonal deficiencies, peripheral ulcerative corneal diseases, neurotrophic keratopathy, pterygium and idiopathic limbal deficiency[78,79]

B) Depending on the extent of deficiency they can also be classified as-

1. **Partial / Focal LSCD**- is characterized by partial/ focal loss of stem cell function with rest of the limbus being normal, e.g.- multiple surgeries at limbus, cryotherapy, pterygium, cryotherapy, less severe chemical/ thermal burns, etc.
2. **Total LSCD**- When it is more severe there is total loss of limbal stem cells without any normal area spared and it is called as total stem cell deficiency e.g.- Steven Johnson syndrome, advanced cicatricial pemphigoid, contact lens wear.

C) Limbal stem cell dysfunction versus destruction-

Dysfunction is usually primary or hereditary and can be a part of other ocular or systemic anomalies. Due to abnormal microenvironment of the limbal tissues, the stem cells never achieve their normal function. The condition is usually bilateral and less severe as the rest of ocular surface may be normal e.g. Aniridia, keratitis associated with multiple endocrine deficiencies.

Destruction is an acquired loss of functioning stem cells. The condition can be unilateral or bilateral and associated with severe ocular surface damage Eg.- chemical/

thermal burns steven Johnson syndrome, multiple surgeries pemphigoid, cryotherapy to limbus, contact lens wear etc.

e) DIFFERENTIAL DIAGNOSIS: [53, 54]

1. **Pseudo-pterygium:** This may be situated anywhere on the limbus in contrast to the true pterygium. A history of some corneal trauma like a marginal ulcer, fascicular ulcer, lime burns always precede. A probe can easily be passed under the neck of a pseudo-pterygium.
2. **Pinguecula:** A pinguecula seldom encroaches on the cornea except when it is very large, when the distinction from pterygium becomes difficult.
3. **Epithelioma:** This sometimes grows in the limbal area and resembles a pterygium. The difference lies in the greater irregularity of its surface, lack of thickening of subconjunctival connective tissue at the caruncle and absence of orientation of the blood vessels into the characteristic pterygial shape.
4. **Bowen's tumor:** This is a rare tumor that can be mistaken for the much commoner pterygium. Its features are much the same as for epithelioma.
5. **Epithelial hyperplasia:** These cases show increase in the subconjunctival connective tissue and the development of white or gray plaques surrounded by erythema giving the appearance of a pterygium.
6. **Squamous cell carcinoma of the limbus:** It is a very rare pathology but its differential diagnosis may be difficult with respect to other pathologies of the limbus, including a pterygium. Like a pterygium, it would also appear to be the result of chronic exposure to UV radiation.

   The most common site is the infero-temporal zone of the limbus. The definitive diagnosis is obtained by histological examination.

7. **Conjunctival papilloma:** It is a small active neo-formation in small cauliflower. It is highly vascular and bleeds easily. Compared to a pterygium differential diagnosis is easy but a certain diagnosis is histological. It is of vital origin.
8. **The limbal dermoid:** It is a rare congenital pathology which appears as a round yellow-red neo-formation between the limbus and the edge of the cornea. There is no abnormal visualization. The preferred site for the dermoid is the infero-temporal sector.
9. **Phlyctenular keratoconjunctivitis:** It is a small circumscribed conjunctival neo-formation with a gel-like appearance and surrounded by twisted capillaries and is associated with conjunctival hyperaemia. The pathogenesis is linked to delayed hypersensitivity to foreign bacterial or food proteins. This pathology is generally localized, but in some cases can lead to new vessel formation in the cornea and successive surface opacity. It is common in infancy or childhood.
10. **Lymphoma of the conjunctiva:** It is a very rare lesion that involves the inferior and nasal bulbar conjunctiva. This is a salmon-pink subconjunctival lesion which is poorly vascularized and almost flat. The definitive diagnosis is obtained histologically.
11. **Nodular episcleritis:** it is an inflammation of the episclera and the over-lying conjunctiva; in the nodular forms, it is localized. Young adult females are most affected and the pathology is observed as a bright red, almost flat nodule. 1t consists of twisted and injected conjunctival and episcleral capillary vessels. When it first appears, episcleritis is associated with pain but it disappears following several weeks' treatment with anti-inflammatory drugs. However, it

tends to recur. The differential diagnosis of pterygium should also include conjunctival intraepithelial neoplasia, squamous cell carcinoma, a corneal macropannus and limbal dermoid. The characteristic features of these entities should distinguish these disorders from a pterygium.

f) MANAGEMENT OF PTERYGIUM

Conservative therapy for pterygium is warranted unless one of the following circumstances arises: [20,29,35]

1. Loss of visual acuity either because of induced astigmatism or encroachment onto the visual axis.
2. Marked cosmetic deformity.
3. Marked discomfort & irritation unrelieved by medical management.
4. Limitation of ocular motility secondary to restriction.
5. Documented progressive growth toward the visual axis suggesting that visual loss will ultimately occur. In such circumstances, surgical intervention is required. Because recurrences after pterygium excision are frequent and aggressive, firm indications for surgical removal should exist before primary excision.

Medical Approaches

Basically treatment of pterygium is surgery. But medical management can be tried in cases where the pterygium is early, small inactive with minimal vascularisation.

1) Hyaluronidase : Acts by deploymerizing the hyaluronic acid in turn increases the tissue permeability. This causes ballooning of the pterygium away from the sclera. The injections are repeated at weekly intervals for 5 – 6 weeks.

2) Corticosteroids : In cases of early pterygium they act by inhibiting the fibrovascular and epithelial proliferation, thereby retarding or regressing the further growth of pterygium. They also bring down the hyperemia and reduce the bulk of pterygium. But pterygium does not disappear. They are used in the form of topical drops and eye ointments. They are also recommended postoperatively after pterygium excision to check the recurrence.
3) Lubricants, tear replacements vasoconstrictors have only evoked passing interest in the treatment of pterygium

Surgical Approaches

The fact that numerous different techniques exist for the surgical treatment of pterygium underscores the point that no single approach is universally successful.

Indications for Surgical Removal of Pterygium : are

1) For cosmetic reasons
2) Periodic inflammations
3) Diminution of vision because of
    a) Induced astigmatism,
    b) Progressive Pterygium involving the central region of the cornea.
4) Interference with ocular motility and development of diplopia.

Different Surgical techniques for the treatment of pterygium:

Evulsions:

A horse hair or flax thread was used as early as seventh century. Other methods described included use of squint hooks and corrugated silver wires.[80] The suture was passed underneath the body of the pterygium and, with a sawing motion toward the cornea, the head was dissected from the underlying corneal tissue.

Transplantation of the head of the pterygium:

Various techniques originated in the nineteenth century to redirect the head of the pterygium away from the cornea to prevent recurrences. The surgical procedure consisted of burying the pterygium head underneath the normal conjunctival edge inferiorly after surgical dissection of the head from the cornea (Desmarres 1855, McReynolds 1902). Unfortunately, recurrence rates of 30-75% were reported with these techniques. Such transplantation procedures have been largely abandoned secondary to high recurrence rates and poor post-operative cosmetic results.[31,81]

Pterygium excision/avulsion:

Avulsing a thin, relatively transparent, primary pterygia by mechanically shearing off the pterygium head from the underlying cornea with the use of forceps was recommended by Rich to avoid deep lamellar dissections. Advantages cited for this method include a resultant smooth corneal surface, rapid epithelialization, and minimal scarring postoperatively. It should be noted that many pterygia cannot be avulsed from the cornea in a smooth continuous plane and must be excised.[37] As a general rule, care should be taken to only perform a superficial corneal dissection, just deep enough to remove the pterygium. Deep lamellar keratectomies offer no distinct advantages, since the resection may produce post-operative ocular surface abnormalities and alter corneal tensile strength.

Bare sclera Technique

After pterygium excision, numerous authors in the past advocated a 'bare-sclera' technique in which the resultant scleral and corneal defects would be left to epithelialize post-operatively (Scarpa 1811, D'Ombrian 1948).

It was theorized that a pterygium recurrence would be prevented if the corneal epithelium could heal before the conjunctival epithelium reached the limbus.[82,28] Many authors claimed impressive success rates with this bare sclera technique. Unfortunately, controlled studies were not performed to validate the reports. Indeed, using a similar bare-sclera technique, Youngson reported a pterygium recurrence rate of 37% and concluded that the procedure is unsound, and 'pterygia should not be treated surgically'.[83] Karg and Ehlers reported a 91% recurrence rate (20 of 22 patients) using a baresclera technique in combination with excimer laser corneal ablation to smooth the corneal surface.[84]

Conjunctival Flaps and Conjunctival autografts

Various surgical strategies for the treatment of pterygium have been developed using the premise that close approximation of healthy conjunctival tissue at the denuded limbus after pterygium excision prevents recurrences. The three basic variations on this theme include excision with primary conjunctival closure, excision with conjunctival flap formation, and conjunctival autografts.

Pterygium Excision with Primary Conjunctival Closure

Primary conjunctival closure is achieved by undermining adjacent normal superior and inferior bulbar conjunctiva and pulling the cut conjunctival edges together to achieve primary conjunctival closure after pterygium excision (Arlt 1850, Arruga 1956). Patient age less than 40 years and aggressive pterygium activity have been cited as risk factors for recurrences.[19, 25]

Pterygium Excision with Rotational Flap

Rotational conjunctival flaps to cover the pterygium excisional site have been employed since the 1940s. *Aratoon* in 1967 reported a recurrence rate of less than 1 %

in a series of 150 consecutive procedures by using a conjunctival pedicle flap after pterygium resection.[85] A report by *Wilson and Bourne* discussed a redirectional conjunctival flap technique originally described by *Stocker* known as a conjunctival Z-plasty, the procedure involved rotating a flap of normal conjunctiva into a limbal position while simultaneously rotating the remaining pterygium body laterally onto the bulbar conjunctiva after resecting the pterygium head from the cornea. While no recurrence figures were quoted, the authors cited two advantages of the procedure, the preservation of normal conjunctiva for possible future free grafting and the formation of a barrier of normal conjunctival tissue adjacent to the limbus to prevent recurrent pterygium growth onto the cornea.[86]

Mc Coombes et al reported a recurrence rate of 3.2% by using a sliding conjunctival flap after primary pterygium excision.[87]

Kenyon et al described conjunctival free graft transplantation as a treatment for pterygium in 1985. In this technique; a tree conjunctival graft from the supratemporal bulbar conjunctiva is used to resurface the exposed scleral surface after pterygium resection. A 5.3% recurrence rate was reported. The authors recommended this treatment modality for advanced primary and recurrent secondary pterygium, especially when concurrent fornix reconstruction is required or when conjunctival scarring involves the extra-ocular muscles. *Lewallen* reported a randomized trial of conjunctival free graft versus a bare sclera technique for pterygium in the Caribbean. There was a lower recurrence rate for conjunctival freegraft (3 of 19 cases) as compared to a bare sclera control group (6 of 16). Overall, recurrence rates after conjunctival autograft are low. Pooling data from eight studies using conjunctival autograft in the treatment of pterygium gives an overall recurrence rate of 7.9%.[11]

Description of the general procedural technique for conjunctival free graft (Kenyon et al 1985)[11]

After the excision of the pterygium, the size of the scleral defect created is measured with Castroviejo calipers. The globe is then rotated downwards using the stay sutures to expose the superior bulbar conjunctiva. The dimensions of the intended conjunctival graft (adjacent to the limbus) are marked with a gentian violet marking pen based on the previous measurements of the recipient bed. The gentian violet marks not only aid in the excision of an approximately sized donor graft but are invaluable in preventing inadvertent upside down orientation of the graft in the recipient bed. *Allan* et al[88] noted that free grafts as large as 15 mm by 15 mm can be prepared and used without difficulty. Balanced salt solution is then injected subconjunctivally outside of the gentian violet marks to elevate the conjunctiva to aid in the conjunctival dissection. Blunt Westcott's Scissors are used to incise the posterior border of the graft. The conjunctiva is then undermined using blunt dissection with care taken to not include underlying Tenon's capsule in the final graft. The lateral edges of the donor graft are incised outside of the gentian violet marks as the dissection is carried forward. It is important to note that the graft is purposely excised outside of the gentian violet marks so that these marks can be used for later orientation. The donor conjunctival graft should be as thin as possible so that post-operative healing will occur with less shrinkage. It is also important that the limbal conjunctiva is incised last after the entire graft has been dissected forward to the limbus. This assures that the graft will not retract and become difficult to handle. Handling of the donor conjunctival tissue only occurs with nontoothed forceps (e.g. McGregor conjunctival forceps) so as to avoid a buttonhole in the conjunctiva.

At this point, the graft is oriented with the unmarked limbal donor edge adjacent to the limbus in the recipient bed and the gentian violet marks on the exposed surface of the conjunctiva. *Allan* et al advocated securing the graft with 8.0 vicryl sutures. Kenyon et al routinely secured the graft to the recipient conjunctival edge and underlying episclera with numerous 10-0 nylon sutures (buried knots) to avoid a post-operative graft dehiscence. The majority of these sutures usually extrude on their own by 1 month post-operatively, while the rest usually epithelialize and remain buried. Patient discomfort is usually not a problem due to the use of permanent sutures. The occasional exposed stitch can be removed after adequate conjunctival healing in the early post-operative period. The donor harvest site is left to epithelialize on its own, which usually occurs in the first several post-operative days. Kenyon et al advocate the post-operative steroid and antibiotic drop six times a day during the first 1 or 2 weeks and switch to a steroid drop alone after that time. Drops are titrated according to the degree of inflammation and may be continued for 4-8 weeks, depending on the clinical circumstances.[11]

The primary disadvantage of the conjunctival free graft technique is the prolonged operative time required when compared to other bare sclera or primary closure techniques. Additionally, an operating microscope is required for optimum results, which can be a problem for ophthalmologists in developing countries. However, these disadvantages are outweighed by the lack of sight-threatening complications and the relatively low recurrence rates after conjunctival free grafts.

Limbal conjunctival autograft[89] :

Limbal transplantation was described by Barraquer in 1964. More recently, Kenyon & Tseng (1989) described a large series of limbal autografts in patients with unilateral ocular surface disease, which involved the transplantation of healthy limbal

epithelium from the unaffected fellow eye. A repository of conjunctival stem cells was postulated (Dua &Forrester, 1990) and latter demonstrated to be located at the fornices (Wei et al. 1993). The presence of two distinct populations and locations of stem cells on the ocular surface would suggest that they serve as progenitors of two different phenotypes of epithelial manner from the limbus (Dua & Forrester, 1987), conjunctival epithelial wounds heal in a centripetal manner from the fornix (Dua, 1998).

Limbal autograft transplantation is based on the concept that the limbal epithelium contains the stem cell population for corneal epithelial cellular proliferation and differentiation and has been advocated for a variety of unilateral ocular surface disorders with suspected limbal stem cell disease (Tan et al., 1996).
Guler et al. (1994) described the technique of limbal conjunctival autograft transplantation (LCAT), in cases with recurrent pterygium, as follows:

Using retrobulbar block and akinesia of lids, a rigid lid speculum was placed and stay sutures of 6-0 silk were inserted at the 6 & 12 o`clock limbus to provide maximum surgical exposure. The operation was accomplished by means of an operation microscope in the operating room.

After the excision of the pterygium, the size of the conjunctival defect created is measured with Castroviejo calipers. The globe is then rotated downwards using the stay sutures to expose the superior bulbar conjunctiva. The conjunctiva is then dissected to free the body of pterygium. Superficial keratectomy is done to clean the cornea at the area covered by the head of pterygium using a Beaver blade. Minimal cautery is used to control bleeding and the area of bare sclera is measured. A superotemporal limbal conjunctival autograft incorporating a small portion of limbal stem cells, and measuring approximately 0.5-1 mm larger than the recipient bed, is

harvested from the same eye. The graft was dissected towards the cornea with a number 15 scalpel blade to include 0.5 mm of the superficial limbus. Dissection of the conjunctival autograft is done superotemporally from the fornix to the limbus. Care is taken not to include Tenon's capsule. The graft is then transferred to the recipient bed and secured with 10/0 or 8/0 Vicryl sutures. The graft is oriented such that harvested limbal stem cells are positioned adjacent to the cornea. The host area is left with Tenon's capsule exposed

Lamellar keratoplasty and penetrating keratoplasty

If significant corneal thinning is present as a consequence of previous pterygium surgery, a lamellar keratoplasty may be indicated to restore the normal ocular surface integrity. Additionally, various authors have recommended a lamellar keratoplasty as a barrier to pterygium regrowth.

While the reported series are small, recurrence rates after lamellar keratoplasties using lyophilized donor tissue have been reported between 0% and 60%. In severe cases where the visual axis is affected by thinning and scarring, a penetrating keratoplasty may be indicated to visually rehabitate the eye (Castroviejo 1950, Friede 1953).[90]

Amniotic membrane transplantation: Human amniotic membrane reduces inflammation and formation of fibrovascular tissues. This has been used with success to cover the bare sclera after pterygium excision.[91,13] It serves as a useful alternative to conjunctival tissue in situations where there is a large conjunctival defect and shortage of healthy conjunctival tissue to cover the bare sclera as seen in recurrent pterygium.[27,29] However preparation of a fresh transplantable amniotic membrane is a tedious process.

Mucous membrane grafts and skin grafts

Other grafting substances included buccal mucous membrane, skin taken from the flexor surface of the forearm, behind the ear, or from the redundant skin of the upper lid. In cases in which sufficient conjunctiva is not available for a pedicle graft, Trivedi et al recommended the use of a mucous membrane graft from the lower lip after a pterygium excision. The clinical circumstance of generalized conjunctival disease preventing rotational flaps or free graft is uncommon.

Wrong reported that a split thickness skin graft decreases the incidence of recurrences in cases of secondary recurrent pterygia and presents an acceptable "white" eye post-operatively. Post-operative appearances show a "white" patch in the area of the previously excised pterygium. The cosmetic appearance of skin grafting does not approach the excellent results achieved by conjunctival rotational flaps or autograft. Based on the paucity of reports using skin grafts, the technique has not gained widespread acceptance in the treatment of pterygia.[92,93]

Fibrin adhesive:

Cohen et al first described the use of fibrin glue for pterygium surgery.[94] Fibrin glue is now preferred over sutures for anchoring conjunctival graft or amniotic membrane. Use of fibrin glue reduces both the operation time and postoperative discomfort. However cost and availability are the limitations

COMPLICATIONS OF CONJUNCTIVAL GRAFTING

These are infrequent and not generally sight threatening [20,29,33,95]

Intra-operative

- Hemorrhage
- In advertant corneal perforation

- Injury to the medial rectus muscle
- Donor site hemorrhage
- Loss of orientation, Dipping of the graft
- Button holing of the graft

Post operative

- Conjunctival graft edema
- Corneoscleral dellen
- Epithelial inclusion cysts
- Tenon's granuloma which usually occurs in the first two weeks. It is often associated with recurrence and should be excised.
- Wound dehiscence's graft retraction
- Subconjunctival fibrosis at harvest site causing EOM restriction and
- diplopia
- Symblepharon formation more with inferior donor sites
- Giant papillary conjunctivitis due to suture irritation
- Corneal scarring

For optimal surgical results, careful dissection of the Tenon's tissue from the conjunctival graft and recipient bed, minimal manipulation of tissues, and accurate orientation of the graft is essential.

Adjunctive therapy

In an effort to lower the recurrence rates after primary pterygium excision alone, investigators have combined excisional techniques with various adjunctive treatment modalities. In the circumstance of secondary recurrent pterygium, the

known aggressive clinical course certainly warrants some additional treatment strategy other than standard treatment modalities.

The following adjunctive therapies have been variably recommended for both advanced primary and secondary recurrent pterygium.

Lasers:[96] Insler and Caldwell have reported a less than 2% incidence of recurrent pterygium with the use of argon laser in selected cases post operatively following surgical excision. Any early evidence of recurrence of pterygium is treated with laser burns to the neo-vascular fronds. The power is adjusted to minimize conjunctival epithelial burning and shrinkage.

