A STUDY OF THE CLINICAL AND MICROBIOLOGICAL CHARACTERISTICS OF FUNGAL CORNEAL ULCER

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LIST OF ABBREVIATIONS

T2 DM	Type 2 diabetes mellitus
IOP	Intraocular pressure
AS	Anterior segment
KOH	Potassium hydroxide
AC	Anterior chamber
ASOCT	Anterior Segment Optical coherence tomography
B scan	Brightness Scan
RBS	Random Blood Sugar
IVCM	Invivo confocal microscopy
FK	Fungal Keratitis

LIST OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

ABSTRACT

BACKGROUND

Corneal blindness is the 4th most common cause of blindness in the world with a prevalence of 5.1% and is a major public health problem according to World Health Organization reports. Hence, it is rightfully termed as a "silent epidemic," imposing a heavy financial burden on the healthcare system, especially in developed countries.

Fungal keratitis is a severe disease in which diagnosis can be challenging. The incidence in India ranges from 44% to 47%, due to tropical climate and a large agricultural population at risk. It is associated with systemic immunosuppression and ocular trauma in agriculturists

Fungal keratitis, if remains unmanaged, can have severe complications resulting in blindness.

In this region of North Karnataka, being a predominantly agricultural population, the risk of corneal injury is high, this risking the development of fungal keratitis. Therefore, prompt diagnosis necessary to provide evidence-based guidance for the successful empirical management of fungal keratitis.

AIM & OBJECTIVES

This study aims to analyze and assess the clinical and microbiological characteristics in fungal corneal ulcer

.

MATERIALS & METHODS

This study is cross-sectional and time-bound, conducted on patients attending the outpatient and inpatient departments of Ophthalmology, B.L.D.E. (D.U.).'s Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura.

All patients with corneal ulcer that visited our outpatient and inpatient department were examined, around 147 patients were screened and a total of 52 patients with KOH mount positive and growth positive for fungal culture were included in the study. They were screened by complete ophthalmic examination, including detailed History, best-corrected visual acuity, slit-lamp examination, fluorescent staining, relevant investigations like Random Blood sugar, Complete blood count, rapid HIV Test, HbsAg spot test, Gram stain, 10%KOH Mount, lactophenol cotton blue stain, and fungal

cultures are performed using 2 sets of Sabouraud's Dextrose Agar (SDA), of which one is incubated at room temperature. The other is incubated at 37 degrees celsius, and both sets are examined for the growth of fungus. Anterior segment optical coherence tomography was done to measure the endothelial plaques.

RESULTS

The total patients included in the study were 52 who were KOH mount and culture positive for fungal elements, having the mean age of 50.88 years. 53.8% were famers by occupation and 81% were illiterate.55.6% had history of trauma with organic matter. Majority presented with redness, pain, pricking sensation, photophobia, blurring of vision and watering. The common signs noted were ciliary congestion, irregular, dry looking, central corneal ulcer measuring 2-5mm extending 20-50% deep, with mid stromal infiltration with satellite lesions and surrounding stromal edema. 51.9% presented with endothelial plaque which were detected with ASOCT, thus showing a positive correlation ($p<0.001$). 11 presented with perforation. Majority presented with the best corrected viual acuity of hand movements (32.7%). The KOH mount positive were found in 46.7% among the screened patients. Out of 147 screened, 69 patients were KOH mount positive out of which 52 were culture positive and 17 were KOH mount positive but did not yield any growth on culture. Among the KOH mount positive 60% had septate hyphae. The majority of the organisms found in fungal culture were aspergillus fumigatus 61.5, making filamentus fungi predominant cause of mycotic keratitis.

CONCLUSION

Fungal keratitis is commonly associated with trauma. Farmers are prone for developing it. Anterior segment optical coherence tomography can be used to detect endothelial plaques that was most commonly presented in fungal keratitis. Thus it can be used as an adjunct to monitor the disease. On microbiological evaluation filamentous fungi contributed the most. It was associated with poor visual prognosis. Therefore, Early diagnosis and treatment can help in better management.

INTRODUCTION

Corneal infections can lead to corneal scarring and blindness if not diagnosed quickly and managed appropriately [(1)]. The second most significant global contributor to infectious blindness is a corneal ulcer. Additionally, it is the leading contributor to ocular morbidity and visual impairment in developing nations. Every year, 1.5 to 2 million new cases of monocular blindness caused by corneal disorders are reported worldwide. About 6.8 million people in India are blind as a result of corneal conditions [(2,3)].

Rural areas of india, where majority of populations are farmers by occupation and are prone for accidental trauma to the cornea People who work in other professions , such as manufacturing, building, carpentry, and stone cutting, are also more likely to sustain corneal wounds. The majority of fungal keratitis patients report of redness, discomfort, epiphora, photophobia, and decreased vision along with a corneal ulcer. The diagnosis and treatment of these patients present a challenge to the treating ophthalmologist. Therefore, receiving the best care possible at the right time can lessen major complications including corneal abscess, perforation, corneal scaring [(4)].

The goal of the current study was to determine the demographic, clinical, and microbiological characteristics of patients who reported to our centre with fungal keratitis. The significance of demographic risk factors, typical presenting

symptoms, and diagnostic considerations in cases of fungal keratitis in the north Karnataka region is highlighted by this study.

NEED FOR THE STUDY

- The problem of blindness is universal (5). Blindness due to corneal pathologies ranks 4th in the world, after cataract, glaucoma, and age-related macular degeneration (ARMD), with a prevalence of 5.1%. 1.5- 2 million new cases of corneal ulcers are recorded every year establishing a major public health problem according to World Health Organization reports [(6)]. In India, approximately 6.8 million people have corneal blindness [(7)]. Hence, it is rightfully termed as a "silent epidemic," imposing a heavy financial burden on the healthcare system, especially in developed countries[(8)]
- Fungal keratitis is a severe disease in which diagnosis can be challenging [(9)]. It is ubiquitous in tropical areas. The incidence in India ranges from 44% to 47%. A fungal corneal ulcer is common in India due to the tropical climate and a large agricultural population at risk [(10)].
- Keratitis by filamentous fungi are most often associated with ocular trauma attained while performing agriculture related activities, whereas keratitis by yeasts are seen in patients with immunosuppression [(11)].
- If left untreated fungal keratitis can result in severe complications, like corneal abscess, perforation and corneal scaring, finally resulting in blindness [(11)].

- An essential key to restore vision in fungal corneal ulcers is by diagnosing the infection, commencing prompt treatment regimen at the earliest which is a significant challenge for the treating ophthalmologist [12].

  In this region of North Karnataka, being a predominantly agricultural population, the risk of corneal injury is high, so it risks developing fungal keratitis [13]. Therefore, prompt diagnosis necessary to provide evidence-based guidance for the successful empirical management of fungal keratitis.

AIMS AND OBJECTIVES OF THE STUDY

1. To assess the clinical characteristics in fungal corneal ulcer

2. To evaluate the microbiological characteristics in fungal corneal ulcer

REVIEW OF LITERATURE

1. An Indian study was done in 2019 by Palanisamy Manikandan on mycotic keratitis found that rapid detection, and antifungal susceptibility of fungal isolates from corneal scraping found that among fungal aetiologies, Fusarium 52.5% and Aspergillus 16.5% were predominant. While the study revealed a male preponderance with both the fungal keratitis [(24)].

2. A study conducted in 2020 on the Endothelial Plaques as Sign of Hyphae Infiltration of Descemet's Membrane in Fungal Keratitis by Xiaolin Qi et al. concluded that Endothelial plaques considered as a sign of hyphae infiltrating Descemet's membrane. Penetrating Keratoplasty should be performed once plaques are detected in the endothelium during the surgery[(25)].

3. Sun et al in 2012 demonstrated that corneal tissue necrosis removal with implantation of conjunctival autograft flap under the guidance of AS-OCT was safe and effective option in the treatment of mycotic keratitis. which were not sensitive or aggravate for antifungal drugs [(26)].

4. Jin min et al did a study in 2022 in which he observed viral corneal ulcer may be seen as subepithelial infiltrates and specific stromal hyperintensive signals in AS-OCT but unspecific in nature, they concluded that AS-OCT imaging may provide useful information for the diagnosis and monitoring of herpetic keratitis.AS-OCT showed the unclear corneal endothelium–endothelial plaque boundary in fungal keratitis in previous work [(21)].

5. A study by mabrouk et al in 2022 found that Corneal trauma by a vegetative matter was the commonest risk factor associated with infective keratitis in 92 cases (61.3%), 60 cases were fungal (72.3%), Aspergillus species was the commonest fungal species isolated in fungal keratitis. Only six cases (4%) required evisceration due to aggressive presentation from the start and keratoplasty was performed for two cases (1.33%) [(27)].

6. Vaibhav mishra et al in the year 2022 found that trauma was the key predisposing factor of keratitis because of filamentous fungi. The commonest causative agent of fungal keratitis in current study was Fusarium species followed by Curvularia species [(28)].

7. Tawde et al did a study in 2022 and found that the presence of diabetes, hypertension, blurred vision, and corneal discoloration was significantly higher in patients with FK compared to those without FK. Aspergillus sp. (52.1%) and Fusarium sp. (47.61%) were the predominant etiological agents isolated from cases in North and Northeast India, respectively. FK due to melanized fungi was associated with diabetes, trauma with animal tail, and corneal discoloration [(29)].

8. Divya arunachalam et al conducted a study in 2022 by combining the transcript analysis data from cell lines and primary cultures, we showed the up regulation of immune defense genes in A. flavus infected cells. At the same time, chemokine signaling and B cell signaling pathways are downregulated. The variability in the expression levels in the immortalized cell line and the primary cultures is likely due

to the variable epigenetic reprogramming in the immortalized cells and primary cultures in the absence of any changes in the genome. It highlights the importance of using both cell types in host-pathogen interaction studies [30].

9. Maylander et al in 2022 concluded in his study that fungal keratitis has poor visual outcomes and is a great challenge. Infections with filamentous fungi predominated over yeast and were generally treated more aggressively both medically and surgically. Filamentous and yeast keratitis had similar durations of infections and visual outcomes. Antifungal susceptibility testing influenced treatment in 80% of cases in which it was performed [31].

10. Suman saha in his study concluded that fungal keratitis is an important cause of microbial keratitis with injury to the cornea being a leading predisposing factor. Although Aspergillus sp. was implicated in most of the patients in our study population, Candida sp. were found in higher numbers than previously reported. Keratitis caused by filamentous fungi responds adequately to medical management. Therapeutic keratoplasty continues to remain an important treatment modality in infections with Candida sp. Early diagnosis with prompt identification of the pathogenic organism is mandatory to initiate appropriate therapy and thereby reduce morbidity [32].

11. Ravula hasika and her collegues conducted a study in 2019 on the clinical profile of pythium keratitis found that The classic clinical features of this keratitis were

multiple linear tentacle-like infiltrates and the presence of dot-like infiltrates, the use of confocal microscopy can help in diagnosing Pythium keratitis [33].

