Dissertation on

A CLINICAL STUDY ON PERIPHERAL ULCERATIVE KERATITIS OF NONINFECTIVE ETIOLOGY

Submitted in partial fulfillment of requirements of

M. S. OPHTHALMOLOGY

BRANCH III

Of

REGIONAL INSTITUTE OF OPHTHALMOLOGY

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI-600 003

MAY - 2019

CERTIFICATE

This is to certify that this dissertation titled **"A Clinical Study on Peripheral Ulcerative Keratitis of noninfective Etiology"** is a bonafide record of the research work done by **Dr.SUDARVIZHI.A**., Post graduate in Regional Institute of Ophthalmology, Madras Medical College and Research Institute, Government General Hospital,Chennai-03, in partial fulfillment of the regulations laid down by The Tamil Nadu Dr.M.G.R. Medical University for the award of M.S.Ophthalmology Branch III, under my guidance and supervision during the academic years 2016-2019.

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I wish to express my sincere thanks to my family, friends and all my colleagues and my heartful gratitudeto all my patients without whom this endeavor would not have been possible.

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled, **"A CLINICAL STUDY ON PERIPHERAL ULCERATIVE KERATITIS OF NONINFECTIVE ETIOLOGY "** is a bonafide and genuine research work conducted by me under the guidance of **Prof. Dr.M.ANANDA BABU, M.S., D.O.,** Head of Department of Cornea and Contact lens services, Regional institute of ophthalmology & Government Ophthalmic hospital. Chennai-600008.

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Place: Chennai

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CERTIFICATE OF APPROVAL

To
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Dear Dr.Sudarvizhi.A.

The Institutional Ethics Committee has considered your request and approved your study titled **"A CLINICAL STUDY ON PERIPHERAL ULCERATIVE KERATITIS OF NON INFECTIVE ETIOLOGY" - NO.07102017**

The following members of Ethics Committee were present in the meeting hold on **10.10.2017** conducted at Madras Medical College, Chennai 3

1. Prof.P.V.Jayashankar :Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., Dean,MMC,Ch-3 : Deputy Chairperson
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8. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
9. Thiru K.Ranjith, Ch- 91 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

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CONTENTS

ABBREVIATION

PUK	-	Peripheral ulcerative keratitis.
RA	-	Rheumatoid Arthritis.
MUC	-	Membrane Associated Mucins.
MMP	-	Matrix Metalloproteinase.
TIMP	-	Tissue inhibitor of matrix metalloproteinase.
ANA	-	Anti-nuclear antibodies..
ANCA	-	Anti-nuclear cytoplasmic antibodies.
TNF-α	-	Tumor necrosis factor .
ASOCT	-	Anterior segment optical coherence tomography.
RS	-	Respiratory system
CVS	-	Cardio vascular system
CNS	-	Central nerves system.
AMG	-	Amniotic membrane graft.
HIV	-	Human immuno deficiency virus.
HBV	-	Hepatitis B virus.
HCV	-	Hepatitis C virus.

PART 1

INTRODUCTION

Peripheral corneal ulceration is defined as acrescent-shaped destructive inflammation at the margin of corneal stroma, that is associated with an epithelial defect, presence of stromal inflammatory cells, and progressive stromal degradation and thinning.

It causes progressive necrosis of the corneal stroma, which will leads to perforation and blindness.

The peripheral corneais different from central cornea in morphologic and immunologic characteristics and so it prone to inflammatory reactions. Complications of PUK can be prevented by early detection and early treatment.

REVIEW OF LITERATURE

Sharma N et al conducted a prospective study in which seventy six eyes of 65 consecutive patients were evaluated over an 18 month period and were followed for a period of 3 years.This study concluded that ,

- Mooren's ulcer was the leading cause and collagen vascular diseases, infections are next important causes of PUK in developing countries.
- Surgical intervention in perforated cases had good anatomical success and visual prognosis.[1]

Tauber et al conducted an study in which they had evaluated 61 eyes with PUK to report on guidelines for systemic chemotherapy.

This study concluded that historical review of systems should be through.[2.]

D M Squirrell et al,J Winfield et al and R.S .Amos et alconducted a study on 9 cases who developed RA associated PUK.

This study concluded that RA associated PUK often has a poor visual outcome and its appearance may herald the transformation of a patient's RA into systemic vasculitic phase. It should be managed with aggressive immunosuppression, if the associated morbidity and mortality are to be avoided. Cell mediated mechanisms appear to be important in aetiopathogenesis of PUK and a combination of corticosteroids and cyclosporine is therefore probably the regimen of choice.[3]

Thomas et alhad evaluated three patients with rheumatoid arthritis andkeratolysis who were not responding to steroids &immunosuppressents were giveninfliximab infusion. Theconjunctivalinjection was reduced and epithelial defects healed.On methotrexate administration synergistic action was noted and concluded that infliximab is an alternative to cases not responding corticosteroids and methotrexate[4]

Ngan et al conducted a study of 18 eyes of 14 patients with Mooren'sulcer, amniotic membrane graft was done with complete epithelializationof defect in mean time of 12.4 days. In 10 eyes vision improved to 6/12or better.

Thus it concluded that amniotic membrane graft can be an alternative when systemic immunosuppressive drugs cannot be given[5.]

Jia Yet al conducted a study in which amniotic membrane transplant was done for 12 paitents with PUK. They concluded that steroid therapy prevents the recurrence & promote the healing process.[6.]

Raizman MB et al conducted a study in which tectonic keratoplastywas done for 17 eyes progressive ulceration. They concluded that tectonic keratoplastypreserves the anatomical integrity of eyes[7].

D A R Bessant et al conducted a study on 10 cases of corneal ulceration with associated rheumatoid arthritis,Steven johnson syndrome and Mooren's ulcer these 10 cases undergone lamellar keratoplasty.

They concluded that Lamellar keratoplasty preserves the globe and maintains useful vision[8.]

ANATOMY OF CORNEA

Cornea is the principal refractive surface of human eye. It is a transparent structure which forms the one sixth of outer covering of the eyeball. It contains the intraocular pressure and provides a protective surface with the environment.

Adult corneal dimensions are vertically 10.5 mm and horizontally 11.5 mm in anterior surface. In posterior surface both the horizontal and vertical dimensions are 11.5 mm.

Corneal thickness in the centre is 520 to 540 microns and in the periphery it is 670 microns.

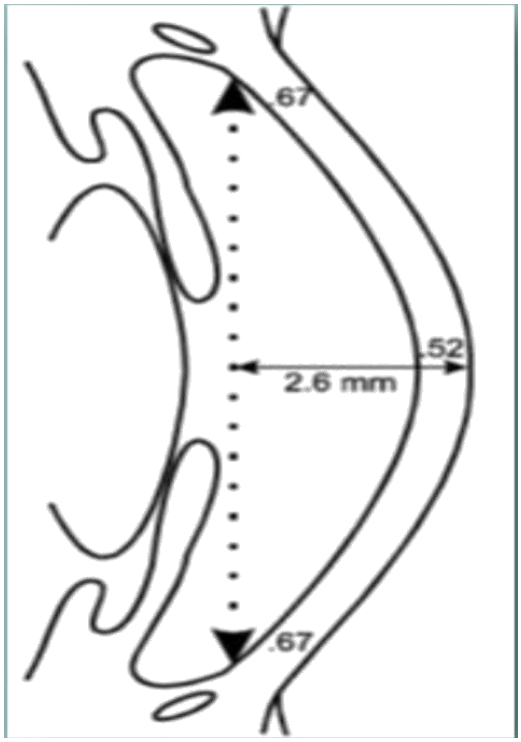


Figure 1 showing corneal thickness

RADIUS OF CURVATURE

Anterior surface:7.8 mm

Posterior surface:6.5 mm

REFRACTIVE POWER OF CORNEA - +43 D

REFRACTIVE INDEX- 1.38

The curvature of cornea is larger than the rest of the globe. The junction of the cornea and Sclera forms the limbus which is a transition zone of 1 to 1.5 mm.

It contains 6 layers from without inwards:

1.Epithelium

2.Bowman’s membrane

3.Stroma or substantia propria

4.Dua’s layer or pre descemet's membrane

5.Descemet’s membrane

6.Endothelium

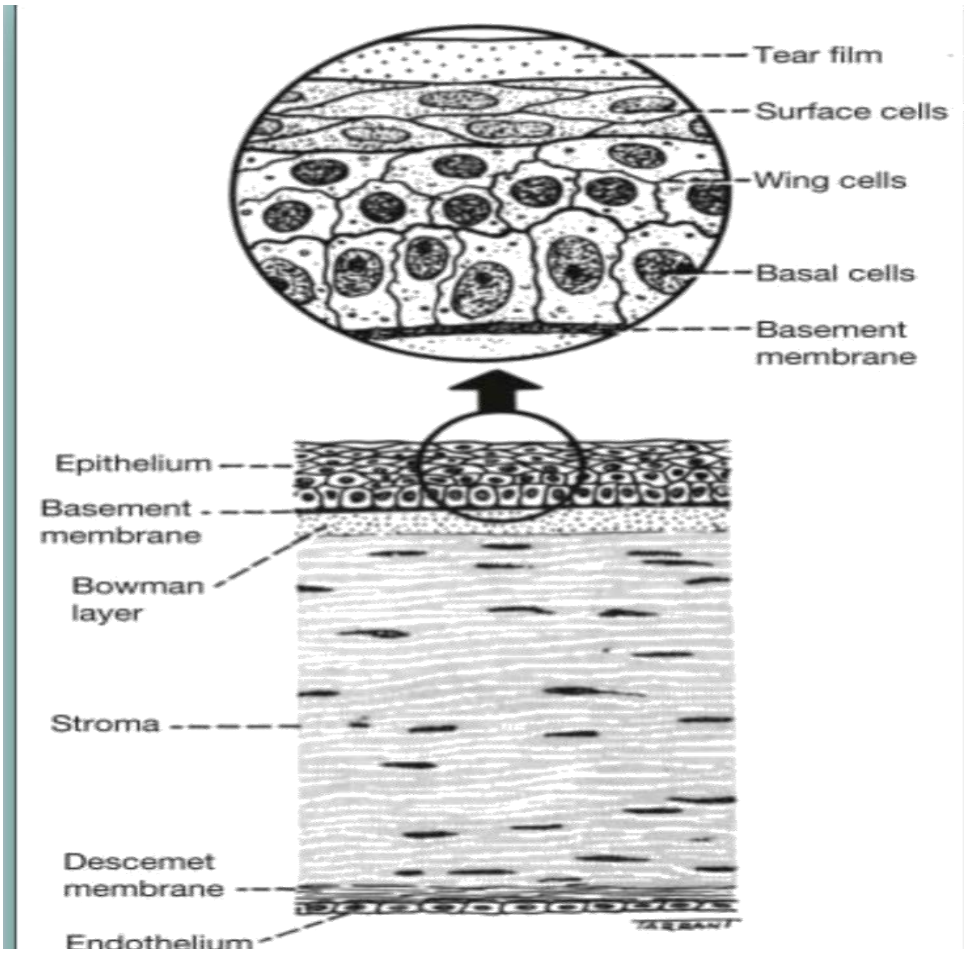


Figure 2 showingEpithelial cell layer zones

EPITHELIUM

It constitutes 10% of total corneal thickness and measures about 50 to 90 microns. It consists of 5 to 7 layers of stratified squamous non-keratinised epithelium.

It constitutes 3 zones,

1.Superficial squamous zone

2.Middle wing cell layer zone

3. Deep Basal cell layer zone

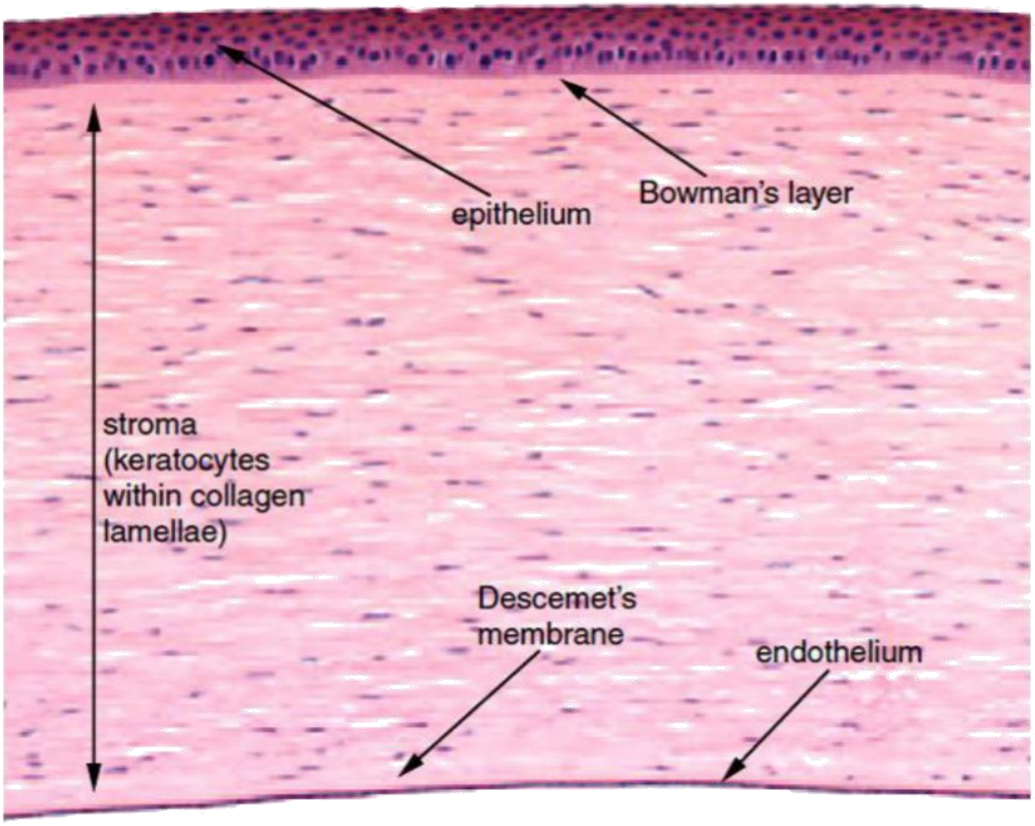


Figure 3histological section of layers of cornea

SUPERFICIAL ZONE

It has 1 to 2 layers of flattened nucleated cells called squamous cells. It has micro projections called microvilli or microplicae. The cells turn over is 7 to 14 days. It has desmosomes and tight junction complexes.

MIDDLE ZONE

It contains 2 to 3 layers of wing cells which has wing like extensions from round cell body. It has desmosomes and gap junctions.

DEEP BASAL ZONE

It is a single layer of cuboidal to columnar basal cells supported by basal lamina. It is metabolically active layer.It has some permeability for glucose,sodium,O2 and CO2.
It is attached by hemidesmosomes to basement membrane which contains collagen type 4, 7 and glycoproteins. Basal lamina is further divided into

- Lamina Lucida
- Lamina Densa (deeper layer)

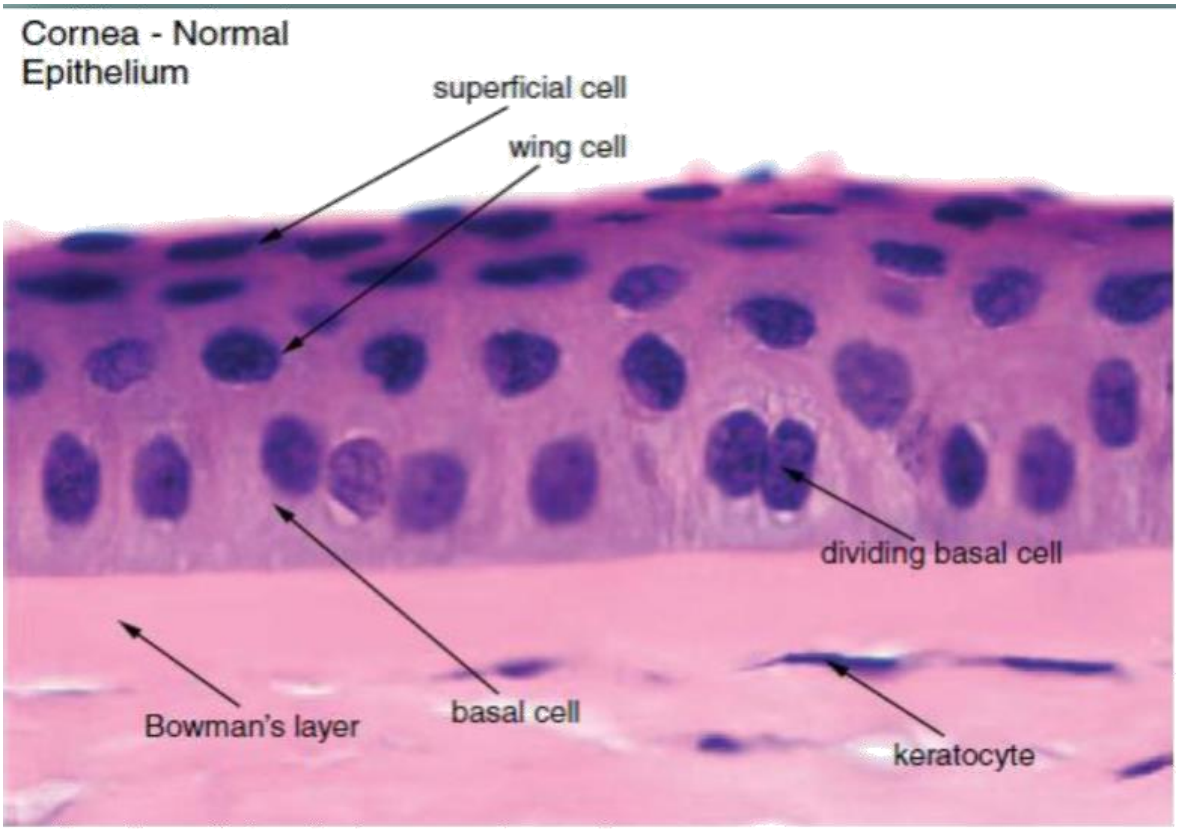


Figure 4 showing histological section of epithelial cell layer

The integrity of corneal epithelium plays vital role in protection against many pathogenic organisms like neisseria gonorrhoeae and corynebacterium diphtheriae. The loss of integrity of epithelium predisposes the cornea to infection.

Bowman's membrane

It lies subjacent to the basal lamina of epithelium and measures 8 to 14 microns in thickness. It has compact arrangement of collagen type 1, 3 and it contains numerous

pores for corneal nerves. It is relatively resistant to trauma, if destroyed it cannot be re-regenerated.

Stroma or substantia propria

It constitutes 90% of the corneal thickness and measures 500 microns. It is made up of collagen type 1(major), type 3 and 6.

Collagen fibrils are arranged in 200 to 250 bundles ,each extent to the width of cornea. It is of 9 to 260 nm wide.Fibrils are regularly arranged parallel to the surface equally spaced which forms the 3D diffraction grating to scatter 98% of incoming light rays.

The collagen fibrils are embedded in glycasaminoglycan ground substance in a ratio of 3:1 keratan sulphate and chondroitin sulphate.

Keratocytes which are modified fibroblasts constitutes 2.5 to 5 % of the stromal volume .keratocytes are responsible for the synthesis and maintanence of collagen and proteoglycan substance.These are long ,thin ,flattened cells positioned between lamellae.

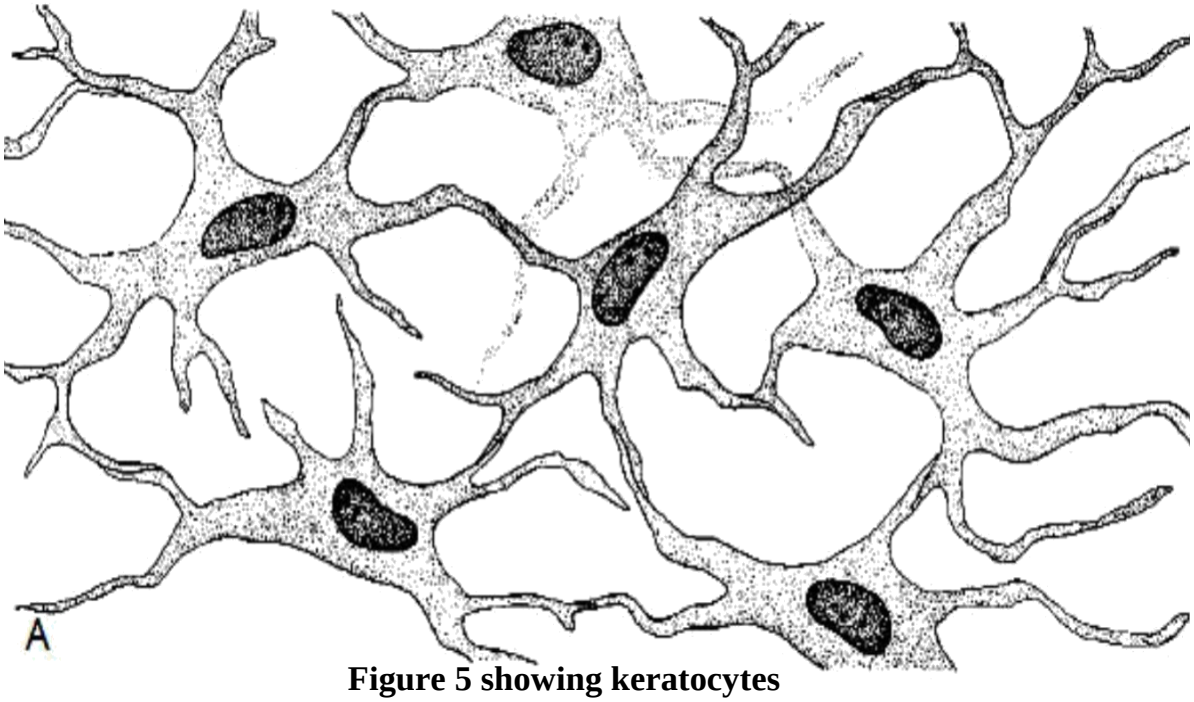


Figure 5 showing keratocytes

Dua’s layer or pre descemet's membrane

Though it is thin it is very strong.