Chemotherapy

THIOTEPA:[29,97] the nitrogen mustard analog thiotepa, N, N', N'', triethylene thiophosphoramide, has been advocated as an adjunctive measure to reduce the post-operative recurrence of pterygium since 1962. Thiotepa is an alkylating agent that interferes with normal mitosis and cell division in all rapidly proliferating tissues. It was postulated that thiotepa reduced the recurrence of pterygium by inhibiting vascular endothelial proliferation at the operative site.

Common recommended form is to mix 15 mg of thiotepa m 30 ml of Ringer's solution for a final dilution of 1:2000 strength. The patient uses the medication topically every 3 hours during the day starting 2 days postoperatively for a total of 6 – 8 weeks time.[29]

While no systemic toxicity of topical thiotepa therapy has been reported, complications reported include early and late onset poliosis and periorbital skin depigmentation that can be permanent (especially in darkly pigmented patients), prolonged conjunctival injection, irritation, epithelial toxicity leading to delayed

epithelialization of the cornea, conjunctival deposition of black pigment, allergic reactions and scleral perforation. Sun exposure during therapy was suggested as a contributing factor in the skin and lash depigmentation. The periorbital skin depigmentation has been cited, as the major reason thiotepa has not gained widespread acceptance in the post-operative treatment of pterygia.

Mitomycin C:[10,98,99,100,101,102] Mitomycin C is an antibiotic that was first isolated from Streptomyces ceaspitosus by Hata in 1956. Clinical trials with mitomycin C in the United States began in the late 1960s for a variety of solid tumors to include breast, prostate, gastric and bladder cancers. Since that time, numerous investigators have reported that topical mitomycin C is efficacious in decreasing recurrence rates after pterygium excision. Systemic therapy with mitomycin C carries risks of myelotoxicity, hemolyticuremic syndrome, pneumonitis, hepatic veno-occlusive disease, and rate cardiotoxicity. Following reductive activation, mitomycin C interacts with DNA to form monofunctional adducts as well as covalent crosslink between the two complementary strands of DNA. The preferred molecular target in DNA are responsible for the antibiotic and anti-neoplastic activity of mitomycin C because molecular synthesis cannot progress normally with such permanent structural alterations. Additionally, the production of toxic oxygen free radicals from mitomycin C in vivo has been postulated that could cause significant damage to any membrane with unsaturated lipids. Overall, mitomycin C has the greatest anti-proliferative effect on those cells showing the highest rate of mitosis.

Kunimoto and Mari first used mitomycin C to treat pterygia with a dose of 0.4 mg/ml used 4 times daily for a period of 1-2 weeks. Following reports of complications, the efficacy and safety of lower doses was established by Hayasaka and associates in 1988 (0.2 mg/ml 2 times daily for 5 days) with a recurrence rate of

6.9%. The use of topical mitomycin C eye drops of 0.2- 0.4 mg/ml strength 2 - 4 times daily after pterygium surgery was popularized in the United States by Singh et al. These drops were dispensed in dark bottles and patients were advised to keep the drops refrigerated and to strictly discontinue use after 1 week. But reported incidences of complications with doses a low as 0.4 mg/ml 1 time daily for 2 days led to MMC being applied in one dose intraoperatively. This was applied to the bare sclera area left behind after pterygium excision. Typically, a 5 mm X 5 mm pledget was soaked in solution of 0.25 mg/ml of MMC and applied to the bare sclera directly for 1-3 minutes. Because the dosage could be monitored the complications as compared to that of topical medications were less.[98,99] A double- masked trial of pterygium excision with and without mitomycin C eye drops found recurrences to be 89% in the placebo group versus 2.3% in the mitomycin group. Subsequent investigations by other authors have confirmed the low recurrence rates after treatment with 0.2-0.4 mg/ml topical mitomycin with recurrence rates between 5% and 9%. Overall, these studies indicate that mitomycin C is effective in reducing recurrences after pterygium excision.

Complications following Mitomycin C include:[101,102]

- Scleral ulceration, necrotizing scleritis, scleral calcification
- Severe secondary glaucoma
- Corneal edema, corneal perforation
- Iridocyclitis
- Cataract
- Infection
- Photophobia and pain

Mitomycin C after pterygium excision is contraindicated in patients with:

- Keratitis sicca
- Sjogren's syndrome
- Neurotrophic keratitis
- Severe meibomian gland dysfunction
- Blepharitis

Radiation Therapy:[29, 103,104]

Until the 1950s, radon bulbs, radium plaques, Grenz rays and X-rays were employed in the treatment of pterygia with variable success. In 1952, strontium 90 was introduced for the treatment of neoplastic disease and has been extensively used for the treatment of pterygia since that time. Strontium 90 decays to yttrium 90, with a half-life of 64 hours, which in turn, decays to zirconium 90, which is stable. Beta rays from strontium 90 have an average energy of 0.21 MeV per disintegration while beta rays from yttrium 90 have an average of 0.89 MeV per disintegration. This low penetration profile of strontium 90 is important, since cataracts may develop should the dose to the crystalline lens approach 1500 to 2500 rep (1 rep = 1.08 rad). Recurrence rates after pterygium excision with beta irradiation have varied widely, with a low of 0.8% to a high of 80% reported in literature. The mechanism of action of beta irradiation in reducing recurrences is thought to be through the inhibition of mitosis in rapidly dividing cells such as vascular endothelial cells.

The optimal dose is between 1000 and 3000 rad given at the time of surgery or within a few days after surgery. Applying the beta irradiation at the time of surgery may also help in better control and localization of the treatment and may save the patient additional time and expense.

Complications following beta irradiation include:

- Scleral necrosis/scleromalacia
- Pseudomonas endophthalmitis secondary to scleral necrosis
- Radiation-induced cataract
- Epithelial defects/corneal thinning/corneal ulcers/pseudomonas keratitis
- Symblepharon

The latency between the beta irradiation and the onset of the complications is long (14.5 years). Because scleral necrosis and possible late infectious complications occur years after the original surgery, it is not surprising that numerous short and intermediate term studies deemed beta irradiation safe. Because conjunctival autograft offers a low rate of pterygium recurrence and is free from long term sight-threatening complications, it appears that autograft offers patients a safer alternative when compared to beta irradiation or mitomycin therapy.

h) RECURRENCE [103,104]

The perfect result of a pterygium excision would be a normal appearance of the conjunctiva with no appearance of blood vessel orientation into the characteristic pterygial shape. More often, the initial stages consist of a few blood vessels growing in a triangular fashion.

Recurrence following operation has been attributed by various authors to the fallowing factors.

a) Incomplete dissection of head of pterygium from cornea.

b) Incomplete removal of pterygium tissue.

c) Remnants of connective tissue left at the corneoscleral junction.

d) Failure to create a smooth area next to limbus.

e) In case of thick graft the extra thickness which is made of connective tissue usually permits pterygium to grow beneath it.

This proceeds to definite recurrence in which the blood vessels are accompanied by a variable amount of subconjunctival connective tissue. Sometimes a few blood vessels reach 1 or 2 mm onto the cornea (Gibson's vascularized scar).
A frank recurrence is sometimes referred to as 'malignant recurrence' where the growth is well over the cornea within 1 month post-operatively. It is thick and fleshy and in its course of growth drags over the caruncle and the plica. It is usually very firmly adherent to the cornea and the sclera, more than the primary pterygium, and is usually more symptomatically distressing.

The majority of the recurrences can be detected during the 1st month post-operatively and almost all occur by 3 to 6 months.

PATHOPHYSIOLOGY OF RECURRENCE

The mechanism that explains the recurrence is the reactivation of the inflammatory process present in the primary form. Surgical trauma acts as an inflammatory response enhancer.

If after surgery, fibroblastic tissue is active then the consequence is an increase of proliferative cytokines and growth factors (VEGF), which induce the fibrovascular proliferation, while increasing the synthesis of metalloproteinases that destroy the Bowman membrane and stromal collagen, facilitating progress of pterygium[105,106]

In most cases there are signs of more aggressiveness, more violent inflammatory reaction with fibroblastic proliferation, thickening and irregularity of

the affected tissues. Sometimes the process can produce cicatricial symblepharon and limitations in ocular motility.

Lewallen S et al[107] (Ophthalmology 1989) carried out a randomized trial of conjunctival autograft treatment of pterygium for preventing recurrence and compared it with bare sclera excision.After months follow-up, recurrence was 21%(3 of 19) in the autograft group and 37%(6 of 16) in the bare sclera group. It was seen that younger patients were much more likely to have recurrence and all were noted within 6 to 8 weeks of surgery.

Riordan-Eva P et al[108] (Eye 1993) in a retrospective survey of 117 operations for primary or recurrent pterygium compared conjuctival autograft with both,excision without conjuctival closure(Bare sclera excision) and excision with complete conjunctival closure.The probability of recurrence at 36 months after surgery was determined by survival cure analysis.Conjunctival autografting (n=15) resulted in a 14% probability of recurrence compared with 70% for bare sclera excision(n=50) and 69% for excision with complete conjunctival closure (n=20).In previously operated cases conjunctival autografting (n=17) resulted in a 7% probability of recurrence, compared with 82% for bare sclera excision(n=15).They concluded that conjunctival autograft was more likely to produce an improvement in visual acuity compared to other forms of surgery.

Guler et al[109] (Acta Ophthalmol 1994) studied limbal conjunctival autograft transplantation in cases with recurrent pterygium.31 out of 49 patients were treated by limbal conjunctival autograft transplantation and the other 18 treated by Czermak technique i.e. by suturing the upper free edge of the conjunctiva to the lower edge after two lines of limbal cauterization intra-operatively which was used as a control

group.Mean follow up period was 10months.They observed a recurrence rate of 13.3% in conjunctival limbal autograft transplantation group as compared to 50% recurrence rate in control group (p=0.02,<0.05).Postoperatively graft edema was observed in all cases but disappeared mostly in 10days.Tenon's granuloma was seen in 5 cases(16.1%), graft rejection in 2cases (6.4%), haematoma under the graft in 1 case (3.2%).

Hille K et al[110] (Ophthalmology 1996) conducted a prospective study of surgical management of pterygium i.e. bare sclera technique vs. free conjunctival limbal transplant.They used bare-sclera technique in 21 eyes and performed free transplantation of conjunctiva in 34 eyes.The duration of follow-up was 14 months. They concluded that in patients with free limbal transplant, no recurrence was noted but the bare-sclera technique was associated with a recurrence rate of 35.5%(P<0.01).

Shimazaki et al[111] (Ophthalmic Surg Lasers 1996) conducted a study to determine the usefulness of limbal autograft transplantation in the treatment of recurrent and advanced ptygeria.11 patients with recurrent ptygeria and 16 with advanced pterygia(mean age ranged from 61±13.1years) were treated with limbal autograft transplantation.Once a pterygium had been excised,superior limbal tissue was taken with conjunctival flap and transferred to the excised area.Although recurrence was noted in 2 cases (7.4%),subconjunctival tissue invasions were limited to less than 1mm.Their results indicate that limal autograft transplantation was effective for the treatment of recurrent and advanced pterygium.

Srinivas Rao et al[112] (Indian J Ophthalmol 1998)carried out conjunctival limbal autograft in 51 patients(mean age ranged from 42.7 ± 14.5 years) with pterygia having visual impairment, cosmetic disfigurement, motility restriction, recurrent

inflammation, interference with contact lens wear. No significant intra-operative complications were noted except button holing. Post-operatively, most cases had moderate graft edema in the first two weeks with accumulation of serous yellow tinged fluid which resolved spontaneously, 1 case had corneal dellen, 2 cases had graft retraction which was due to cut through of the suture with retraction of conjunctiva at graft host junction and 1 eye had giant papillary conjunctivitis due to exposed sutures. Recurrence was noted in 2(3.8%), eyes at 3.5 months and 9.2 months. The recurrence was across the graft, asymptomatic and was detected on routine follow-up. Satisfactory postoperative cosmesis was achieved in all eyes and this was subjectively graded by the patient as excellent in 27(75%), good in 4(11.4%) and fair in 5 eyes(13.9%). They recommended conjunctival limbal autograft as a procedure of choice for surgical management of both primary and recurrent pterygium.

Essex RW et al[113] (Clin Experiment Ophthalmol 2004) conducted a study on amniotic membrane grafting in the surgical management of primary pterygium on 28 pterygia of 26 patients and observed a recurrence of pterygium within 12 months. They concluded that amniotic membrane graft for primary pterygium was associated with an unacceptably high recurrence rate.[125]

Fernandes M et al[114] (Eye 2005) conducted a retrospective analysis of 920 patients (989 eyes) with primary and recurrent pterygia. They analyzed that CAG appears to be an effective modality for primary and recurrent pterygia. Also concluded that males and patients below 40 years face a greater risk of recurrence. They also noted that bare sclera technique had an unacceptably high recurrence rate.

Al Fayez et al[115] (Opthalmology 2002) conducted a randomized, prospective clinical trial to compare the safety and efficacy of limbal versus conjunctival autograft transplantation for advanced primary and recurrent pterygia in 79 eyes. 24 eyes with primary and 12 eyes with recurrent pterygia underwent free conjunctival autograft transplantation (group A), and 28 eyes with primary and 15 eyes with recurrent pterygia underwent limbal-conjunctival autograft transplantation (group B). With a 3-year of follow-up,2 cases of primary (8.3%) and 4 cases of recurrent (33.3%) pterygia with free autograft showed recurrence. None of the patient treated with limbal-conjunctival autograft transplantation developed recurrence. They concluded that though both techniques were effective in cases of advanced primary pterygia with no statistically significant difference. Limbal transplantation appeared more effective than free conjunctival transplantation for treatment of recurrent pterygia ($P<0.05$).

Bekibele CO et al[116] (Eye 2006) described a randomized controlled prospective study by using 5-FUas adjuvant treatment compared to conjunctival limbal autograft in pterygium. In this study, 35 eyes with large pterygium treated with bare sclera along with intraoperative application of 5-FU (50mg/ml). They compared with 33 eyes treated with conjunctival limbal autograft transplantation. Recurrence was observed in 4 (11.4%)eyes treated with 5-FU and 4(12.1%) eyes treated with conjunctival autograft ($P>0.05$) after 2 years of follow-up. They concluded that 5FU is marginally superior to conjunctival limbal autograft.

Mohamed A.E et al[89] (Oman J Ophthalmol 2009) carried out Pterygium excision was performed followed by superotemporal limbal stem cells and conjunctival autograft transplantation in 42 eyes of 42 patients with grade I-III primary pterygium. Recurrence of pterygium occurred in two eyes (2/42; 4.75%). No

significant complications were noted. Apart from re-operation in the two recurrent cases, no further surgical interventions were needed in any case. They concluded that limbal stem cells and conjunctival autograft transplantation is a safe and effective technique for the treatment of different grades of pterygium. It is very useful in preventing pterygium recurrence, which is a major problem in pterygium surgery.

Abdel Rehman et al[117] (Saudi J Ophthalmol 2011) carried out a prospective randomized comparative study including 60 eyes of 48 patients with recurrent pterygia. The study included 36 males and 12 females of age ranged from 28 to 52 years. The recurrence rate was 2 eyes in group 1 (10%) (limbal stem cell transplantation + conjunctival autograft), 6 eyes in group 2 (30%) (AMT) and 4 eyes (20%) in group 3 (MMC + AMT). The rate of recurrence was significantly different between the three groups ($P < 0.001$). They concluded that limbal stem cell transplantation together with conjunctival autografting proved to be more effective in prevention of pterygium recurrence and in rapid restoration of normal epithelial morphology.

MATERIALS AND METHODS

SOURCE OF DATA:

It was a hospital based study of patients who were operated for Pterygium in which 50% patients underwent Pterygium excision with limbal stem cell transplantation and 50%patients underwent Pterygium excision with conjunctival autograft. All patients were inpatients of Department of Ophthalmology at B.L.D.E.U's Shri. B.M.Patil Medical College Hospital and Research Centre, Bijapur.

STUDY DURATION: Duration of this study was from October 2011 to February 2013.

STUDY DESIGN: Prospective randomized comparative hospital based study.

SAMPLE SIZE:

With 3% prevalence rate of pterygium[2], 95% confidence level and 5% margin of error, sample size for this study was 46, using the following statistical formula:-

$n = 4pq/ L^2$

STATISTICAL ANALYSIS:

- Diagrammatic presentation, Proportions, Mean ± Standard deviation, Fishers exact test, Wilcoxon matched pairs test, Mann Whitnall U test.

METHODOLOGY

Preoperative Evaluation

Patients admitted for Pterygium surgery during the study period were included in the study. The data was categorized into age, sex and occupation.

- Detailed history was taken regarding the duration of symptoms and treatment history.
- Visual acuity recording
- Slit lamp examination
- Refraction
- Anterior segment photography

After slit lamp examination, pterygium was graded on the basis of amount of encroachment of the pterygium on the cornea

Grade I: < 2mm from limbus

Grade II: 2-4mm from limbus

Grade III: >4mm from limbus

- Investigations like blood and urine examination, random blood sugar, HIV, HBsAg were done.
- Medical fitness for surgery will be taken if required. All patients will be admitted a day before surgery and local antibiotic drops will be started preoperatively. Surgery will be performed under peribulbar anaesthesia. Steroid- antibiotic drops was instilled post operatively for 4- 6 weeks.

Method of Randomization:

Patients selected for the particular procedure by giving serial numbers, patients with odd number will be subjected for Pterygium excision with conjunctival autograft and those with even number for Pterygium excision with limbal stem cell transplantation.

Following day of surgery, detailed slit lamp examination of the graft and post operative visual acuity was assessed. Other parameters like pain, edema and congestion etc. were studied in both procedures. Follow up was done on day 1, first week, 4th week, 3rd month to know any complications and recurrence after surgery.

INCLUSION CRITERIA:

Patients who came to hospital and got operated for primary Pterygium, during the study period with written informed consent.

EXCLUSION CRITERIA:

- Pregnant women.
- Those with predisposing conditions to corneal ulceration or poor wound healing such as immunocompromised patients, Sjogren's syndrome,atopic keratoconjuctivitis or herpetic keratitis.
- Patients with scleritis, rheumatoid arthritis and glaucoma.
- Recurrent Pterygium
- Those with history of previous intraocular surgery.
- Those without written informed consent.

Surgical steps:

1. Surgical procedure of simple excision with conjunctival autograft (Group A):

After peribulbar anaesthesia, surgical area is painted with 10% povidone iodine antiseptic solution. A wire speculum is placed. Superior rectus bridle suture is taken to stabilize the globe. After the excision of the pterygium, the size of the conjunctival defect created is measured with Castroviejo calipers. The globe is then rotated downwards to expose the superior bulbar conjunctiva. The dimensions of the intended conjunctival graft (adjacent to the limbus) are measured and marked using

calipers. Balanced salt solution is then injected subconjunctivally to elevate the conjunctiva to aid in the conjunctival dissection. The conjunctiva is then undermined using blunt dissection taking care not to include underlying Tenon's capsule in the final graft. The donor conjunctival graft should be as thin as possible so that post-operative healing will occur with less shrinkage. Minimum handling is done so as to avoid a buttonhole in the conjunctiva.

The graft is then oriented adjacent to the limbus in the recipient bed and secured with 8-0 vicryl sutures. The donor harvest site is left to epithelialize on its own, which usually occurs in due course of time.