12. Sharma et al in her study in 2018 found that coherence tomography. In addition, it also provides insight into the activity of keratitis. ASOCT is very useful in monitoring fungal keratitis especially in cases with aggressive stromal infiltration and endothelial plaques, she monitored the infiltrate area, width and thickness using ASOCT[34].
13. Jayashree MP et al in their study in the year 2020, concluded that delicate balance exists between cornea and surrounding environment that helps cornea maintain its integrity in-spite of continuous exposure to pathogens. Corneal ulceration may result when the balance is disrupted and defence mechanisms compromised. Mycotic and bacterial keratitis should be suspected in patients with a corneal lesion and should be ruled out before commencing steroids or antibiotics in order to save the sight. KOH mount microscopy method is more reliable in early detection and fungal culture is most sensitive method for diagnosis. Trauma is the most important predisposing factor. Aspergillus spp is the predominant fungus and streptococcus pneumonia is the predominant bacteria causing keratitis. Early detection and prompt treatment is important to minimize permanent visual loss. Preventive aspects like washing hands, wearing protective glasses when required should be advised to patients [35].

I. ANATOMY OF CORNEA

- Cornea is an avascular and transparent structure
- It has concave inner surface and convex outer surface.
- Elliptical shaped anterior surface
- Circular shaped posterior surface.
- Derived from a Latin word “corneus” meaning a horn [14].
- The central 1/3 rd – has 5.4mm optical zone.
- 1/6 of outer fibrous coat of eyeball is formed.
- The anterior vertical diameter - 11mm.
- Anterior horizontal diameter - 12 mm.
- Posterior diameter -11.5 mm.
- Radius of curvature of central - 7.8mm anterior and 6.5 mm posterior.
- Refractive index- 1.376.
- +43D out of +58.3D of total diopter is contributed by cornea.
- Central corneal thickness- 0.52mm and at the periphery - 0.67 mm.
- It has the largest amount of free nerve endings [15]

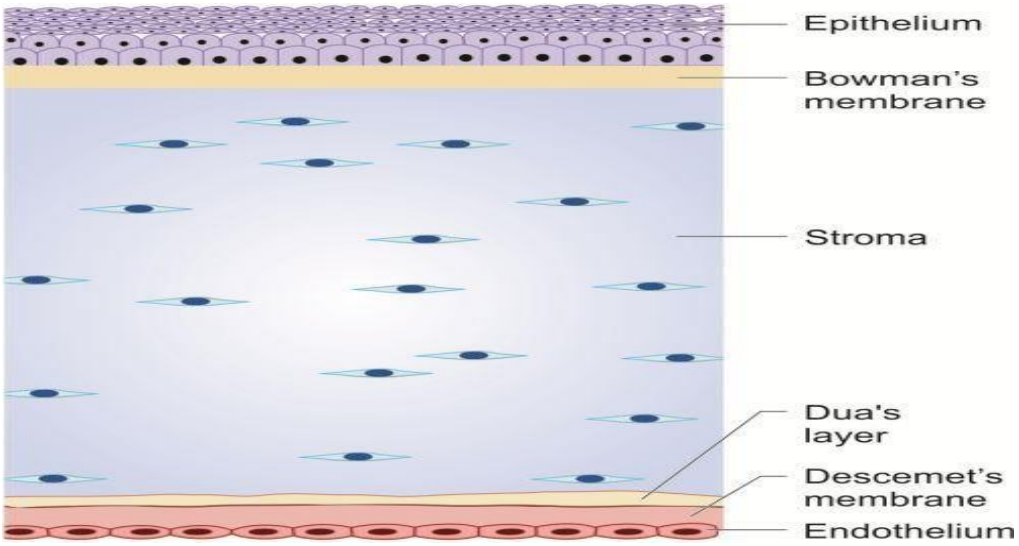


Figure 1: layers in cornea

II. LAYERS in CORNEA

There are six layers in cornea

A. Epithelial layer

B. Bowman's layer

C. Stroma

D. Predescemet's layer of Dua

E. Descemet's layer

F. Endothelial layer

1. **Epithelium**:

- It is a non keratinized, stratified squamous and is continuous with bulbar conjunctiva
- 50-90mms thick.

- Consists of 5-7 layer of cells
- Lower-most– basal layer: it has tall columnar polygonal shaped cells.
- Mid epithelial 2-3 layers- wing/ umbrella cells
- Superficial most 2 layers- flat cells
- This layer sloughs off at regular intervals
- The growth of basal layers replaces it in 6-8 days [16].

a) Basal layer- comprises of tall columnar, polygonal shaped cells arranged in palisade like manner on basement membrane.

- Width – 12micrometer
- Density 6000 cells/mm^2
- Germinal layer of epithelium
- Undergoes mitosis to produce daughter cells which migrate anteriorly into wing cell layer
- Basal cells have oval nucleus and cytoplasm has few organelles and mitochondria, suggesting low aerobic oxidation and more dependent on pentose shunt for metabolism
- Basal cells are joined firmly laterally and anteriorly by zona occludens and desmosomes
- This accounts for epithelial transparency and resistance to flow of

water, electrolytes and glucose- barrier function.

b) Non epithelial cell- they appear within the corneal epithelial layer especially in peripheral cornea, these cells include histiocytes, macrophages, lymphocytes and pigmented melanocytes. Antigen presenting langerhan's cells are formed peripherally and move centrally with age or in response to keratitis

c) Basal lamina: the basement membrane of the basal cells is PAS positive structure

- Posteriorly, It blends into bowmann's membrane
- Anteriorly, firm adhesions are formed with the basal cells by adhesion complex made up of hemidesmosomes and type 7 collagen fibrils.
- Abnormality in basement membrane results in recurrent erosions and epithelial defects

d) Wing cells: they form 2-3 layers of polyhedral cells with flattened nucleus and are adhered to each other and basement membrane anteriorly via tight junctions.

e) Flattened cells: constitutes the 2 most superficial cell layers, they have highest level of differentiation and are chronologically oldest epithelial cells

- These cells are long and has flat nucleui
- Desmosomal attachments and maculae occludentes are numerous in them
- Zonulae occludentes are present laterally
- The anterior cell wall of the superficial cells has microvilli – tear film stability
- They form junctional complexes that maintains the barrier function of the epithelium.

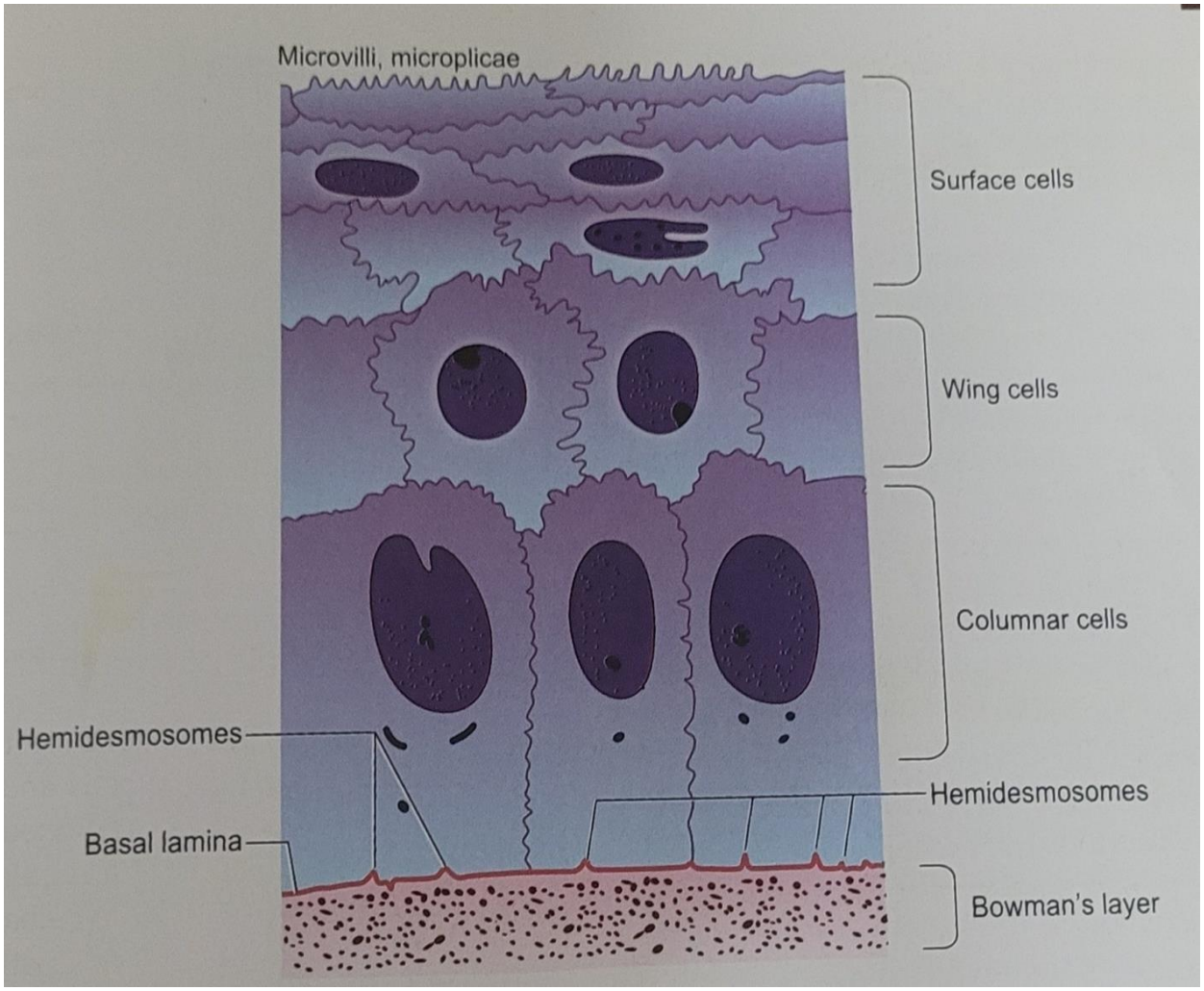


Figure2: microscopic structure of corneal epithelium

2. Bowman's layer:

- An acellular mass of condensed collagen fibrils.
- Thickness: 8-14micrometers.
- Binds to corneal stoma posteriorly and basement membrane of epithelium anteriorly.
- It is the condensed superficial part of stroma.
- It is secreted during embryogenesis by the anterior stromal keratocytes and epithelium.
- Composed of type 1 and 5 collagen fibres that are enmeshed in a matrix consisting of glycoproteins and proteoglycans.
- It shows resistance to injury and infection.
- It doesn't regenerate if destroyed
- It acts as a smooth base for uniformity of epithelium and helps in refraction

3. Stroma / substantia propria:

- Contributes approximately about 90% of the cornea's overall thickness.
- o.5mm thick
- It is made up of cells and collagen fibrils that are enmeshed in a hydrated proteoglycan matrix (ground substance)

a) Corneal lamella

- Consists of collagen 1,3,5,6

- Collagen type 1 predominates
- Type7 forms the anchoring fibril of epithelium
- They are arranged in many layers (200-250)
- They are in sync with one another and also with corneal plane and is continuous with the sclera lamellae at the limbus
- They have an oblique orientation in the anterior 1/3rd of stroma
- Posterior 2/3rd of stroma -the lamellae are alternated at right angles to one another
- Central parallel arrangement of corneal fibrils extends to the periphery where they form a weave at the limbus
- They run in 2 different orientation in the centre and run circumferentially at the periphery forming a peripheral collagen ring.
- This imparts considerable strength to the peripheral cornea amd maintains its curvature and optical properties.
- When performing superficial keratectomies and lamellar keratoplasty, the parallel organisation of the lamellae makes it simple to dissect the intralamellar layer.

b) Stromal cells

- Consists of Keratocytes, wandwerng macrophages, histiocytes and few lymphocytes.