Descemet’s membrane

It forms the basement membrane of corneal endothelium. The major collagen is type 4 collagen. It’s peripheral termination forms the schwalbe’s line. It is 3 to 5 microns in birth and 12 microns in adult. It has regenerative potential.

It is divided into anterior one third banded form which is laid down in utero and posterior two third nonbanded form which is laid down throughout life by endothelium.

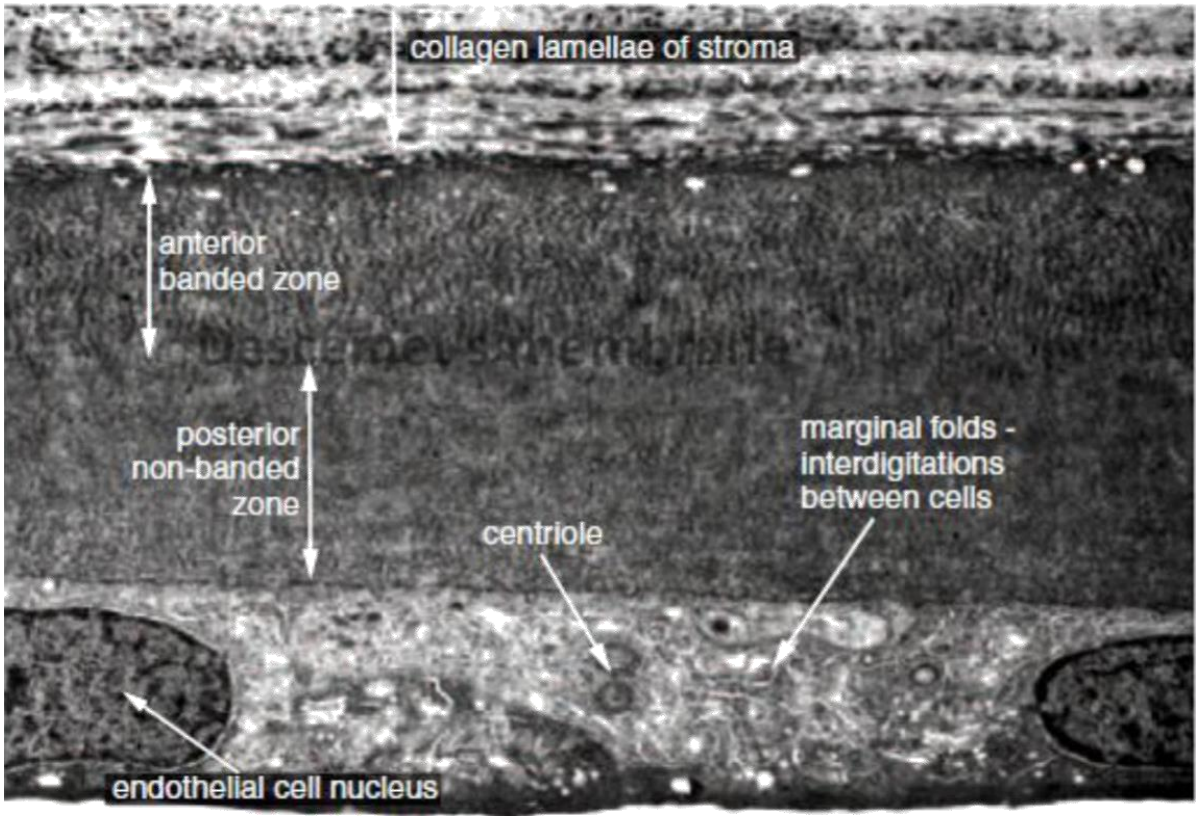


Figure 6 showing layers of descemet membrane

ENDOTHELIUM

It is a single layered low cuboidal hexagonal cells. It measures 4 to 6 microns in thickness. Endothelial cell count at birth is about 3500 to 4000 cells /mm2.It decreases 0.3 to 0.6 % per year with age. In adults it decreases upto 1400 to 2500 cells/mm2.The decrease in cell count will occur atincreased age,increased IOP ,following surgery. If the cell count decreases upto 400 -700,corneal edema will occur.

It prevents the seepage of aqueous into stroma by its tight lateral interdigitations.It plays major role in maintaining the relatively low stromal hydration of 78% through Na+K+ activated ATPase pump in basolateral border of cells.

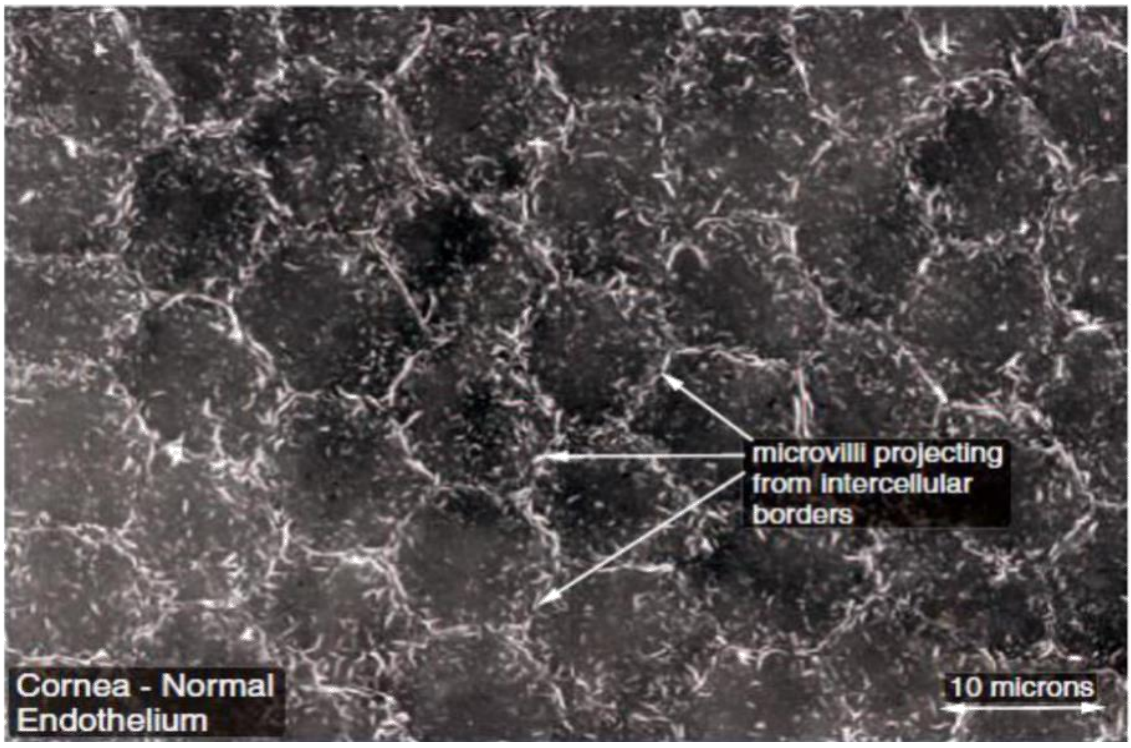


Figure 7 showing endothelium of cornea

VASCULAR SUPPLY OF CORNEA

Cornea is avascular structure but the peripheral cornea receives blood supply from limbal vessels which in turn formed from anterior ciliary arteries.These vessels extend into peripheral cornea of about 0.5 mm.

The venules from the peripheral cornea drain into the orbital veins along with venules from episclera.

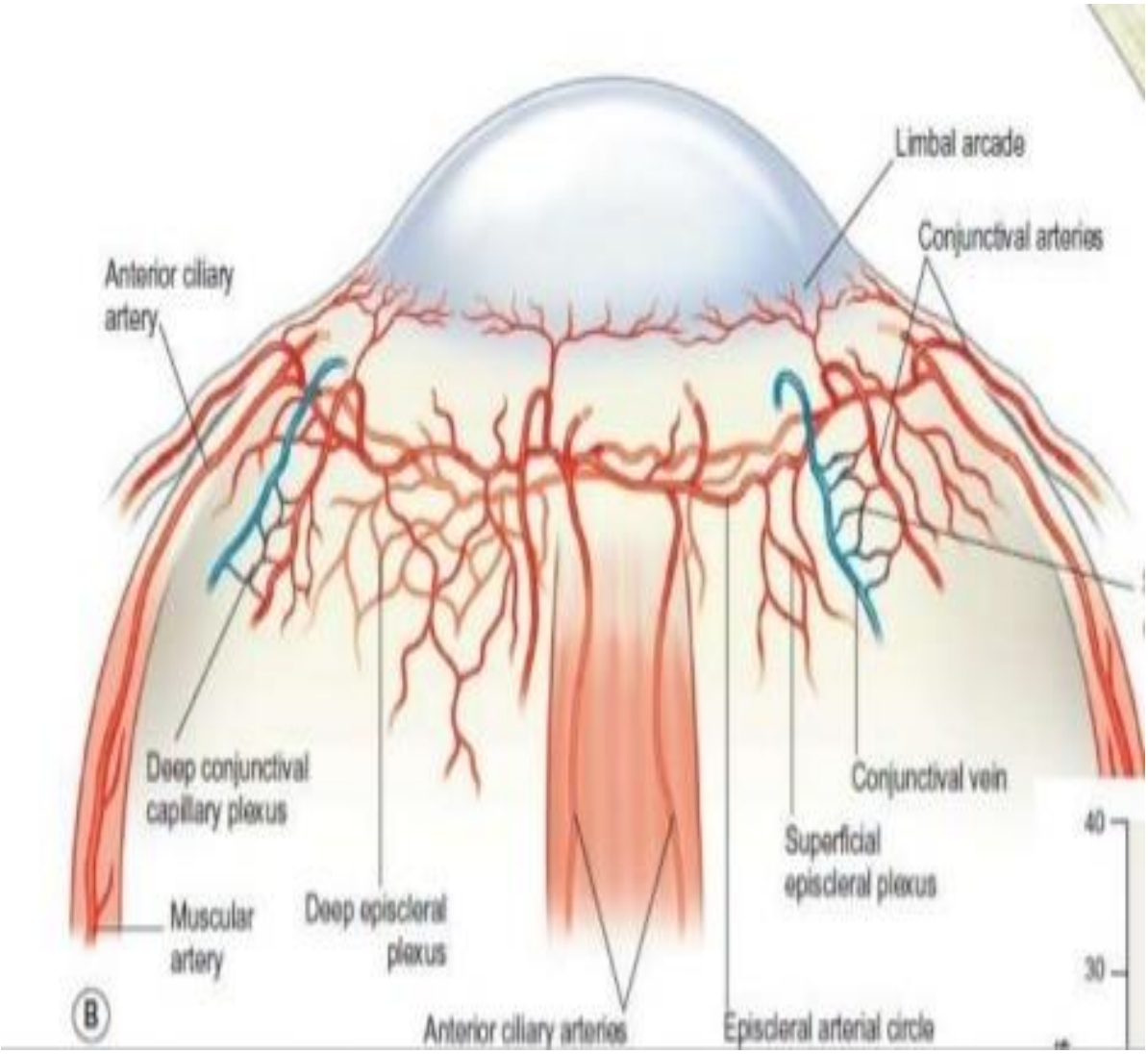


Figure 8 showing vascular supply of cornea

NERVE SUPPLY OF CORNEA

Cornea has rich innervation by both sensory & autonomic nerve fibers. The sensory supply is from ophthalmic division of trigeminal nerve & sympathetic supply is from superior cervical ganglion and it receives parasympathetic fibers from ciliary ganglion. The ophthalmic division of trigeminal nerve divides into nasociliary and ciliary nerves. The ciliary nerves enter the peripheral cornea as bundles forming the limbal plexus. The nerve trunks from the limbal plexus enter stroma and repeatedly branch to form the anterior stromal plexus.

The superficial layer of the anterior stromal plexus is located just beneath bowman's membrane and it forms the subepithelial plexus. The branches of subbasal plexus ascend vertically to reach the epithelium forming the intra-epithelial nerve terminals.

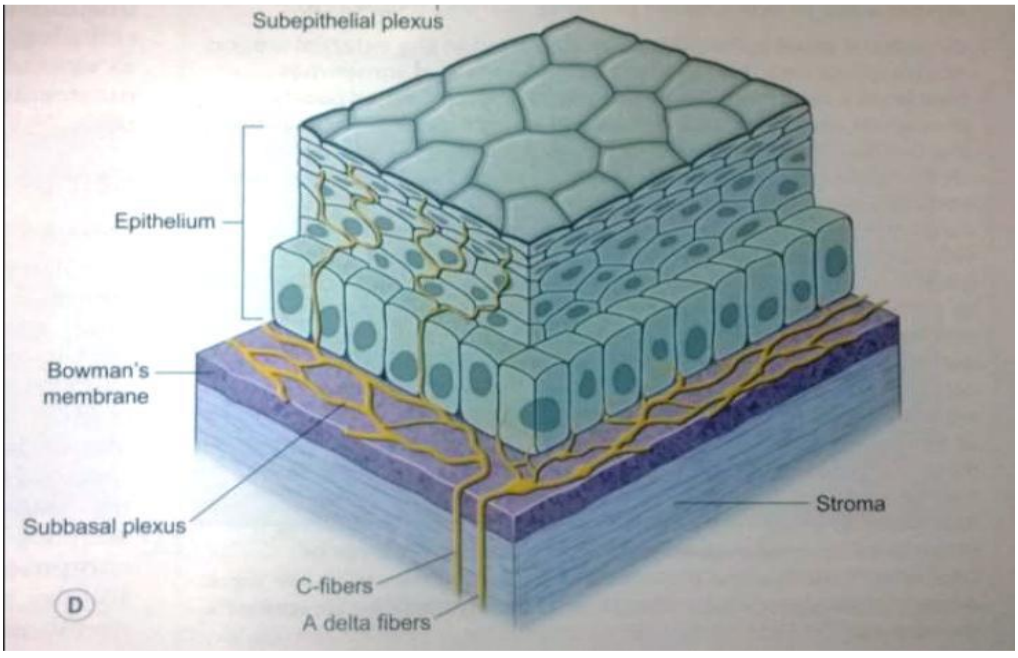


Figure 9 showing nerve supply of cornea

PHYSIOLOGY OF CORNEA

Corneal transparency

It is attributable to physiological factors as follows

1. Regular lattice arrangement of collagen fibrils.
2. Corneal epithelium and tear film.
3. Corneal avascualrity.
4. Non myelinated nerve fibres.
5. Relative deturgescence state of normal cornea.

Factors affecting corneal hydration

1.Glycasaminoglycans induced stromal swelling pressure.

2.Barrier function of epithelium and endothelium.

3The relative dehydration of cornea is maintained by active pump systems of endothelium.

•The enzyme pump systems are –

- Na^+/K^+ ATPase pump system.
- Carbonic anhydrase enzyme system
- Na^+/H^+ pump.
- Bicarbonate dependent ATPase

4.Evaporation of H2O from corneal surface.

5. Intraocular pressure.

PROTECTIVE FACTORS

- An intact corneal epithelial surface with its tight junctions formed by the desmosomes and hemidesmosomes protects the surface of eye from infectious agents. Eyelid forms the physical barrier.
- The tearfilm constitutes immunoglobulins, lysozyme, lactoferrin.
- The normal ocular flora prevents the growth of exogenous organisms.
- The conjunctiva contains subepithelial mucosa associated lymphoid tissue.

UNIQUE FEATURES OF THE PERIPHERAL CORNEA

- Peripheral cornea is 1mm inthickness which is greater than the central cornea.
- Tight adherent nature of epithelium to the underlying structures .
- Epithelial stem cells are highly concentrated in the peripheral cornea.
- Peripheral cornea has more access to blood vessels and lymphatics
- Endothelial cells in peripheral cornea have maximum mitogenic activity.
- Collagen fibers are loosely arranged.
- Nerve fibres are less dense in the peripheral cornea wherein the central cornea is heavily innervated.So the peripheral cornea is less sensitive than central cornea.
- Peripheral cornea depends upon the blood vessels from the edge of the cornea for nutrients whereas the central cornea derives its nutrients from aqueous humour.

- The Membrane associated Mucins MUC 4 is present in higher levels in the periphery which may be associated with serum albumin from the capillaries of peripheral cornea.
- Unique immunological features of peripheral cornea are more concentration of Langerhan's cells, IgM, C1 (first component of complement cascade), immune complexes due to diffusion from limbal vessels because of its large size.

Thus, vascular inflammatory disorders, limbal infections, collagen vascular disorders, neoplastic diseases and local degenerations affect the peripheral cornea in a distinct way.

LIMBUS

Limbus is the peripheral area, 1mm wide which forms a transition between transparent cornea and opaque sclera. It is rich in blood vessels & nerve endings like conjunctiva, it is divided into anatomical limbus, histological limbus and surgical limbus. Anatomical limbus is formed by junction of conjunctival & corneal epithelium where the limbal stem cells undergo differentiation.

Histological limbus is the junction of cornea & sclera in histological cross sectional views.Surgical limbus is blue grey transition zone of approximately 1.2mm wide which is seen after reflecting the conjunctiva away from the limbus.

Limbus is composed of only 2 layers, the epithelium & the stroma. The epithelium is still stratified squamous with 10 or more layers and the basal layer cells are more closely

packed with scanty cytoplasm. The stroma loses its regular arrangement and it has numerous blood vessels.

The limbus consists of stem cells which can undergo differentiation and proliferation.

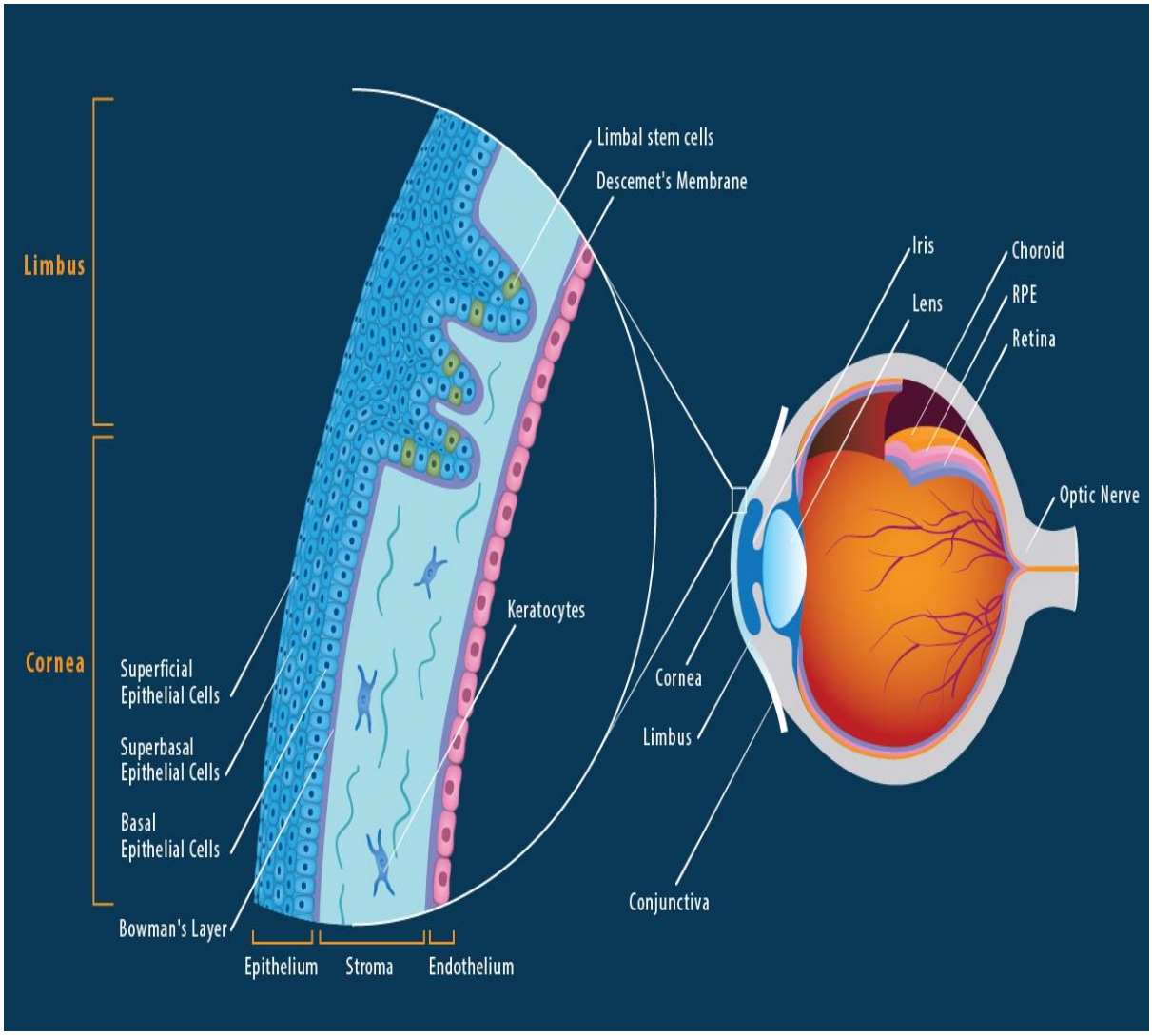


Figure 10 showing limbus of cornea

PERIPHERAL ULCERATIVE KERATITIS

It is destructive inflammatory disease of the juxta-limbal corneal stroma that is associated with a crescent shaped inflammation with an epithelial defect, the presence of inflammatory cells in the stroma and progressive stromal melting. It is associated with various ocular and systemic infectious and non-infectious diseases.