2. Surgical procedure of simple excision with limbal stem cell transplantation (Group B):

After peribulbar block, the head of the pterygium is lifted from the underlying cornea and then dissection carried over the conjunctiva to free the body of pterygium. After the excision of the pterygium, the size of the conjunctival defect created is measured with Castroviejo calipers Superficial keratectomy is done to clean the cornea at the area covered by the head of pterygium and the area of bare sclera is measured. A superotemporal limbal conjunctival autograft incorporating a small portion of limbal stem cells, and measuring approximately 0.5-1 mm larger than the recipient bed, is harvested from the same eye. The graft was dissected towards the cornea with a number 15 scalpel blade or a crescent blade to include 0.5 mm of the superficial limbus. Dissection of the conjunctival autograft is done superotemporally from the fornix to the limbus. Care is taken not to include Tenon’s capsule. The graft is then transferred to the recipient bed and secured with 8-0 Vicryl sutures. The graft

is oriented such that harvested limbal stem cells are positioned over the limbus of the donor site. The host area is left with Tenon's capsule exposed

Post-operative treatment:

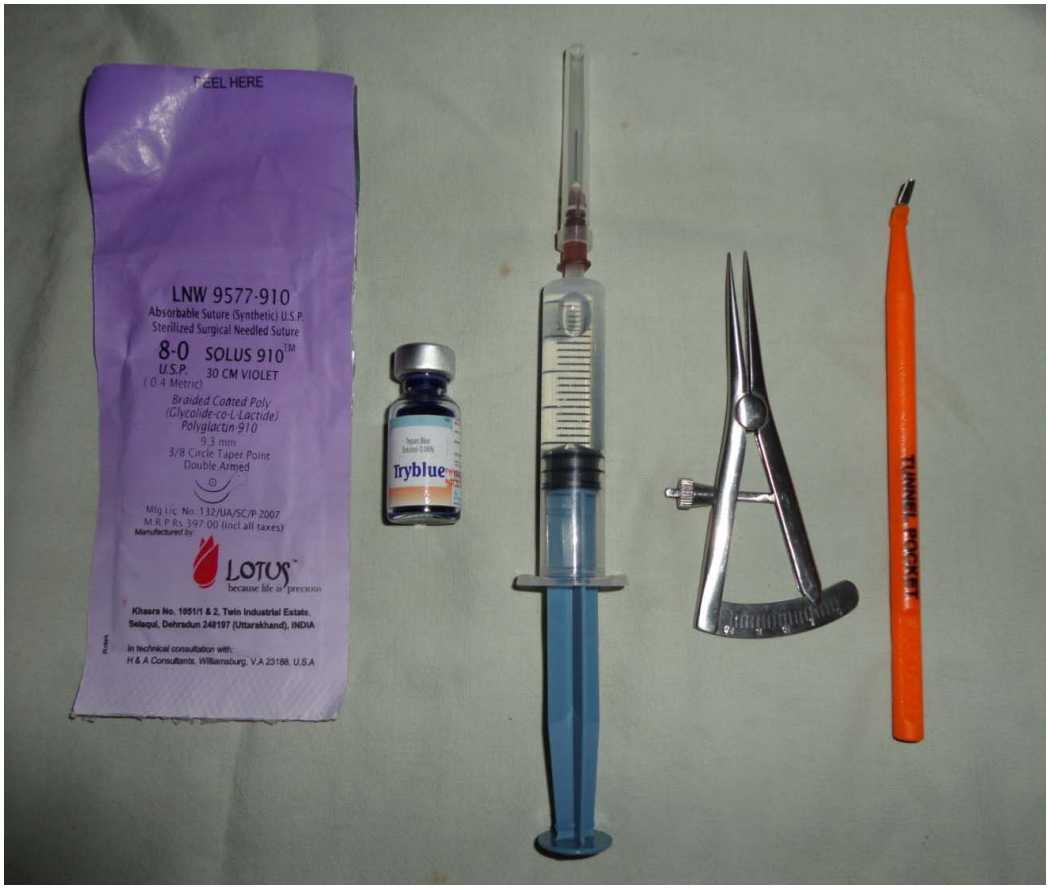
Postoperatively all patients in group A and group B were treated with combination of antibiotic and steroid eye drops, initially 6 times a day and then tapered over a period of four weeks. Lubricating eye drops were advised 4 times a day for 1 month.

Follow-up:

Patients were examined in the follow up visits as per the schedule given in the study proforma

Growth of any fibrovascular tissue past the limbus onto the clear cornea in the area of previous Pterygium constituted recurrence.

Figuare 1 : SURGICAL INSTRUMENT SET



SURGICAL STEPS IN CONJUNCTIVAL AUTOGRAFT

(GROUP A)

Figure 2

a) Pre-operative photograph of LE nasal pterygium

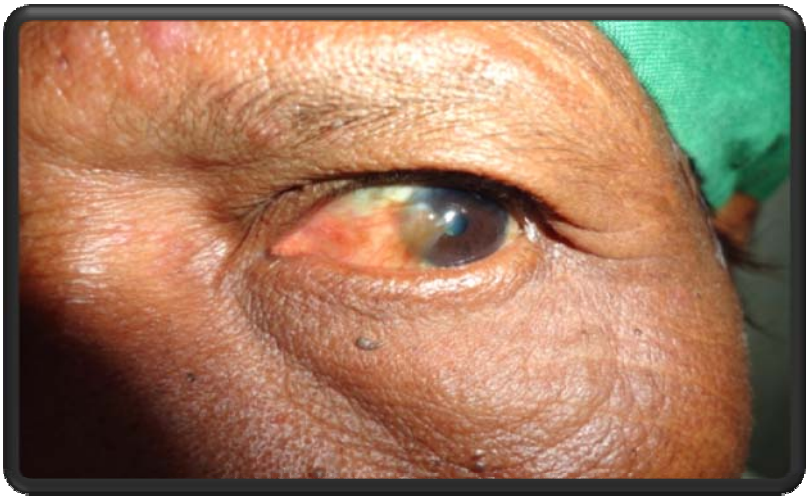


Figure 3

b) The head of the pterygium is lifted from the cornea and dissection is carried out to free the body of pterygium from the underlying conjunctiva

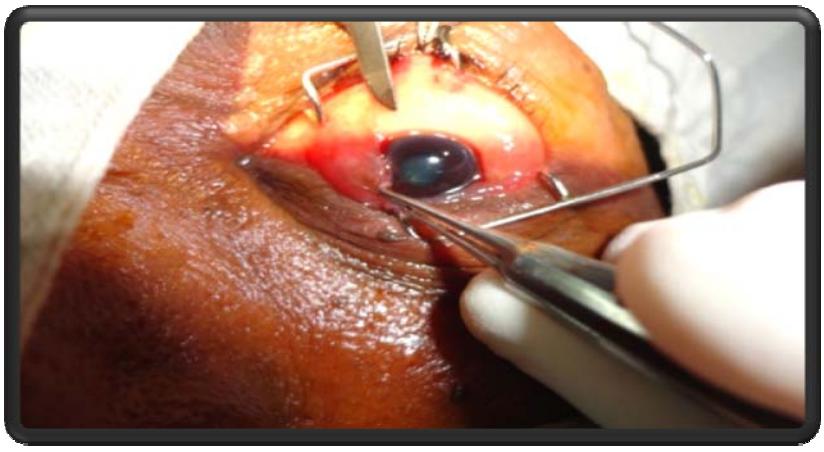


Figure 4

c) Graft is harvested from the donor site after precise measurement

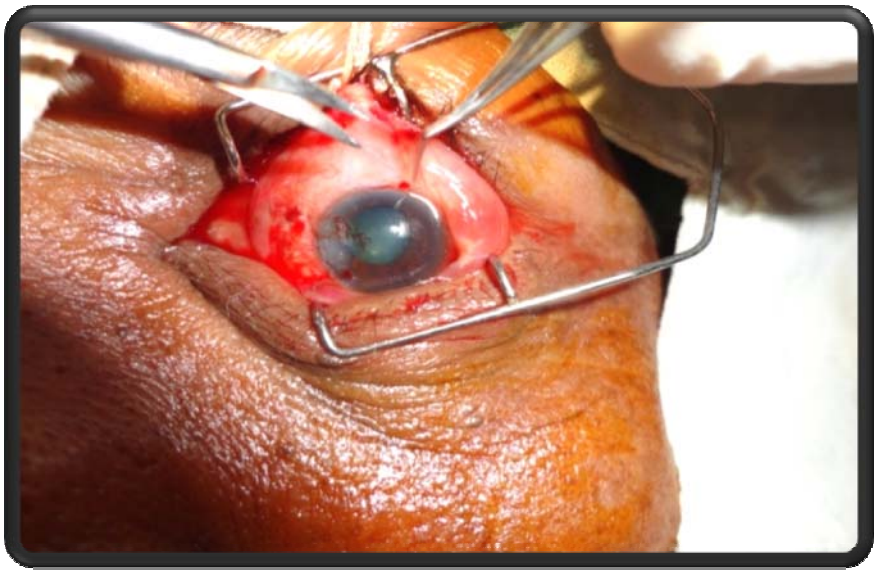
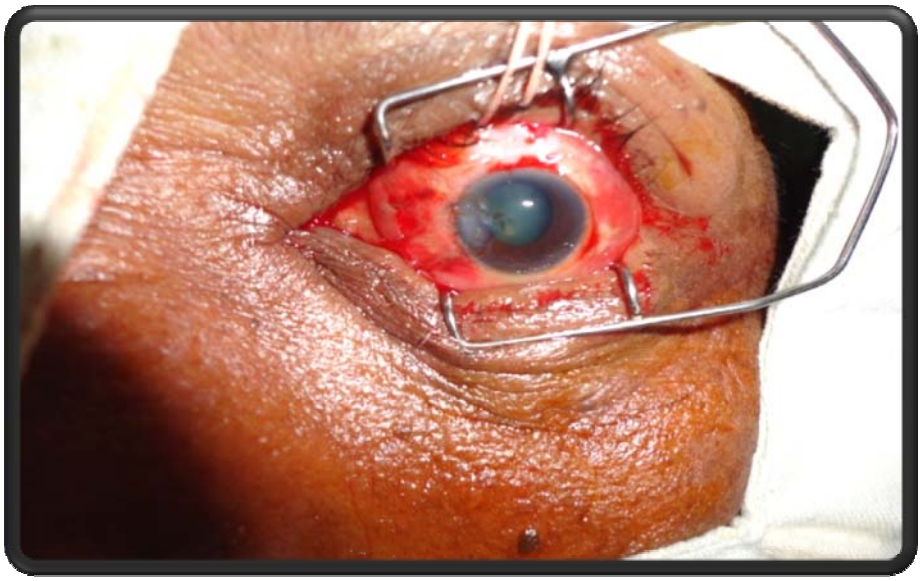


Figure 5

d) Graft is placed over the scleral bed and sutured with Vicryl 8-0 sutures.



SURGICAL STEPS IN CONJUNCTIVAL AUTOGRAFT WITH LIMBAL STEM CELL TRANSPLANTATION (GROUP B)

Figure 6

a) Pre-operative photograph of LE nasal pterygium

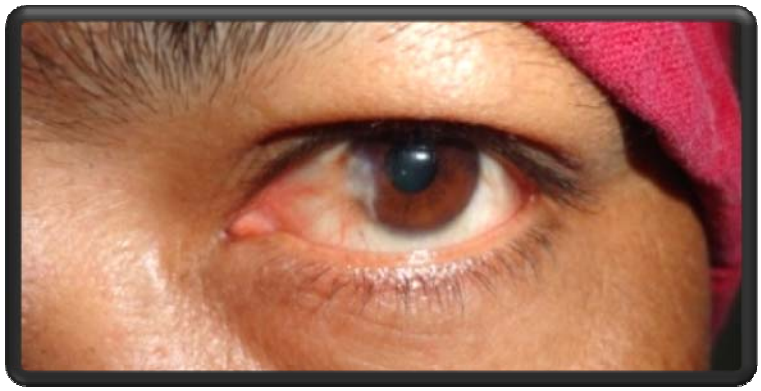


Figure 7

b) After the excision of pterygium, dimensions of bare sclera is measured by calipers.

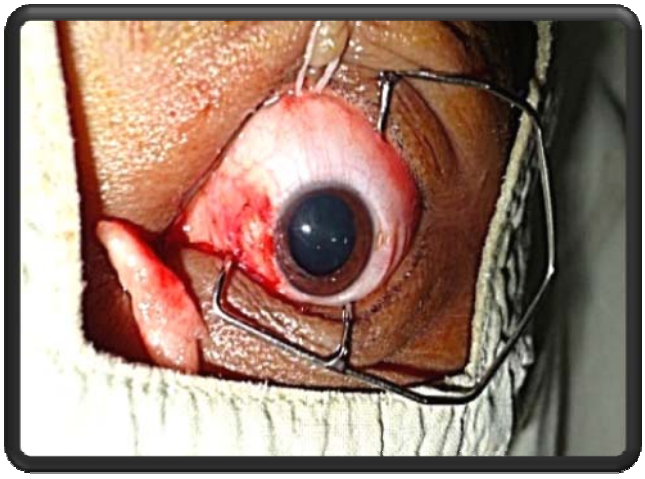


Figure 8

c) A superotemporal limbal conjunctival autograft including 0.5mm of superficial limbus is dissected out using crescent blade.

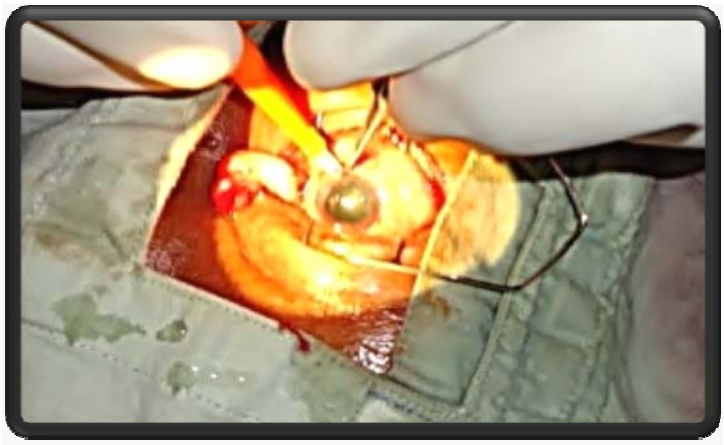


Figure 9

d) Graft is then slided over from donor site to recipient site

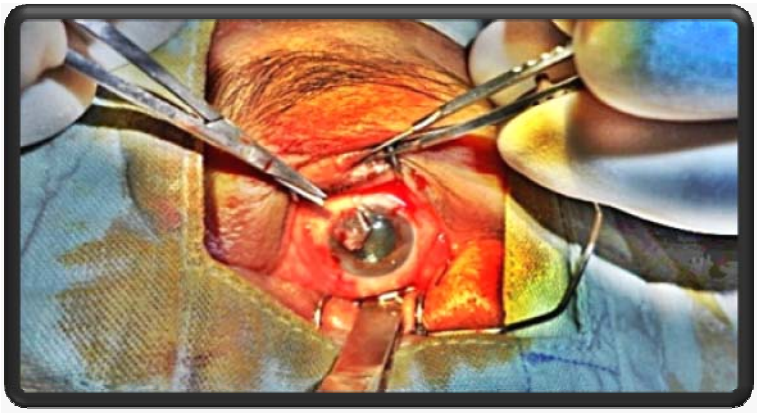
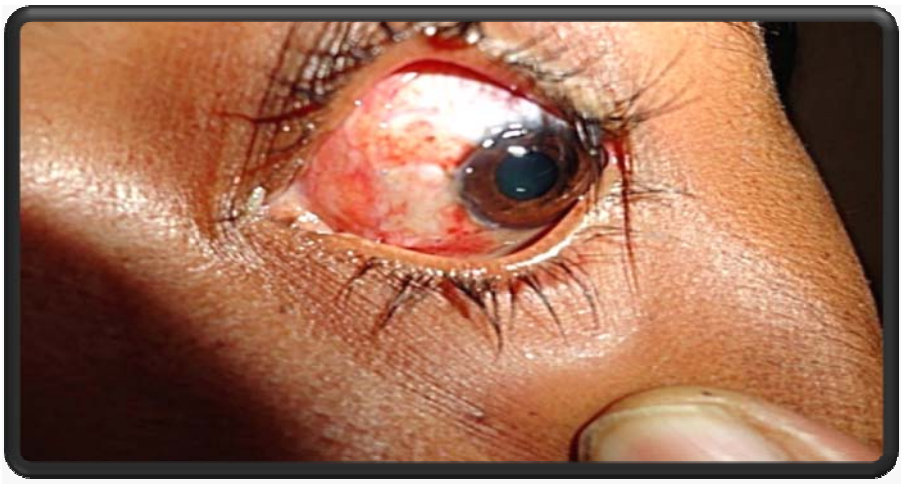


Figure 10

e) The graft is then secured to the host bed with vicryl 8-0 sutures in such a way that the harvested limbus stem cells lie on the limbus of donor site



OBSERVATIONS AND RESULTS

Table No. 1: Age wise distribution of the study population:

In the present study, 14 (30.43%) patients were in the age group of 31 to 40 years, and 12 (26.08%) patients in the age group of 41-50 years. The average age and standard deviation in group A and B were 43.26±14.70 and 41.565±11.63 years respectively.

Age in years	**Group A**	**Group B**	**Total**
21-30	5	6	11(23.91%)
31-40	9	5	14(30.43%)
41-50	4	8	12(26.08%)
51-60	1	2	03(6.52%)
61-70	3	2	05(10.86%)
71-80	1	0	01(2.17%)
Total	23	23	46
Mean±SD	43.26±14.70	41.565±11.63	42.42±13.165

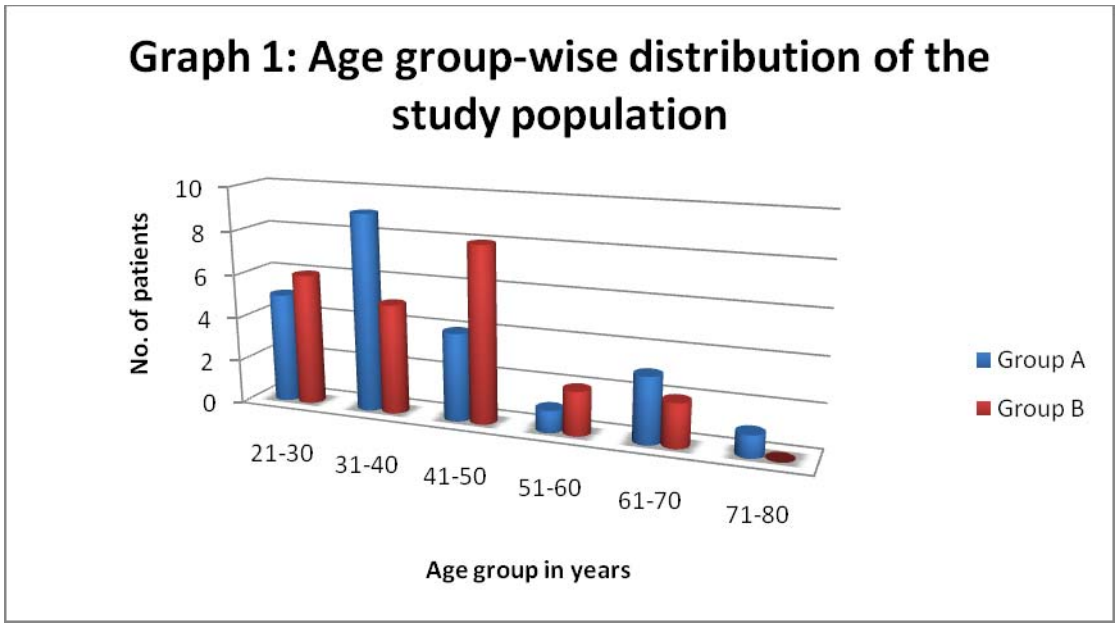

Graph 1: Age group-wise distribution of the study population
No. of patients
10
8
6
4
2
0
21-30
31-40
41-50
51-60
61-70
71-80
Age group in years
Group A
Group B

Table No. 2: Age and Sex wise distribution of the patients:

In the present study, 14 (30.43%) patients were in the age group of 31 to 40 years, and 12 (26.08%) patients in the age group of 41-50 years. The average age and standard deviation in group A and B were 43.26±14.70 and 41.565±11.63 years respectively. There was no statistically significant difference in age and sex distribution between group A and group B. Mean age was 42.42 years. Majority of them were females(69.56%).