- Corneal keratocytes- 2,4 million in number and constitutes 2-4% of volume of stroma. These are fibrocytes that are found throughout the stroma extending into the lamellae. They flattened cell body, large eccentric nucleus and long branching processes, During development and in response to injury, they create ground substances and collagen fibrils.
- At the site of injury, the stromal cells travel in loops of the corneal blood vessels.

c) Ground substance of cornea

- Consists of hydrated matrix of proteoglycans that run along and between the collagen fibrils.
- The primary glycosaminoglycans of stoma are keratin and chondroitin sulphate in the ratio 3:1
- Chondroitin sulphate- maximum in periphery
- Keratin sulphate- maximum in centre
- These glycosaminoglycans are charged and are responsible for swelling property of stroma
- The keratocytes within the lamellae synthesize both the collagen and proteoglycans

➢ Function of stroma- acts as a window to the right passage and meshes with surrounding sclera connective tissue to form a rigid frame for maintaining

intraocular pressure.

4. Predescemet's membrane:

- It was introduced by Dr.Harminder Dua in the year 2003.
- 15mm thick
- Also refered as dua's layer
- Acellular structure
- Impervious to air
- Composed of type 1 colagen primarily, collagen 4, 5 and 6 also present
- Proteoglycans – lumicans, mimecan and decorin
- No keratocytes
- Doesn't extend to periphery

5. Posterior elastic lamina or Descemets membrane:

- It is the sturdy, uniform layer that lies between the stroma and the pre-descemets membrane.
- It forms the basement membrane of endothelium.
- It contains glycoproteins and collagen with no elastic.
- Elasticity is one of its physical characteristics.
- It is very resistant to trauma, chemicals and infection.
- It maintains the structure of the eye even when the entire stroma is sloughed off.

- It gets regenerated, if destroyed
- It holds its tension and folds back on itself after being torn.
- In the periphery- it ends at the anterior end of trabecular meshwork- **Schwalbe's line**.
- In electron microscopy, it can be divided into 2 regions
    A. Anterior 1/3rd – vertically banded pattern
    B. Posterior 2/3rd – amorphous and granular
    - The posterior surface at the periphery has round wart like excrescence- **hasssal henle bodies**
    - Central excrescence - **guttae**

6. Endothelial layer:

- It is the cornea's innermost layer.
- Consists of closely spaced flat hexagonal cells arranged in a mosaic design.
- At birth - Cell density is 6000 cells/mm^2 and in adults- decreases to 2400-3000 cells/mm^2.
- Enlargement (polymegathism) of the remaining cells fills the gap left by the dying cells.
- It has a considerable fuctional reserve- corneal decompensation occurs only when the count is <500cells/mm^2
- Best evaluated by specular microscope.
- They are joined laterally to one another by tight interdigitating junctional

complexes.

and anteriorly to the Descemet's membrane by hemidesmosomes.

- The intercellular space is sealed off from the anterior chamber by the continuous desmosomal linkages and zonulae occludentes that surround the entire cell.
- This calcium dependent linkage – maintains endothelial barrier function.
- Additionally, the endothelium has two active pumping mechanisms: active secretion and active protein synthesis.
- This layer has high metabolism and high energy production- abundant mitochondria, free ribosomes, golgi complexes and rough and smooth endoplasmic reticulum present in cells.
- Corneal hydration is controlled by the endothelial pumps-
    a. Sodium potassium ATPase pump system- more active extrusion of sodium from tissue.
    b. HCO^-_3 ATPase- present on mitochondria and depletion of it induces swelling.
    c. Carbonic anhydrae enzyme- regulation of fluid transport, produces bicarbonate and hydrogen ions.
    d. Na^+/H^+ pump: maintains proper fluid/ionic balance.

LIMBUS

- 2 types – anatomical and surgical
- **Anatomically**- it is a circumcorneal transitional zone of sclerocorneal junction and conjunctivo-corneal junction.

❖ **Conjunctivocorneal junction-**

- The underlying structures are firmly attached to the bulbar conjunctiva.
- Its epithelium continues but substantia propria ends
- The epithelium thickens and is disorganised in the transitional zone.
- These cells contain melanin
- **Limbal stem cells- basal cells at limbus**
  - ✓ They are undifferentiated pluripotent stem cells present in limbal basal epithelium of palisades of vogt and the interpallisades rete ridges
  - ✓ They are the source of new corneal epithelium
  - ✓ These slow cycling cells divide and raises the progeny of daughter cells which amplify and proliferate continuously, migrate in centripetal direction towards the centre of the cornea, thus maintaining the corneal epithelium
  - ✓ Damage of this layer leads to chronic epithelial surface defects.
  - ✓ Such deficiencies lead to conjunctivalization of cornea with

vascularization of cornea, appearance of goblet cells and an unstable, irregular epithelium.

❖ **Sclerocorneal junction**

- The oblique, circular, and opaque fibres of the sclera merge with the clear corneal lamellae to form a continuous structure.
    - The corneoscleral junction begins centrally in a plane connecting the end of the bowman layer and the schwalbe line, which is the termination of descemets membrane.

❖ Other structures found at limbus – corneoscleral stroma and acqueous outflow apparatus.

❖ Internally the postererior limit is anterior tip of sclera spur.

- **Surgical limbus**
    - It is a circumcorneal transitional zone between the cornea and sclera
    - It is 2mm wide
    - Characterized by external landmarks.

i. Anterior limbal border- prominent ridge created by the insertion of conjunctiva and tenons capsule into cornea, it overlies the termination of bowman's membrane

ii. Mid limbal border – the junction between blue zone and white zone. It overlies the region where the descemet's membrane terminates.

iii. Posterior limbal border – 1mm posterior to mid limbal border- overlies sclera

spur & only seen with use of sclerotic scatter.

- **2 zones**

a. **Blue limbal zone-** 1mm in superior, 0.8mm inferior and 0.4mm nasal and temporal

b. White limbal zone- 1 mm wide, constant**.**

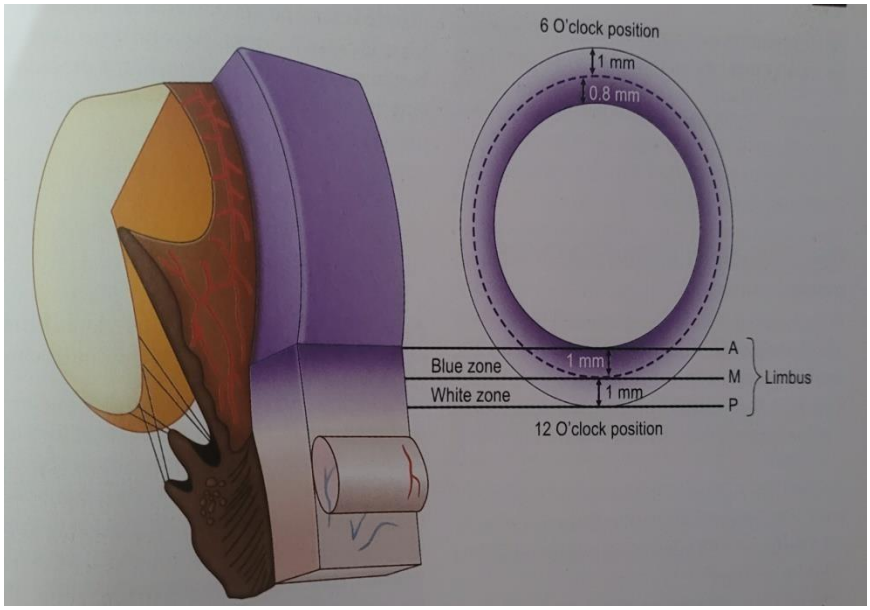


FIGURE 3: ANATOMY OF LIMBUS

TOPOGRAPHY OF CORNEA:

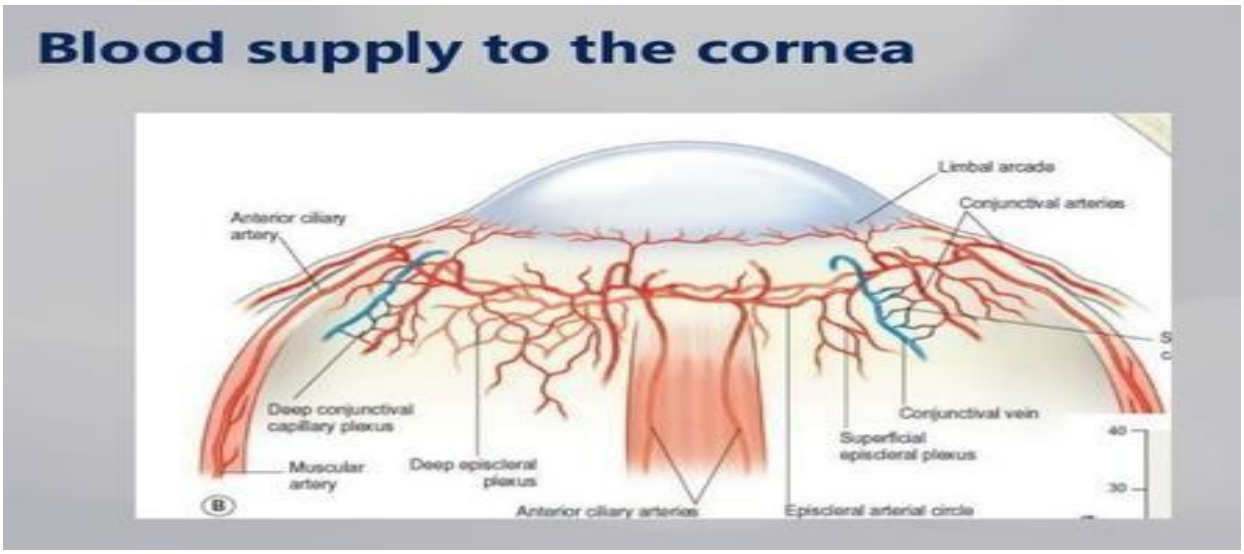
- It flattens on convergence.

- From the apex to the limbus, the curve changes, becoming flatter in the nasal and superior regions.
- The word "corneal apex" or "cap" refers to the small, spherical area of the anterior curvature that is correctly centred for the pupillary aperture but decentered with respect to the visual axis.
- In men, it is flatter than in women [(17)].

COMPOSITION OF HUMAN CORNEA:

- Around 78 % is water
- Collagens: **Type I** – **most abundant**-50-55 %
  Type III – 1 %
  Type IV – 8-10 %
  Type VI – 25–30 %
- 0.7 % and 0.3 %- keratin and chondroitin sulphate respectively
- Salt around 1 %

VASCULAR SUPPLY OF CORNEA



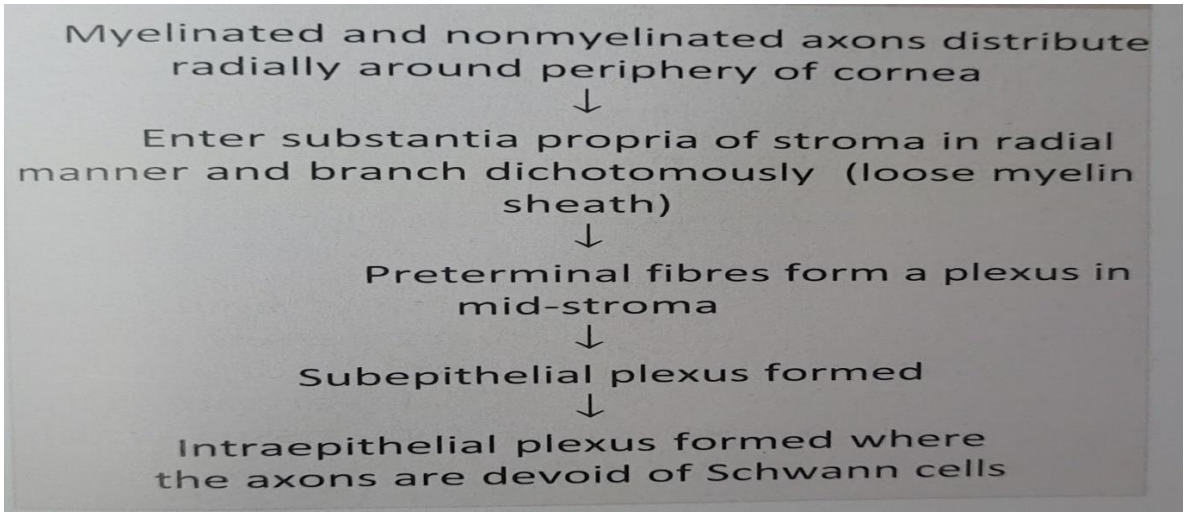
- The cornea is avascular
- Perilimbal plexuses of blood vessels(1mm periphery) -Anterior ciliary artery-> anterior ciliary vessels-> small loops in the subconjunctival tissue overlapping the cornea [(16)].