Etiology of peripheral ulcerative keratitis

	Infectious	**Non-infectious**
Ocular	Bacterial: Staphylococcus, Streptococcus, Moraxella, Haemophilus Gonococcus Viral (Herpes simplex, herpes zoster) Acanthamoeba Fungal organisms	• Mooren's ulcer • Terrien's marginaldegeneration • Pellucid marginal degeneration • Blepharitis • Keratoconjunctivitis sicca • Neurotrophic andNeuroparalytic • Nutritional deficiency • Ocular chemical injury • Contact lens • Trauma • Post-surgical

Systemic	Tuberculosis Syphilis Hepatitis C Varicella zoster Gonorrhea	• Rheumatoid arthritis • Polyarteritis nodosa • Giant cell arteritis • Wegener's granulomatosis • Systemic lupus erythematosis • Sjögren's syndrome • Relapsing polychondritis • Progressive systemic sclerosis • Churg-Strauss syndrome • Crohn's disease • Ulcerative colitis • Rosacea • Steven Johnson's syndrome • Sarcoidosis • Behçet's disease • Psoriasis • Malignancy • Cryoglobulinemia • Schönlein-Henoch purpura • Serum sickness

		• Pyoderma gangrenosum • Erythema devatumdiutinum

ETIOPATHOGENESIS

It is associated with various ocular and systemic infectious and noninfectious causes.The exact pathophysiologic mechanism is not known.

The peripheral cornea is unique in morphological and physiological characteristics which predisposes it to inflammation.The peripheral cornea recieves its oxygen and other nutrients from the perilimbal capillary arcades which extends 0.5mm to the clear cornea.This perilimbal capillary arcades act as reservoir for immunocompetenet cells such as macrophages,langerhans cells,plasma cells.Langerhans cells which are antigen presenting cells concentrated more in these limbal vessels.

The immune complexes present in the patients with collagen vascular diseases tends to lodge here because of its size and molecular sieving properties of cornea.Peripheral cornea has more concentration of complement C1 which can cause chemotaxis of neutrophils.Ig M directed against rheumatoid factor Ig G also gets concentrated here and form immune complexes.These immune complexes deposition in the peripheral cornea causes inflammation and ulceration.The proximity of the peripheral cornea to these results in peripheral ulcerative keratitis.

Keratocytes plays vital role in maintenance and turnover of corneal matrix.The rate of matrix turnover depends upon balance between the collagenases and the tissue inhibitors.Collagenases are mainly produced by fibroblasts and mononuclear cells.

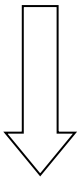
The local imbalance between collagenases such as MMP-1 and the tissue inhibitors such as TIMP-1 results in rapid keratolysis and PUK.

Any inflammatory stimulus in the peripheral cornea that is caused by invasion of microbial organisms (bacteria, virus, fungi, and parasites), immune complex deposition (in systemic immune diseases), trauma, malignancy, or dermatologic conditions may produce local and systemic immune responses, resulting in neutrophil recruitment and complement activation at the limbus.

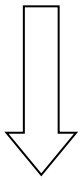
Activated complements increase the vascular permeability and produces chemotactic factors such as c3a,c5a and recruits neutrophils.These neutrophils releases enzymes, proteolytic and collagenolytic,proinflammatory substances suchas leukotreines ,prostaglandins,platelet activating factor. The inflamed conjunctiva also produces collagenases which can cause stromal degradation

Flow chart of Pathogenesis of PUK

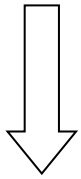
Various etiologies



Inflammation of the peripheral cornea

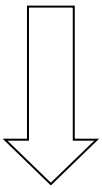


Damage to the vessel wall and increased vessel permeability causing leakage

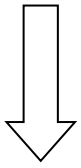


Generates proinflammatory cytokines and chemotactic factoers for neutrophills

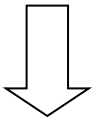
C3a and C5a



Neutrophills release collagenolytic and proteolytic enzymes



Matrix metalloprotienase produced by local resident cells



Destruction of the corneal stroma

Systemic diseases that may cause immune complex deposition at the peripheral cornea and cause PUKinclude collagen vascular diseases such as rheumatoid arthritis (RA), Wegener's granulomatosis (WG),polyarteritis nodosa (PAN), relapsing polychondritis(RP), and systemic lupus erythematosus (SLE).

Infectious conditions, whether systemic (hepatitis,syphilis) or local (herpes simplex keratitis, funga lkeratitis), and noninfectious local disorders (Mooren'sulcer, marginal keratitis) also may cause PUK.

MATRIX METALLOPROTEINASE

Activated matrix metalloproteinase I (MMP-Ior collagenase I), is a lytic enzyme against type I collagen of corneal extracellular matrix, has been identified as causative agent of PUK.

It is also suggested that MMP-I is produced by the cornea lkeratocytes or infiltrating macrophages.

Expression of MMP-8 (a neutrophil collagenase) has been associated with inflammatory conditions and plays a crucial role in wound healing and tissue remodelling.

Production of MMP-2 & MMP-9 has been implicated in the progression of PUK and causes perforation by breaching the basement membrane.

CLINICAL FEATURES

OCULAR FEATURES

SYMPTOMS

1. Ocular Redness
2. pain
3. watering
4. Photophobia
5. Foreign body sensation
6. Defective vision

In acute cases visual acuity may be normal or mild reduction can be there. In long standing cases visual acuity may be reduced due to induced astigmatism or corneal opacity.

It can be associated with scleritis and anterior uveitis.

Pain out of proportion to the severity of ulcer & without is characteristic of mooren's ulcer.

SLIT LAMP EXAMINATION

- Crescent shaped destruction at the juxtalimbal cornea with associated vascularisation.
- Epithelial defect will be present.
- Yellow white infiltrates which are inflammatory cells.

- Varying degrees of corneal thinning. Vascularization of the bed of the ulcer present up to leading edge.
- The ulcer typically involves superficial one-third of the stroma initially then its spread concentric to the limbus. The leading edges are undermined and de-epithelized.
- In early disease there may be patchy epithelial involvement with near normal stromal thickness.
- corneal melting can occur at any clock hours with or without intervening clear space from the limbus.
- Frequently associated with limbal ,episcleral and ciliary injection.

In advanced case most of the cornea is lost & only central island will be present surrounded by thinned scared vascularized cornea.

- Scleritis if present indicates underlying systemic disease associated with PUK

Complications include perforation,secondary bacterialinfections,severe astigmatism,cataract , glaucoma.

CLASSIFICATION

Based on depth of thinning,

- <25% – grade 1
- 25-50% - grade 2
- 50- 75%- grade 3
- 75 – 100% - grade 4

Based on clock hours & extension of PUK

MILD - 2’ clock hours, superficially upto anterior stroma

MODERATE - 2’ - 4’ clock hours, with anterior stromal involvement/

any clock hours with mid stromal involvement

SEVERE- Extends upto Descemet’s membrane/ perforation

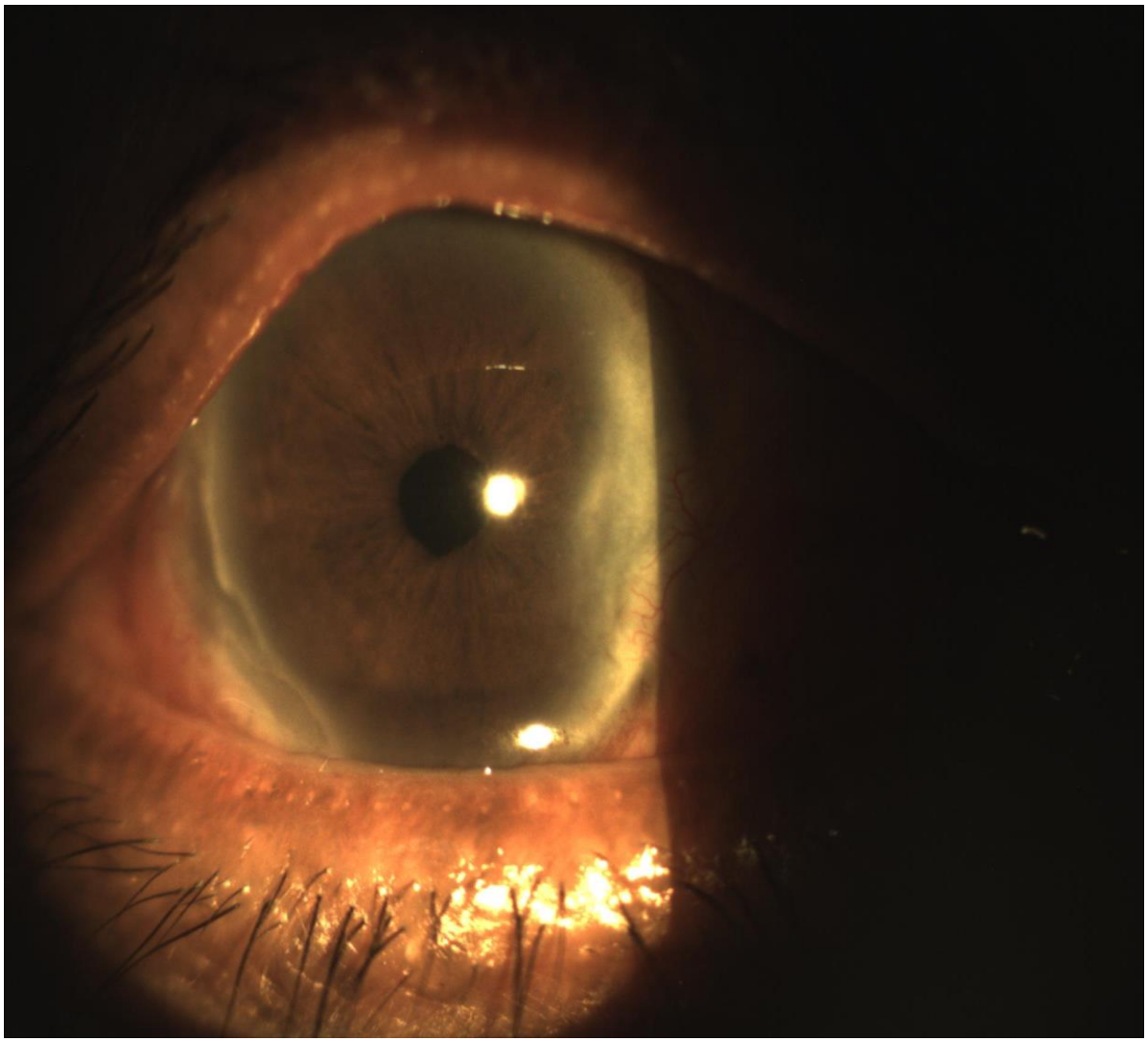


Figure 11 showing slit lamp image of PUK from 7 to 10 clock hours of grade 2

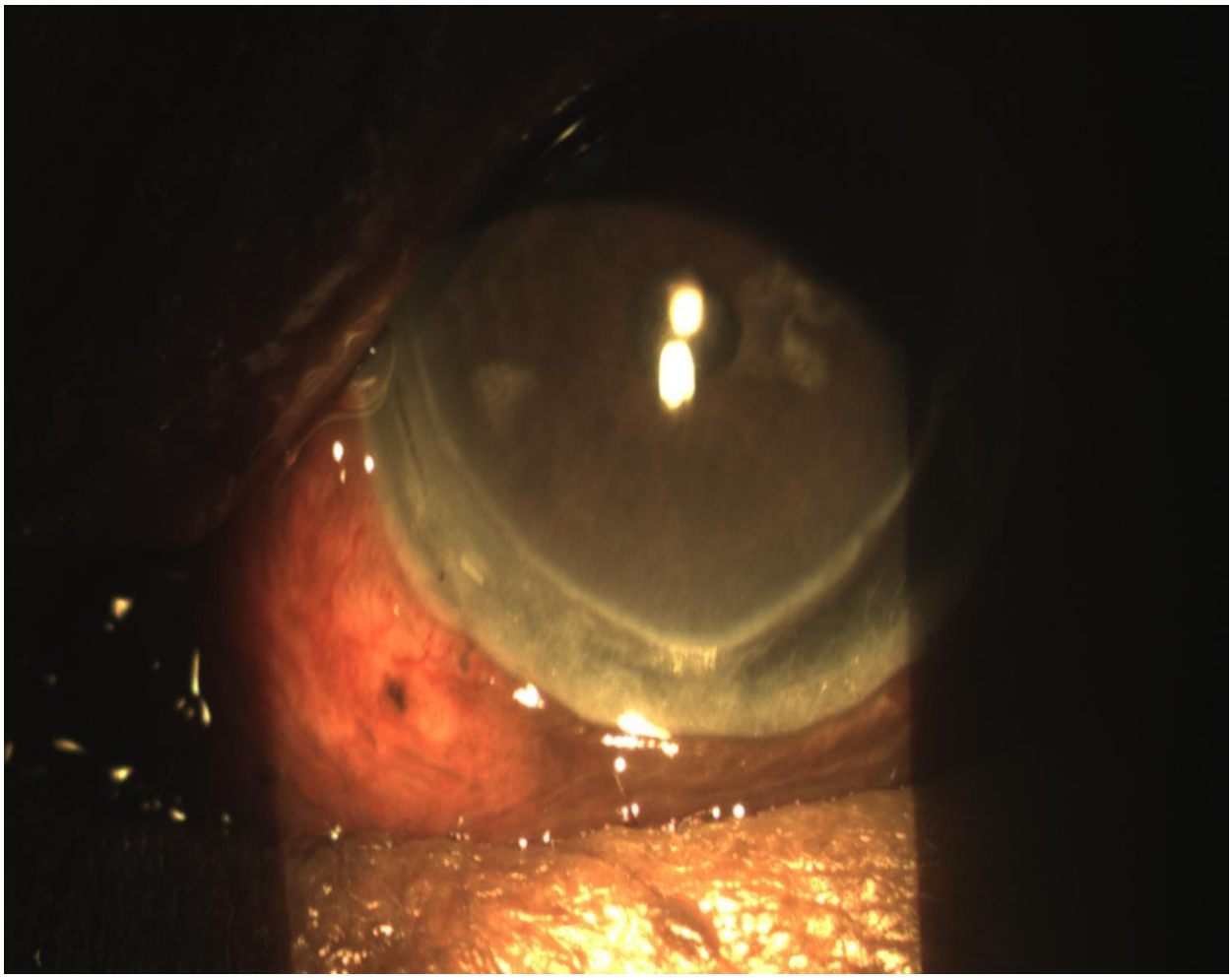


Figure 12 showing slit lamp image of PUK from 3 to 9 clock hours of grade 3

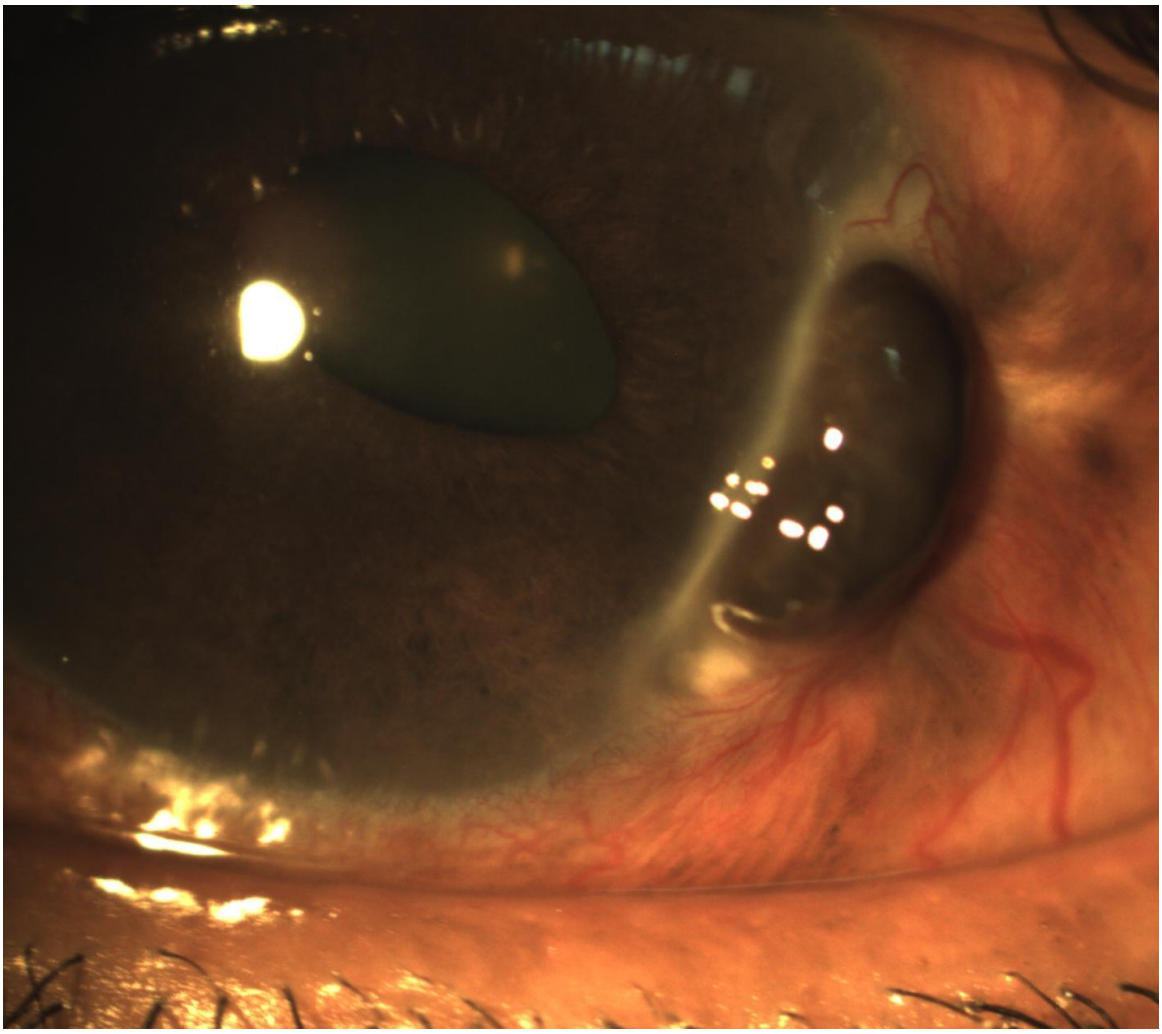


Figure 13 showing slit lamp image of perforated PUK from 3 to 5 clock hours of grade 4

SIGNS OF RESOLUTION :

- Regression of conjunctival inflammation.
- Epithelisation of the cornealsurface with residual thinning and vascularised scar.

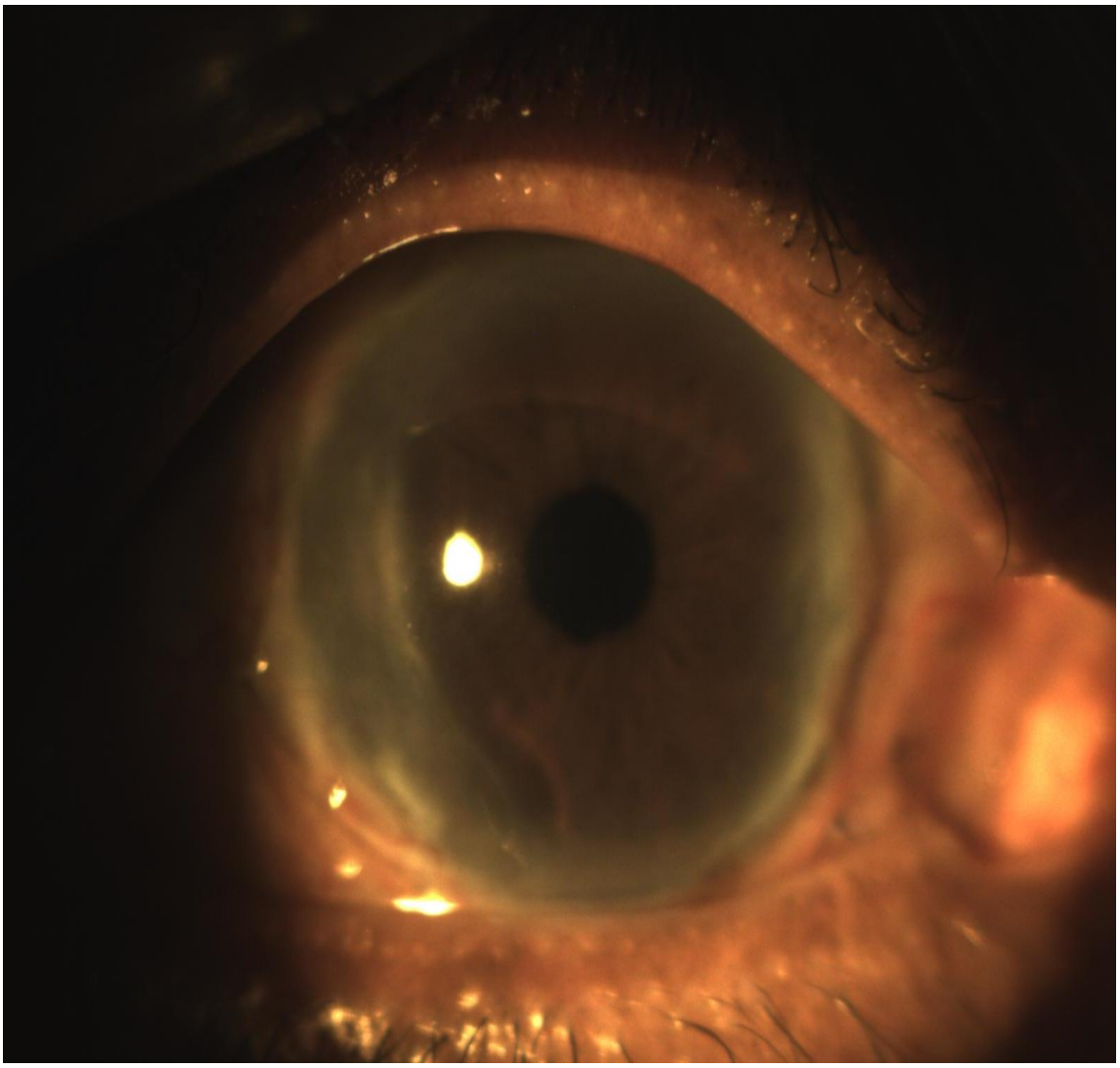


Figure 14 showing healed PUK

Systemic Features

The PUK may be a manifestation of underlying systemic illness detailed systemic history including past history and family history are very important.