Age in years	Group A (n=23)		Group B (n=23)		Total (n=46)	
	Male	Female	Male	Female	Male	Female
21-30	2	3	0	6	2	9
31-40	5	4	2	3	7	7
41-50	0	4	3	5	3	9
51-60	0	1	1	1	1	2
61-70	1	2	0	2	1	4
71-80	0	1	0	0	0	1
Total	8(34.78%)	15(65.21%)	6(26.08%)	17(73.91%)	14(30.43%)	32(69.56%)
Mean±SD	43.26±14.70		41.565±11.63		42.42±13.165	

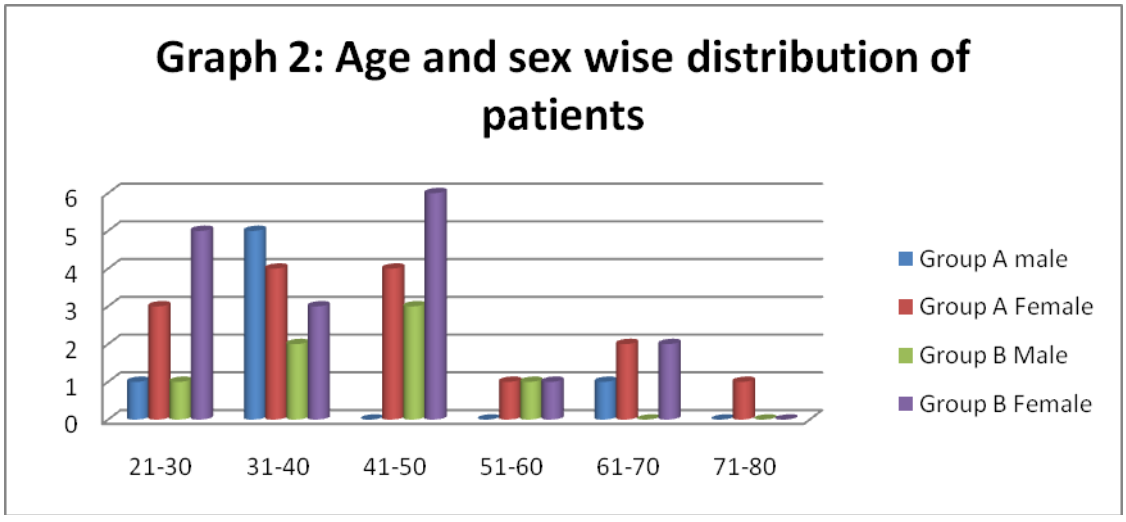


Table No. 3: Distribution of patients as per the nature of work

In this study, 56% were outdoor workers and 43.4% were indoor workers. Incidence of pterygium was higher in outdoor workers

Occupation	No. of patients(%) (n=46)
Outdoor	26(56.5%)
Indoor	20(43.4%)

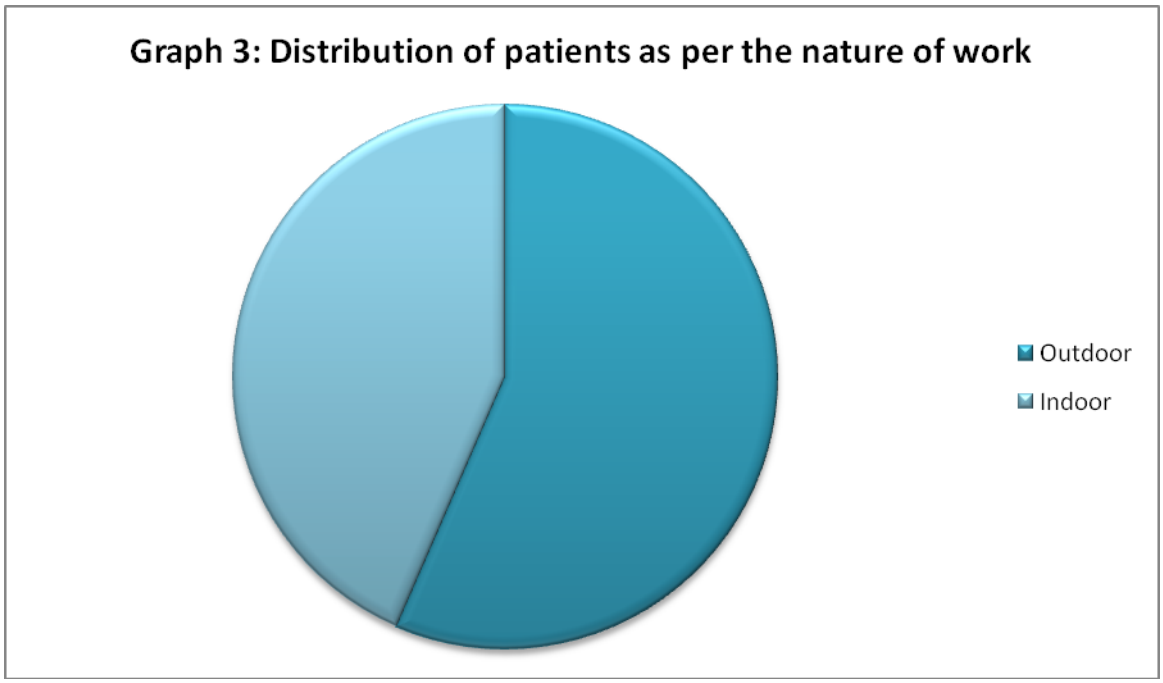


Table No. 4 : Sex- wise distribution of the patients as per the nature of work

Among 32 female patients, 12 of them were outdoor workers, 20 were indoor workers. All males were outdoor workers.

Occupation	Male	Female	Total
Outdoor	14	12	26
Indoor	0	20	20

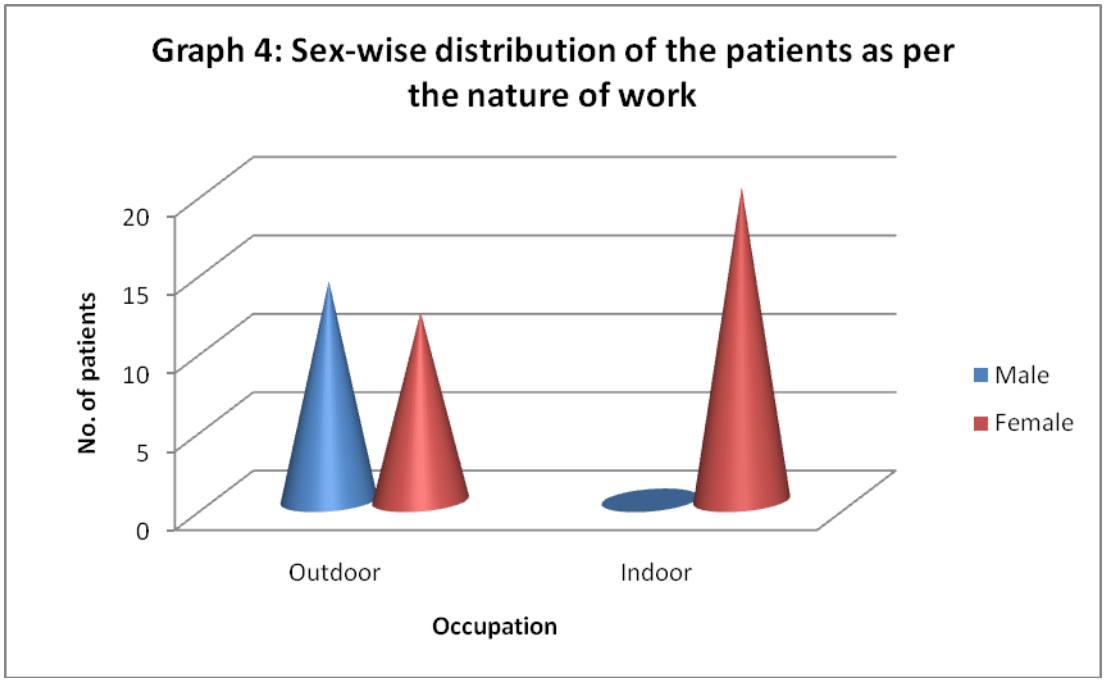


Table No. 5: Distribution of patients according to symptoms

Majority of the patients in the present study needed surgery for the cosmetic reason (26.08%). The next common complaint was foreign body sensation (15.21%)

Symptoms	**No. of patients n(%)**
Burning sensation	2(4.34%)
Cosmetic	12(26.08%)
Foreign body sensation	7(15.21%)
Foreign body sensation & redness	4(8.6%)
Foreign body sensation & watering	1(2.17%)
Pain	4(8.6%)
Pain & burning sensation	1(2.17%)
Pain & diminution of vision	1(2.17%)
Pain & foreign body sensation	5(10.86%)
Pain & redness	4(8.6%)
Pain & watering	2(4.34%)
Redness & burning	1(2.17%)
Redness & diminution of vision	2(4.34%)

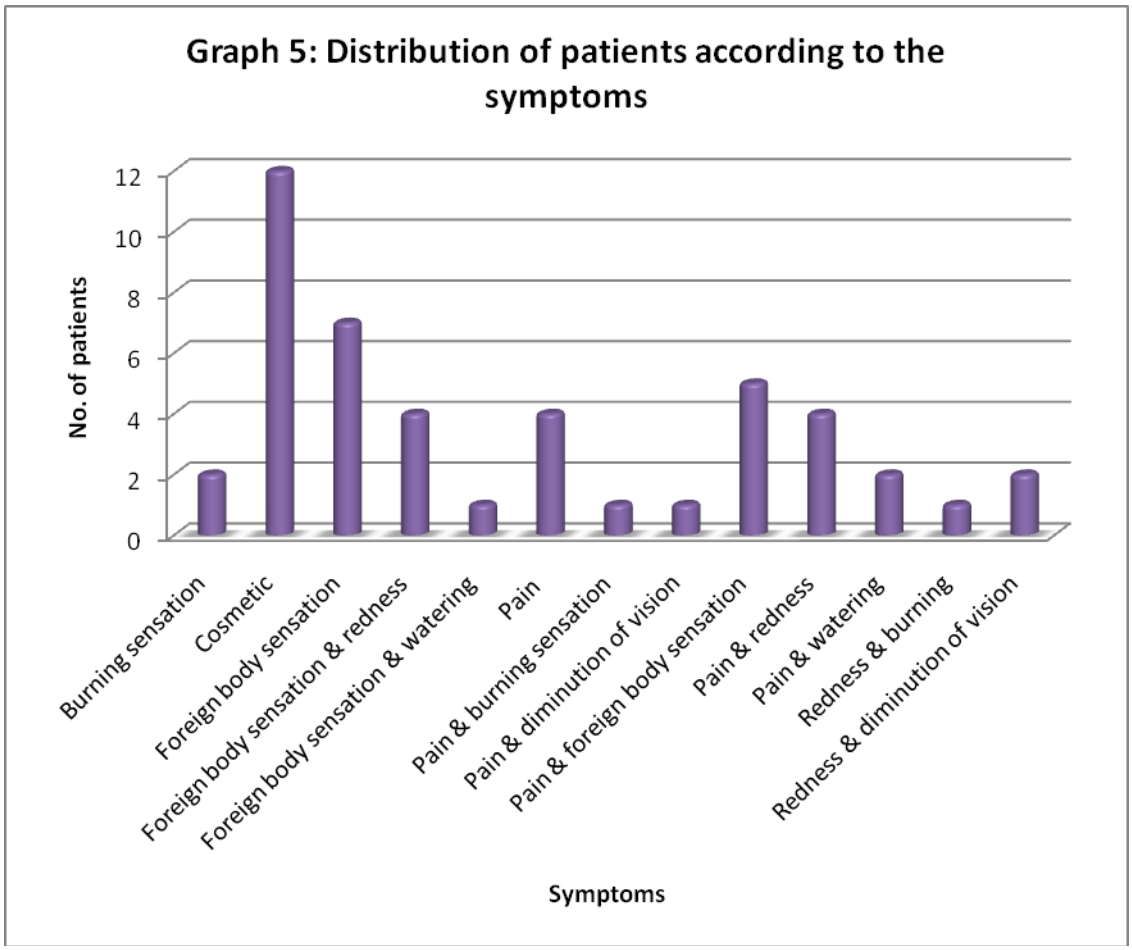

Graph 5: Distribution of patients according to the symptoms
No. of patients
12
10
8
6
4
2
0
Burning sensation
Cosmetic
Foreign body sensation
Foreign body sensation & redness
Foreign body sensation & watering
Pain
Pain & burning sensation
Pain & diminution of vision
Pain & foreign body sensation
Pain & redness
Pain & watering
Redness & burning
Redness & diminution of vision
Symptoms

Table No. 6: Distribution of patients as per the site of pterygium

The occurrence of pterygium was more on the nasal side. Among 46 patients, 45(97.82%) had nasal pterygium and only 1(2%) had temporal pterygium

Site of pterygium	**No. of patients (%)** **(n=46)**
Nasal	45
Temporal	01

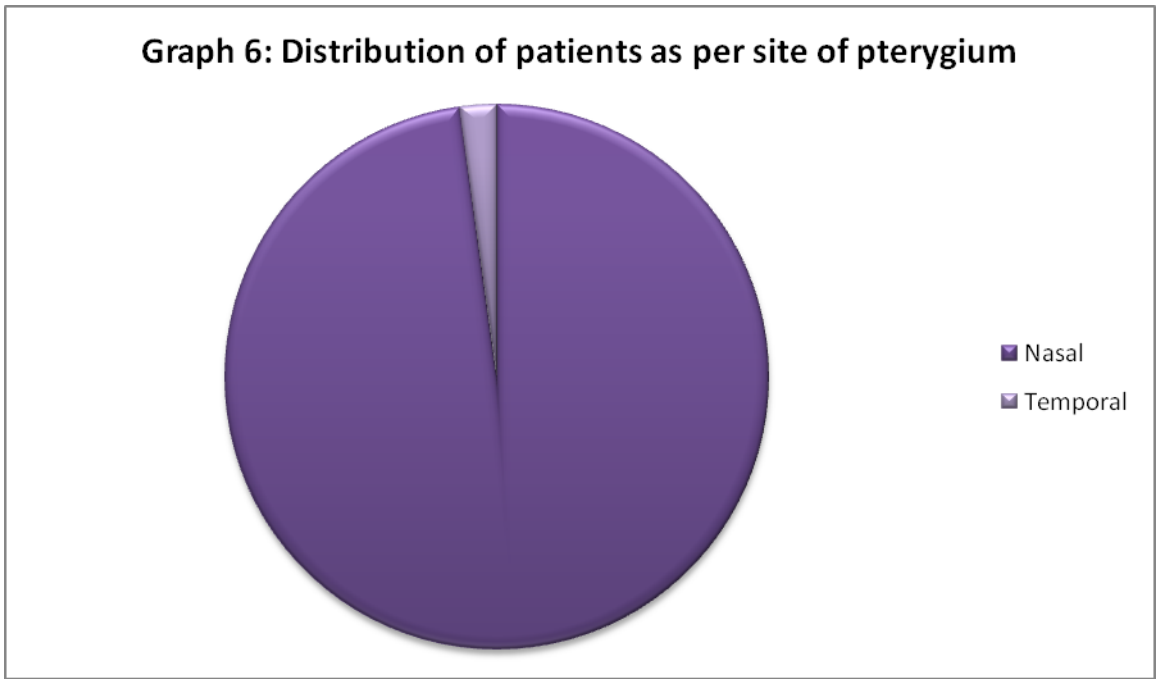


Table no. 7: Comparison of pre and post-operative visual acuity

Out of the 46 patients, majority of the patients had one line improvement of visual acuity in Snellen's chart. Few of them had 2 lines improvement.

VISUAL ACUITY		No. of patients n (%) Total=46
PRE-OP	**POST-OP**	
6/60	6/36	04(8.69%)
6/60	6/24	02(4.34%)
6/36	6/24	01(2.17%)
6/36	6/18	01(2.17%)
6/18	6/12	01(2.17%)
6/12	6/9	05(10.86%)
6/12	6/6	03(6.5%)
6/9	6/6	10(21.7%)
6/6p	6/6	19(41.3%)

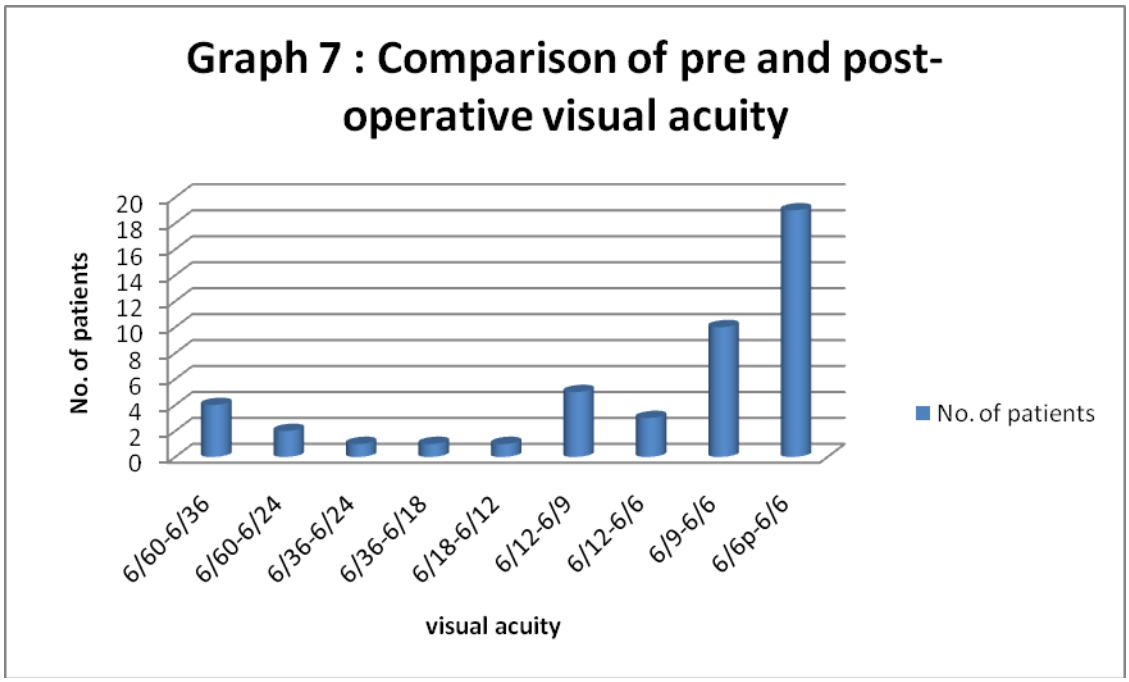


Table No. 8: Comparison of grades of Pterygium in group A and B

Out of 46 patients, 23 patients belonged to grade II and 13 patients to grade III pterygium.

Grade	Group A	Group B	Total
I	04(17.39%)	06(26.08%)	10(21.73%)
II	10(43.47%)	13(56.52%)	23(50%)
III	09(39.13%)	04(17.39%)	13(28.26%)
Total	23	23	46

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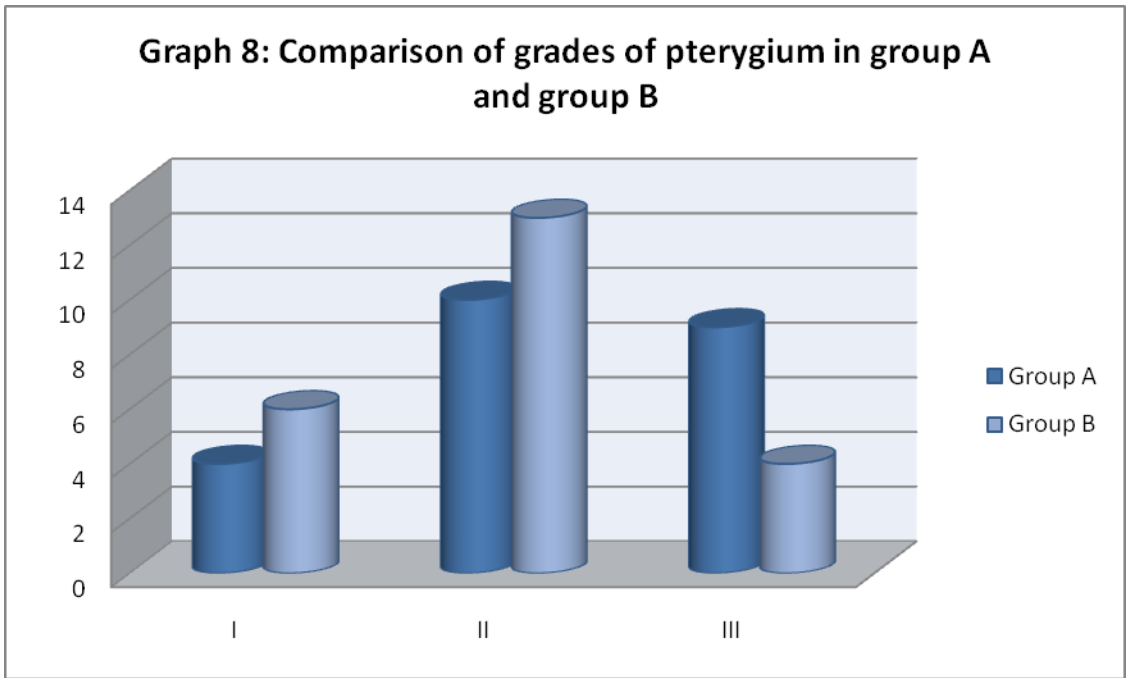


Table no. 9: Comparison of pre-operative and post-operative astigmatism in group A

All patients in group A had with-the rule astigmatism. The average preoperative astigmatism was 0.652 and average postoperative astigmatism was 0.3587. By applying Wilcoxon matched pairs test, the difference in the pre and postoperative astigmatism was found to be highly significant ($p < 0.0001$).