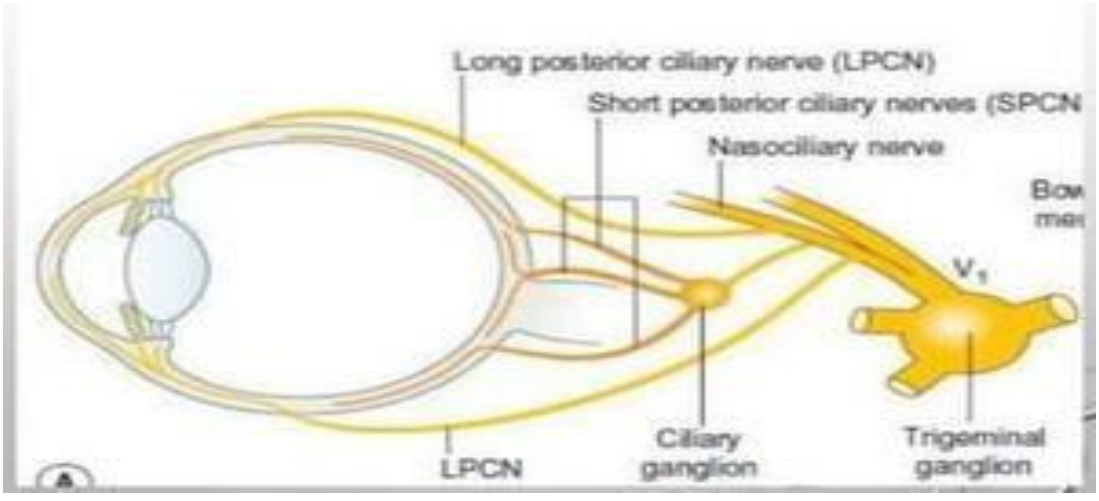
NERVE SUPPLY OF CORNEA :

- Cornea is rich in sensory nerve supply derived from ophthalmic division of trigeminal nerve via long

  and short ciliary nerves.

- A Pericorneal plexus is formed outside the limbus which penetrates into cornea as 60- 70 trunks.
- These nerves are demyelinated as they reach the cornea.
- Proprioceptive sensation is absent in cornea [16]
- Most sensitive at the superior limbus
- Sensitivity lowest in the morning and highest at night
- Sensitivity decreases with age.





BIOMECHANICS OF THE CORNEA:

Cornea provides a tough and resistant outer coating of eye.

- Cornea's biomechanical properties are mainly contributed by its stroma and

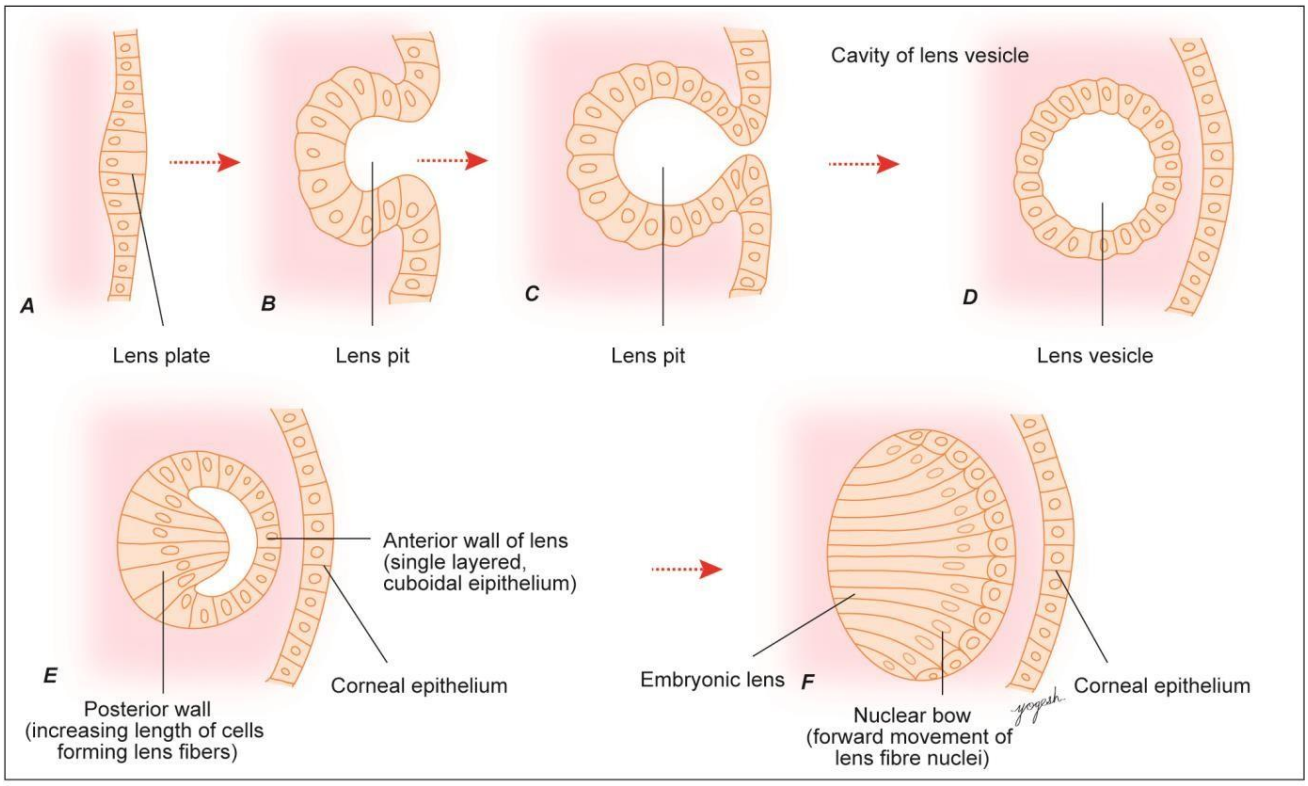
bowmann's membrane

- The dysfunction of these biomechanical properties results in corneal ectasia, distorting the corneal shape, resulting in irregular astigmatism and vision loss [17]

EMBRYOLOGY

The formation of cornea is induced by the lens and optic cup by 7 weeks of intrauterine life.

- Epithelium- derived from Surface Ectoderm
- Bowman's membrane – derived from Mesenchyme
- Stroma – Mesenchyme and Neural crest
- Descemets membrane -Synthesized by endothelium
- Endothelium- Neural crest [17].



PHYSIOLOGY

The following features are essential for the functionality of cornea:

- Transparency
- Refraction of light
- Maintainance of Intraocular pressure
- Provision of protective interface

FACTORS RESPONSIBLE TO MAINTAIN TRANSPARENCY OF CORNEA:

1. Anatomical factors:

- Avascularity
- Presence of demyelinated nerve fibres
- The uniform arrangement of collagen fibres in the stroma
- The uniform arrangement of endothelial and epithelial cells
- Absent keratinization in surface epithelium
- Tear film interface
- Absent cellular pigmentation
- Decreased cells in the stroma

2. Stroma is relatively dehydrated dur to the following reasons

- Endothelial sodium potassium ATP-ase pump

- The intercellular junction in corneal endothelium
- The epithelial impermeability to water

3. The Intra ocular pressure changes

- Any acute raise in intraocular pressure will cause corneal edema [17].

CORNEAL ULCER:

It is defined as loss of corneal epithelium with infiltration into the surrounding and underlying stroma [16].

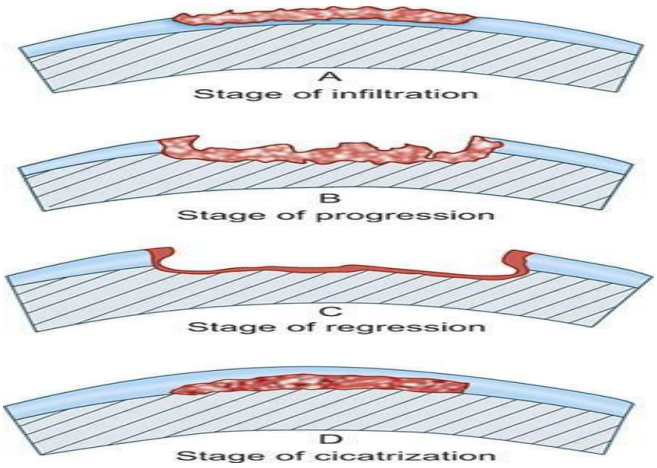
It can be infectious and non infectious.

INFECTIOUS	NON INFECTIOUS
Viral	**Peripheral ulcerative keratitis**
Bacterial	**Moorens ulcer**
Fungal	**Neurotrophic keratopathy**
Parasitic	**Exposure keratopathy**
	Drug induced keratopathy

The following are the commensals normally present on the ocular surface:

- Staphylococcus epidermidis and aureus
- Propionibacterium acne
- Streptococcus pneumonia and viridans
- Diphtheroids [16]

STAGES OF CORNEAL ULCER:



1. Stage of infiltration
2. Stage of active ulceration
3. Stage of regression
4. Stage of cicatrisation

1. **Stage of progressive infiltration** :

- Here the immune cells like polymorphonuclear cells and lymphocytes from the peripheral blood vessels infiltrate the corneal epithelium and causes necrosis

- Based the strength of hosts defence mechanism and virulence of invading organism the decides the course of the disease [15].

2. **Stage of active ulceration:**

- Progressive tissue necrosis and sloughing of epithelial and stroma – sharp demarcated ulcer with surrounding stromal neutrophillic infiltration

1. There is hyperemia and exudation .

2. If the virulence of organism is more, or in absence of antimicrobial agents- progresses deeper.

3. Grey zone of infiltration is noted around the epithelial defect.

4. If it progresses deeper- descemetocele and perforation can occur [17].

3. **The stage of regression** :

- Improvement in clinical symptoms and signs.
- A line of demarcation occurs - Digestion of necrotic material.
- The blood vessels helps in healing and gives access the immune system to reach at the site of infection.
- This stage is reached when the hosts immune response is stronger than pathogen promoting phagocytosis of organism and cellular debris.
- It is associated with regular orientation of infiltrates and curbing of the ulcer edges.