GENERAL EXAMINATION IN A CASE OF PERIPHERAL ULCERATIVE KERATITIS:

Skin		**Ear**	
Rashes/ulcer	All vascular syndromes, SLE	Deafness	RP,WG,GCA,Sjog
Sunburn easily	SLE,PSS	Swollen ear lobes	RP
Depigmentation	SLE	Ear infections	WG,RP
Loss of Hair	PSS,SLE,GCA	**Nose/sinus**	
Painful Cold fingers	PSS	Nasal mucosal ulcers	WG,SLE
Puffy hands and feet	Sjog,CS,WG,RP	Rhinitis/nosebleeds	WG
Respiratory		Swollen nasal bridge	RP
Constant coughing	WG,SLE	Sinusitis	WG

Coughing blood	SLE,CS,WG,PSS,RP	**Mouth/throat**	
Shortness of breath	WG,SLE,PAN,CS,RP	Oral mucosal ulcers	SLE,Sjog
Asthma attacks	CS	Dryness	Sjog
Pneumonia	CS,WG,Sjog,RP	Persistent hoarseness	SLE,RP
Genitourinary		**Neurological**	
Blood in urine	WG,SLE,PAN,CS,RP	Headaches	SLE,GCA,RP
Testicular pain	PAN	Numbness/tingling	All vasculitic syndromes
Rheumatologic		Paralysis	SLE,WG,RP
Painful joints	RA,PAN,GCA,PSS,Sjog	Seizures	SLE,RP
Muscle aches	PAN,GCA,PSS,Sjog	**Psychiatric**	SLE
Gastrointestinal			
Abdominal pain	PAN,SLE,CS		
Nausea, vomiting	SLE		

Regurgitation	PSS		
Jaundice	SLE		
Blood in stool	PAN		

SLE -Systemic lupus Erythamatosus,RA Rheumatoid Arthritis,RP Relapsing Polychondritis,PSS Progressive systemic sclerosis,PAN Polyarteritis nodosa,Sjog Sjogren syndrome,WG Wegener's Granulamatosis,CS churg strauss,GCA Giant cell arteritis.

MOOREN'S ULCER

It is diagnosis of exclusion, if PUK is not associated with any systemic illness & scleritis. Corneal perforation may occur in 35%-40% of cases with minor trauma to the weekend cornea.

Watson classified this into unilateral mooren's ulcer , bilateral aggressive and bilateral indolent.

Unilateral mooren's ulcer :

It is a rare type that affects patients aged more than 60 years, it may progress slowly or extremely rapidly from the single focal point.

Bilateral aggressive Mooren's Ulcer

The age group usually affected is between 14 & 40 years.

Bilateral Indolent

It affects patients in the fifth decade or older. It progresses slowly.

PUK Associated with systemic diseases

Rheumatoid Arthritis

It is most common systemic disease associated with PUK. RA observed in 34% to 42% of PUK cases. It can be associated with scleritis. And rheumatoid PUK often occurs in destructive nodular RA of longer duration & in patients with high titers of rheumatoid factor & anti CCP antibodies .The occurrence of PUK in RA suggest life threatening stage & should be treated as emergency with immunosuppressants .

Wegener' s granulamatosis

It is characterised by vasculitis involving upper and lower respiratory tract and glomerulonephritis.Ocular complications include scleritis,conjunctivitis, PUK. Ocular involvement is about 50% to 60%.

In contrast to RA,PUK often manifest at the onset of wegener's granulomatosis leading to the diagnosis of this underlying condition.

Polyarteritisnodosa

It is a rare multisystmeic disease characterized by necrotising vasulitis of small and medium sized vessels.Scleritis,PUK,retinal vasculitis are the ocular features.Hepatitis B surface antigen is present in about 50 percent of patients.

INVESTIGATIONS

- Microbiological workup of ulcer should be done to rule out infective etiology which includes corneal scraping and sample should be sent for smear and culture and sensitivity.

Basic hematological investigations that is mandatory in all patients include

- Complete blood count-Hemoglobin ,Total count, Differential count, Erythrocyte Sedimentation rate
- Renal and Liver function test.
- Urine analysis.

Tests to rule out underlying systemic infections include :

- Serology for syphilis,
- Chest xray and skin test for tuberculosis,
- Serological test for Hepatitis B and Hepatitis C infections.

Tests for underlying immunological disorders include:

- ANA antinuclear antibodies,
- Rheumatoid factor,
- Antineutrophil cytoplasmic antibodies ANCA,
- Anti CCP - anti cyclic citrullinated peptides antibodies.

AS-OCT ,B mode ultrasonography can be considered if associated scleritis is suspected.

MANAGEMENT

A systematic logical approach should be followed based on history,clinical examination and tailored investigative modalities.

For Infectious PUK

Specific antimicrobial therapy should be instituted for microbial keratitis.

Microbial infections are treated with antibacterials such as fluoroquinolones,fortifed antibiotics such as fortified cefuroxime and fortified ceftazidime for gram positive and

gram negative bacteria perse and antifungals such as topical natamycin and topical azole agents.

Systemic treatment for tuberculosis with antituberculous therapy,syphilis with parenteral penicillin,hepatitis infections with antivirals .

For Non Infectious PUK

It includes both medical and surgical therapy.

A tailored approach specific for each patient is needed based on the treatment guidelines.

MEDICAL THERAPY

It can be either local or systemic therapy.

Local therapy:

- Preservative free lubricants,
- Topical collagenase inhibitors (1% medroxyprogesterone and 20% N-acetylcysteine).
- Prophylactic topical antibiotics.
- Topical corticosteroids -Topical corticosteroids should be instituted earlier are advocated in the early therapy. In eyes with perforation its use should be cautious as it interfere with collagen synthesis.
- Topical cyclosporine 0.05% - 2% BD /QID -immunomodulator agent by suppressing helper T cells which can be used as steroid sparing agent

SYSTEMIC THERAPY

- Oral tetracycline derivatives (Tablet Doxycycline 100 mg BD)
- Oral ascorbic acid
- Systemic corticosteroids (Oral prednisolone 1 mg/kg /day)
- Disease specific immunomodulators

Indications for systemic immunosuppression with chemotherapeutic agents include :

* PUK with active systemic autoimmune disorders such as rheumatoid arthritis, polyarteritis nodosa,relapsing polychondritis,wegeners granulamatosis

*PUK with scleritis

*PUK with ocular vasculitis

*PUK with bilateral simultaneous involvement

*PUK with progressive worsening despite adequate conventional medical and surgical therapy.

Systemic immunomodulators which can be given include

1. Glucocorticoids
2. Immunosuppressives/immunomodulators.
3. Biologic agents

Glucocorticoids

Systemic steroids are the first line therapy for acute cases of PUK. .The usual starting dose is 1 mg/kg/day followed by tapering based on clinical response. Pulse therapy with intravenous methylprednisolone 1g/day for 3 consecutive days followed by oral therapy might be started in imminent danger of vision loss.

Systemic steroids alone often unable to control the disease process and so immunosuppressive drugs or biologic agents can be administered for steroids resistant cases and when steroids are contraindicated.

Immunosuppressives/immunomodulators

The categories indicated in PUK are as follows

1.Antimetabolites,

2.Alkylating agents,

3.T cell inhibitors, and

4.Biologic agents.

Methotrexate, azathioprine, mycophenolate mofetil, and leflunomide aresuitable antimetabolite agents.

Methotrexate and azathioprine are more commonly used antimetabolites in recalcitrant rheumatoid PUK. Oral methotrexate in doses ranging from 7.5–25 mg/week and azathioprine 1.0–2.5 mg/kg/day are effective. Mycophenolate mofetil (1.0 g twice daily) has better inflammatory control and fewer side effects than methotrexate or azathioprine. Leflunomide is also efficacious in the treatment of ocular inflammation.

The alkylating agents, cyclophosphamide and chlorambucil,are indicated in cases unresponsive to methotrexate or other antimetabolites.

Cyclophosphamide may be administered orally at doses of 1–2 m/kg/day or as pulsed intravenous therapy every 3–4 weeks under rheumatologic or internal medicine guidance.

Cyclosporine is a calcineurin inhibitor that inhibits T cell activity.It is given in dose of 2.5 - 5 mg/kg/day.The side effects associated with this drug are gum hyperplasia,hyperkalemia,hirsutism,convulsions.

Biologic agent

Infliximab is a US FDA approved drug.It is indicated in connective tissue and autoimmune associated vasculitic diseases and accompanying PUK and other ocular inflammatory states such as necrotising scleritis and uveitis

It is a specific, chimeric monoclonalantibody against proinflammatory cytokine tumor necrosisfactor alpha (TNF-α), which stimulates production of the matrix metalloproteinases responsible for corneal stromallysis in PUK. It binds both soluble and transmembrane TNF-α by blocking its receptor. Cells expressing transmembrane TNF-α bound to infliximab may also be susceptible to complement-mediated lysis, potentially increasing its anti-inflammatory effect.

Dosing of infliximab varies from 3 mg/kg intravenously for rheumatoid arthritis to 5 mg/kg intravenously for Crohn’s disease, and is administered at weeks 0, 2, and 6,and then every 8 weeks for up to 18 months. Improvement usually occurs 1–2 weeks after the

first infusion. The maintenance of remission must be weighed against potential adverse events, because the long-term efficacy and safety of biologics for use in ocular inflammation is unknown.

Theside effects are malignancy,opportunistic infections, diarrhea, cardiac failure, anaphylaxis ,lymphoproliferative disorders, endogenous endophthalmitis, hepatotoxicity.There is increased risk of thrombosis which can cause branch retinal vein occlusion to myocardial infarction.

Other biologics are etanercept and rituximab . Etanercept is a human recombinant dimeric fusion protein that acts similar to soluble TNF-α receptors. It is also used for the treatment of necrotizing scleritis, and keratitis, but

is less efficacious than infliximab for the treatment of ocular inflammation. This is because infliximab can bind to membrane-bound TNF-α, in addition to free-floating cytokines.

Rituximab, a chimeric antibody against CD20-α, which depletes B lymphocytes, has been used to treat refractory PUK associated with Wegeners granulomatosis.

Surgical Management

Surgical intervention is undertaken either as adjunct to medical therapy, when medical therapy proves inadequate to halt disease progression, or when complications arise for restoring tectonic integrity.

Various surgical options include Conjunctival resection,,Amniotic membrane transplantation , corneal gluing ,bandage contact lens,Patch graft,penetrating keratoplasty.

CONJUNCTIVAL RESECTION

Resection of the perilimbal conjunctiva upto 4mm from limbus removes immune complexes, decreases collagenases and proteinases, and causes resolution of inflammation.

AMNIOTIC MEMBRANE GRAFTING

An amniotic membrane reduces inflammation and promotes re-epithelization. The biologic properties of amniotic membrane that reduces inflammation are expression of Fas ligand and human leucocyte antigen-G ,activation of suppressor T cell mechanisms.

TISSUE ADHESIVES

It is indicated in patients with impending perforation and perforations less than 2.0 mm, and it can be combined with application of a bandage contact lens to prevent discomfort.

Keratoplasty Indications:

1. Tectonic/therapeutic: Increasing depth of melt leading to descemetocele formation or impending perforation.

2. Tectonic/therapeutic: Advancing extension of melt circumferentially and/or centrally.It halts the progression of information

3. Optical: After the active disease process has been treated—for visual rehabilitation of ectasia and induced astigmatism, and for structural stability of the residual thinning.

Postoperative considerations :

- Continue medical management for the underlying illness.
- Graft management:
    - Topical and systemic anti inflammatory drugs such as steroids and immunosuppressants.
    - Topical Antibiotics to prevent infections.
- Preservative free lubricants.
- Associated ocular complications such as steroid induced glaucoma and cataract should be treated.
- Visual rehabilitation with appropriate and timely suture removal and (astigmatic correction.)

TREATMENT PROTOCOL FOR MOOREN'S ULCER

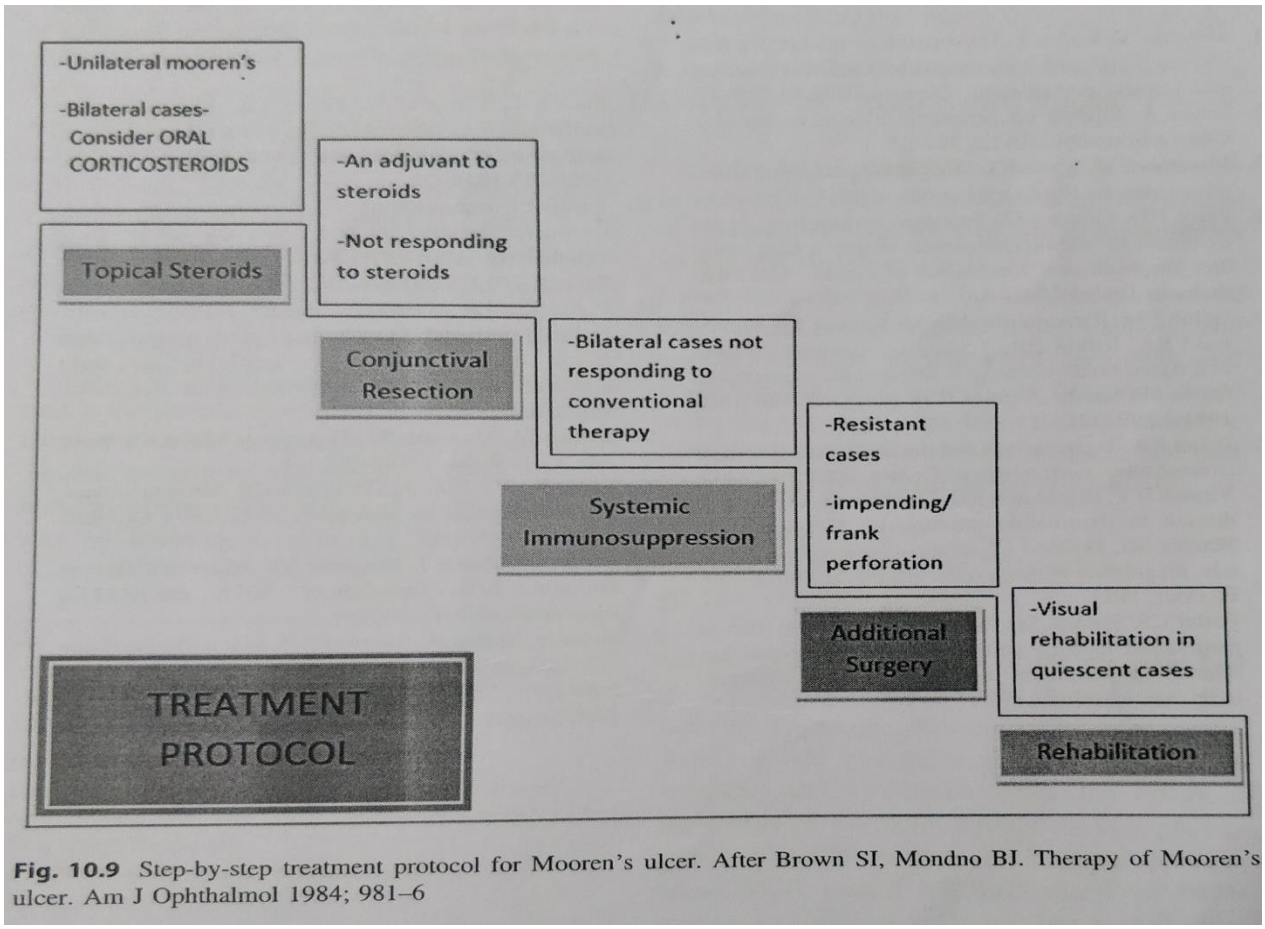


Fig. 10.9 Step-by-step treatment protocol for Mooren's ulcer. After Brown SI, Mondno BJ. Therapy of Mooren's ulcer. Am J Ophthalmol 1984; 981–6

Fig 15 – Treatment protocol of Mooren's ulcer

PART 2

AIM:

To study on the aetiology ,clinical presentation and outcome of various treatment modalities of peripheral ulcerative keratitis of Non infective Etiology.

OBJECTIVES:

1.To study on the various aetiological factors and systemic associations of Peripheral ulcerative keratitis.

2.To study on the various modes of presentation of Peripheral ulcerative keratitis.

3.To study on the outcome of various treatment modalities.

SAMPLE SIZE :40

MATERIALS & METHODS:

This prospective study was conducted at Cornea services Department, RIOGOH, Madras Medical College, at Egmore, Chennai-08, for a period of 12 months.

Methodology:

Patient presenting with Peripheral Ulcerative Keratits to Cornea services department, RIOGOH was registered, evaluated and followed up during the study period.

- A detailed history of the patient , complete general examination with vitals measurement,examination of RS, CVS ,CNS was done.
- Test for best corrected visual acuity using Snellen chart , local ocular and adnexa examination and detailed slit lamp anterior segment evaluation was done.
- Fundus examination with direct ophthalmoscopy, slitlamp biomicroscopy with 90D,indirect ophthalmoscopy , intraocular pressure measurement using noncontact tonometry / rebound tonometry was done.

- Corneal smear examination with gram staining and KOH mount was done.
- Urine analysis and other blood investigations - random blood sugar, hemoglobin ,complete blood count including erythrocyte sedimentation rate, liver function test ,renal function test,Rheumatoid factor, Anti nuclear antibodies was done.Test for HIV and VDRL ,mantoux skin test ,chest x ray ,serology for HBV and HCV.

Patients has been referred to general physician and rheumatologist for expert opinion. Patients has been treated with either medical management with topical and systemic steroids and immunosuppresives or surgical management or both.

Response of the patients to the treatment and occurence of complications in them was assesed in the follow up period.

INCLUSION CRITERIA:

1. Patients presenting with Peripheral Ulcerative Keratitis of Non infective etiology.
2. Age>18 years.

EXCLUSION CRITERIA:

1. Patients with Peripheral Ulcerative Keratitis due to Infectious causes.

SCREENING PROCEDURES/ VISIT:

- Detailed history of present illness,
- Ocular symptoms and signs on presentation
- Visual acuity using Snellen's acuity chart
- Slit lamp biomicroscopy of anterior segment

- Fundus examination of the same and other eye
- Laboratory Investigations and radiological imaging.
- Treatment given and Outcome.

Follow up Procedures / Visits:

First two visits weekly, next two visits biweekly, thereafter monthly follow up. If sudden development of symptoms visit as early as possible or immediately

ASSESSMENTS OF PARAMETERS:

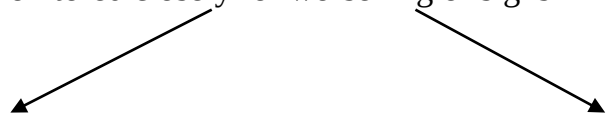
1. Ocular findings during presentation and subsequent follow up.
2. BCVA during presentation and subsequent follow up.
3. Treatment given and its outcome.

Management done in our study.

Non infective Peripheral ulcerative keratitis

Topical steroids initially for every 2 hrs along with topical lubricants, topical collagenase inhibitors, Oral doxycycline for two weeks and oral ascorbic acid. Topical cycloimmune was started for perforated cases and severe thinning cases.

Patients were monitored closely for worsening of signs



IMPROVEMENT SEEN NO IMPROVEMENT SEEN/ WORSENING

Continue topical steroids and taper accordinglyOral steroids (prednisolone 1mg/kg/day)

Oral immunosuppressants

Surgical intervention

RESULTS:

Statistical analysis plan – Analysis of data

Data collected were entered in Excel Spread sheet and analyzed using STATA statistical software package release 11. We used the two-sided independent-samples t test to compare

means across dichotomous variables (i.e. men v. women); the one-way ANOVA test for comparison of means across multilevel variables. Simple calculations like Percentages,Proportions and Mean values were derived. A type I error of 0.05 was considered in all analyses.