Astigmatism in Diopters	**Group A**	
	Pre-operative Number of patients (%)	**Post-operative Number of patients (%)**
0-0.5	06(26.08%)	13(56.52%)

0.5-1	16(69.56%)	04(17.39%)
Mean±SD (SE)	0.652±0.257 (0.058)	0.3587±0.27(0.056)

p< 0.0001 Highly significant

Table no. 10: Comparison of pre-operative and post-operative astigmatism in group B

All patients in group B had with-the rule astigmatism. By applying Wilcoxon matched pairs test, the difference in the standard error between pre and post operative patients was highly significant (p< 0.0001).

Astigmatism in Diopters	**Group B**	
	Pre-operative Number of patients (%)	**Post-operative Number of patients (%)**
0-0.5	11(47.82%)	13(56.52%)
0.5-1	11(47.82%)	0

Mean±SD	0.576±0.276(0.057)	0.1739±0.175(0.036)

p< 0.0001 Highly significant

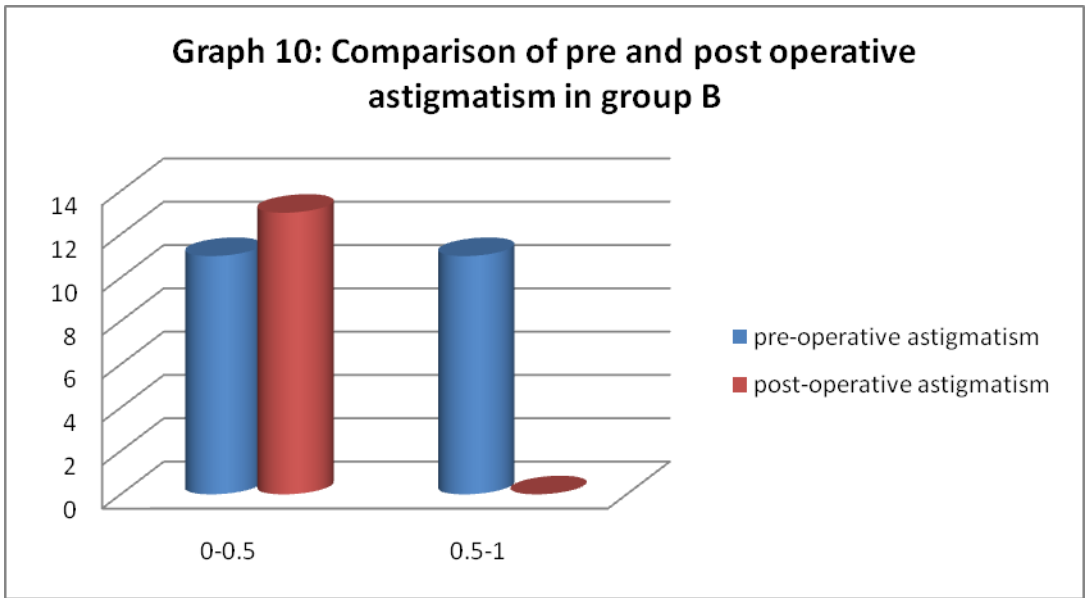


Table No. 11: Average change in amount of post-operative astigmatism after surgery

In the present study, all patients had with-the rule astigmatism ranging from 0.25 to 1 D. Average post operative astigmatism in Group A was 0.3586 and in group B was 0.1739. Thus there is a significant difference in astigmatism in both the groups. By applying Mann Whitney U test, the difference between the means of the two groups was found to be highly significant (U= 67.000 p< 0.0001).

	Group A	Group B
Mean±SD (SE)	0.3586±0.27 (0.056)	0.1739±0.156 (0.036)

p< 0.0001 highly significant

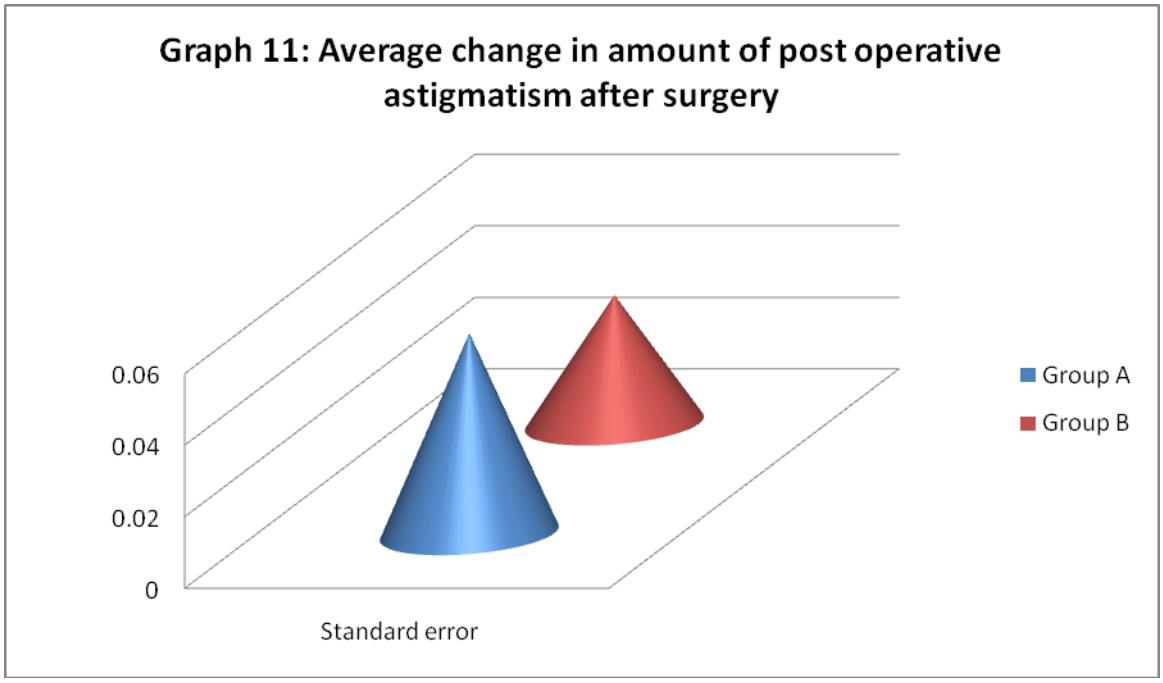

Graph 11: Average change in amount of post operative astigmatism after surgery
0.06
0.04
0.02
0
Standard error
Group A
Group B

Table No 12: Distribution of patients as per the signs & complications at first week follow up

At the first week follow-up after sugery, conjunctival hyperaemia(26.08%) was the most frequent sign encountered in group A patients, whereas in group B few sutures had given away at first week follow-up(13.04%).

	Group A n(%)	Group B n(%)
Graft oedema+ Conjunctival hyperaemia	1(4.34%)	-
Chemosis + Subconjunctival haemorrhage+graft oedema	2(8.6%)	-
Conjunctival hyperaemia	6(26.08%)	2(8.6%)
Few Sutures given away	2(8.6%)	3(13.04%)
Subconjunctival haemorrhage	1(4.34%)	2(8.6%)
Graft oedema	-	2(8.6%)

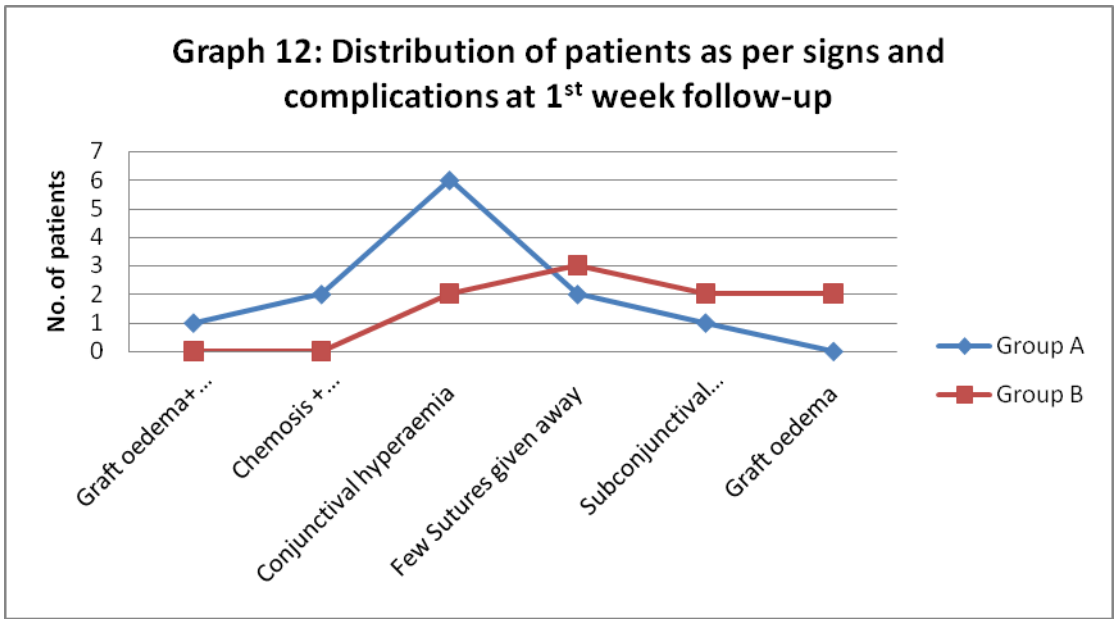


Table no.13: Distribution of patients as per the signs & complications at 1 month follow up

At one month follow-up, all the signs previously noted had resolved, but 2(8.69%) patients in group A showed signs of recurrence. There was no recurrence in group B.

	Group A	Group B
Graft oedema+ Conjunctival hyperaemia	Resolved	Resolved
Chemosis + Subconjunctival haemorrhage+graft oedema	Resolved	Resolved
Conjunctival hyperaemia	Resolved	Resolved
Few Sutures given away	Resolved	Resolved
Subconjunctival haemorrhage	Resolved	Resolved
Graft oedema	Resolved	Resolved
Recurrence	2(8.69%)	0

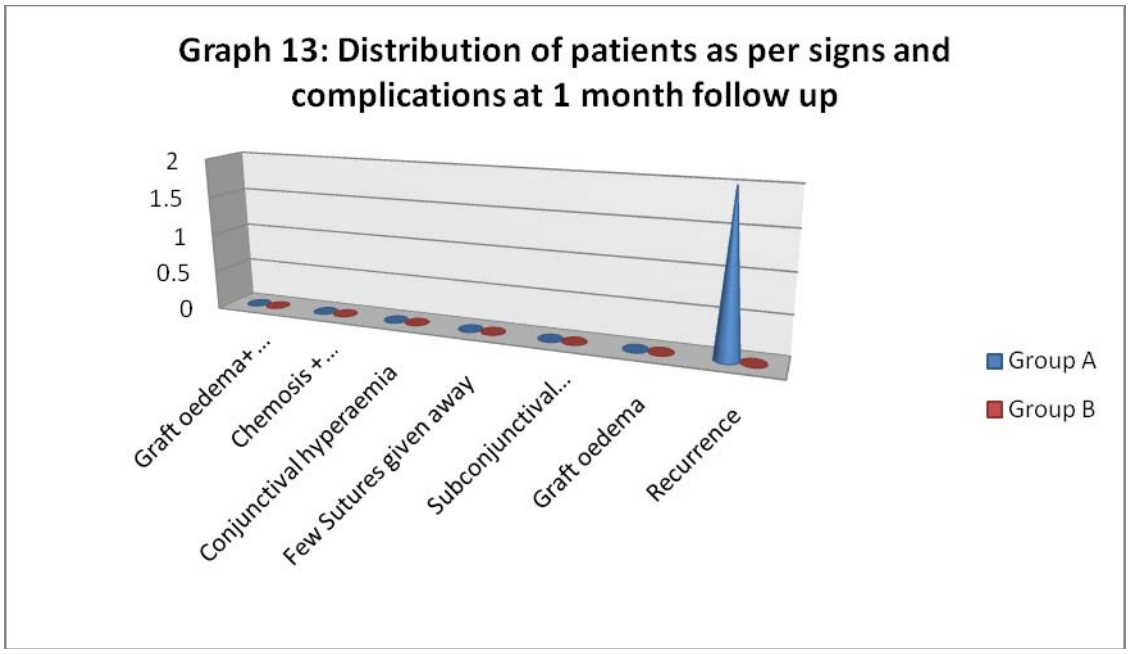


Table no. 14: Distribution of patients as per the complications at 3 months follow up

At 3 months post operative follow up, 1more patient in group A had recurrence.

	Group A	Group B
Recurrence	1	0

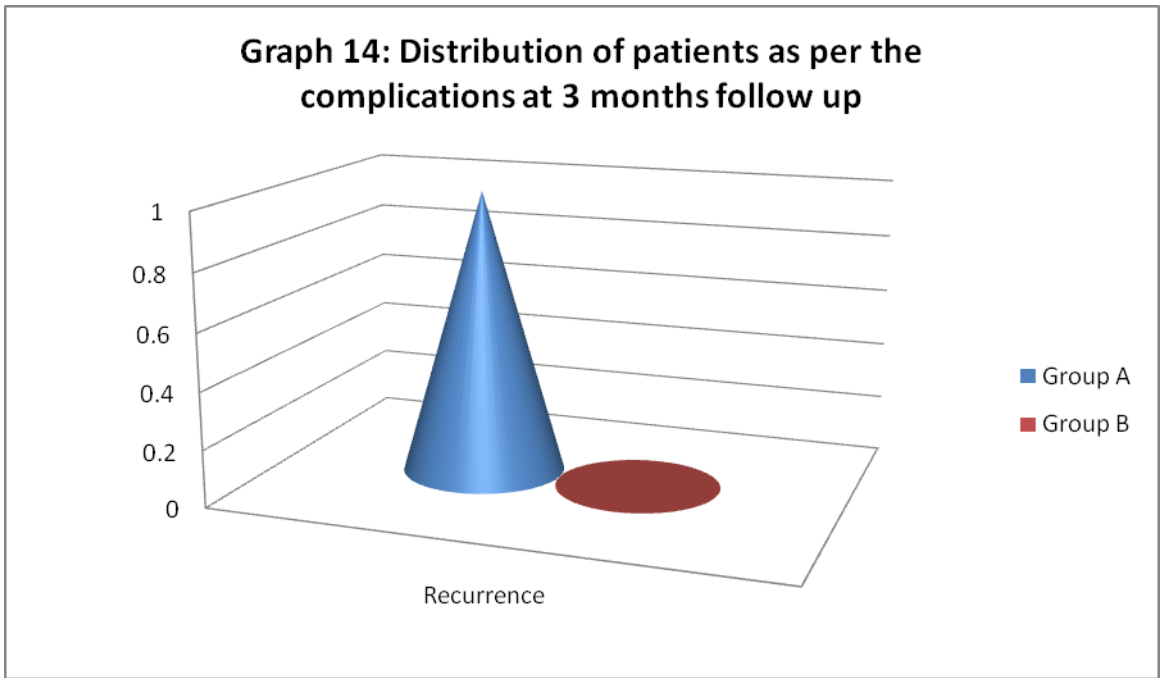
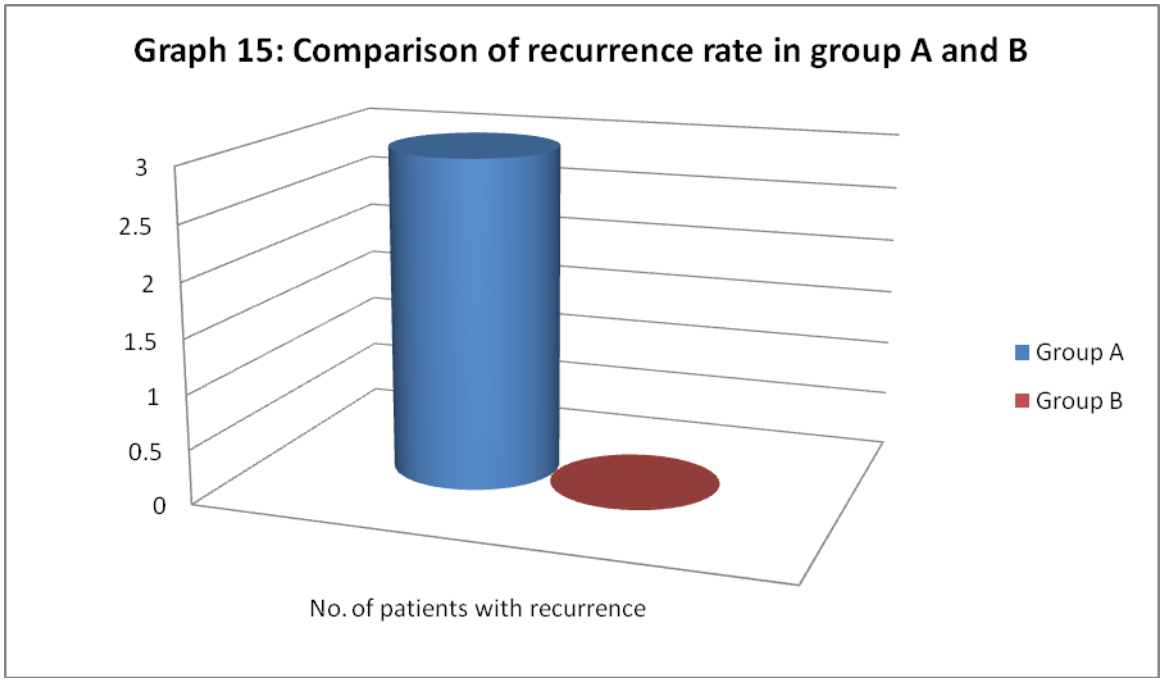


Table No. 15: Comparison of recurrence rate in group A and group B

In the present study, recurrence was seen in 3 patients in Group A and patients in Group B did not show recurrence. By applying Fishers exact test, the result was not statistically significant (p=0.233).