4. **Stage of healing/ cicatrisation**:

- Epithelization of ulcerated region→ the activate fibroblasts- lays down collagen fibrils over necrotic tissue resulting in scar formation
- If there is involvement of only epithelium- no scar is seen, complete healing occurs

- Based of the extent of involvement – the opacity proced by scar tissue can be

A. Nebula- Opacity involving < 1/3rd corneal thickness, iris details can be made out through the opacity
B. Macula- Opacity from 1/3rd to ½ corneal thickness, iris is seen, but details are illdefined.
C. Leucoma- Opacity involving >1/2 of corneal thickness, irirs details are not seen.
D. Adherent leucoma- Leucomatous opacity with incarceration of iris into the opacity [17].

GRADES OF ULCERS:

FEATURES	MILD	MODERATE	SEVERE
SIZE	**< 2mm**	**2-5mm**	**>5mm**
DEPTH OF ULCER	**< 20%**	**20-50%**	**>50%**
STROMAL INFILTRATE	**Dense superficial**	**Dense upto mid stroma**	**Dense deep stromal**
SCLERAL INVOLVEMENT	**-**	**-**	**Present**

COLOUR CODING OF CORNEAL PATHOLOGY [18]

COLOR	ANTERIOR SEGMENT STRUCTURE / PATHOLOHY
BLACK	Scars, degenerations, dystrophy, foreign bodies, sutures, contact lens, band keratopathy
BLUE	Diffuse stromal edema (shading), epithelial edema (small circles), fold in Descemet's membrane (wavy lines) and epithelial bullae (omega- on slit view)
BROWN	Epithelial iron lines, epithelial melanosis, old keratic precipitates and krukenberg's spindles
RED	Blood vessels, rose Bengal (dots), ghost vessels (straight dotted lines), congestion (ciliary, conjunctival and mixed), hemorrhages
GREEN	Filaments (line), punctuate epithelial keratopathy (dots), epithelial defect(shades), dendrites, lenticular changes
YELLOW	Hypopyon, infiltrates and fresh keratic precipitates

SIGNS OF HEALING CORNEAL ULCER:

- Reduction in the infiltrate density of corneal stroma
- Reduction of edema in the corneal stroma
- Reduction in the size of endothelial plaque
- Reduction in the cells in anterior chamber
- Hypopyon size reduction
- Presence of Re-epithelialization of cornea
- Betterment of corneal thickness

FUNGAL CORNEAL ULCERS

- Patients typically have a history of injuries with vegetative matter or animal tails. Injury history in farming fields.
- It most frequently affects farmers.

- People with dry eyes, those on long-term steroid medication, and immunocompromised patients may also exhibit these symptoms [15]

FUNGUS RESPONSIBLE FOR CORNEAL ULCERS:

1. FILAMENTOUS

A. With Septate

1. Not pigmented

- Aspergillus spp (fumigatus, flavus and niger)
- Fusarium spp. (solani, oxysporum, moniliforme)
- Acremonium

2. Those with Pigmentation

- Cladosporium
- Senegalensis
- Verruculosa
- Curvularia Pallescens
- Lasiodiplodia
- Colletotrichum
- Helminthosporium

B. Nonseptated

- Rhizopus
- Mucormycosis
- Absidia

II. Yeast

- Candida Albicans, parapsilosis Krusei, tropicalis
- Cryptoccus neoformans
- Rhinosporidium

III. Dimorphic fungi

- Histoplasmosis

- **Aspergillus is the most frequent fungus found in north India [19].**
- **Fusarium is the most prevalent fungus found in south India [19].**

- **Typical fungal corneal ulcer characteristics.**

❖ Symptoms are never in line with signs

❖ Greyish white infiltrates

❖ Dry looking base

❖ Feathery looking infiltrate margins

❖ Irregular border

❖ Satellite infiltrate lesions around the ulcer

❖ With deeper extension of pathogens -Endothelial plaques

❖ A non sterile, cheesy, fixed, hypopyon with convex upper border- due to extension of fungal hyphae

❖ On scraping, a gritty sensation is felt

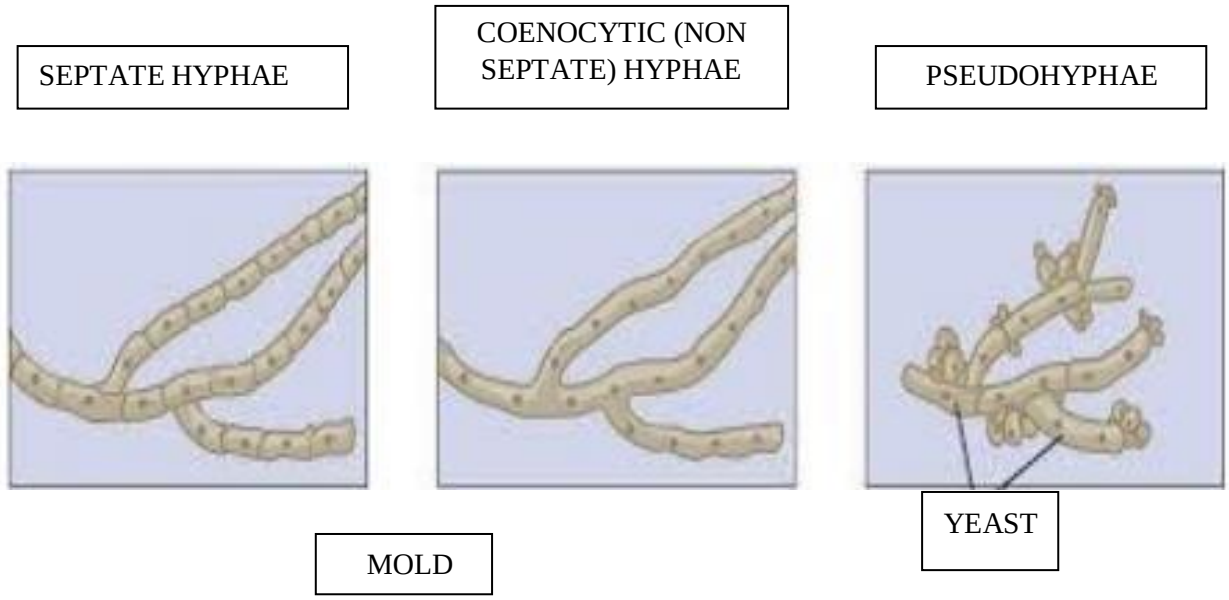
❖ Immune ring formation

INVESTIGATIONS

- **Corneal ulcer scraping**

- Scraping samples should be sent for 10% KOH mount, which is used to find fungus hyphae.
- Due to the presence of chitin, KOH will stain Acanthamoeba cysts as well as fungal filaments.
- 10 percent glycerol added to KOH acts as a mordant and preserves the smear for six

months.



- Culture media used in diagnosis of fungal keratitis are

1. (SDA agar)Sabouraud's dextrose agar
2. (PDA agar)Potato dextrose agar
3. Brain-heart infusion agar
4. Blood agar

- The majority of the fungi that cause keratitis become visible after 2-3 days of culture.
- Since colony development typically takes 1-2 weeks, the culture must be kept going for at least 2 weeks before it can be ruled out as negative [15].

TREATMENT

- Natamycin (antifungal medication) should be begun right away based on the clinical diagnosis after cycloplegics have always been used to ease ciliary spasm and pain.
- The majority of regularly used antifungal medications have low corneal penetration.
- As a result, the necrotic material covering the ulcer bed needs to be removed in order for the medications to reach the therapeutic level by penetrating deeply into the stromal layer.
- Necrotic tissues are scraped with a blunt-end Bard Parker no. 11 blade under topical anaesthetic and daily under a slit light [15].

❖ ANTIFUNGAL AGENTS [20]

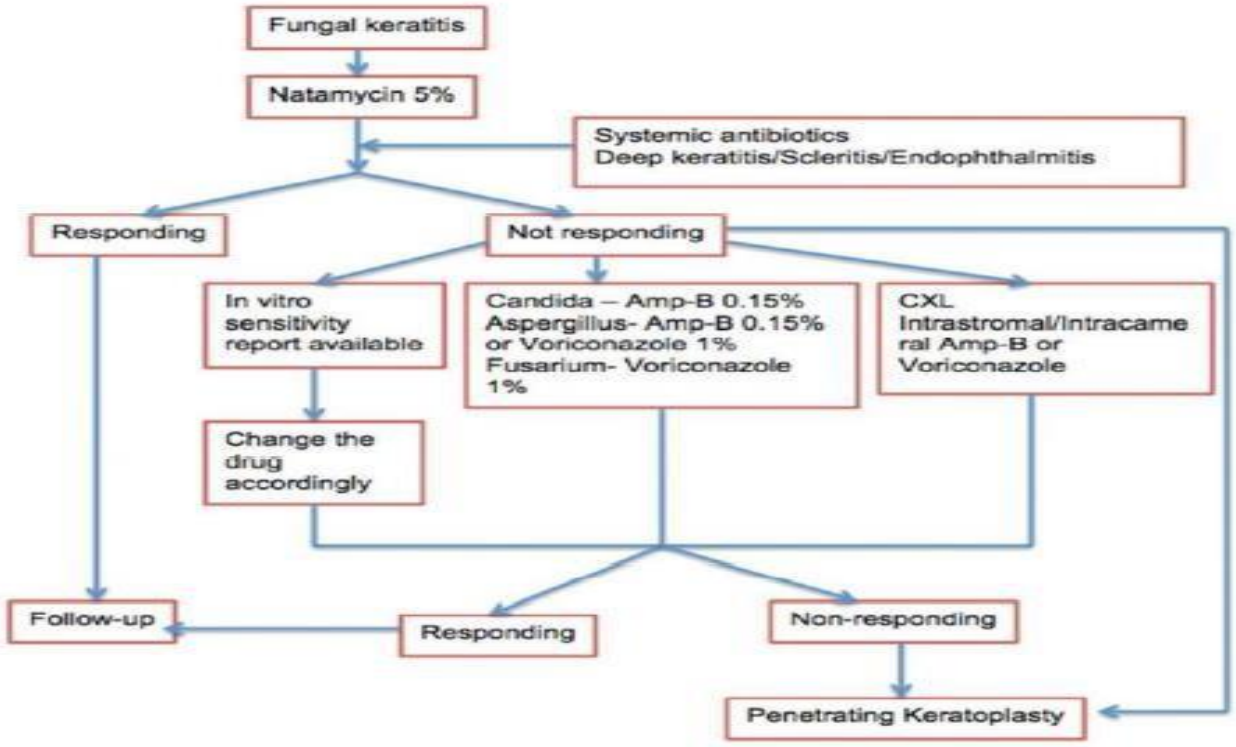
GROUP	DRUGS	MECHANISM
POLYENE ANTIFUNGALS	Amphotericin B, Nystacin, Natamycin	Binds to ergosterols and makes holes in cell wall
AZOLES (IMIDAZOLES & TRIAZOLES)	**Imidazoles**: miconazoles, ketoconazoles **Triazoles:** Fluconazoles,voriconazoles, posaconazole	Acts through cytochromes
PYRAMIDINE ANALOGUES	Flucytocine	Inhibits the fungal cell wall
ECHINOCANDINS	Caspofungin, micafungin	Inhibits 1,3-beta glucan synthesis

- The preferred treatment for filamentous fungus, notably Fusarium, is **natamycin.**
- The non filamentous fungi like candida are better treated with **amphotericin B** (19)
- Candida can be more effectively treated with **voriconazole** for deep stromal involvement, systemic ketoconazole, and topical Amphotericin B.
- Amphotericin B cannot penetrate as deeply as Natamycin.(19)