RESULTS AND ANALYSIS

Age groups	Frequency	Percentage
20 - 30 years	7	17.5%
30 -40 years	2	5%
40-50 years	4	10%
50- 60 years	6	15%
60-70 years	13	32.5%
70 - 80 years	6	15%
>80 years	2	5%
Total	40	100%

Table 1 Age distribution in the study group

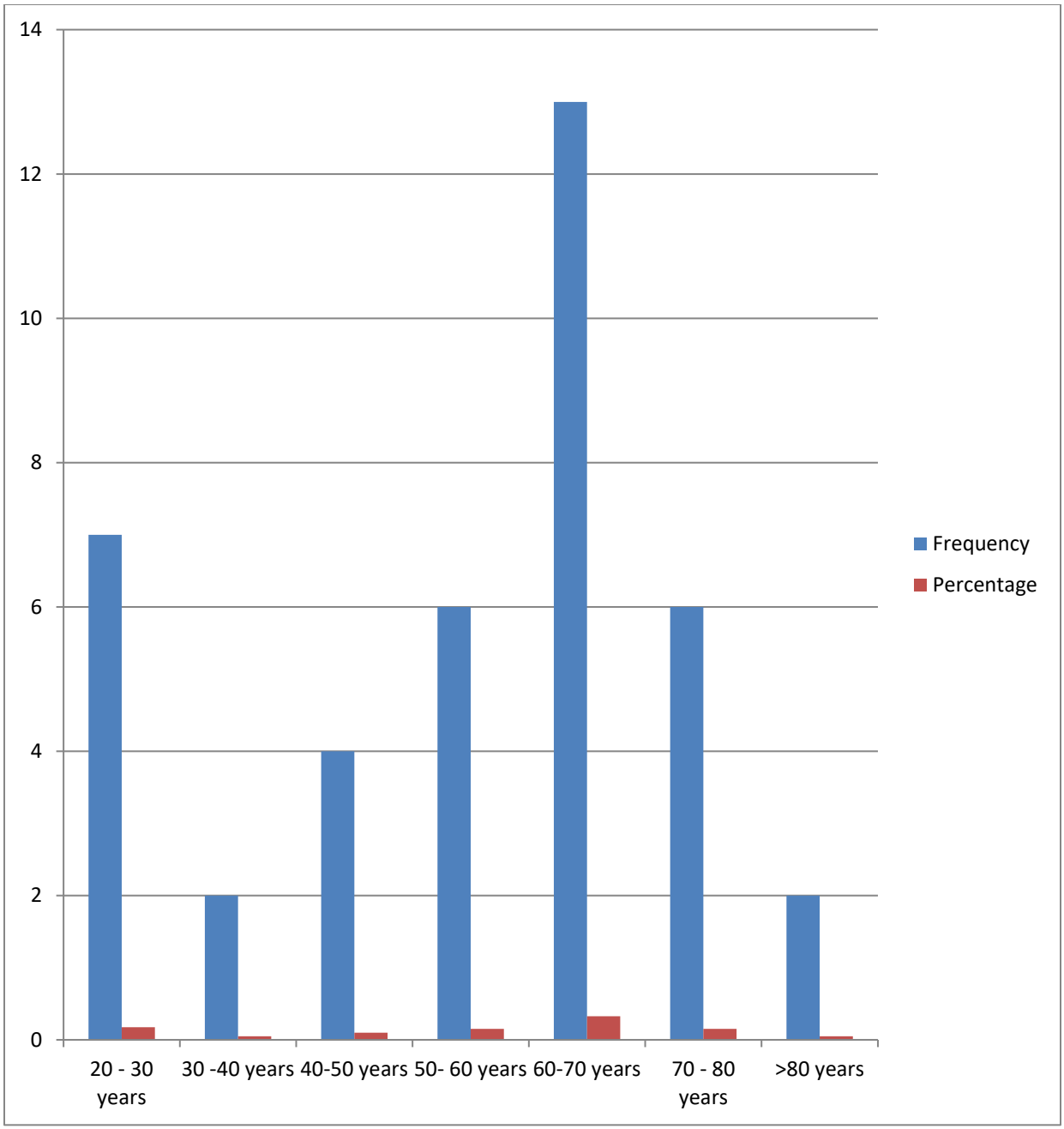


Chart 1Age distribution in the study group

In our study most common age group affected was 60-70 years (32.5%)

SEX DISTRIBUTION

Gender	Frequency	Percentage
Male	24	60%
Female	16	40%
Total	40	100%

Table 2 showing sex distribution in the study group

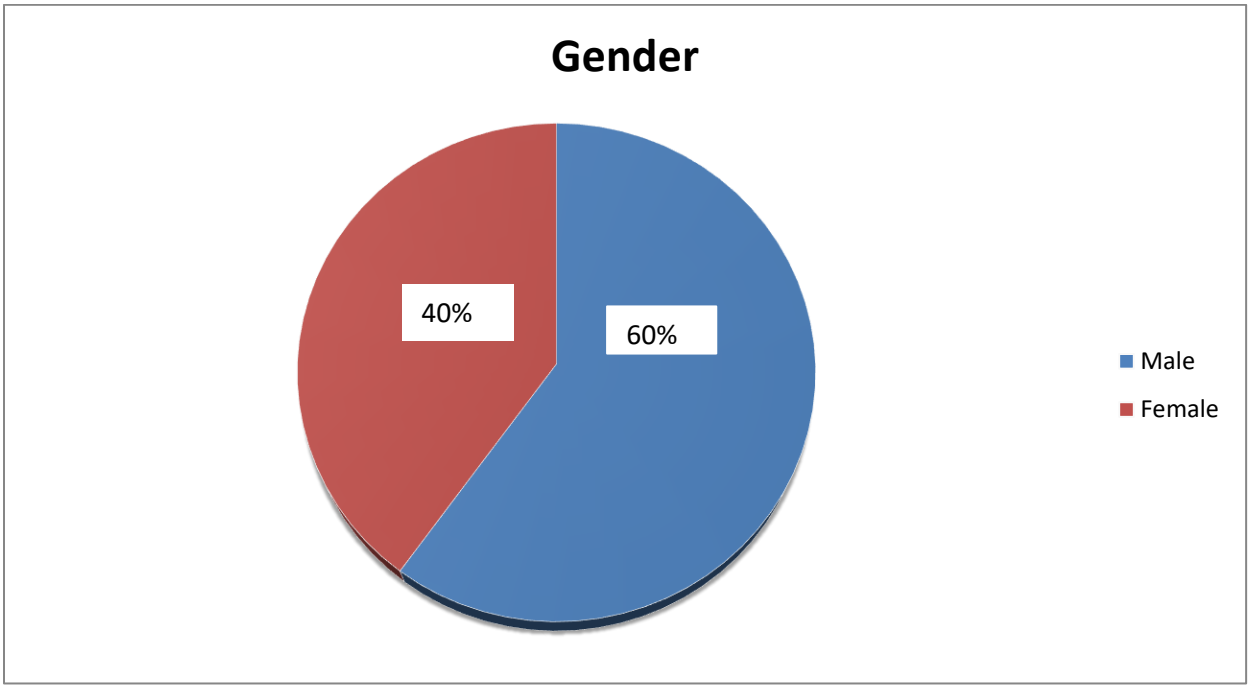


Chart 2 -Pie chart depicting gender distribution in the study group

Men (60%) were more commonly affected than women in our study group.

.LATERALITY

Laterality	Frequency	Percentage
Unilateral	26	65%
Bilateral	14	35%
Total	40	100%

Table 3 showing laterality in this study group

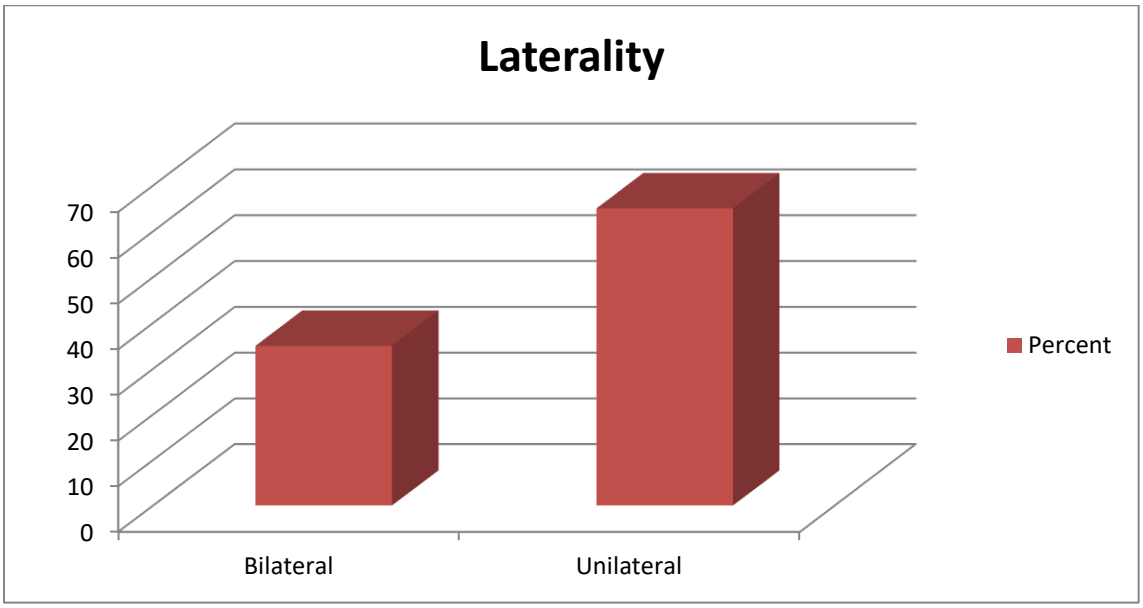


Chart 3- Laterality in the study group

Unilateral cases were 65% and bilateral cases were 35%.Unilateral presentation was the most common presentation.

EYEINVOLVED

Eye involved	Freq.	Percent
Left	21	38.89
Right	33	61.11
Total	54	100

Table 4 showing PUK involved eye

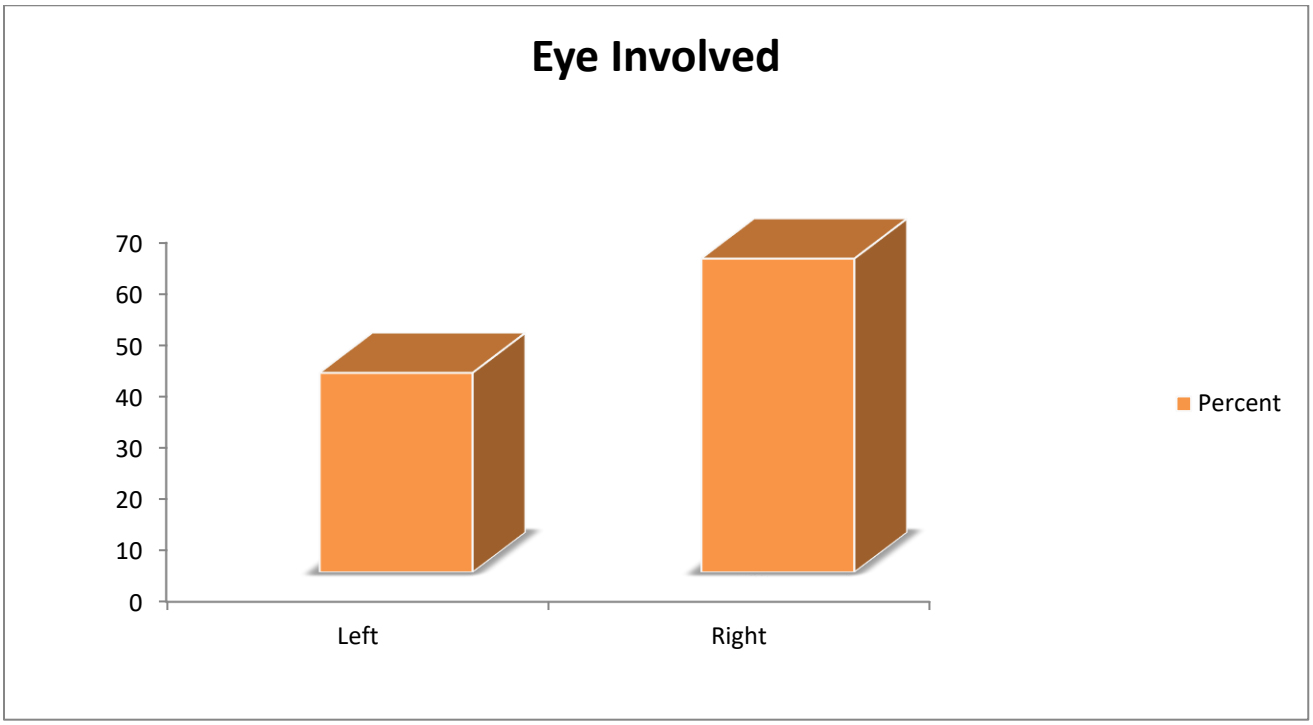


Chart 4 -Bar diagram showing PUK involved eye in study group.

Right eye (61.11%) is involved more than the left eye (38.89%) in the study group.

GRADING OF DEPTH OF THINNING

Grading	Freq.	Percent
I	4	7.41
II	27	50
III	11	20.37
IV	12	22.22
Total	54	100

Table 5- Grading of depth of thinning of PUK

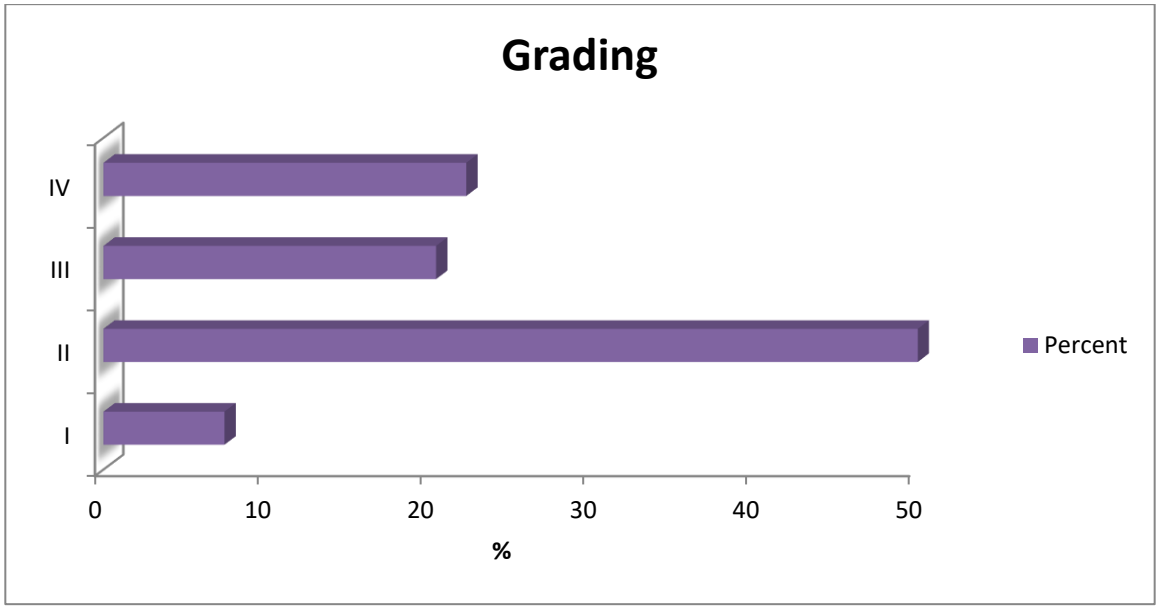


Chart 5 -Grading of depth of thinning of PUK

Most common presentation of gradeof depth of thinning was 2 followed by grade 4 in the study group.

SEVERITY OF PUK

Severity of eyes	Frequency	percentage
mild	7	13.0%
Moderate	22	40.8%
Severity	25	46.2%
Total	54	100%

Table 6 showing severity of eyes affected with PUK.

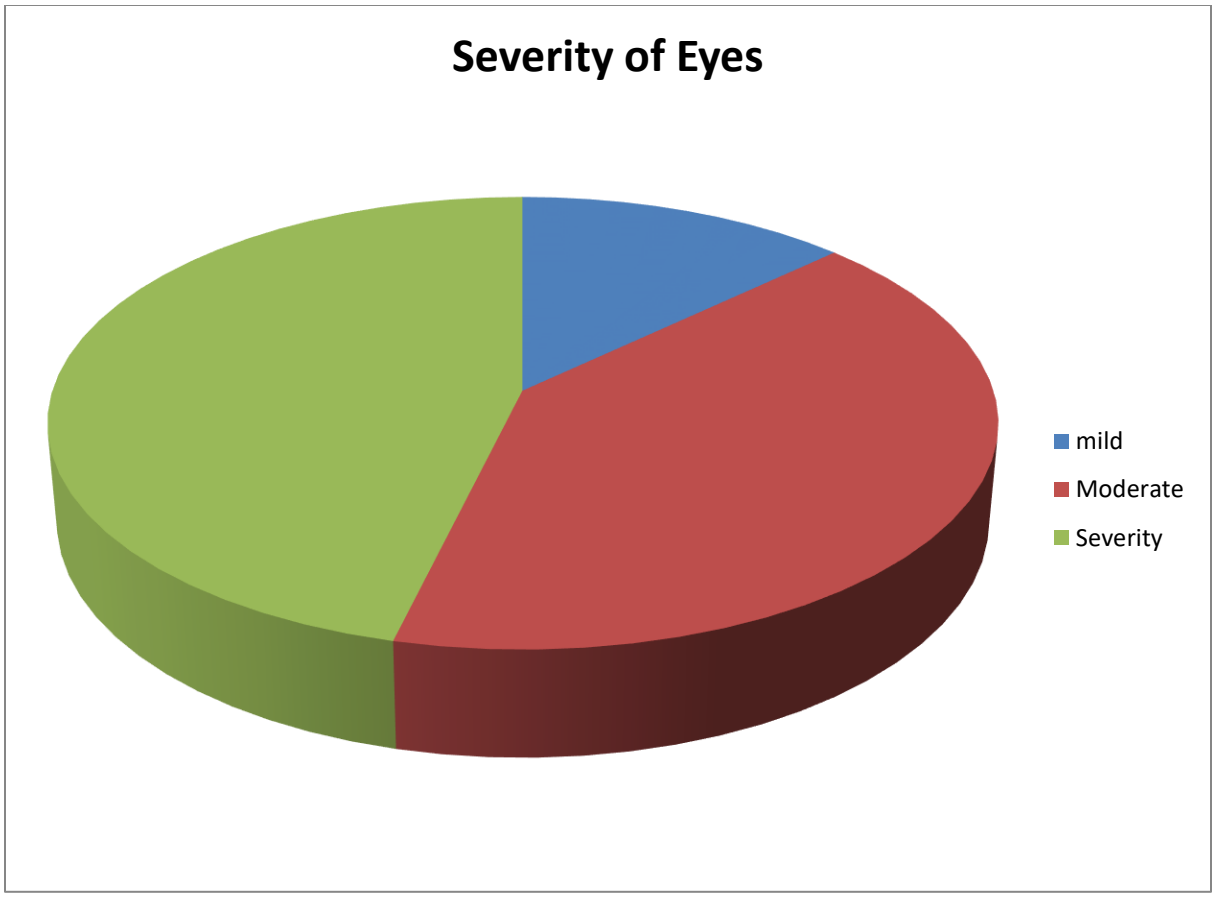


Chart 6 Showing Severity of eyes affected with PUK

In this study group 13% of eyes had mild involvement40.8 % eyes had moderate involvement.46.2 % eyes had severe involvement. Severe cases was the most common presentation. This classification has taken into account both the extent of clock hours involvement & depth of thinning.

INCIDENCE OF PERFORATED PUK

Perforation	Freq.	Percent
Absent	43	79.63
Present	11	20.37
Total	54	100

Table 7 Incidence of perforated PUK in the study group

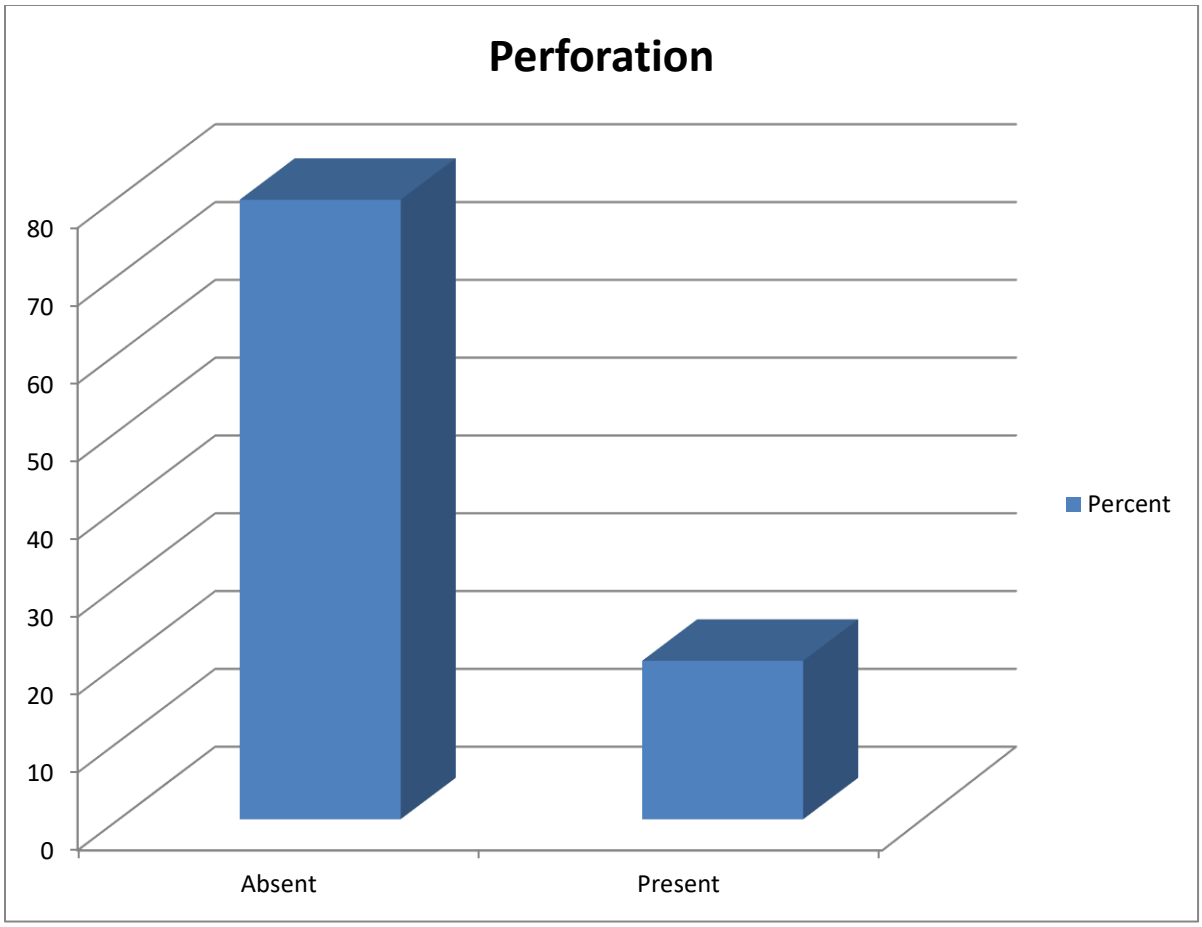


Chart 7-Incidence of perforated PUK

The incidence of perforated PUK in the study group was 20.37%. The number of cases with perforation at the time of presentation was 7 eyes& during the course of therapy was 4 eyes.