Groups	Group A (n=23)	Group B (n=23)	p value
No. of patients with recurrence(%)	03(13.04%)	0	0.23



GROUP A

Figure 11

CASE NO. 45

PRE-OPERATIVE PHOTOGRAPH

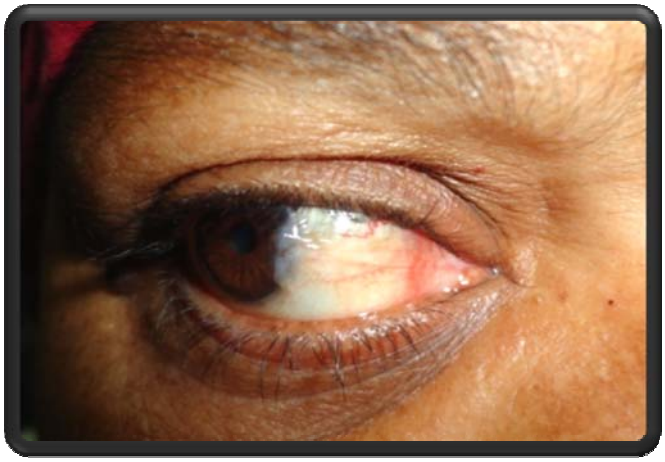


Figure 12

POST OPERATIVE PHOTOGRAPH AT 1 WEEK

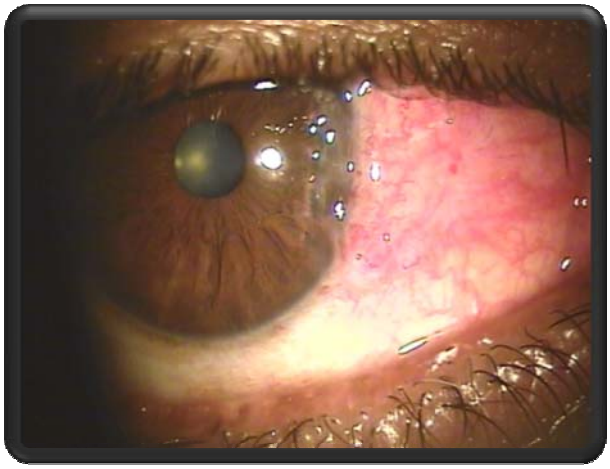


Figure 13

POST OPERATIVE PHOTOGRAPH AT 3 MONTHS

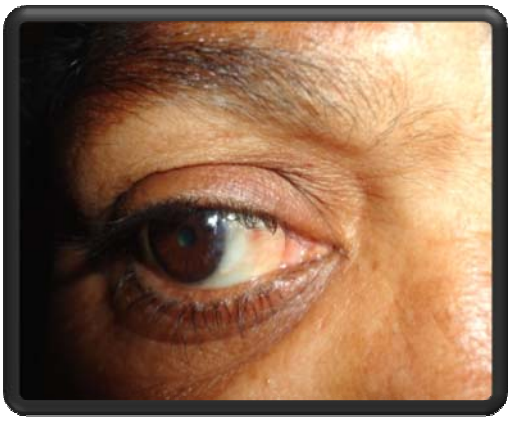


Figure 14

CASE NO. 39:

PRE-OPERATIVE PHOTOGRAPH

Figure 15

POST OPERATIVE 1 WEEK FOLLOWUP

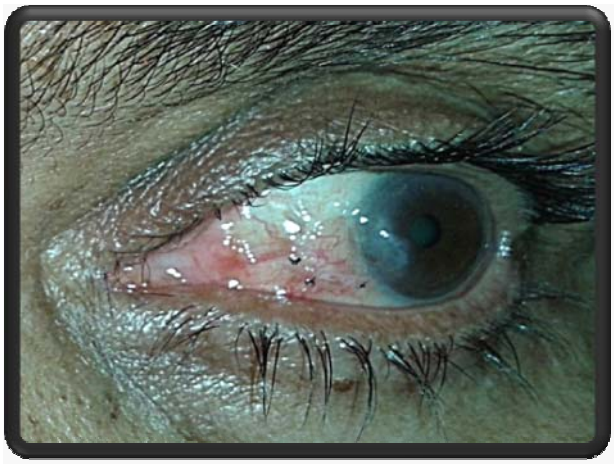


Figure 16

POST OPERATIVE FOLLOWUP AT 3 MONTHS

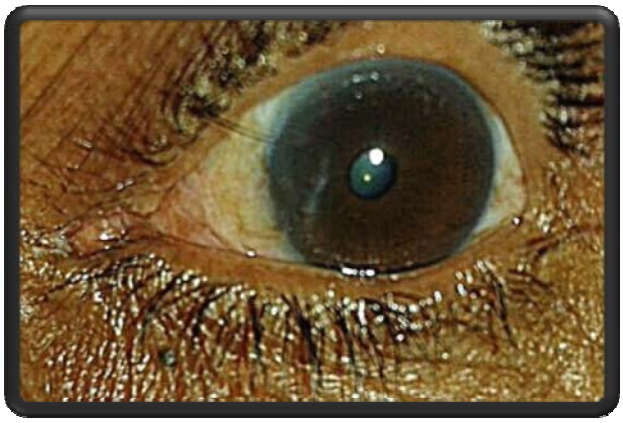


Figure 17

CASE NO. 26

PRE-OPERATIVE PHOTOGRAPH

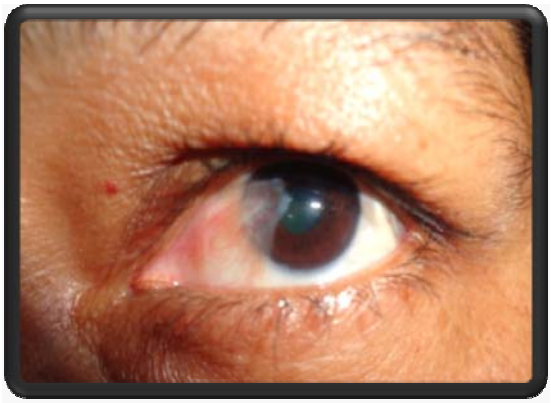


Figure 18

POST OPERATIVE PHOTOGRAPH

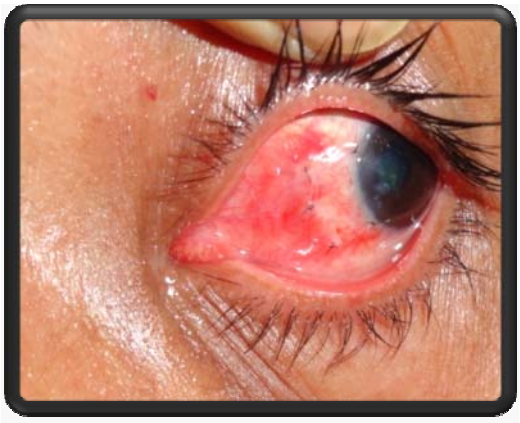
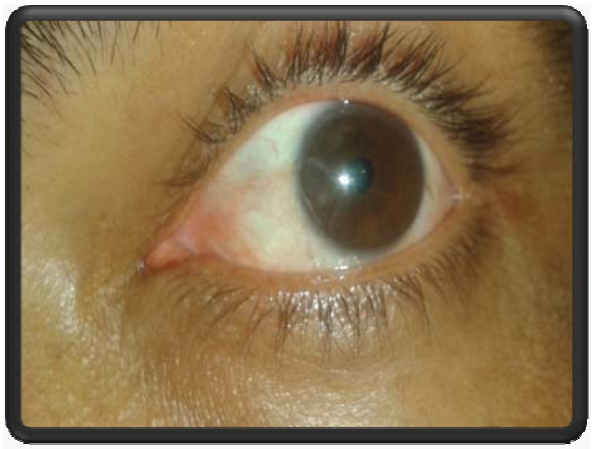


Figure 19

POST-OPERATIVE PHOTOGRAPH AT 3 MONTHS



GROUP B

Figure 20

CASE NO. 38

PRE-OPERATIVE PHOTOGRAPH

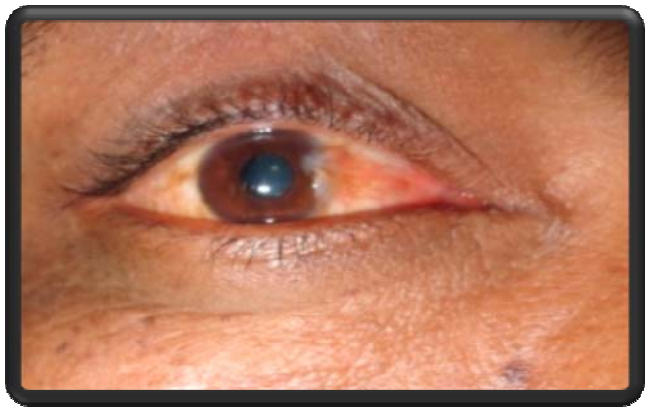


Figure 21

POST OPERATIVE 1 WEEK FOLLOWUP

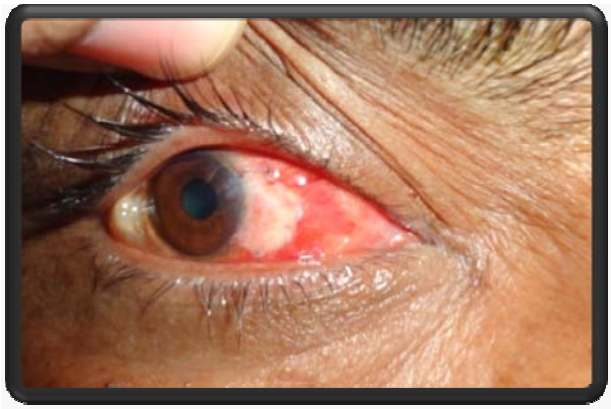


Figure 22

POST OPERATIVE 3 MONTHS FOLLOWUP

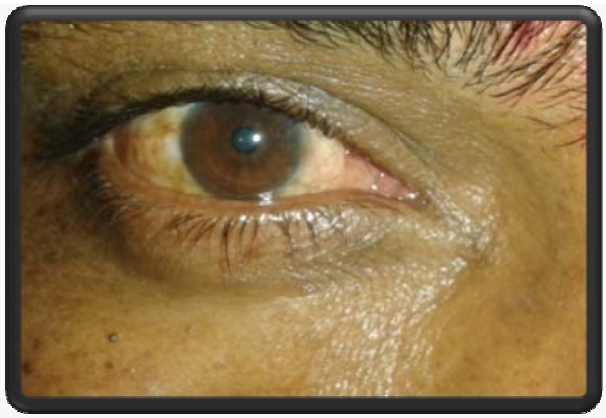


Figure 23

CASE NO. 41

PRE-OPERATIVE PHOTOGRAPH

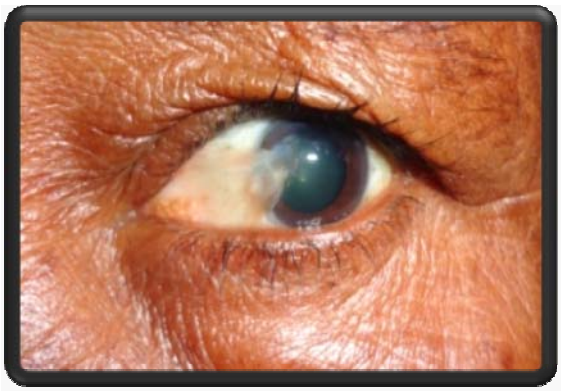


Figure 24

POST-OPERATIVE PHOTOGRAPH AT 1 WEEK

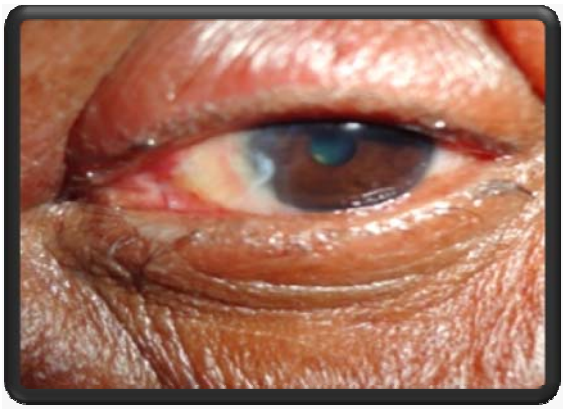
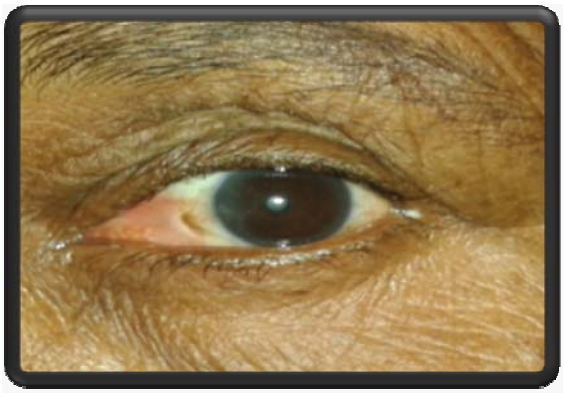


Figure 25

POST-OPERATIVE PHOTOGRAPH AT 3 MONTHS



POST-OPERATIVE PHOTOGRAPH OF THE DONOR SITE SHOWING RE-EPITHELIASATION

Figure 26

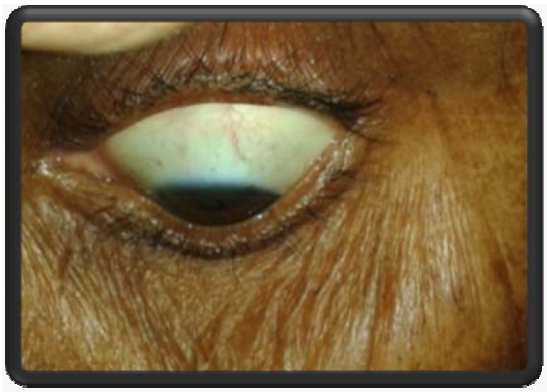


Figure 27

CASE NO. 20

PRE-OPERATIVE PHOTOGRAPH

Figure 28

POST-OPERATIVE PHOTOGRAPH AT 1 WEEK

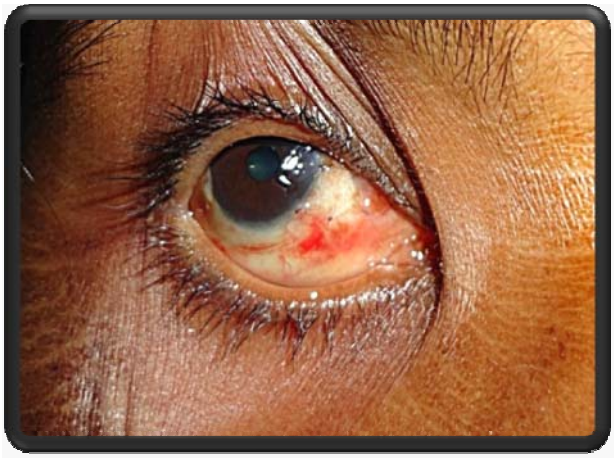
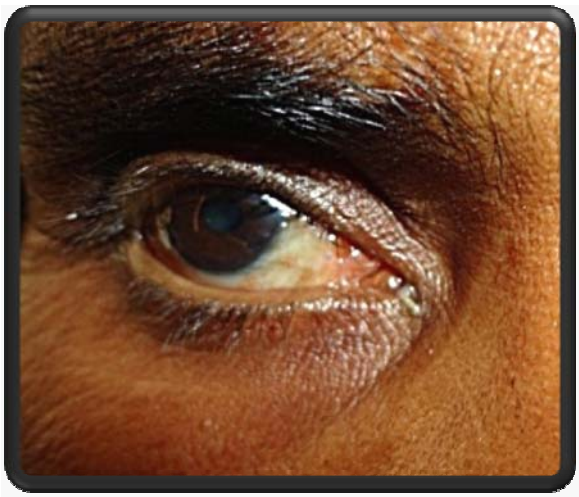


Figure 29

POST-OPERATIVE PHOTOGRAPH AT 3 MONTHS



DISCUSSION

Pterygium is the most common ocular surface disorder characterized by conjunctivalisation of the cornea due to localized ultraviolet induced damage to the limbal stem cells[2]. Surgical treatment of pterygium is directed at excision, prevention of recurrence, and restoration of ocular surface integrity. A myriad of techniques, some combined with others, have been described for achieving these goals. The main complication of these procedures has been the recurrence, which has been estimated as high as 30%-70%.[9]

In this study, 46 patients were treated for primary progressive pterygium. 23 patients underwent pterygium excision with conjunctival autograft and 23 patients underwent pterygium excision with limbal stem cell transplantation.

AGE:

In the present study, 14 (30.43%) patients were in the age group of 31 to 40 years, and 12 (26.08%) patients in the age group of 41-50 years. The mean age was 42.42 years. The average age in group A and B were 43.26 and 41.56 years respectively. This is in close concordance with the findings of Michele Gerundo[26] who reported the range of incidence of age between 30- 56 years. Herbert E. Kaufman et al[118] in his book "The Cornea" had also shown that actively growing pterygia typically occur in the young age group i.e. 25-40 years. Another study by Shrinivas et al[112], the mean age was 42.7±14.5 years.

SEX:

Pterygium is more often seen in males than females. Certain studies report an equal occurrence of pterygia in males and females. In a study done by Pandey et al[119], pterygium was predominantly found in males. However, in the present study it was found to be more in female population. This finding is consistent with reports from two other studies conducted by Peng Lu et al and Liu et al in China.[120,121] Sharma et al also found female preponderance in their study.[122] In the present study, majority of them were females(69.56%).Though the literature documents male preponderance, our study showed female preponderance in both the groups, which may be due to the fact that quite majority of patients come with cosmetic disfigurement and treatment. Also, as most of the women are exposed more to 'chullah' smoke, it may point towards one of the etiological factors in development of pterygium. Thus it is possible that the reported differences in prevalence rates for males and females reflect different exposure rates to environmental risk factors.

OCCUPATION:

The incidence of pterygium is high in outdoor workers. This is well correlated with our study, in which 56.5% were outdoor workers. H.Taylor et al, Mc Reynolds et al, and Moran et al have shown strong association between outdoor work related environmental factors like exposure to UV radiation, heat, dust and incidence of pterygium.[2,3]

Remaining 43.4% patients doing indoor activities also showed pterygium, probably indicating multiple etiopathogenetic factors like genetic predisposition/ heredity playing role in the formation of pterygium.

PRESENTING SYMPTOMS:

Majority of the patients in this study had a complaint about growth on the inner side of the eye and they complained about cosmetic disfigurement caused by this growth. Some patients had foreign body sensation, redness and watering either as a single complaint each or associated with the growth. Only few patients had complaints of diminution of vision which on examination was found to be due to pterygium, as it produces astigmatism. No patients came with diplopia. These findings correlates well with the views of majority of authors, that pterygium does not produce many symptoms especially in the early stage and majority of the patients are either worried about the growth and consulted the doctor for cosmetic reason, but later on when it encroaches the pupillary area, it produces marked diminution of vision[1]. Generally pterygium excision is indicated if the visual axis is threatened or if the pterygium causes extreme irritation.[53] Diminution of vision in early stages can be attributed to astigmatism produced by causing stretch over the cornea and in the later stages due to covering of pupillary area and corneal opacity at the head of pterygium. Pull of the pterygium over cornea causes flattening of the corneal curvature in the horizontal meridian, demonstrated by Ponico E. Carreras and Bedrossian, Robert M[123] also reported that marked changes in refractive status and corneal curvature may be produced by a pterygium before it enters the optical zone of cornea and removal of pterygium would result in change in corneal curvature in about 45% of the individual.

SITE OF PTERYGIUM:

In the present study, 97.82% cases pterygium was on the nasal side and 2% cases had it on the temporal side. Higher evidence of pterygium on nasal side was attributed due to flow of tears towards medial canthus carrying with it sand and dust particles. Possibility of less exposure of conjunctiva due to greater amount of bowing

of outer 2/3rd of the upper lid could explain presentation of the pterygium more commonly on nasal side.

Srinivas K Rao[112] in a study on 51 patients, found that pterygium was nasal in 46 (86.8%) eyes, temporal in 4 (7.5%) eyes and both nasal and temporal in 3 (5.7%) eyes. 97.8% of the pterygia in this study were nasal which co-relates well with the study done by Srinivas et al.

Doloezalovo[124] in his study on 1388 patients found only 1 case of unilateral temporal pterygium.

GRADE OF PTERYGIUM:

In this study it was observed that 21.7% belonged to grade I, 50% to grade II and 28.26% to grade III. In a study done by Sharma et al[122], 76% patients had grade II pterygium. Mohamad AE[89] et al in his study of 42 eyes with pterygium, found 59.52% of grade II and 33.33% of grade III. Patients usually present with grade II and grade III pterygium as it leads to cosmetic blemish and visual disturbance due to astigmatism.

ASTIGMATISM:

Pterygium induces astigmatism due to flattening of the cornea horizontally leading to with-the rule astigmatism. This being the most common type, observed in all patients. This is supported by studies done by Maheshwari et al, Lindsay RG et al, Avisar et al.[125,126,127] Maheshwari et al found that the preoperative refractive cylinder in 36 eyes with primary pterygium, decreased from 4.60±2D to 2.20±2.04D (p=0.00001) after excision of pterygium. They concluded that pterygium usually causes with-the rule astigmatism which is reversible to some extent after excision. In our study, the average measurement of astigmatism preoperatively was 0.652±0.257

D and 0.576±0.276D in group A and B respectively which reduced to 0.3587±0.27D and 0.1739±0.175D in group A and B respectively($p<0.0001$). In all 46 patients irrespective of the surgical technique, preoperative astigmatism found to be reduced significantly after the excision of pterygium.

COMPLICATIONS:

In the present study, 23 patients in group A underwent pterygium excision with conjunctival autograft, and 23 patients in group B underwent pterygium excision with limbal stem cell transplantation. No major intra-operative and post-operative complications were noted in both the groups.