INDICATIONS FOR ORAL ANTIFUNGAL:

1. Deeper ulcers, not responding to topical medications
2. Ulcer involving the limbus and extending to sclera

- In such cases oral ketoconazole tablets 200 mg BD can be used after assessing liver function test



DRUG	ROUTE	DOSING	THERAPEUTIC INDICATION
AMPHOTERICIN B	**Topical** **Intrastomal** **Intracameral** **intravitreal**	**0.15%-0.5%** **5-10mcg/0.1ml** **5-10mcg/0.1ml** **1-0mcg/0.1ml**	**1st choice in keratitis with yeast** **Keratitis with less response to topical treatment** **Keratitis affecting anterior chamber/lens** **1st choice in yeast or filamentous fungal endophthalmitis**
NATAMYCIN	**Topical**	**5% suspension**	**1st choice – fungal keratitis with filamentous fungi**
MICONAZOLE	**Subconjunctival**	**1.2-10mg/1ml**	**Given along with topical treatment in patients low adherent to treatment**
ECONAZOLE	**Topical**	**2% solution**	**Alternative to NTM for filamentous fungi**
KETCONAZOLE	**Oral**	**100-400mg 12h**	**Deep keratitis along with topical therapy**
ITRACONAZOLE	**Oral**	**400mg/day**	**Deep keratitis by yeasts**
FLUCONAZOLE	**Topical** **Subconjunctival** **Oral**	**2mg/ml** **2mg/1ml** **200-400mg/d**	**Alternative to polyene in candida keratitis** **With topical therapy in low adherence treatment** **Deep keratitis**

VORICONAZOLE	**Topical** **Intrastomal** **Intracameral** **Intravitreal** **Oral**	**1%** **50mcg/0.1ml** **50mcg/0.1ml** **50mcg/0.1ml** **200mg 12h**	**Fungal keratitis resistant to polyenes/triazoles** **Deep keratitis with partial response to topical treatment** **Deep keratitis+ andterior chamber/lens** **Associated with AMP in fungal keratitis** **Deep keratitis**
POSACONAZOLE	**Topical** **Oral**	**4% suspension** **200mg every 6h/ 40omg every 12h**	**Fungal keratitis resistant to polyenes/triazoles** **Deep keratitis/ endophthalmitis**
FLUCYTOSINE	**Topical**	**1% solution**	**Given with AMB in candida keratitis**
CASPOFUNGIN	**Topical**	**0.15%-0.5%**	**Fungal keratitis by yeast resistant to polyenes/ first line triazoles**
MICAFUNGIN	**Topical**	**0.1%**	**Fungal keratitis by yeast resistant to polyenes/ first line triazoles**

NON HEALING CORNEAL ULCERS:

There are 3 main causes for non healing

1. Patient-factor
2. Microbiological factor
3. Orbital pathology

PATIENT- FACTOR: patients not compliant to drugs and follow ups

MICROBIOLOGICAL FACTOR: The virulence of the organism

ORBITAL PATHOLOGY: Entropion ,blepharitis, ectropion, dacryocystitis and all orbital pathologies have to be ruled out

MANAGEMENT OF NON HEALING CORNEAL ULCERS:

Treatment varies with each case.

1. Dacryocystectomy- dacrocystitis
2. In ulcers that are not healing with topical medication- voriconazole is injected intrastromally.
3. In case of impacted foreign body- foreign body removal is done
4. In case of secondary glaucoma - oral acetazolamide + topical hypotensive drugs.
5. Exposure keratitis- Tarsorrhaphy

Therapeutic penetrating keratoplasty- last resort for recalcitrant and non healing ulcers

- THERAPEUTIC PENETRATING KERATOPLASTY PRINCIPLES IN CORNEAL ULCER MANAGEMENT

- Its aims to treat the infection and is performed in conjunction with peripheral iridectomy.
- The infective issue with 1mm healthy tissue is removed.

1. INDICATIONS FOR PERFORMING KERATOPLASTY IN CASES OF MYCOTIC KERATITIS

- Keratitis that has perforated
- Keratitis resulting in impending perforation
- Keratitis not healing despite adequate treatment.

COMPLICATIONS OF CORNEAL ULCERS

Subdivided into

1. Pre- perforation
2. Perforation
3. Post- perforation

2. Pre- perforation
    1. Iritis/ iridocyclitis- due to reaction caused by diffused toxins in AC
    2. Corneal opacity can be nebula, Macula, Leucoma
    3. Decematocele- descemet's membrane bulges out as a transparent bubble called decematocele

4. Formation of cataract

3. Perforation : the descematocele disrupts due to sudden jerky movements and strain , resulting in sudden decrease of intraocular pressure.

Disruption of descemtocele
⇩
peripheral anterior synechiae
⇩
anterior chamber flattens
⇩
Eyeball becomes hypotonus
⇩
Iris prolapses through it
⇩
Inflammatory exudates over the ulcer with iris plugging the perforated site noted

4. Post perforation
    1. There is iris tissue prolapsing through the perforation
    2. Adherent Leucoma- Healed perforated corneal ulcer, it is associated with poor visual prognosis.
    3. Pseudocornea
    4. PAS- peripheral anterior synechiae
    5. Endophthalmitis
    6. Panophthalmitus
    7. If there is a significant perforation, the iris may prolapse through it. Iris has deposits of grayish-yellow exudate. A very thin layer of connective tissue is formed by the exudate. The newly created cicatricial tissue and iris are too frail to handle the pressure and bulges inside the eye. The term "anterior staphyloma"

refers to the ectatic cicatrix where the iris is imprisoned.

8. Phthisis bulbi - the eye may contract as the intraocular pressure decreases. Due to the text muscles' strain on the hypotonous eye, it takes on a quadrilateral shape. There are degenerative alterations that prevent the sense of light.
9. Decematocele
10. Secondary glaucoma - raise in intraocular pressure due to dense exudates blocking the trabecular meshwork.

Anterior Segment Optical Coherence Tomography (AS-OCT)

- It is an optically based technique for tomographic imaging of the tissues in the anterior part of the eye. It creates detailed cross-sectional photographs of cornea and this is utilized to examine the corneal morphology in individuals with corneal pathologies, including keratoconus, bullous keratopathy, and post keratoplasty [(56)].
- This AS-OCT device can capture pictures of the entire AS in a single frame and can perform 30,000 A-scans / second using axial resolution of < 10 mm using a 1310-nm wavelength. For all patients, imaging by AS-OCT was carried out in a light-filled environment (990 lux)[(56)].
- Previous studies have shown the use of AS-OCT being instrumental in the treatment of infectious keratitis [(56)].
- Soliman et al. observed that patients with mycotic keratitis, early focal and diffuse necrotic stroma were easily localized by ASOCT. High resolution and noncontact are two of its qualities.

- It has been extensively employed in research and is currently used in the treatment of keratitis, the assessment of corneal thickness, the measurement of the angle in the AC, and keratoplasty [21].

(IVCM) In Vivo Confocal Microscopy

- It is utilized for non-invasive, quick examination of the living cornea, management of infectious keratitis, corneal transplantation, refractive surgery, dry eye disease, imaging of corneal nerves, evaluation of the ocular surface in glaucomatous patients, and examination of the ocular surface in contact lens wearers.
- Instillation of one drop of topical anaesthetic and one drop of gel tear substitute into the lower conjunctival fornix before procedure.

- With the aid of a series of galvanometer scanning mirrors and a coherent high-intensity light source, the more recent generation of microscopes can produce higher-contrast, in vivo pictures of the cornea at various depths, ranging from the epithelial layer to the endothelial layer.

- The pictures of fungal elements are quickly obtained, allowing for the early diagnosis and treatment.

- Additionally, it offers images of the corneal structures at a much greater resolution and makes it easier to analyse the epithelial and marginal structures of the cornea. Its 800x magnification is more than the 380x of 1st generation microscopes. This

level of enhancement of optical properties is sufficient to see delicate and minute corneal cells, such as yeast and fungus hyphae.

- This technique is also incorporated for yeast visualisation is also enhanced by the higher resolution of the current generation confocal microscopes.

- There are a few drawbacks, such as the lesion being positioned at a deeper layers of the cornea, presence of excessive stromal edoema , which influence the picture quality.

- However, studies have shown that it has good sensitivity and specificity in the diagnosis of acanthamoeba keratitis and mycotic keratitis [22, 23, 41].

MATERIALS AND METHODS

The study was executed on patients attending the department of Ophthalmology, B.L.D.E(Deemed to be University)'s Shri B. M. Patil Medical College, Hospital and Research center, Vijayapura, during the period of JANUARY 2021-JULY 2022.

STUDY DESIGN: - Cross-sectional study

DURATION OF STUDY: JANUARY 2021-JULY, 2022. [18 months]

SOURCE OF DATA

147 patients were screened out of which a total of 52 patients with both KOH mount and fungal culture positive patients, coming to the outpatient and inpatient department , were enrolled in the study. They were included only after the complete clinical and microbiological diagnosis of mycotic corneal ulcer.

They were screened by complete ophthalmic examination, including detailed History.

1. **HISTORY**

All patients underwent a thorough history check that included questions about their demographics, occupation, the types and duration of their symptoms, their nature, any prior truma to the eye, their nature, and any systemic comorbidities.

2. **OCULAR EXAMINATION**

- Snellens chart was used to assess visual acuity
- Slit lamp biomicroscopy was used to evaluate the anterior segment
- Lacrimal syringing was performed to rule out chronic dacryocystitis

3. INVESTIGATIONS

The study's purpose was communicated to the patients, and their written informed consent was obtained after institutional approval.

The patient's history, clinical examination, and investigational findings were all noted.

Routine blood tests to look for any systemic comorbidities, such as RBS, CBC, HIV, and HbsAg.

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CORNEAL SCRAPING AND SMEAR PREPARATION[36]

Prerequisites needed for scraping of cornea

a. Speculum (optional)
b. Topical anaesthesia
c. Instruments to retrieve the specimen-15 no.surgical blade/ 26 ½ guage needle
d. 3 glass slides
    1. KOH wet mount
    2. Gram stain
    3. Optional slide –Giemsa, and Calcofluor stains.
e. Cover slips
f. Culture plates

i. Blood agar

ii. Sabrodauds dextrose agar

Anaesthesia :

- Topical proparacaine has the ability to provide adequate anaesthesia within one minute of instillation, and does not produce a strong stinging sensation. Corneal scraping is conducted with topical anaesthesia, preferably instillation of two drops of 0.5% proparacaine in the inferior fornix.
- Patients with mental impairment, children, or difficult adults may need general anaesthesia and sedation..

Instrument

- The following instruments are used to collect the sample: • Bard-Parker blade #57; 26 G needle; Kimura's spatula, needle; a surgical blade no. 11; a Ca^{2+} alginate swab; a spatula made of platinum (which can be quickly sterilised).
- Great caution is suggested in cases of larger and denser mycotic ulcers.
- As with any procedure, we must fully explain the justification for the process and solicit the patient's cooperation in order to obtain an appropriate sample.
- The scraping should ideally be carried out under a slit lamp.
- By using scrapings from the ulcer's margin and the centre, the yield of the scraping can be increased.