Ocular Association of PUK

Ocular Assosciation	Frequency	Percentage
Meibomitis	**15**	**27.77**

Table 8- Ocular Association of PUK

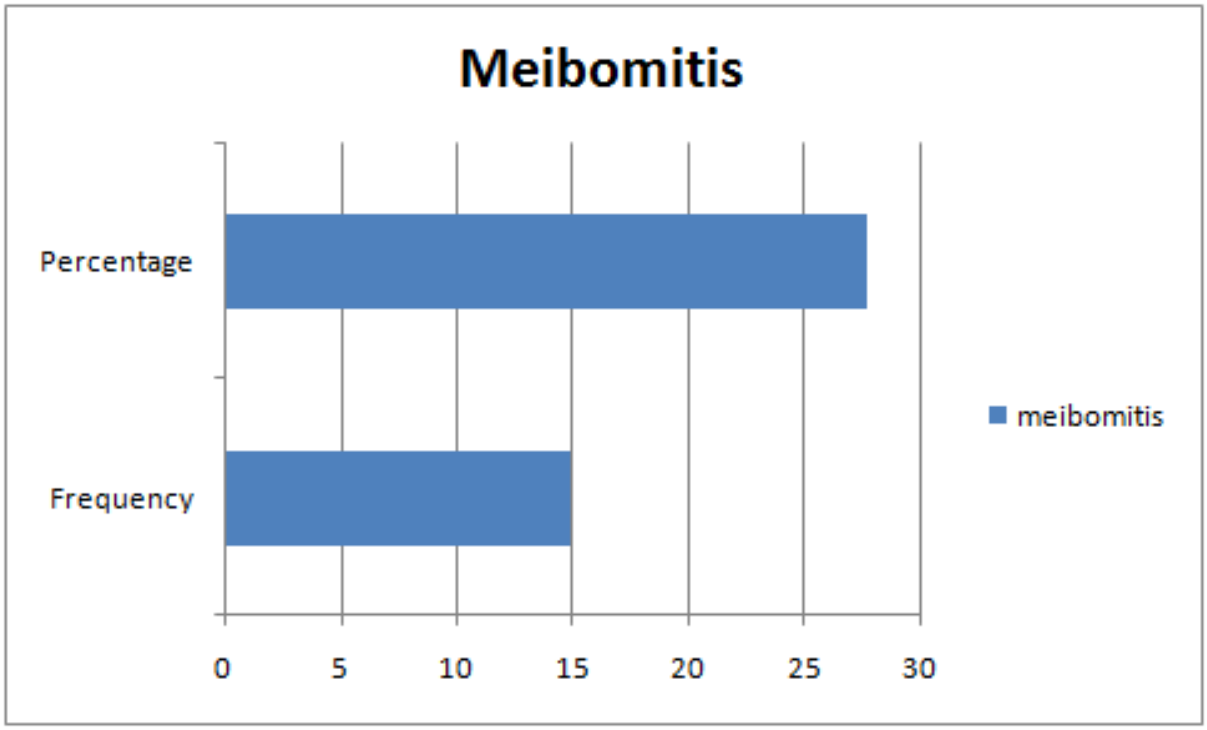


Chart 8- Ocular Association of PUK

In our study 15 eyes (27.77%) had meibomitis.

ETIOLOGY

Etiology	Freq.	Percent
Idiopathic	18	45
Mooren's	13	32.5
RA	8	20
SLE	1	2.5
Total	40	100

Table 9 -Etiology of PUK

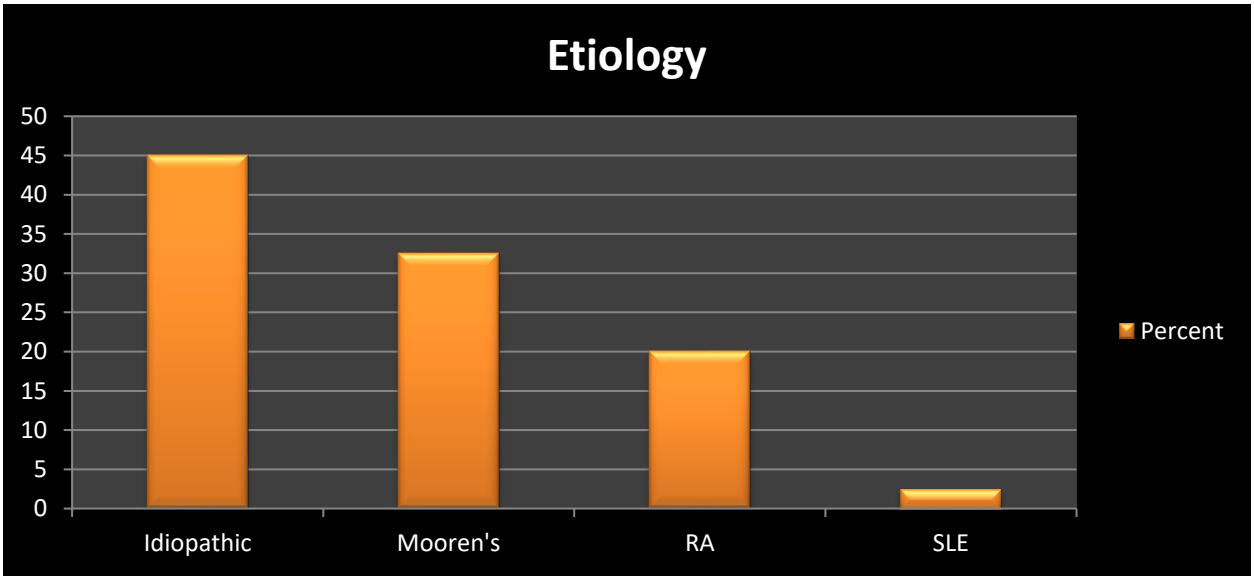


Chart 9-Etiology of PUK in the study group

In this study group ,most common etiology was mooren's ulcer (32.5%) followed by Rheumatoid arthritis(20%) and Systemic Lupus Erythematosus (2%).

MANAGEMENT

MEDICAL MANAGEMENT-

Topical therapy

Topical Management	Percent	Frequency
Cyclosporine	18.51	10
Steroid	55.6	30
Both	25.92	14
Total	100	54

Table 10 - Topical therapy given to PUK cases

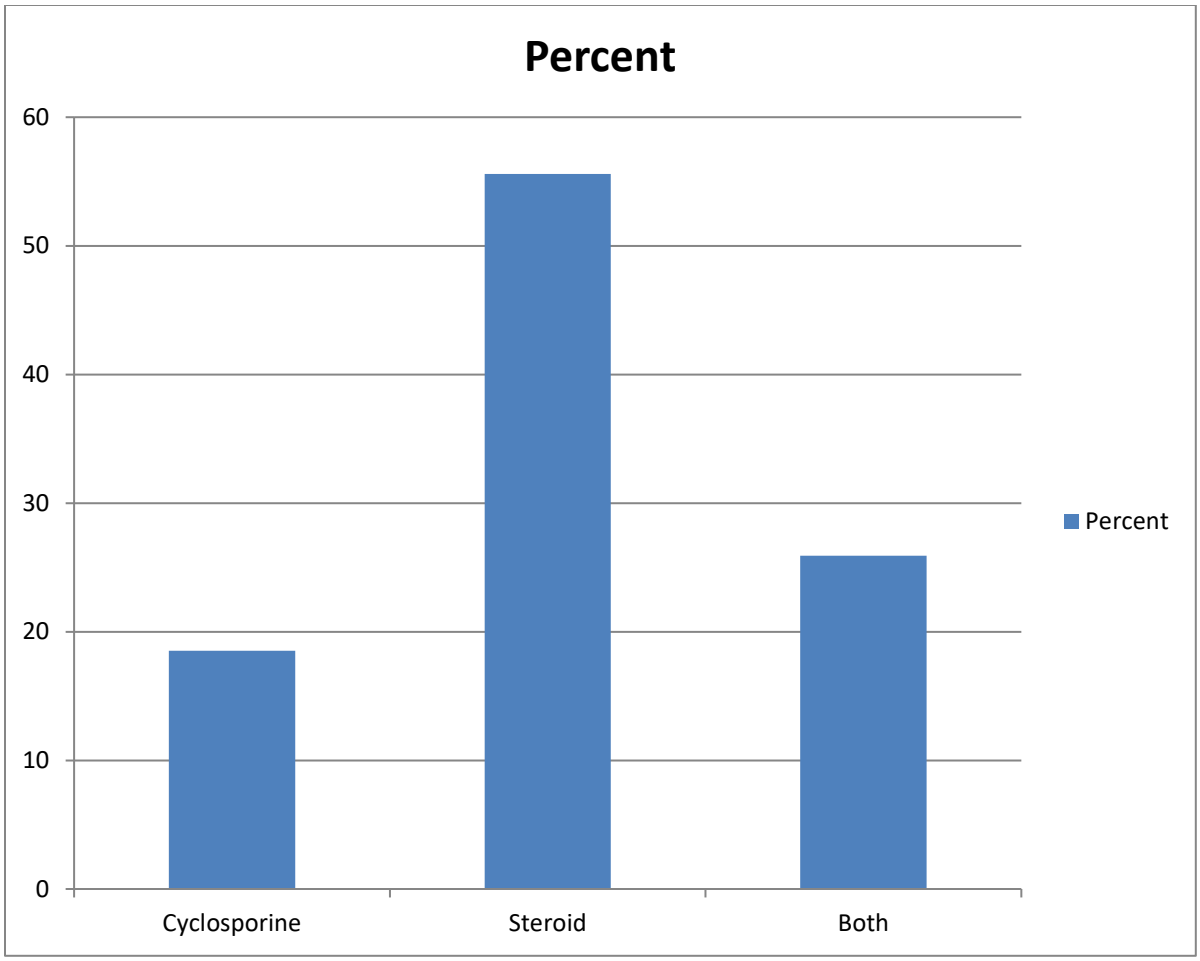


Chart 10 -Topical therapy given to PUK cases.

Among the topical therapy,topical cyclosporine alone was given to 18.5% eyes (10),topical steroids prednisolone acetate 1% eye drops was given 55.6% of eyes (30), both were given to25.92% eyes(14).

SYSTEMIC THERAPY

ORAL STEROIDS

Oral Steroids	Freq.	Percent
Not Used	3	5.56
Used	51	94.44
Total	54	100

Table 11 Oral Steroid therapy to PUK

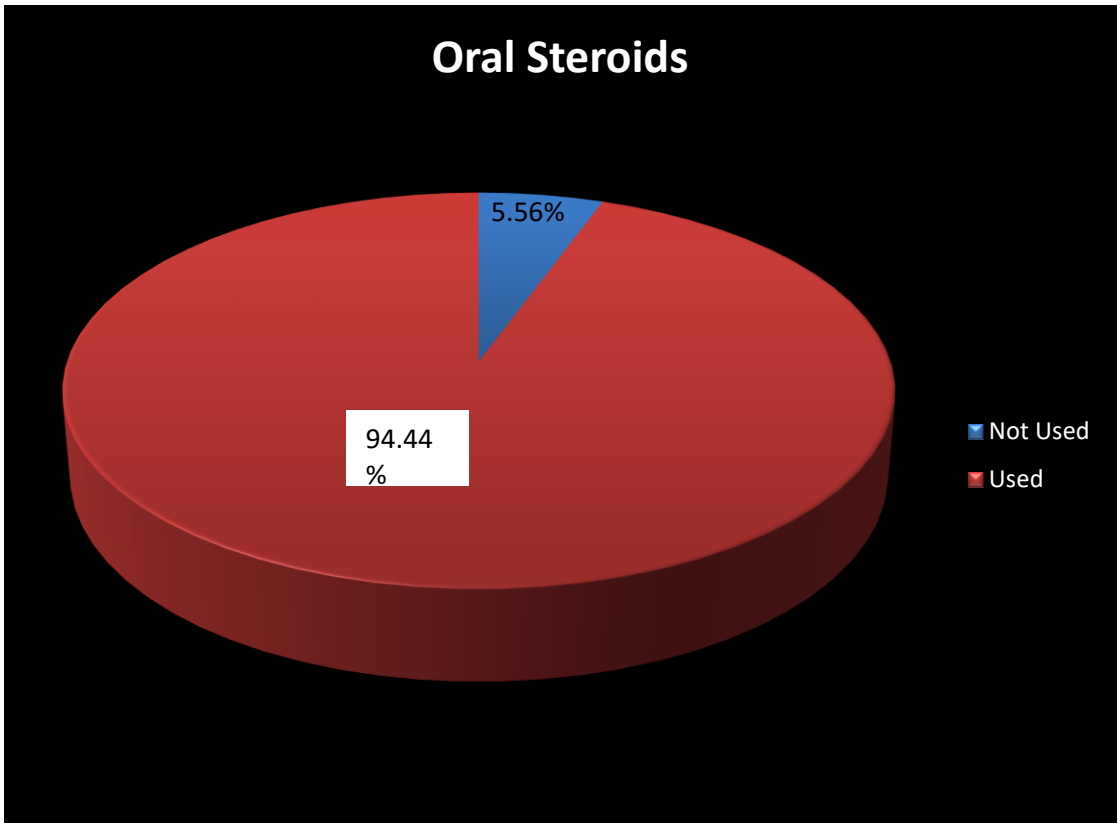


Chart 11- Oral Steroid therapy to PUK

Oral steriod was given to 94.44% of eyes(51/54).

IMMUNOSUPPRESSANTS

ImmunosupressantsUsed	Freq.	Percent
Azp 1mg/kg/d	1	1.85
Mtx 10mg/wk	8	14.81
Nil	45	83.33
Total	54	100

Table 12- Systemic immunosuppressant therapy given to PUK eyes

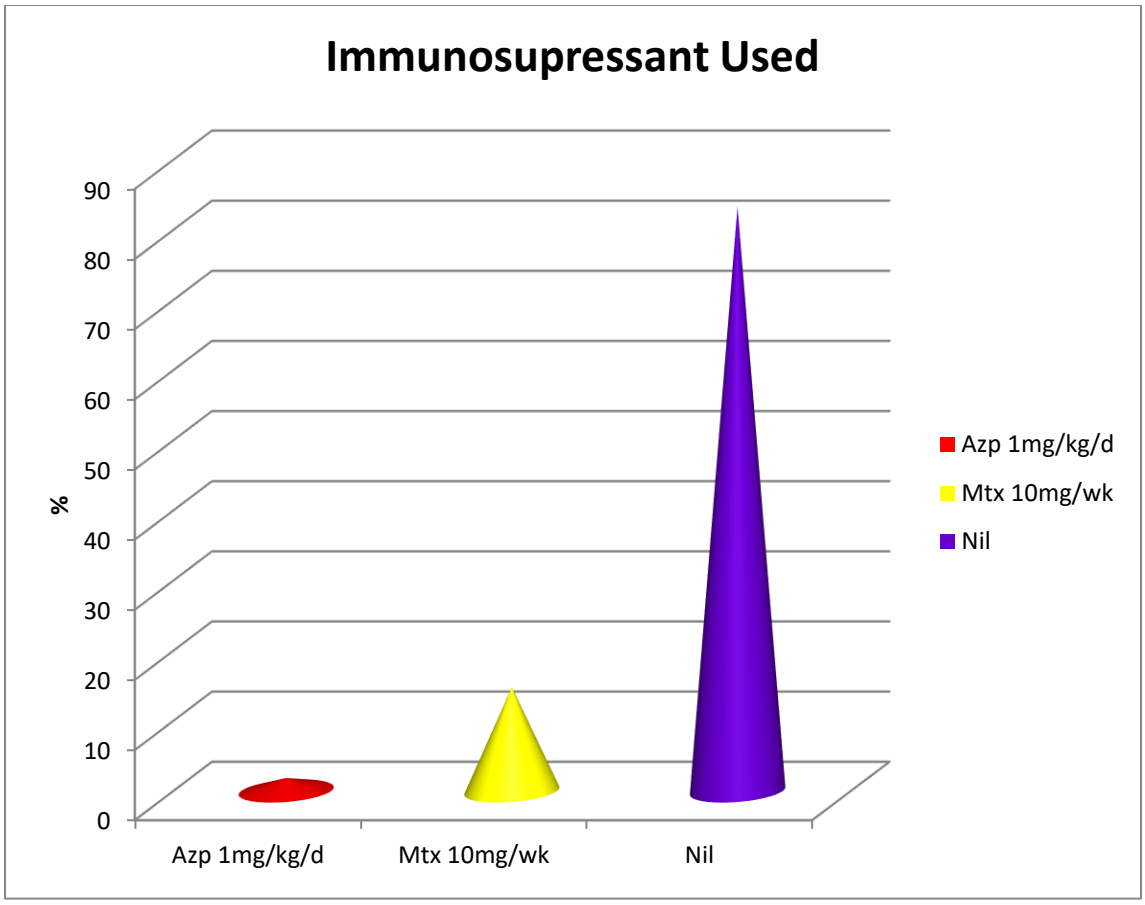


Chart 12- Systemic Immunosuppressants given to PUK eyes

Systemic immunosuppressants- oral methotrexate 10 mg /wk was given to 8 eyes(14.81%) and oral azathioprine 1 mg/kg/day was given to 1 eye (1.85%) as these eyes were severe PUK and associated with underlying systemic collagen vascular disease.

SURGICAL MANAGEMENT

Surgical Management	Freq.	Percent
Patch graft	8	14.81
Peritomy	2	3.7
Peritomy with AMG	10	18.52
Total	20	37.03

Table 13 Surgical management of PUK eyes

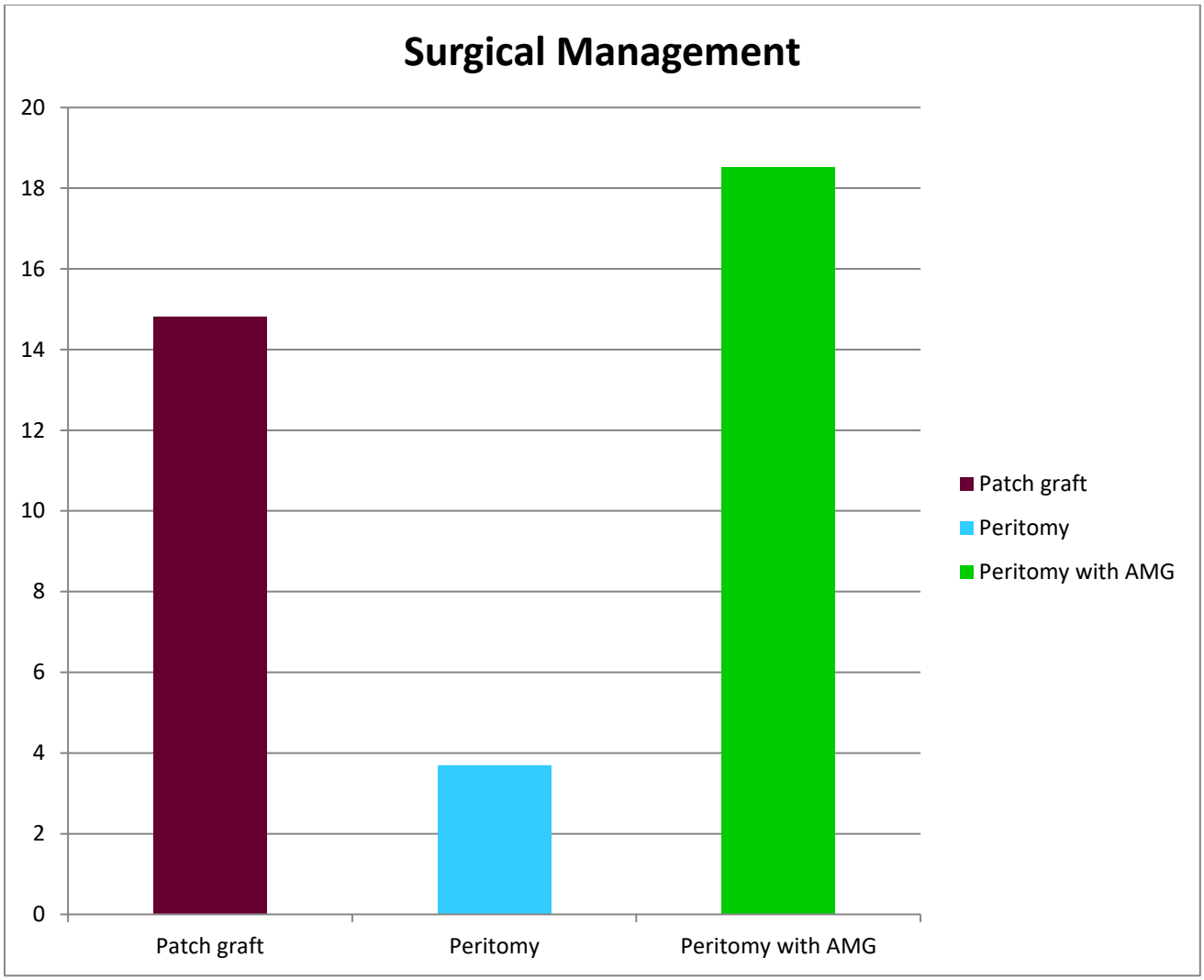


Chart 13- Surgical management of PUK eyes

Among the surgical management, Patch graft was done for 8 eyes(14.81%),Peritomy was done for 2 eyes (3.7%) and Peritomy with amg was done for 10 eyes (18.52%).