At the first week follow up, graft oedema and subconjunctival haemorrhage were seen in 4.34% each of patients in group A which resolved in the subsequent visits. In group B, 2 patients(8.6%) had graft oedema and 2 patients had subconjunctival haemorrhage. These subsequently resolved with instillation of antibiotic steroid eye drops. The incidence of graft oedema is less in the present study because of the minimal handling of the graft during surgery. Starck et al **(47)** in their study have pointed out towards the possibility of graft edema in early post operative period due to limbal – fornix disorientation of the graft. However, in our study, limbal– fornix disorientation did not occur in any eye.

Few sutures had given way in 2(8.6%)in group A and 2(8.6%) in group B because of loosening of knots, however these did not not pose any problem.

At Subsequent follow up, recurrence was seen in 03(6.52%) patients in group A and no recurrence was seen in group B. These patients were followed up subsequently every 3 months and it was not intervened surgically if the recurrent pterygium was stationery and asymptomatic.

No complications like graft retraction, graft loss or dehiscence, corneoscleral dellen, tenon granuloma, epithelial cysts were noted in the present study and none of the patients developed any donor site complications. Serious complications such as pyogenic granuloma, symblepharon formation, scleral melt or scleral avascularity were not encountered in any of the patients eye throughout the followup period in both the groups.

All patients were followed up for a minimum period of 3 months and both the procedures seemed to be relatively free from severe complications, and resulted in satisfactory cosmetic appearance.

RECURRENCE:

Despite the various surgical procedures that have been described for the treatment of pterygium, recurrence remains a significant problem after surgical excision. 23 eyes of 23 patients who underwent pterygium excision with conjunctival autograft showed a recurrence rate of 6.52%.

Kenyon et al.[11] (1985) reported 3 recurrences in 57 eyes (5.3 %) with advanced and recurrent pterygia treated by conjunctival autografting after a mean follow-up of 24 months. No recurrences were observed in the 16 primary pterygia and in 41 recurrent pterygia .

In a study by Chen PP et al[128], a recurrence rate of 39% in 23 eyes was reported after mean follow up of 13.5 months

In the study by Bruce Allan et al[88], the recurrence rate with conjunctival autograft in 93 eyes was 6.5%

In the study by P. Riordan Eva et al[108], a recurrence rate of 14% was found in 15 eyes.

Since the report by Kenyon et al[11] of low recurrence associated with conjunctival autografting after pterygium excision, the method became one of the procedures of choice for the surgical management of pterygium. However, prospective, randomized studies of conjunctival autografting after pterygium have shown higher recurrence rates (16%–39%) in high-risk populations.

Serial no.	Authors	Recurrence rate with conjunctival autograft(%)
1	Kenyon et al	5.3%
2	Bruce Allan et al	6.5%
3	P. Riordan Eva et al	14%
4	Chen PP et al	39%
5	Present study	6.52%

.

The group B patients underwent pterygium excision with limbal stem cell transplantation. Among 23 eyes none of the patients had recurrence. Different investigators reported variable recurrence rates after limbal autografting for pterygium. In a long-term study, Pulte et al[129] observed two recurrences in a group of 70 patients with pterygia (62 primary; 8 recurrent) who underwent limbal-conjunctival autograft transplantation, with a mean follow-up of 45 months. Shimazaki et al[111] noted minimal subconjunctival tissue invasion (less than 1 mm) in 2 of 27 patients with advanced and recurrent pterygia followed up for a mean of 11 months after limbal-conjunctival autograft transplantation. Rao et al[112] reported 2 recurrences (3.8%) in a group of 53 (36 primary; 17 recurrent) pterygia after a mean

follow-up of 18.9 months after limbal-conjunctival autograft transplantation. Gris et al[130] performed limbal conjunctival transplantation for repeatedly recurrent pterygia, and none of the seven patients showed signs of recurrence after a minimum follow-up of 14 months. Similar results were obtained in the present study but for primary pterygia.

In a group of 41 cases of recurrent pterygia, Mutlu et al[131] reported a 14.6% recurrence rate with a minimum follow-up of 15 months

Al Fayez et al[115] performed conjunctival limbal transplantation for advanced and recurrent pterygia and none of the 43 patients showed recurrence after a minimum follow up of 3 years, supporting the effectiveness of conjunctival limbal autograft. Mahamad AE et al[89] reported very low recurrence rate(4.7%) in his study.

Serial no.	Authors	Recurrence rate with conjunctival limbal stem cell autograft
1	Mutlu et al	14.6%
2	Shrinivas Rao et al	3.8%
3	Mohamad AE et al	4.7%
4	Gris et al	0
5	Al Fayez et al	0
6	Present study	4.34%

No recurrence in group B indicates that limbal stem cell transplantation proves to be a better outcome surgical technique. Inclusion of the limbal tissue in the autograft definitely improves the ocular surface at host site and helps in repairing it. Both conjunctival autograft and conjunctival autograft with limbal stem cell transplantation are technically demanding and time consuming, and paying attention

to surgical details such as complete removal of episcleral scar tissue, harvesting a graft of proper size and free of Tenons tissue, and meticulous dissection and handling of the graft tissue is important. Recurrence and graft failure were related to lack of surgical experience in performing limbal and conjunctival grafting by several authors[131] and to inadequate postoperative anti inflammatory therapy.[111]

CONCLUSION

Both the surgical methods of excision of pterygium that is Conjunctival autograft and Limbal stem cell transplantation were effective in the management of pterygium.

Limbal stem cell transplantation together with conjunctival autografting proved to be more effective and safe in prevention of pterygium recurrence and in rapid restoration of normal epithelial morphology

Limbal conjunctival autograft achieves accurate anatomical reconstruction of the ocular surface and restores the limbal barrier. It provides excellent cosmetic results.

Thus we recommend Limbal stem cell transplantation as a procedure of choice for the surgical treatment of pterygium.

SUMMARY

This study is a prospective randomized controlled hospital based study to compare the effectiveness of conjunctival autograft with limbal stem cell transplantation.

- Fourty six eyes of 46 patients were randomized into 2 groups after a detailed ocular examination. Odd numbers were grouped under Group A and even numbers in Group B. Those in Group A underwent Conjunctival autograft following pterygium excision and those in Group B underwent Conjunctival autograft with limbal stem cell transplantation following pterygium excision.
- A total of 46 patients were included in the study. Each group had 23 eyes.
- All cases of primary progressive pterygium were included in the study.
- Mean age in Group A was 43.2 years and 41.5 years in Group B.
- In this study it was observed that 21.7% belonged to grade I, 50% to grade II and 28.26% to grade III.
- Maximum incidence of pterygium (30.43%) was seen in the age group of 31–40 years followed by 41-50 years(26.08%).
- Majority of them were females (69.56%).
- Majority of the patients in the present study came with the complaints of red fleshy mass and they wanted surgery for the cosmetic reason (26.08%). The next common complaint was foreign body sensation (15.21%).

- In this study, 56% were outdoor workers and 43.4% were indoor workers. Incidence of pterygium was higher in outdoor workers.
- Among 46 patients, 45(97.82%) had nasal pterygium and only 1(2%) had temporal pterygium.
- In all the 46 patients there was improvement in the visual acuity. Most of them had one line improvement in visual acuity.
- In this study we did not encounter any serious intra operative or post operative complications. At the first week follow up, graft oedema and subconjunctival haemorrhage were seen in 4.34% each of patients in group A which resolved in the subsequent visits. In group B, 2 patients (8.6%) had graft oedema and 2 patients had subconjunctival haemorrhage. These subsequently resolved with instillation of antibiotic steroid eye drops
- At Subsequent follow up, recurrence was seen in 03(6.52%) patients in group A and no recurrence was seen in group B.
- Serious complications such as pyogenic granuloma, symblepharon formation, scleral melt or scleral avascularity were not encountered in any of the patients eye throughout the follow up period in both the groups.
- After a minimum followup period of 3 months, both the procedures' seemed to be relatively free from complications. But no recurrence in group B indicates that limbal stem cell transplantation proves to be a better outcome surgical technique. Inclusion of the limbal tissue in the autograft definitely improves the ocular surface at host site and helps in repairing it.

Thus in this study we found with limbal stem cell transplantation is a safe and effective procedure in reducing the recurrence rate after pterygium excision.

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ANNEXURES

RESEARCH SAMPLE INFORMED CONSENT

Consent will be taken from each patient before procedure.

TITLE OF PROJECT	**:**	**COMPARATIVE STUDY OF CONJUNCTIVAL AUTOGRAFT WITH LIMBAL STEM CELLS TRANSPLANTATION FOR PREVENTION OF RECURRENCE OF PTERYGIUM**
GUIDE	:	Dr. SUNIL G.BIRADAR
P.G. STUDENT	:	Dr.RADHIKA

PURPOSE OF RESEARCH:

I have been explained about thereason for doing this study and selecting patients as subjects of the study.

This study is for better understanding of the effectiveness and safety of the two procedures inPterygium which will help in future for better selection of the procedure for Pterygium surgery.

PROCEDURE:

I understand that I will undergo Pterygium surgery by random selection.

RISKS AND DISCOMFORTS:

I clearly understand the risk involved in the procedure.

BENEFITS:

I understand that my participation in this study willhelp in selection of safe and effective procedure for Pterygium surgery.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of institutional record and will be subjected to confidentiality and privacy regulations of the said institute. Information of a sensitive personal nature will not be a part of medical record, but will be stored in investigators research file and identified only by a code number. The code key connecting name two numbers will be kept in a separate secured location.

If the data are used for publication in the medical literature and for teaching purposes no names will be used and other identities such as photographs, audio and video tapes will be used only with my special written permission. I understand I may see the photographs and the video tapes and have the audio tapes before giving this permission

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. Dr. Radhika is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. And for careful reading a copy of this consent form will be given to me.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or withdraw consent and discontinue participation in the study at any time

without prejudice. I also understand that Dr. Radhika may terminate my participationin the study after she has explained the reasons for doing so.

INJURY STATEMENT:

I understand in the unlikely event of injury to me resulting directly from my participation in this study, if such injury werereported promptly, then medical treatment will be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to_____(patient's/relevant guardian) the purpose of the research, the procedure required and the possible risk and benefits to the best of my ability.

Dr. Radhika Date

(Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that I Dr.Radhika has explained to me the purpose of research, the study procedure, that I will undergo and the possible discomforts as well as benefits that I may experience in my own language and I understand the same. Therefore I agree to give consent to participate as a subject in this research project.

(Participant)Date

_____ _____

(Witness to signature) Date

ANNEXURE

BLDE U'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR

"COMPARATIVE STUDY OF CONJUNCTIVAL AUTOGRAFT WITH LIMBAL STEM CELLS TRANSPLANTATION FOR PREVENTION OF RECURRENCE OF PTERYGIUM"

PROFORMA

Name of the patient :
IP. No / OP No. : Age/ Sex :

Address :

Occupation :

Date of Admission :

Date of surgery :

Date of Discharge :

1)Chief complaints :

2)History of presenting illness :

h/o trauma/ watering/ pain/ photophobia/ itching/ discharge / foreign body sensation/ growing red mass(cosmetic) /burning sensation/ diminuition of vision/ double vision

3)Past history : H/o Chemical burns/Corneal ulcers/ Trauma/ drug allergies/ Pterygium excision/ treatment history. Any history suggestive of rheumatoid arthritis.

4)General physical examination :

5)Preoperative : Right eye Left eye

a)Visual acuity

b)Pin hole

c)Near

d)Refraction

e)IOP

f)Sac syringing

6)Ocular examination :

a)Head posture

b)Extra Ocular movements

c)Adnexa

d)Conjunctiva

Pterygium

Size

Shape

Circumferential extent on the cornea

Radial extent in relation to cornea

Vascularity

Infiltration

Type of Pterygium type 2/type 3

Nasal /temporal

e)Cornea :

Size :

Shape :

Surface :

Transparency :

Sensation :

f)Anterior Chamber :

g)Iris :

h)Pupil :

i)Lens :

j)Direct ophthalmoscopy :

8)Investigations :

a)Hb% :

b)Urine sugar :

c)Random blood sugar :

d)HIV :

e)HBsAg :

9)Treatment :

Pterygium excision with a)Conjunctival autograft

b)Limbal stem cell transplantation

Surgeon's name :

Intraoperative complications :

Intervention :

10)Post operative treatment

11)Post operative follow up :

	1st day	1st week	4th week	3rd month
i)Pain				
ii)Foreign body sensation				
iii)Photophobia				
iv)Watering				
v)Conjunctival congestion				
vi)Chemosis				
vii)Graft : - Vascularity - Necrosis -Failure - Others				
viii)Cornea Size Shape Surface Transparency Sensation				
ix)Limbal avascularity				
x)Sclera -Necrosis -Inflammation				
xi)Post-operative recurrence Yes/No				

xii)Status of donor area				
xiii) Any other				
xiv)Intervention				

KEY TO MASTER CHART

M- Male

F- Female

RE- Right eye

LE- Left eye

FB- Foreign body sensation

DOV- Diminution of vision

VA- Visual Acuity

Conj.- conjunctiva

SCH: Sub conjunctival haemorrhage

Ethical Committee
BIJAPUR-586103
OUT WARD
No 27/2011
Date 21-10-11
Shri B. M. PATIL Medical College

B.L.D.E. UNIVERSITY'S

SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 20-10-2011 *at* 10-30 am *to scrutinize the Synopsis/Research projects of postgraduate/undergraduate student/Faculty members of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis/Research project has been accorded Ethical Clearance.*

Title Comparative Study of conjunctival autograft with limbal stem cells transplantation for prevention of recurrance of pterygium.

Name of P.G./U.G. student/Faculty member Dr. Radhika
Dept of Ophthalmology

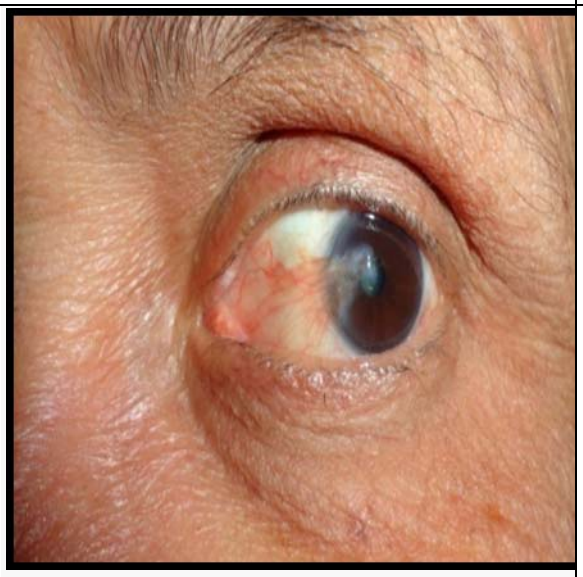
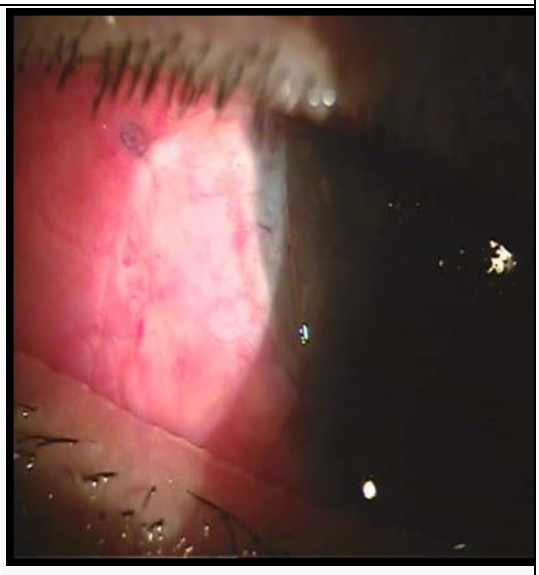
Name of Guide/Co-investigator Dr. S-G. Biradar Prof Ophthalmology

DR.M.S.BIRADAR,
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

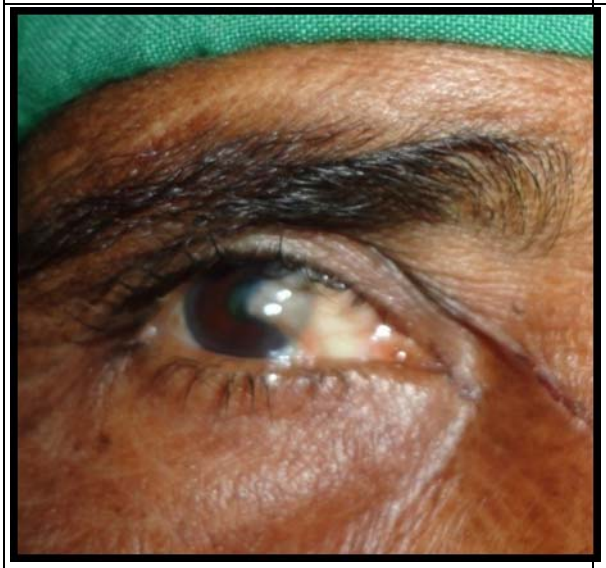
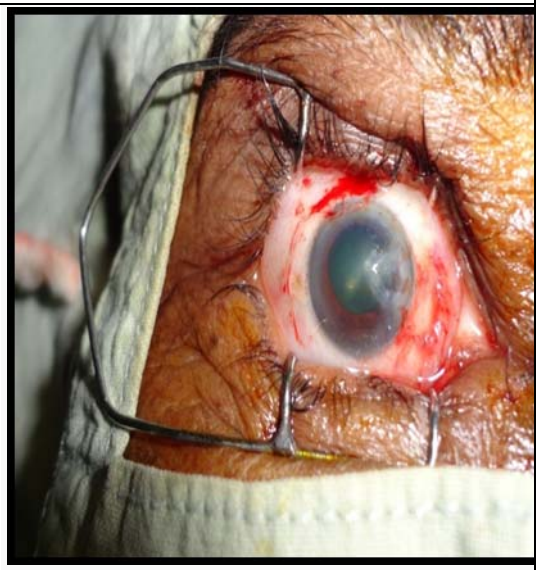
Chairman
Ethical Committee
BLDEA'S Shri. B.M. Patil
Medical College
Bijapur-586103