- As we collect the samples, be careful not to contaminate the instrument with lids or eyelashes. In order to reduce the chance of perforation, keep the sharp edge of the instrument tangential to the surface.
- The margins of the ulcer are scraped with the 11. No blade and placed on a slide. The location of the smear is then marked with a wax pencil or marker.
- The smears have to be labeled properly

4. KOH MOUNT

- On a spotless glass slide, place the specimen. 10% KOH is added in 1 drop.
- To remove any air bubbles, place the cover glass on top of the slide and gently press down. Apply the gauze to the prepared slide to remove any excess solution.
- Place the slide on the microscope's stage and begin the investigation with a low power (10 x). Lower the condenser to lower illumination to reveal epithelial cells
- Look for fungus-like things like hyphae or yeast. Use the 40x settings (high-dry objective) to check further if any hyphae or budding yeast are suggestive of fungus [37].

5. FUNGAL CULTURE- SABOURAD DEXTROSE AGAR (SDA)

- The title sabouraud dextrose agar comprised of 1% peptone, 4% glucose and 1.5-2% agar with a final Ph of 5.6[38]
- The commercial SDA media was prepared according to manufactures instruction.
- Thirty and half grams (30.5 g) of SDA was dissolved in 250 ml of distilled water in 500ml conical flask, sterilized at 121 °C for 15 min, cooled to 45 °C and poured into Petri dishes [39].
- Samples are inoculated onto this agar by streaking in C –shaped which are incubated at 2 temperature degrees: room temperature and 37C° [40].
- The both sets are examined for the growth of fungus.
- Positive fungal cultures are identified based on colony morphology, growth

characteristics on various media, and microscopic features.

- A diagnosis of a fungal corneal ulcer is confirmed in the presence of at least one of the following:

    1) Fungi in Smear of corneal scraping examination.
    2) Growth of the same fungi in two culture media.
    3) Considerable growth of fungi at the inoculated site on a single solid medium.

6. ANTERIOR SEGMENT OPTICAL COHERENCE TOMOGRAPHY

Infected eyes were imaged by using optical coherence tomography specialized for anterior segment scans with optical resolution- 5 μm vertical and 15 μm horizontal scans using the Cornea Cross Line model. The major goal was to determine whether there was a distinct or wavy border to distinquish the endothelial plaque from endothelial cells of cornea. To focus on the interaction between them, AS-OCT scanning is chosen to be performed around the patient's corneal ulcers.

Patient is asked to sit infront of the machine and rest the chin and forehead on the given slot provided and asked to look straight into the machine to observe the green light, the position of the patient is adjusted accordingly and the scans are obtained [21].

7. Statistical tools utilized for the analysis of results and data tables are derived from data analysis tool, which is an add-on tool in

MICROSOFT-excel.

Sample size was calculated using the formula

$$n = \frac{z^2\text{-}pxq}{d^2}$$

Z= statistic at level of significance

d^2 = Absolute error

p= Proportion rate

q= 100-p

The data derived were noted in MICROSOFT-Excel sheet and by utilizing the statistical package for social sciences (Verson 20), the statistical analysis was conducted.

Results will be presented as Mean (Median) ±SD, counts and percentages and diagrams.

The p-value is calculated using the sampling distribution of test statistic under Null Hypothesis, the sample data, type of test being done.

8. INCLUSION CRITERIA:

All patients with both KOH mount and culture positive fungal keratitis attending the outpatient and inpatient department were enrolled in this study, only following examination & clinical diagnosis of mycotic keratitis.

9. EXCLUSION CRITERIA:

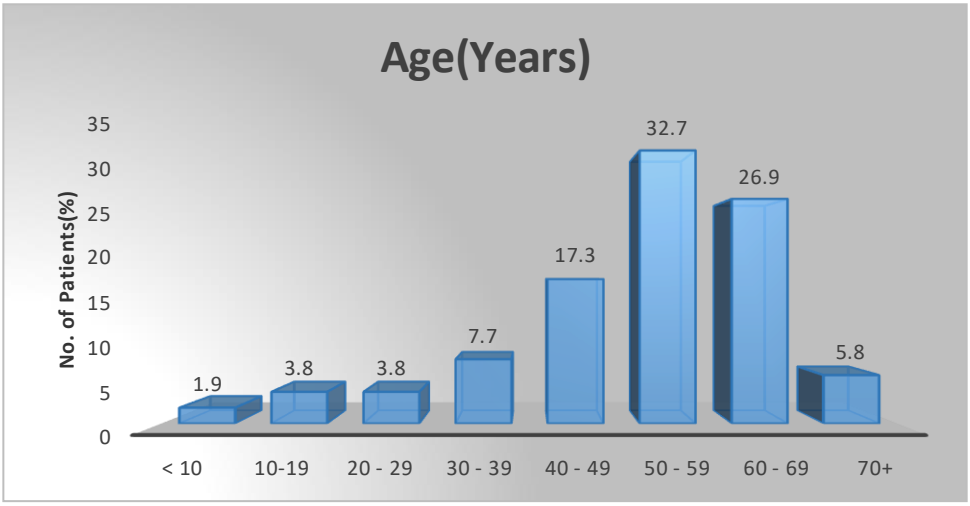
Patients with

1. Bacterial keratitis
2. Viral keratitis
3. Mooren's keratitis
4. Marginal keratitis
5. Neurotrophic keratitis
6. Autoimmune mediated keratitis
7. Interstitial keratitis

RESULTS

A total of 147 patients were screened out of which 52 patients were KOH mount and culture positive, were enrolled in the study. Written informed consents were taken all of them.

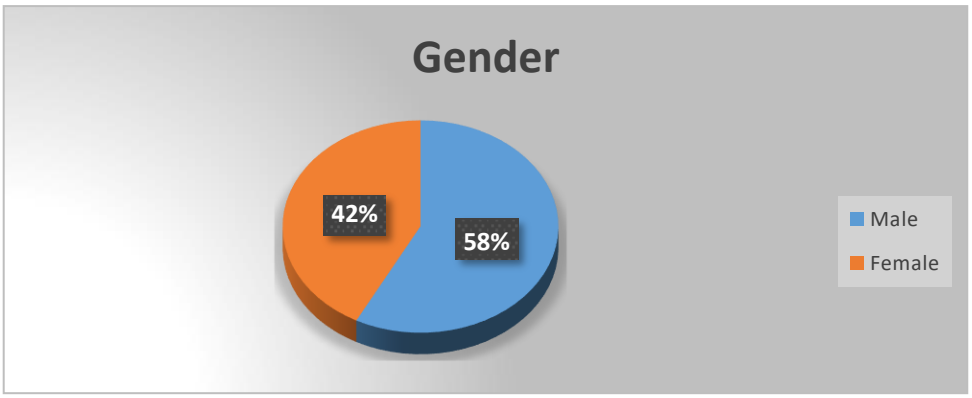
1. AGE DISTRIBUTION



Graph 1. Graph showing Age variation in this study

In this study, patients with ages from below 10 to 70 above years were enrolled, around 32.7% patients were in the range 50-59 years followed by patients with ages between 60-69 years with the mean age being 50.88 years, indicating that ages beyond 50 years are more prone to fungal keratitis.

2. SEX DISTRIBUTION



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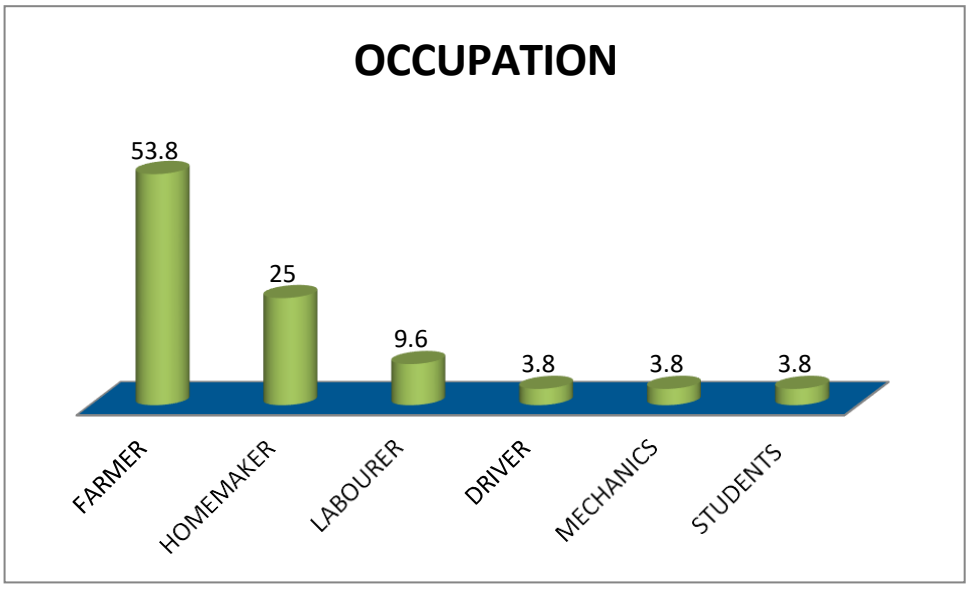
Graph 2. Pie chart showing Sex Distribution

In the study male were affected more (57.7%) when compared females (42.3%). Males were shown to be afflicted in greater numbers, but there was no overly large male preponderance.

3. OCCUPATION

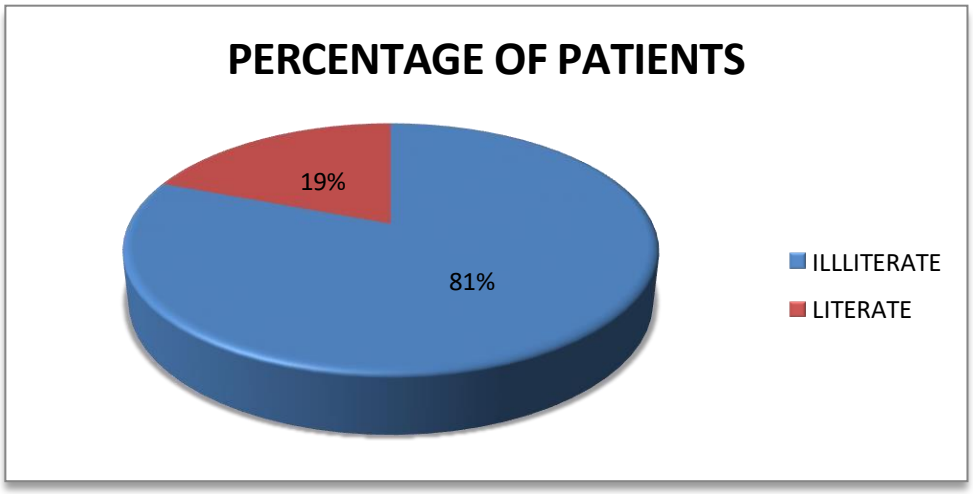


Graph 3. Graph showing various occupation owned by the patients in this study

In the study among the patients enrolled, most of the patients (53.8%) were

farmers by occupation, indicating farmers are at high risk of fungal keratitis, followed by homemakers. Drivers, mechanics and students also contributed to its eitiology.