RESOLUTION OF SIGNS

Resolution of Signs	Freq.	Percent
Absent	4	7.41
Present	50	92.59
Total	54	100

Table 14 -Resolution of signs after treatment among PUK eyes

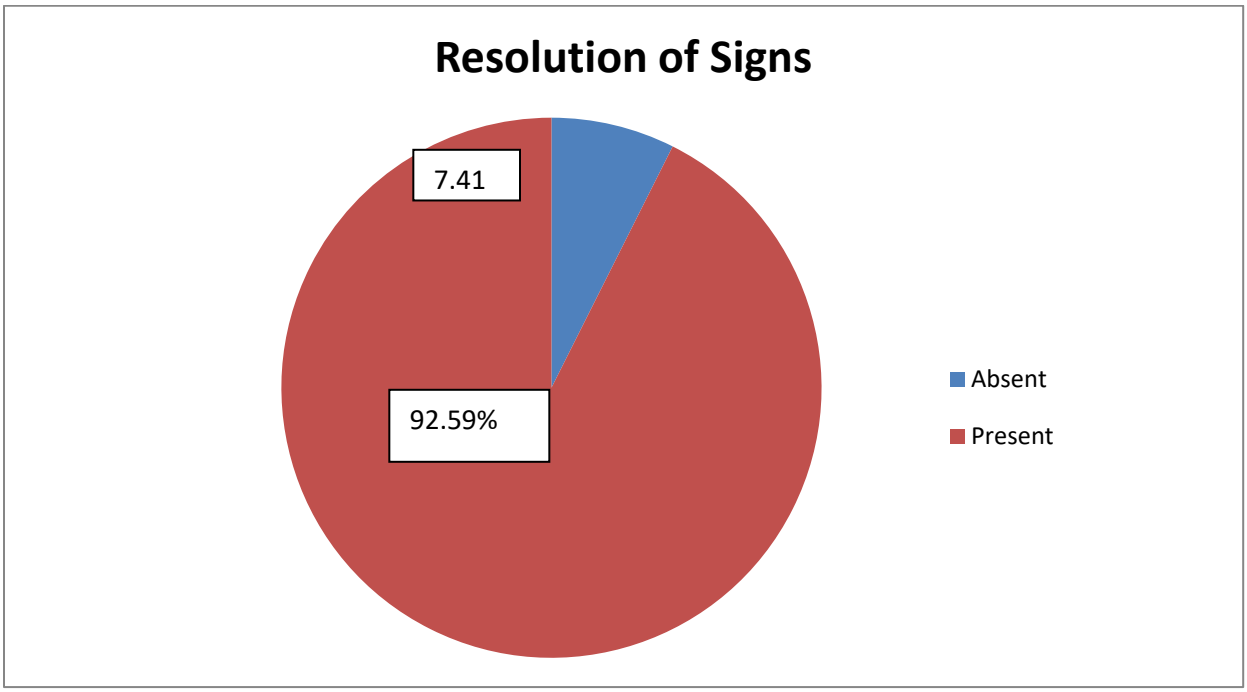


Chart 14 - Resolution of signs after treatment among PUK eyes

Among 54 eyes,resolution of signs of active PUK was seen in 50 eyes(92.59%) after treatment.

Comparison of resolution of signs among various surgical Modalitiess

Resolution of Signs Present	Freq.	Percent
Patch graft	7	87.5
Peritomy	2	100
Peritomy with AMG	7	70

Table 15 -resolution of signs among various surgical modalities

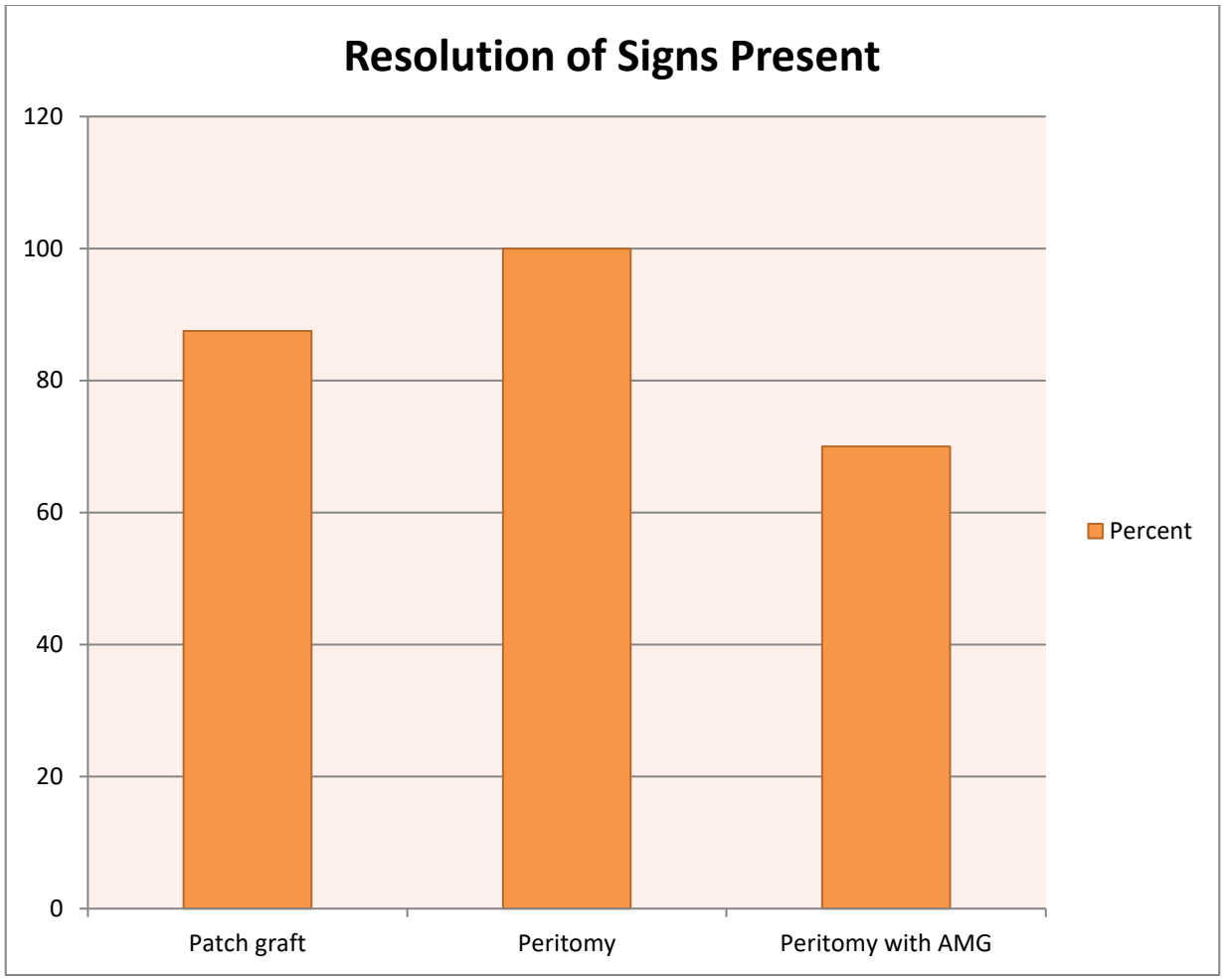


Chart 15 -Resolution of signs among various surgical modalities

Among the various surgical modalities ,patch graft was successful in 87.5%,Peritomy was successful in 100% and Peritomy with amg was successful in 70%.

COMPARISON OF VISUAL ACUITY PRE AND POST TREATMENT

Vision in Log MAR	Obs	Mean	Std. Dev.	Min	Max	P Value
Pre Treatment Vision	54	0.90	0.39	0.3	2	
Post Treatment Vision	54	0.62	0.37	0	2	<0.001

Table 16-Visual acuity in LogMAR pre and post treatment

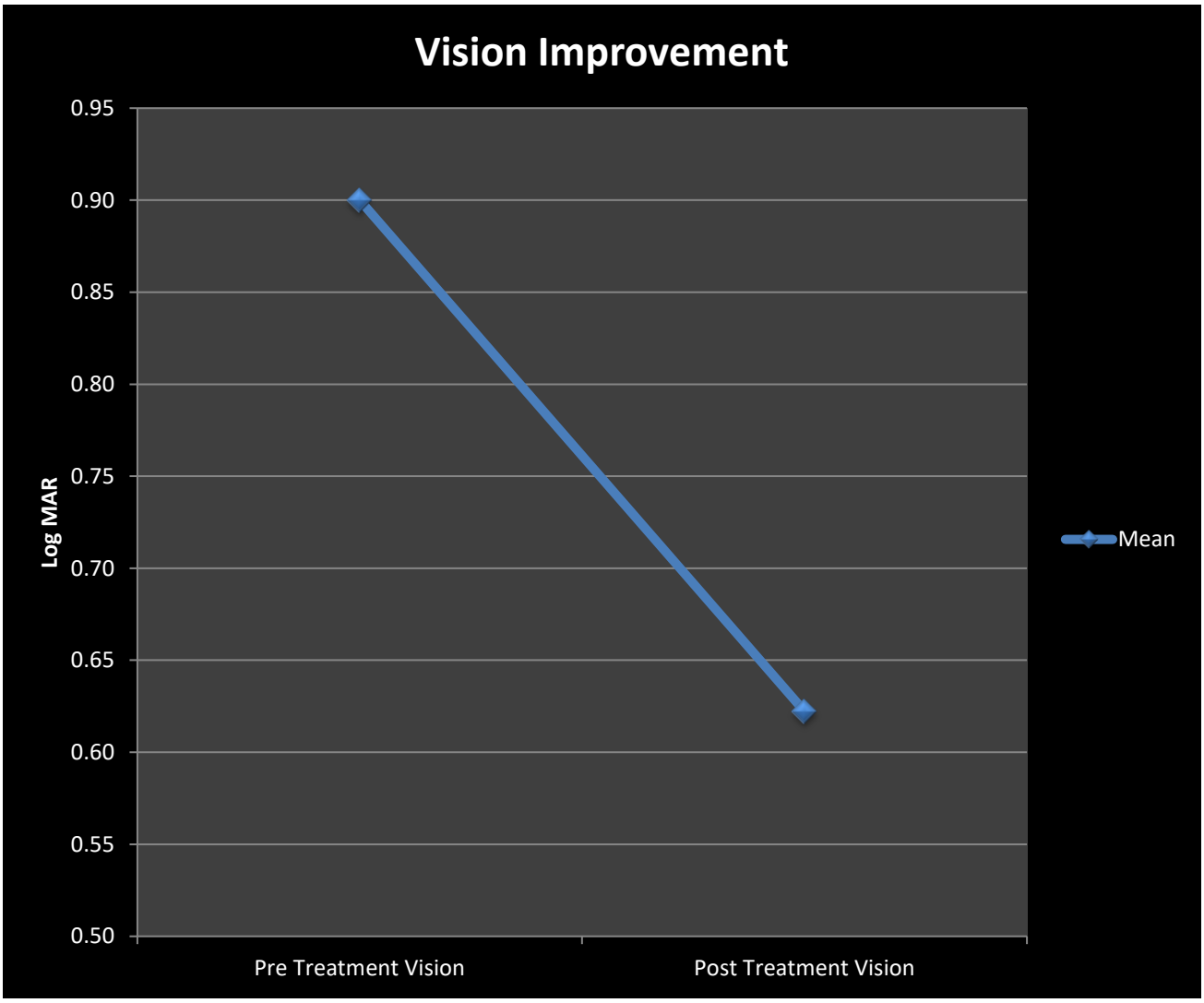


Chart 16 - Visual acuity in LogMAR pre and post treatment.

Comparison of visual acuity shows there is significant improvement between pretreatment and post treatment visual acuity.The mean of pretreatment visual acuity was 0.90(LogMAR) with standard deviation 0.39 and the mean of post treatment visual acuity was 0.62(LogMAR) with standard deviation 0.37 and the P value is <0.001 which is significant.

COMPARISON OF VISUAL ACUITY AMONG VARIOUS SURGICAL MODALITIES

Surgical Management	Pre Treatment Vision	Post Treatment Vision	p value
Patch graft	1.29	0.86	<0.05
Peritomy	0.55	0.20	<0.05
Peritomy with AMG	0.99	0.84	>0.05

Table 17 - Pre and post treatment visual acuity among various surgical modalities

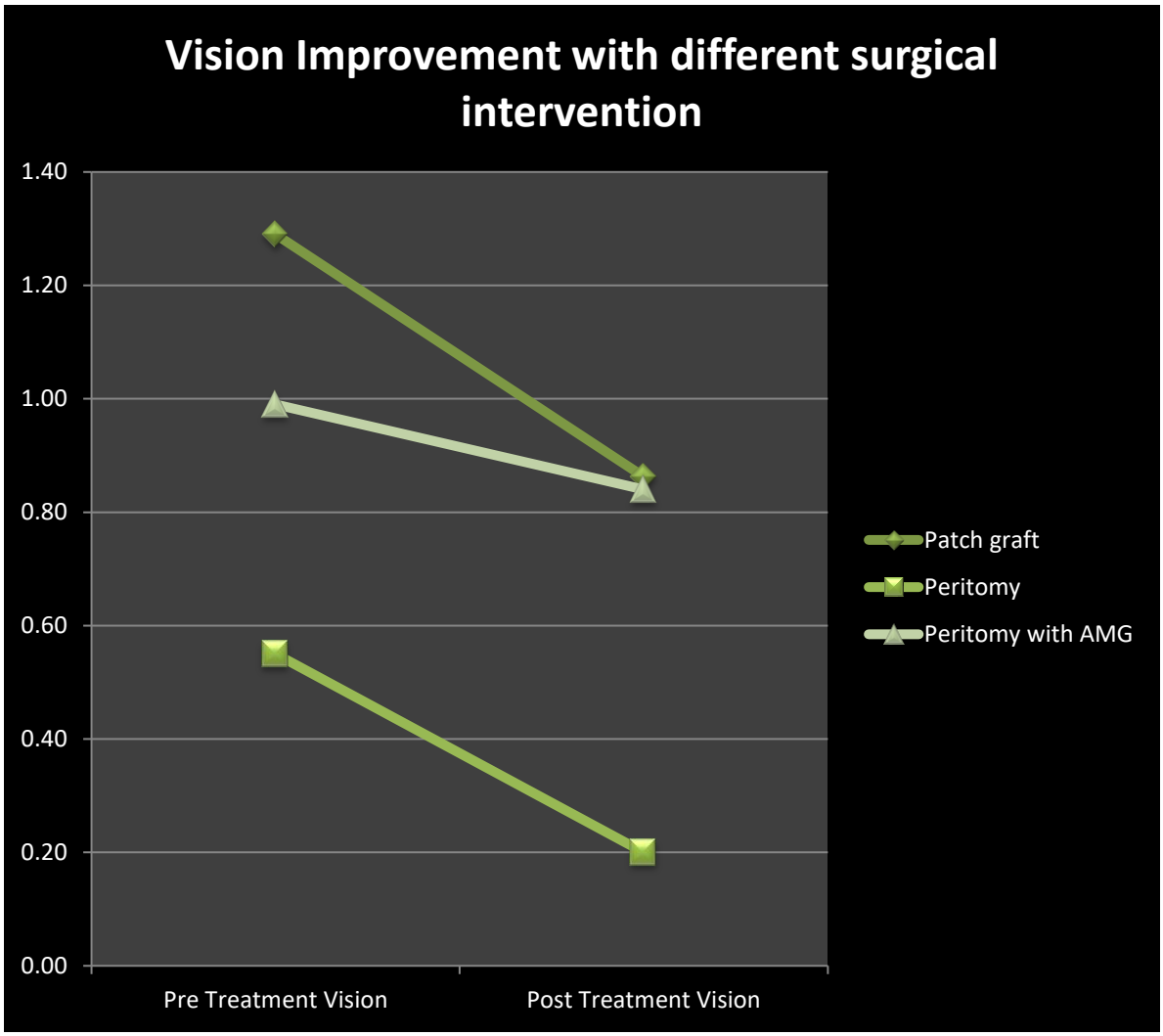


Chart 17- Pre and post treatment visual acuity among various surgical modalities

Among the various surgical modalities,Patch graft has visual acuity improvement from mean of pretreatment vision 1.29 to post treatment vision mean 0.86 and the P value was <0.05 which is significant. For peritomy , mean pretreatment visual acuity was 0.55 and post treatment mean visual acuity was 0.20 and the P value was <0.05.

Among the Peritomy with AMG cases ,the pre treatment mean visual acuity was 0.99 and post treatment mean visual acuity was 0.84 and P value is >0.05 which is not significant.

Limitation here was the number of eyes undergone Peritomy was only 2 and the number of eyes undergone patch graft was 8 and peritomy with AMG was 10.There was gross difference between number and severity of eyes undergone patch graft or peritomy with AMG or peritomy alone.

DISCUSSION

In our study the maximum number of patients(32.5%) were in 60-70 years age group.The mean age in our study group was 57.7±18.33 years.Sixty percent of cases were men and forty percent cases were women.. It is similar to Sharma et al study in which sixty percent of cases were men and the mean age was 45.5±17.9 years.[1]

In our study unilateral cases were 65 % (26 /40) and bilateral cases were 35% (14/40).Unilateral presentation was the most common presentation in our study. Sharma et al study also showed unilateral presentation was 83%(54/65) more common than bilateral presentation.[1]

In our study mean grade of depth of ulceration at presentation was 2.57which is comparable to another study conducted by Tauber et al in which the mean depth of ulceration was grade 2.[2]

In our study 15eyes (27.77%) had meibomitis. It is comparable to sharma et al study where meibomitis was present 22.3% of eyes.(17/76)[1]

In our study the most common etiology was mooren's ulcer 32.5 % (13/40) followed by rheumatoid arthritis 20 % (8/40).This is similar to sharma et al study in which the mooren's ulcer was the most common etiology 31.5 %(24/76 eyes) followed by systemic collagen vascular diseases.[1]

Management

In our study the eyes undergone either medical therapy or surgical therapy or both according to the severity of presentation.

Medical management

The eyes undergone medical therapy alone was 34 eyes (62.96%).All of them were successful.No cases were reported to have treatment failure.

Resolution of signs of PUK was achieved in mild - moderate cases which recieved medical management alone.It is similar to Sharma et al study , where the mild cases treated with medical therapy alone was successful in all eyes.[1]

Surgical Management

In our study group, the eyes undergone patch graft was 8 (14.81%) , peritomy (conjunctival resection) was 2 (3.7%) and peritomy with AMG was 10 eyes (18.52%).

Among the 8 eyes which had undergone patch graft,7 were successful and one failure .Penetrating full thickness keratoplasty was done for the failure eye.Of 2 eyes which had undergone peritomy,all were successful.

Among 10 eyes which had underwent peritomy with AMG,7 were successful and 3 were failure. Penetrating keratoplasty was done for those failure 3 eyes.

Patch graft was successful in 87.5 % eyes (7/8 eyes).Peritomy with AMG was successful in 70% eyes (7/10 eyes).Peritomy alone was done for 2 eyes which was successful 100 % (2/2). On the whole, surgical treatment was successful in 80 % eyes (16/20).

It is similar to Sharma et al study in which the surgical treatment was successful in in 83.3% (30/36 eyes).[1]

In our study on comparison of pre and post treatment visual acuity, visual acuity improvement noted with P value of < 0.001which was significant. Sharma et al study had reported improvement in post treatment visual acuity with P value of 0.085 for mild cases,0.160 for moderate cases,0.001 for severe cases.[1]

SUMMARY

This study was conducted to find out the most common etiology,various modes of presentation of PUK and to analyze the outcome of management modalities.The results are as follows:

- The maximum number of patients(32.5%) were in 60-70 years age group.The mean age in our study group was 57.7 ±18.33 years
- Men (60 %)were more commonly affected than women (40%)in our study group
- Unilateral cases were 65% and bilateral cases were 35%.Unilateral presentation was the most common presentation
- Right eye (61.11%) is involved more than the left eye (38.89%) in the study group.
- Most common presentation was gradeof depth of thinning was 2 followed by grade 4 in the study group.
- In this study group 13% of eyes had mild involvement.40.8 % eyes had moderate involvement 46.2 % eyes had severe involvement. Severe involvement was the most common presentation.
- In our study 15 eyes are meibomitis (27.77%)
- In this study group ,most common etiology was mooren's ulcer (32.5%) followed by Rheumatoid arthritis(20%),Systemic Lupus Erythematosus (2%).
- Medical management in the combination of topical steroids and immunosuppressants and systemic steroids and immunosuppressants were given

according to the protocol. Of 34 eyes which received medical management alone,all were successful.

- Surgical treatment was successful in 80 % eyes (16/20).
- Patch graft was successful in 87.5 % eyes (7/8 eyes).Peritomy with AMG was successful in 70% eyes (7/10 eyes).Peritomy alone was done for 2 eyes which was successful 100 % (2/2).
- On comparison of pre and post treatment visual acuity, there was visual acuity improvement noted with P value of < 0.001which was significant.

CONCLUSION

Peripheral ulcerative keratitis is a condition which can cause severe loss of vision.A thorough investigative search should be made to identify the underlying etiology.Severe PUK &PUK associated with collagen vascular disorders may need systemic immunosuppressants,which should be started in collaboration with rheumatologist.Mild to moderate cases can be well managed medically. Severe perforated cases needs surgical intervention to preserve the anatomical integrity of eyes and visual rehabilitation.The key is identifying the etiology and the treatment should be tailored on individual basis and when necessary,to select and perform the appropriate surgical intervention. Early treatment prevents visual loss which indicates the need for early referral of patients to tertiary care centre.

PART 3

BIBILIOGRAPHY

1. Sharma, Namrata, Gautam Sinha, Himanshu Shekhar, Jeewan S.Titiyal, Tushar Agarwal, Bhavna Chawla, Radhika Tandon, and Rasik B. Vajpayee. "Demographic Profile, Clinical Features and Outcome of Peripheral Ulcerative Keratitis: A Prospective Study."*The British Journal of Ophthalmology*, May 2, 2015. doi:10.1136/bjophthalmol-2014-306008

2. Tauber, J., M. Sainz de la Maza, T. Hoang-Xuan, and C. S. Foster. "An Analysis of Therapeutic Decision Making Regarding Immunosuppressive Chemotherapy for Peripheral Ulcerative Keratitis." *Cornea* 9, no. 1 (January 1990): 66–73

3.Squirrell DM[1], Winfield J, Amos RS.Peripheral ulcerative keratitis 'corneal melt' and rheumatoid arthritis: a case series.Rheumatology (Oxford). 1999 Dec;38(12):1245-8.

4. Thomas JW, Pflugfelder SC. Therapy of progressive rheumatoid arthritis-associated corneal ulceration with infliximab. Cornea. 2005 Aug;24(6):742–4.