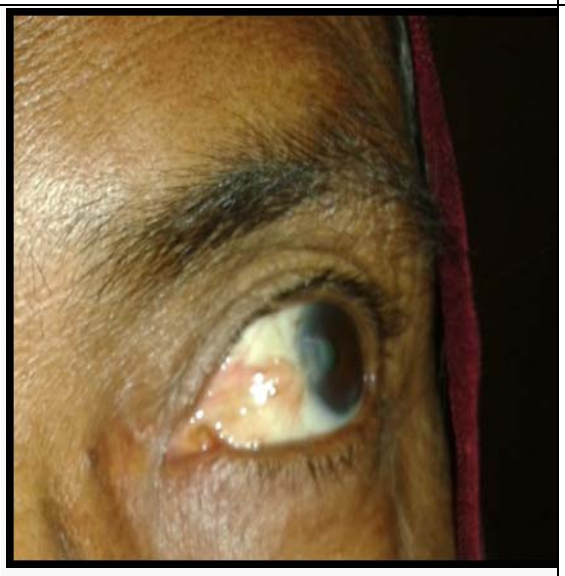
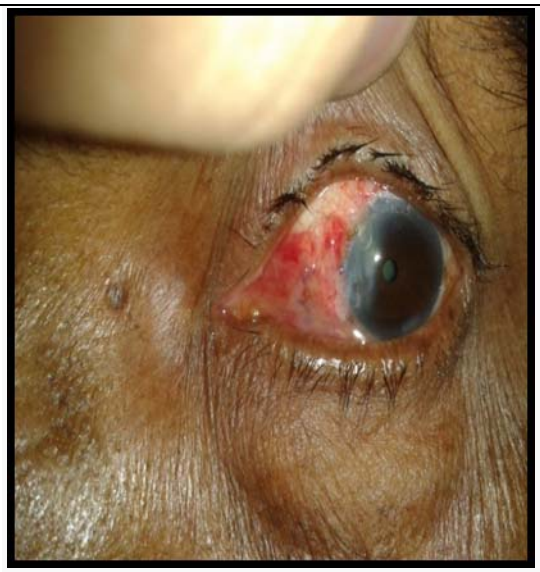
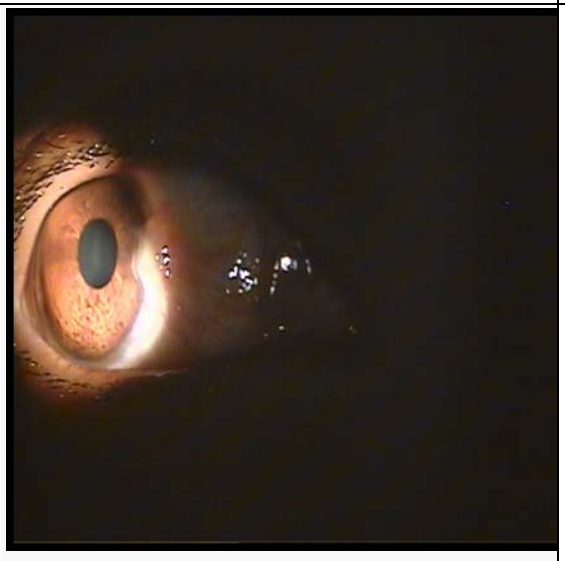
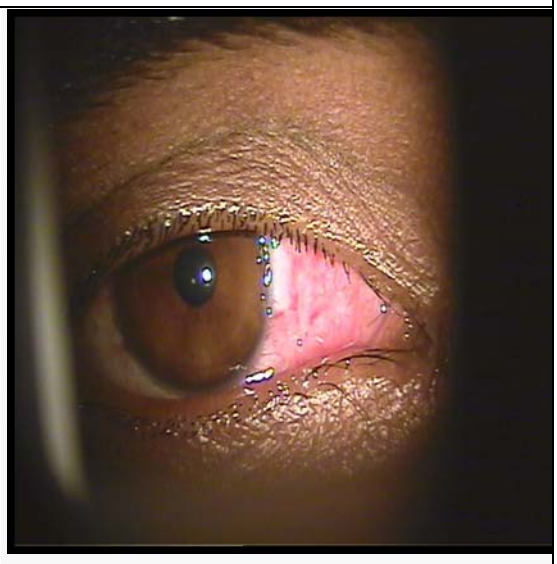
Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ASE NO. 14 (GROUP B)

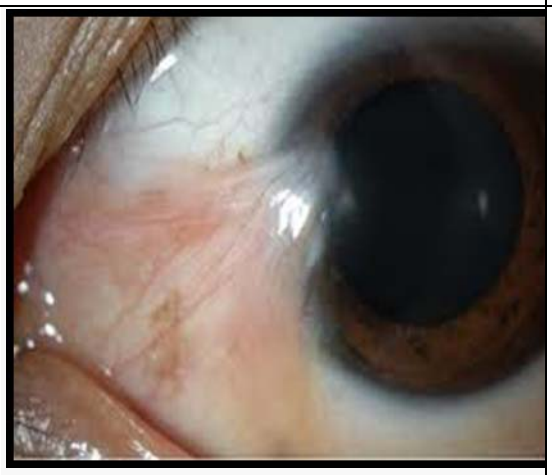
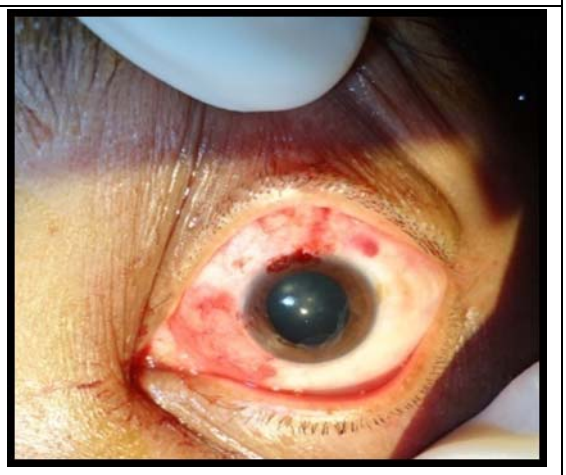
PRE-OPERATIVE PHOTOGRAPH	POST-OPERATIVE PHOTOGRAPH
	

CASE NO. 22 (GROUP B)

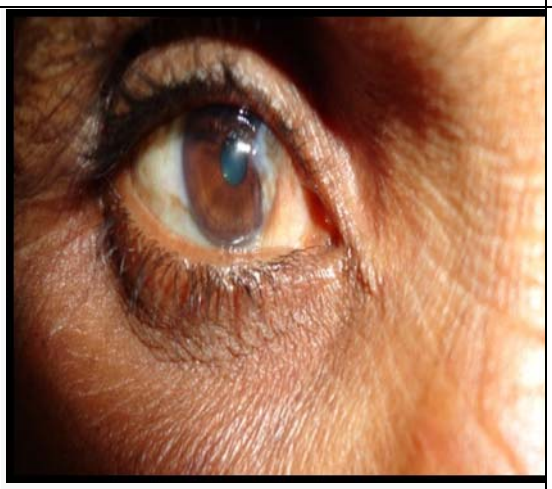
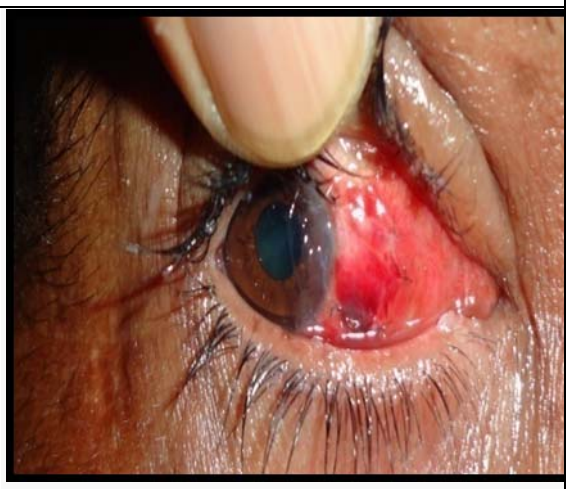
PRE-OPERATIVE PHOTOGRAPH	POST-OPERATIVE PHOTOGRAPH
	

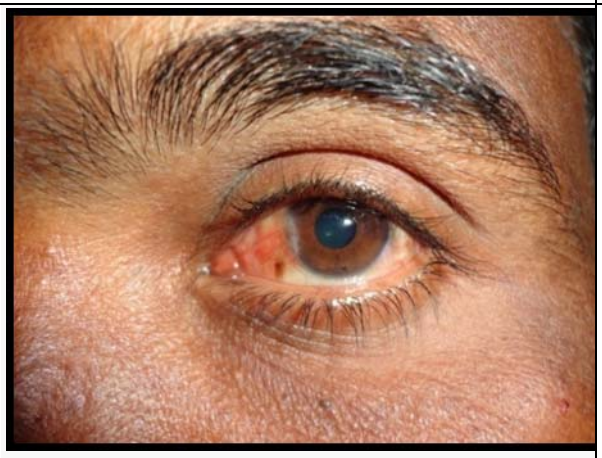
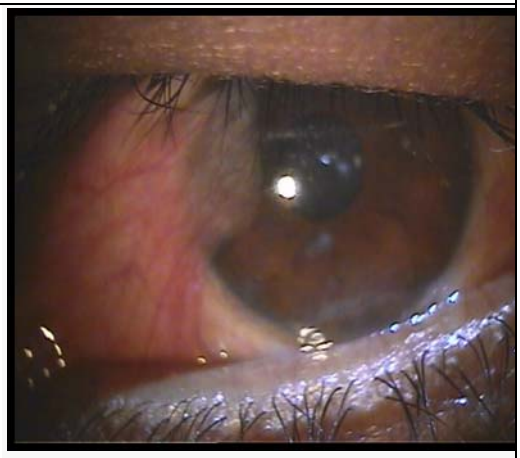
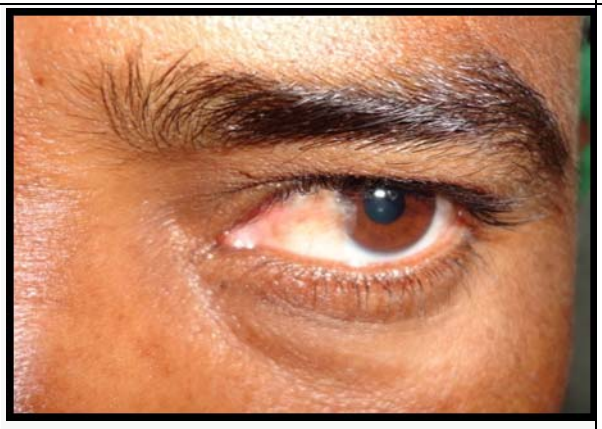
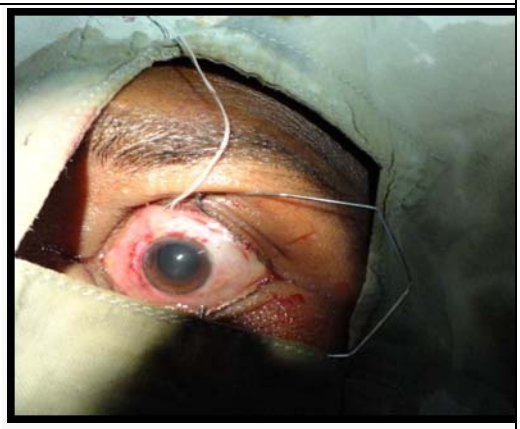
CASE NO. 34 (GROUP B)	
PRE-OPERATIVE PHOTOGRAPH	**POST-OPERATIVE PHOTOGRAPH**
	
CASE NO. 42(GROUP B)	
PRE-OPERATIVE PHOTOGRAPH	**POST-OPERATIVE PHOTOGRAPH**
	

CASE NO. 37 (GROUP A)

PRE-OPERATIVE PHOTOGRAPH	POST-OPERATIVE PHOTOGRAPH
	

CASE NO. 19(GROUP A)

PRE-OPERATIVE PHOTOGRAPH	POST-OPERATIVE PHOTOGRAPH
	

CASE NO. 43(GROUP A)	
PRE-OPERATIVE PHOTOGRAPH	**POST-OPERATIVE PHOTOGRAPH SHOWS RECURRENCE AT 3 MONTHS**
	
CASE NO. 33(GROUP A)	
PRE-OPERATIVE PHOTOGRAPH	**POST-OPERATIVE PHOTOGRAPH**
	

MASTER CHART

Serial No.	Name	IP/OP No.	Age	Sex	Address	Occupation	Site	Symptoms	preop VA	post op VA	Astigmatism	
									pre-op	post op	pre-op	post op
1	Suresh pujari	13949	30	M	Indi	outdoor	LE NASAL	pain	6/9	6/6	0.75	0.5
2	Mukund gouda	19824	38	M	Bijapur	outdoor	RE NASAL	FB sensation	6/6p	6/6	0.5	0.25
3	Giriyamma	14774	45	F	Bijapur	indoor	LE NASAL	pain	6/9	6/6	1	0.75
4	Kalasawwa	22302	65	F	Bijjargi	outdoor	LE NASAL	cosmetic	6/60p	6/36	0.75	0.25
5	Chandramma	14773	48	F	Bijapur	indoor	RE NASAL	FB sensation	6/12	6/9	0.75	0.5
6	Malabai	11201	51	F	Bijapur	outdoor	RE NASAL	FB sensation	6/12	6/6	0.75	0.25
7	Shankaremma K	182816	40	F	Bijapur	indoor	LE NASAL	pain & watering	6/18	6/12	0.75	0.5
8	Yamanavva meti	14770	30	F	Bijapur	indoor	LE NASAL	pain & FB sens	6/6p	6/6	0.25	0
9	Krishna	182817	40	M	Bijapur	outdoor	RE NASAL	burning sens	6/6p	6/6	0.75	0.25
10	Tangemma T	6149	26	F	Babladi	indoor	RE NASAL	cosmetic	6/6p	6/6	0.5	0.25
11	Sangangouda	14857	40	M	Bijapur	outdoor	RE NASAL	pain & watering	6/6p	6/6	0.25	0
12	Sushila	5007	30	F	Bijapur	indoor	RE NASAL	pain & redness	6/6p	6/6	0.25	0
13	Honawwa	21649	60	F	D Hippargi	outdoor	RE NASAL	pain	6/60	6/36p	0.75	0.25
14	Renuka	1896	50	F	Bijapur	indoor	LE NASAL	pain & redness	6/9	6/6	0.5	0

Serial No.	Name	IP/OP No.	Age	Sex	Address	Occupation	Site	Symptoms	preop VA	post op VA	Astigmatism	
									pre-op	post op	pre-op	post op
15	Nagamma	6913	35	F	Bijapur	indoor	RE NASAL	cosmetic	6/6p	6/6	0.75	0.5
16	Ashok patil	83009	42	M	Bijapur	outdoor	RE NASAL	cosmetic	6/6p	6/6	0.75	0.25
17	Draupadi	7014	50	F	Bijapur	indoor	RE NASAL	pain & FB sens	6/6p	6/6	0.75	0.5
18	Indrabai	21700	40	F	Bijapur	outdoor	RE TEMPORAL	FB sensation	6/9	6/6p	0.5	0.25
19	Shankaremma K	4920	30	F	Bijapur	indoor	RE NASAL	burning sens	6/12	6/9	1	0.75
20	Tarabai	23735	30	F	Bableshwar	outdoor	RE NASAL	cosmetic	6/9	6/6	0.25	0
21	Neelamma Motagi	23380	26	F	Bijapur	indoor	RE NASAL	cosmetic	6/9	6/6	0.75	0.25
22	Kalawwa	24661	50	F	Sindagi	outdoor	RE NASAL	redness & DOV	6/60	6/24	1	0.25
23	Girijawwa	13023	80	F	Bijapur	indoor	LE NASAL	FB sens & watering	6/60	6/36	0.75	0.5
24	Indrabai	23786	40	F	Bijapur	indoor	RE NASAL	FB sens	6/36	6/18	1	0.5
25	Chondappa	18165	65	M	Bijapur	outdoor	LE NASAL	FB sens	6/12	6/6p	0.75	0.5
26	Sumitra	20389	32	F	Bijapur	indoor	LE NASAL	cosmetic	6/9	6/6	0.5	0
27	Sangamma	3130	37	F	Bijapur	outdoor	LE NASAL	pain & FB sens	6/6p	6/6	0.25	0
28	Manjula Hosamani	22737	43	F	Bijapur	indoor	LE NASAL	pain & FB sens	6/9	6/6	0.5	0
29	Kalasawwa D	22302	65	F	Bijjargi	outdoor	RE NASAL	redness & FB sens	6/60	6/36p	1	0.75

Serial No.	Name	IP/OP No.	Age	Sex	Address	Occupation	Site	Symptoms	preop VA	post op VA	Astigmatism	
									pre-op	post op	pre-op	post op
30	Rukmani	21865	45	F	Bijapur	indoor	RE NASAL	cosmetic	6/12	6/9	0.75	0.25
31	Paravati Cumate	4039	30	F	Indi	indoor	RE NASAL	FB sens	6/6p	6/6	0.25	0
32	Dundappa	28739	60	M	Bijapur	outdoor	LE NASAL	pain & redness	6/12	6/9	0.75	0.25
33	Sidram	28950	28	M	Taleshwar	outdoor	LE NASAL	pain & burning sens	6/6p	6/6	0.5	0.25
34	Shivalingawwa	2059	65	F	Bijapur	outdoor	LE NASAL	pain	6/60	6/24	1	0.5
35	Chenmallappa	28947	38	M	Tajpur	outdoor	LE NASAL	pain & DOV	6/6p	6/6	0.25	0
36	Paravati soodi	2502	28	F	Kambhagi	outdoor	LE NASAL	cosmetic	6/6p	6/6	0	0
37	Kalyani	4025	32	M	Suragihalli	outdoor	LE NASAL	FB sens & redness	6/6p	6/6	0.75	0.25
38	Baganna	2805	32	M	Bijapur	outdoor	RE NASAL	FB sens & redness	6/12p	6/9	0.75	0.5
39	Kanta	28359	66	F	Bijapur	indoor	LE NASAL	redness & DOV	6/36	6/24	0.75	0.5
40	Basamma	5263	45	F	Bijapur	outdoor	RE NASAL	pain & FB sens	6/9	6/6	0.25	0
41	Modinbee	28941	45	F	Indi	outdoor	LE NASAL	FB sens & redness	6/12	6/6p	1	0.75
42	Prema Masali	5558	26	F	Bijapur	indoor	LE NASAL	cosmetic	6/6p	6/6	0.25	0
43	Rajkumar Kattimani	4447	31	M	Indi	outdoor	LE NASAL	redness & burning	6/6p	6/6	0	0
44	Motisab	6034	44	M	Bijapur	outdoor	RE NASAL	cosmetic	6/9p	6/9	0.75	0

Serial No.	Name	IP/OP No.	Age	Sex	Address	Occupation	Site	Symptoms	preop VA	post op VA	Astigmatism	
									pre-op	post op	pre-op	post op
45	Maheshwari	7186	34	F	Bijapur	indoor	RE NASAL	redness & pain	6/6p	6/6	0.5	0
46	Modisab	8076	44	M	Bijapur	outdoor	LE NASAL	cosmetic	6/9	6/6	0.75	0.25

Grade	Study group	Status of donor area	Complications			
			First day	1st week	1month	3months
II	A	Healthy	graft oedema+conj hyperaemia	graft oedema+conj hyperaemia	graft healthy	graft healthy
II	B	Healthy	graft oedema+conj hyperaemia	graft healthy	graft healthy	graft healthy
III	A	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
II	B	Healthy	chemosis+SCH	SCH	graft healthy	graft healthy
II	A	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
I	B	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
III	A	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
II	B	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
II	A	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
I	B	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
II	A	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
I	B	Healthy	graft oedema+conj hyperaemia	graft oedema	graft healthy	graft healthy
III	A	Healthy	graft oedema	graft healthy	graft healthy	graft healthy
III	B	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy

Grade	Study group	Status of donor area	Complications			
			First day	1st week	1month	3months
II	A	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
I	B	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
II	A	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
III	B	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
III	A	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
II	B	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
I	A	Healthy	SCH	SCH	sch resolving	graft healthy
III	B	Healthy	SCH	SCH	graft healthy	graft healthy
III	A	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
II	B	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
II	A	Healthy	conj hyperaemia	conj hyperaemia	recurrence	recurrence
II	B	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
I	A	Healthy	conj hyperaemia	conj hyperaemia	graft healthy	graft healthy
II	B	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
III	A	Healthy	chemosis+SCH+graft oedema	chemosis +SCH+ graft oedema	graft healthy	graft healthy

Grade	Study group	Status of donor area	Complications			
			First day	1st week	1month	3months
II	B	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
II	A	Healthy	conj hyperaemia	conj hyperaemia	graft healthy	graft healthy
III	B	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
III	A	Healthy	conj hyperaemia+chemosis	conj hyperaemia	graft healthy	graft healthy
II	B	Healthy	graft healthy	few suture given away	graft healthy	graft healthy
I	A	Healthy	conj hyperaemia	few sutures given away	recurrence	recurrence
I	B	Healthy	conj hyperaemia	graft healthy	graft healthy	graft healthy
II	A	Healthy	conj hyperaemia	conj hyperaemia	graft healthy	graft healthy
II	B	Healthy	conj hyperaemia	few sutures given away	graft healthy	graft healthy
III	A	Healthy	chemosis+SCH+graft oedema	chemosis +SCH+ graft oedema	graft healthy	graft healthy
II	B	Healthy	conj hyperaemia+chemosis	few sutures given away	graft healthy	graft healthy
III	A	Healthy	conj hyperaemia+chemosis	few sutures given away	graft healthy	graft healthy
I	B	Healthy	conj hyperaemia	conj hyperaemia	graft healthy	graft healthy
II	A	Healthy	conj hyperaemia+chemosis	conj hyperaemia	vascular	recurrence
II	B	Healthy	graft healthy	graft oedema	graft healthy	graft healthy

Grade	Study group	Status of donor area	Complications			
			First day	1st week	1month	3months
I	A	Healthy	graft healthy	graft healthy	graft healthy	graft healthy
II	B	Healthy	conj hyperaemia	conj hyperaemia	graft healthy	graft healthy