5. Amniotic membrane transplantation for Mooren's ulcer. Clin Experiment Ophthalmol. 2011 Jul;39(5):386–92. Ngan ND, Chau HTM.

6. Jia Y, Gao H, Li S, Shi W. Combined anterior chamber washout, amniotic membrane transplantation, and topical use of corticosteroids for severe peripheral ulcerative keratitis. Cornea. 2014 Jun;33(6):559–64

7. Chen J, Xie H, Wang Z, Yang B, Liu Z, Chen L, et al. Mooren's ulcer in China: a study of clinical characteristics and treatment. Br J Ophthalmol. 2000 Nov;84(11):

51. Raizman MB, Sainz de la Maza

8. Raizman MB, Sainz de la Maza M, Foster CS.Tectonic keratoplasty for peripheral ulcerative keratitis. Cornea. 1991 Jul;10(4):312–6.

9. Dana, M. R., Y. Qian, and P.Hamrah. “Twenty-Five-Year Panorama of Corneal Immunology: Emerging Concepts in the Immunopathogenesis of Microbial Keratitis, Peripheral Ulcerative Keratitis, and Corneal Transplant Rejection.” Cornea 19, no. 5 (September 2000): 625–43.

10. Sangwan VS, Zafirakis P, Foster CS. Mooren’s ulcer: current concepts in management. Indian J Ophthalmol. 1997 Mar;45(1):7–17

11. Watson PG.Management of Mooren’s ulceration. Eye (Lond). 1997;11 (Pt 3):349–56.

12.McKibbin M, Isaacs JD, Morrell AJ. Incidence of corneal melting in association with systemic disease in the Yorkshire Region, 1995-7. Br J Ophthalmol. 1999 Aug;83(8):941–3.

13. Wood TO, Kaufman HE. Mooren’s ulcer. American journal of ophthalmology. 1971;71(1):417–22.

14. Watson PG.Management of Mooren’s ulceration. Eye (Lond). 1997;11 (Pt 3):349–56.

15. Watson PG. Vascular changes in peripheral corneal destructive disease. Eye (Lond). 1990;4 (Pt 1):65–73.

16. Lewallen S, Courtright P. Problems with current concepts of the epidemiology of Mooren's corneal ulcer. Ann Ophthalmol. 1990 Feb;22(2):52–5

17. Foster CS, Forstot SL, Wilson LA. Mortality rate in rheumatoid arthritis patients developing necrotizing scleritis or peripheralulcerative keratitis. Effects of systemic immunosuppression.Ophthalmology. 1984

18. Knox Cartwright NE, Tole DM, Georgoudis P, Cook SD. Peripheral ulcerative keratitis and corneal melt: a 10-year single center review with historical comparison. Cornea. 2014 Jan;33(1):27–31.,

19. Gillette, T. E., J. W. Chandler, and J. V. Greiner. "Langerhans Cells of the Ocular Surface." *Ophthalmology* 89, no. 6 (June 1982): 700–711.

20. Wilson SE, Lee WM, Murakami C, Weng J, Moninger GA. Mooren-type hepatitis C virus-associated corneal ulceration. Ophthalmology. 1994 Apr;101(4):736–45.

21. Isaak BL, Liesegang TJ, Michet CJ. Ocular and systemic findings in relapsing polychondritis. Ophthalmology. 1986 May;93(5):681–9.

22. Yagci, Ayse. "Update on Peripheral Ulcerative Keratitis." *Clinical Ophthalmology (Auckland, N.Z.)* 6 (2012): 747–54.doi:10.2147/OPTH.S24947.

23.Radhika tandon,Anat Galor,Virendar singh sangwan,Manatosh Ray "peripheral ulcerative keratitis -A Comprehensive Guide

24. John, S. L., K. Morgan, A. B. Tullo, and P. J. Holt. "Corneal Autoimmunity in Patients with Peripheral Ulcerative Keratitis (PUK) in Association with Rheumatoid Arthritis and Wegener's Granulomatosis." *Eye (London, England)* 6 (Pt 6) (1992): 630–36. doi:10.1038/eye.1992.136

25. Huerva V, Sanchez MC, Traveset A, Jurjo C, Ruiz A. Rituximab for peripheral ulcerative keratitis with wegener granulomatosis. Cornea. 2010 Jun;29(6):708–10.

26. Keenan JD, Mandel MR, Margolis TP.Peripheral ulcerative keratitis associated with vasculitis manifesting asymmetrically as fuchs superficial marginal keratitis and terrien marginal degeneration. Cornea. 2011 Jul;30(7):825–7

27. Solomon A, Meller D, Prabhasawat P, John T, Espana EM, Steuhl K-P, et al. Amniotic membrane grafts for nontraumatic corneal perforations, descemetoceles, and deep ulcers. Ophthalmology. 2002 Apr;109(4):694–703.

28. Pokharel A, Subedi S, Bajracharya M. Peripheral ulcerative keratitis triggered by bacterial conjunctivitis. Nepal J Ophthalmol. 2010 Jun; 2 (1):71–3.

29. Pfister RR, Murphy GE. Corneal ulceration and perforation associated with Sjögren's syndrome. *Arch Ophthalmol*1980;**98**:89–94.

30. Emery P, Salmon M. Early rheumatoid arthritis: time to aim
for remission. *Ann Rheum Dis* 1995;**54**:944–7.

PROFORMA

PROFORMA

Sl.No:	OP/IP No	Cornea clinic No:	Address
Name:	Age:	Sex:	

Chief complaints **:**

History of presenting illness**:**

	RIGHT EYE	LEFT EYE	DURATION
PAIN			
REDNESS			
LACRIMATION			
PHOTOPHOBIA			
DEFECTIVEVISION			

History suggestive of systemic illness if any :

	On Presentation		On Presentation
Skin		**Ear**	
Rashes/ulcer		Deafness	
Sunburn easily		Swollen ear lobes	
Depigmentation		Ear infections	
Loss of Hair		**Nose/sinus**	
Painful Cold fingers		Nasal mucosal ulcers	
Respiratory		Rhinitis/nosebleeds	
Puffy hands and feet		Swollen nasal bridge	

Constant coughing		Sinus trouble	
Coughing blood		Mouth/throat	
Shortness of breath		Oral mucosal ulcers	
Asthma attacks		Dryness	
Pneumonia		Persistent hoarseness	
Genitourinary		**Neurological**	
Blood in urine		Headaches	
Testicular pain		Numbness/tingling	
Rheumatologic		Paralysis	
Painful joints		Seizures	
Muscle aches		**Psychiatric**	
Gastrointestinal			
Abdominal pain			
Nausea, vomiting			
Regurgitation			
Jaundice			
Blood in stool			

Past history:

History of trauma /previous ocular surgery.

History of diabetes ,hypertension ,tuberculosis ,epilepsy ,cardiac disorder ,any known systemic illness in the past.

Family history:

History of any autoimmune disorder /connective tissue disease.

GENERAL EXAMINATION :

Built, Nourishment ,Pallor , Icterus ,Cyanosis ,Clubbing ,Pedal edema.

	On Presentation		On Presentation
Saddle nose deformity		Rhinophyma	
Pinna deformity		Facial/peripheral ulcer	
Nasal Mucosal Ulcer		Facial taught skin	
Oral/Tongue Ulcer		Temporal Artery Erythema	
Butterfly rash		Raynaud's phenomenon	
Alopecia		Ulcer in finger tips	

Hypopigmentation		Subcutaneous nodules	
Hyperpigmentation		Arthritis in arms and legs	
Loss of facial expression		Facial telangiectasia	

OCULAR EXAMINATION

	Right Eye	Left eye
Visual acuity		
IOP		
Lids		
Conjunctiva		
Sclera		
Cornea (Ulcer Description)		
AC		
Iris		
Pupil		
Lens		
NLD		
Fundus		

INVESTIGATIONS

Corneal smear Examination

BLOOD AND URINE INVESTIGATIONS

	On Presentation		On Presentation
Total Count		Rheumatoid Factor	
Differential Count	P L M B E	Antinuclear Antibody	
Hb		Anti DS DNA Antibody	
ESR		P-ANCA	
Mantoux test		C-ANCA	
Urine Albumin		CRP	
Urine Sugar		Renal function test-urea, creatinine	
Urine casts		Liver function test	

Urine Pus cells/RBC's		HIV and VDRL	
Random Blood Sugar		Serology for HBV and HCV	

Radiological investigations**:** X Ray chest PA:

FINAL DIAGNOSIS :

TREATMENT :

FOLLOW UP :

First two visits weekly, next two visits biweekly, thereafter monthly follow up. If sudden development of symptoms visit as early as possible or immediately

KEY TO MASTER CHART

1. s no - serial number

2. name

3. age – in years

4. gender: m - male ,f- female

5.laterality -

u/l - unilateral

b/l- bilateral

6 .bcva re - Best corrected visual acuity Right eye

7.bcva le - Best corrected visual acuity left eye

8. eye involved

re-Right eye

le - Left eye

9.bcva pre treat of inv eye -Pretreatment best corrected visual acuity of involved eye

10.LogMAR of pretreatment best corrected visual acuity of involved eye

11.Involvement clock hours

12.Grade - Grade of depth of thinning

re-Right eye

le - left eye

13.Perforated

yes,no

14.IOP -Intra ocular pressure mmhg

re-Right eye

le- Left eye

15. Meibomitis

m-Meibomitis

16.Etiology -Underlying sys illness

underlying systemic illness

17 .management

Medical- topical steroids and /or topical immunosuppressants

oral prednisolone 1mg/kg/day -

yes/no

systemic immunosuppressants

Surgical

18.Resolution of signs

yes/no

19.bcva post treatof involvd eye-post treatment best corrected visual acuity of involved eye

20. logmar value of post treatment best corrected visual acuity of involved eye.

21. bcva post treatment - Best corrected visual acuity post treatment.

re - right eye, le - left eye

sn	name	ag	se	laterality	bcva re	bcva le	eye invo lv	pre treat of inv ey	logm	Involv ement clock hou	grad re	le	Perfora ted yes/no	IOP mmh RE	LE	mei bom iti	Etiology Underlying sys illness	management topical steroids and /or topical immunosuppressants	-oral prednisolone 1mg/kg/day yes/no	systemic immunosuppressants	surgical	resolution of signs yes/no	post treato f invo	logmar	bcva po re	reatmer le
			M/F																							
1	Sherin	28	f	u/l	5/60P	6/6P	re	5/60 p	1.1	2	4		yes	10	16		idiopathic	top ste	yes	Mtx 10mg/wk	Patch graft	yes	6/18P	0.6	6/18p	6/6p
2	Kamatchi	50	f	u/l	6/18p	6/9p	re	6/18 p	0.5	2	1		no	16	14		RA	top ste	yes	nil	Nil	yes	6/9P	0.2	6/9p	6/9p
3	Mohan	76	m	u/l	5/60p	6/12p	re	5/60p	1.1	3	4		yes	10	14	m	RA	top cycl	yes	nil	peritomy with amg	no	3/60p	1.3	3/60p	6/12p
4	Nagamal	62	f	u/l	6/36p	6/12p	re	6/36p	0.8	4	1		no	14	12	m	idiopathic	top ste	yes	nil	Nil	yes	6/36P	0.8	6/36p	6/12p
5	muthusamy	65	m	u/l	6/18p	6/9p	re	6/18p	0.5	3	2		no	16	14	m	idiopathic	top ste	yes	nil	Nil	yes	6/12p	0.3	6/12p	6/9p
6	Jayalakshmi	70	f	u/l	cfcf	6/9p	re	CFCF	2	6	3		no	14	16		Mooren's	top ste,top cycl	yes	nil	Nil	yes	6/60p	1	6/60p	6/9p
7	Logan	68	m	u/l	6/24p	6/12p	re	6/24P	0.6	4	3		no	15	14		RA	top ste,top cycl	yes	nil	Nil	yes	6/24p	0.6	6/24p	6/12p
8	Gows shaw	72	m	u/l	3/60p	6/18p	re	3/60P	1.3	8	3		no	17	16	m	Mooren's	top ste,top cycl	yes	nil	Nil	yes	6/60p	1	6/60p	6/18p
9	Selvi	34	f	u/l	6/24p	6/6p	re	6/24P	0.6	6	2		no	15	14		idiopathic	top ste,top cycl	yes	nil	Nil	yes	6/18p	0.5	6/18p	6/6p
10	Selvam	36	m	u/l	6/6p	6/60P	le	6/60p	1.0	3		4	yes	14	10	m	idiopathic	top cycl	yes	nil	peritomy with amg	yes	6/18p	0.5	6/6p	6/18p
11	Kalyani	67	f	u/l	6/18p	2/60p	le	2/60p	1.4	6		4	yes	16	10		Mooren's	top cycl	yes	nil	Patch graft	yes	6/18p	0.5	6/18p	6/18p
12	Tamizhazhagan	22	m	u/l	6/6p	6/12p	le	6/12p	0.3	2		2	no	18	20	m	idiopathic	top ste	no	nil	Nil	yes	6/6p	0	6/6p	6/6p
13	Muthusamy	80	m	u/l	6/18p	6/9p	re	6/18P	0.5	4	3		no	16	16		Mooren's	top ste	yes	nil	peritomy	yes	6/9p	0.2	6/9p	6/9p
14	Devan	21	m	u/l	6/12p	6/6p	re	6/12P	0.3	5	2		no	16	14		idiopathic	top ste	yes	nil	Nil	yes	6/12p	0.3	6/12p	6/6p
15	Duraiarasan	52	m	u/l	6/6p	3/60P	le	3/60P	1.3	3		4	yes	14	10	m	Mooren's	top cycl	yes	Azp 1mg/kg/d	patch graft	yes	6/24p	0.8	6/6p	6/24p
16	Aravindh kumar	32	m	u/l	3/60p	6/6p	re	3/60P	1.3	3	4		yes	12	8		idiopathic	top cycl	yes	nil	peritomy with amg	no	2/60p	1.4	2/60p	6/6p
17	Natarajan	76	m	u/l	2/60p	6/12p	re	2/60P	1.4	8	3		no	14	12	m	Mooren's	top ste	yes	nil	patch graft	no	cfcf	2	cfcf	6/12p
18	Chellama	65	f	u/l	6/18p	6/12p	re	6/18P	0.5	2	1		no	14	18		idiopathic	top ste	no	nil	Nil	yes	6/12p	0.3	6/12p	6/12p
19	Albert	28	m	u/l	6/6p	6/12p	le	6/12p	0.3	2		1	no	14	14		idiopathic	top ste	no	nil	Nil	yes	6/9p	0.2	6/6p	6/9p
20	Sundari	74	f	u/l	6/60P	6/12p	re	6/60P	1.0	5	2		no	14	16	m	idiopathic	top ste,top cycl	yes	nil	Nil	yes	6/18p	0.5	6/18p	6/12p
21	Baskaran	72	m	u/l	6/9p	6/24p	le	6/24p	0.6	2		2	no	16	14		RA	top ste	yes	nil	peritomy	yes	6/9p	0.2	6/9p	6/9p
22	Manikumar	44	m	u/l	6/60p	6/9p	re	6/60P	1	6	4		yes	10	12	m	Mooren's	top cycl	yes	nil	patch graft	yes	6/18p	0.6	6/18p	6/9p
23	Marimuthu	69	m	u/l	6/9p	3/60p	le	3/60p	1.3	6		4	yes	16	10		Mooren's	top cycl	yes	Mtx 10mg/wk	patch graft	yes	6/18p	0.6	6/9p	6/18p
24	kamalammal	65	f	u/l	6/60P	6/12p	re	6/60P	1.0	6	2		no	16	18		idiopathic	top ste	yes	nil	Nil	yes	6/36p	0.8	6/36p	6/12p
25	Padmavathy	61	f	u/l	3/60p	6/18p	re	3/60P	1.3	6	4		yes	10	12		Mooren's	top cycl	yes	nil	peritomy with amg	no	2/60p	1.4	2/60p	6/18p
26	Dhanam	68	f	u/l	6/60P	6/9p	re	6/60P	1.0	3	2		no	14	14		idiopathic	top ste	yes	nil	Nil	yes	6/24p	0.6	6/24p	6/9p
27	Kandapillai	65	m	b/l	6/60P	6/12P	re	6/60 p	1.0	6	2		no	14	14	m	Mooren's	top ste	yes	nil	Nil	yes	6/18P	0.5	6/18P	6/12P
28	Kandapillai				6/60P	6/12P	le	6/12P	0.3	3		2	no			m		top ste	yes	nil	Nil	yes	6/12p	0.3	6/18P	6/12P
29	veeraraghavan	75	m	b/l	3/60p	3/60p	re	3/60 p	1.3	6	2		no	18	16		RA	top ste	yes	nil	Nil	yes	6/36P	0.8	6/36p	6/36p
30	veeraraghavan				3/60p	3/60p	le	3/60P	1.3	3		2	no					top ste	yes	nil	Nil	yes	6/36p	0.8	6/36p	6/36p
31	Subramani	67	m	b/l	6/60P	6/36p	re	6/60P	1.0	6	3		no	12	18		RA	top ste,top cycl	yes	nil	Nil	yes	6/36p	0.8	6/36p	6/24p
32	Subramani				6/60P	6/36p	le	6/36P	0.8	8		3	no					top ste,top cycl	yes	nil	peritomy with amg	yes	6/24p	0.6	6/36p	6/24p
33	Kattamal	60	f	b/l	6/24p	6/24p	re	6/24P	0.6	12	2		no	16	12	m	RA	top ste	yes	Mtx 10mg/wk	Nil	yes	6/18p	0.5	6/18p	6/12p
34	Kattamal				6/24p	6/24p	le	6/24P	0.6	12		2	no					top ste	yes	Mtx 10mg/wk	Nil	yes	6/12p	0.3	6/18p	6/12p
35	Thangavel	85	M	b/l	6/60P	6/18p	re	6/60P	1.0	8	3		no	12	14		RA	top ste	yes	nil	Nil	yes	6/24p	0.6	6/24p	6/12p
36	Thangavel				6/60P	6/18p	le	6/18P	0.5	6		2	no					top ste	yes	nil	Nil	yes	6/12p	0.3	6/24p	6/12p
37	Dhanalakshmi	70	F	b/l	2/60p	2/60p	re	2/60P	1.4	6	3		no	14	16	m	Mooren's	top ste,top cycl	yes	nil	Nil	yes	6/60p	1	6/60p	6/60p
38	Dhanalakshmi				2/60p	2/60p	le	2/60P	1.4	6		3	no			m		top ste,top cycl	yes	nil	Nil	yes	6/60p	1	6/60p	6/60p
39	Nainiappan	82	M	b/l	2/60p	6/60P	re	2/60P	1.4	8	4		no	12	10		idiopathic	top ste,top cycl	yes	Mtx 10mg/wk	Patch graft	yes	6/24p	1	6/24p	6/24p
40	Nainiappan				2/60p	6/60P	le	6/60P	1.0	4		2	no					top ste,top cycl	yes	Mtx 10mg/wk	Nil	yes	6/24p	0.6	6/60p	6/24p
41	Govindasamy	67	M	b/l	6/60P	6/24p	re	6/60P	1.0	6	4		yes	10	12		Mooren's	top cycl	yes	nil	peritomy with amg	yes	6/36p	0.8	6/36p	6/24p
42	Govindasamy				6/60P	6/24p	le	6/24P	0.6	4		2	no					top ste	yes	nil	peritomy with amg	yes	6/24p	0.6	6/36p	6/24p
43	Murugavel	23	M	b/l	6/18p	6/24p	re	6/18P	0.5	4	2		no	18	14		idiopathic	top ste	yes	nil	peritomy with amg	yes	6/12p	0.3	6/12p	6/12p
44	Murugavel				6/18p	6/24p	le	6/24P	0.6	6		2	no					top ste	yes	nil	Nil	yes	6/12p	0.3	6/12p	6/12p
45	Devaraj	66	M	b/l	2/60p	6/60P	re	2/60P	1.4	8	4		yes	10	14		Mooren's	top cycl	yes	Mtx 10mg/wk	patch graft	yes	6/36p	0.8	6/36p	6/24p
46	Devaraj				2/60p	6/60P	le	6/60P	1.0	12		2	no					top ste,top cycl	yes	Mtx 10mg/wk	Nil	yes	6/24p	0.6	6/36p	6/24p
47	Elumalai	30	M	b/l	6/18p	6/18p	re	6/18P	0.5	4	2		no	14	12		Idiopathic	top ste,top cycl	yes	nil	Nil	yes	6/12p	0.3	6/12p	6/12p
48	Elumalai				6/18p	6/18p	le	6/18P	0.5	4		2	no					top ste,top cycl	yes	nil	Nil	yes	6/12p	0.3	6/12p	6/12p
49	Ponnamal	57	F	b/l	6/18p	6/12p	re	6/18P	0.5	3	2		no	14	14		SLE	top ste	yes	nil	Nil	yes	6/12p	0.3	6/12p	6/12p
50	Ponnamal				6/18p	6/12p	le	6/12P	0.3	2		2	no					top ste	yes	nil	Nil	yes	6/12p	0.3	6/12p	6/12p
51	Nirmala	50	F	b/l	6/36p	3/60p	re	6/36P	0.8	8	2		no	14	16		idiopathic	top ste	yes	nil	Nil	yes	6/24p	0.6	6/24p	6/60p
52	Nirmala				6/36p	3/60p	le	3/60P	1.3	10		3	no					top ste	yes	nil	peritomy with amg	yes	6/60p	1	6/24p	6/60p
53	Leelavathi	54	F	b/l	6/36p	6/60P	re	6/36P	0.8	4	2		no	16	14		idiopathic	top ste	yes	nil	Nil	yes	6/24p	0.6	6/24p	6/18p
54	Leelavathi				6/36p	6/60P	le	6/60P	1.0	8		2	no					top ste	yes	nil	peritomy with amg	yes	6/18p	0.5	6/24p	6/18p