4. LITERACY OF THE PATIENTS



Graph 4. Graph representing literacy

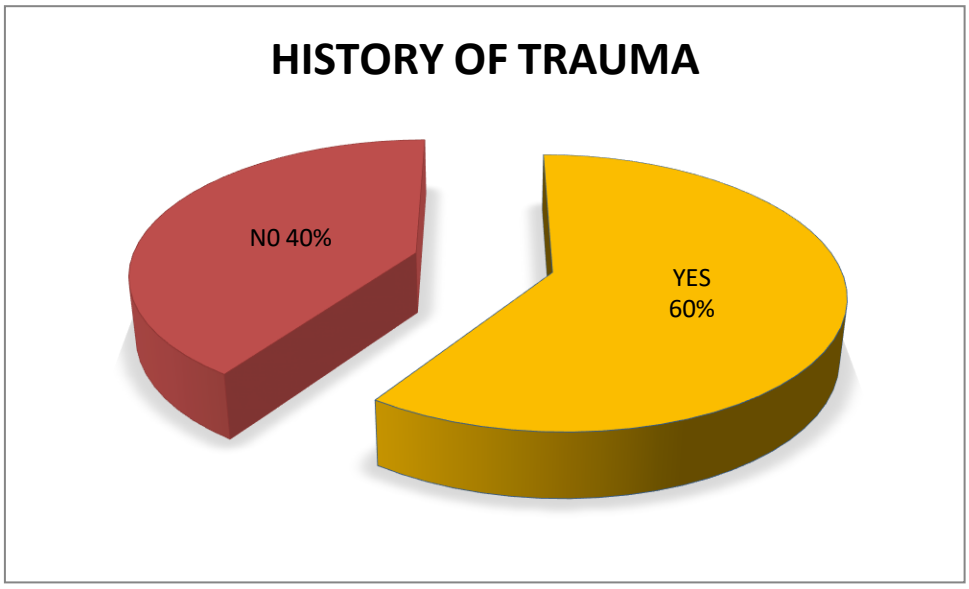
Among the study group 81% were illiterate and 19% were literates indicates that literacy is associated with fungal keratitis.

5. BILATERALITY

EYE	FREQUENCY	PERCENTAGE
LEFT EYE	**25**	**48.1**
RIGHT EYE	**27**	**51.9**

TABLE 5. Table showing bilaterality

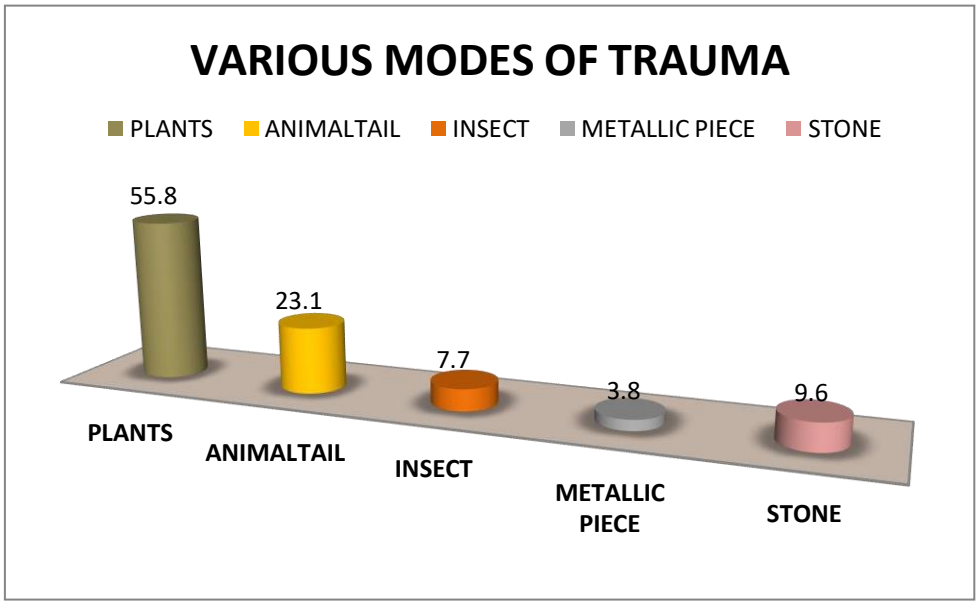
6. HISTORY OF TRAUMA



Graph 5. Graph showing history of trauma

Among 52 patients, 60 % gave history of trauma, thus indicating trauma is most commonly associated with fungal keratitis.

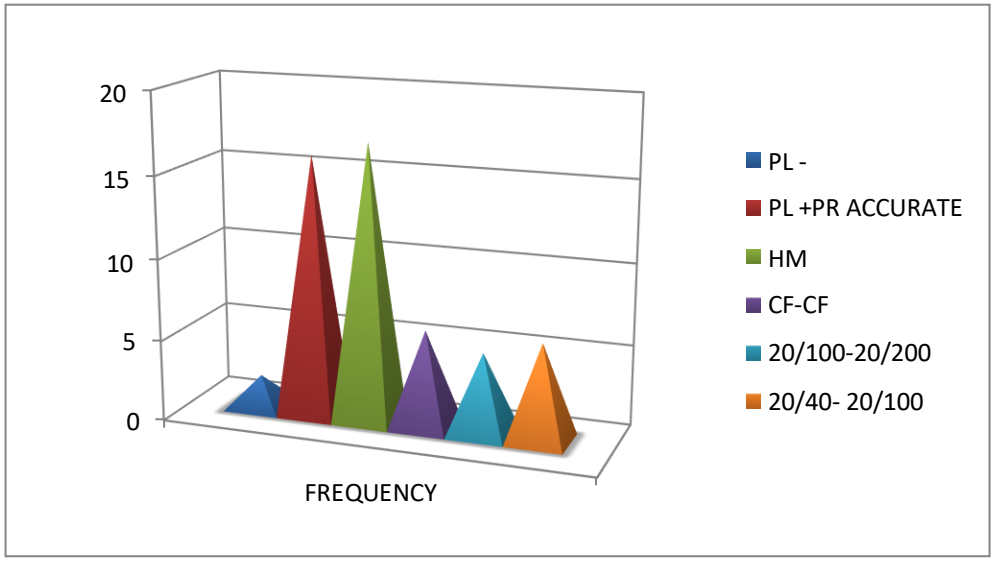
7) TRAUMATIC AGENT



Graph 6. Graph showing various history of traumatic agent

Among the 60% patients with history of trauma , the majority of traumatic agent were plant (55.8%) followed by (23.1%) animal tail.9.6% were unaware of the agents Therefore trauma with organic substances are more prone to develop fungal corneal ulcers.

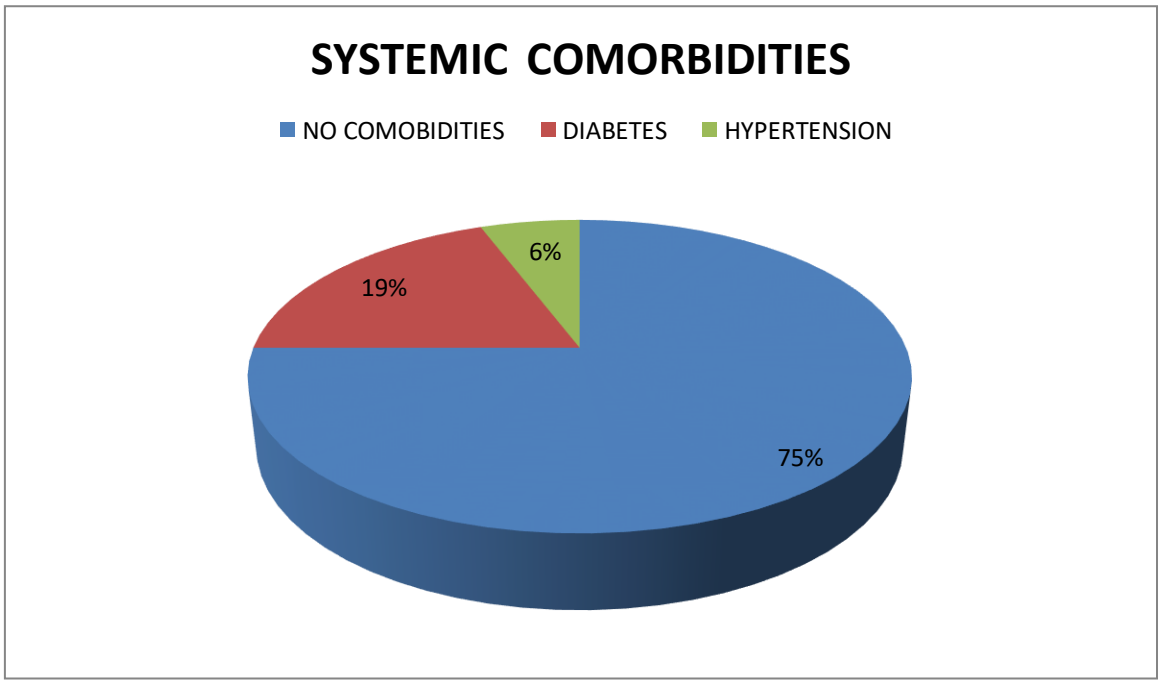
8) BEST CORRECTED VISUAL ACUITY AT PRESENTATION



Graph 7. Graph showing distributions of best corrected visual acuity

Out of the 52 patients , majority presented with BCVA of hand movements followed by perception of light with accurate projection of light in all quadrants, indicating that fungal keratitis with poor visual acuity at presentation.

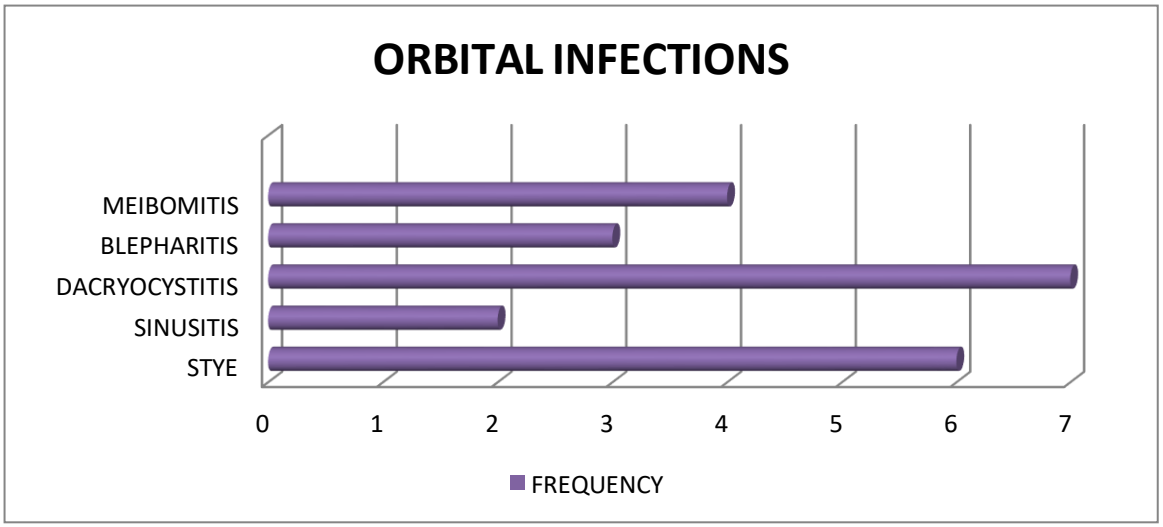
9) ASSOCIATION WITH SYSTEMIC COMORBIDITIES



GRAPH 8 Graph showing the systemic comorbidities associated with fungal keratitis

10 out of 52 were diabetic (19.2%), 3 out of 52 were hypertensive (6%) showing no significant association with fungal keratitis.

10) ADNEXAL INFECTIONS



GRAPH 9: graph showing the association of adnexal infection with fungal keratitis

Among 52 patients, 30 patients had no adnexal infection, whereas among the remaining 22, 13.5% had chronic dacryocystitis followed by stye (11.7%), indicating orbital infections also contributes to fungal keratitis.

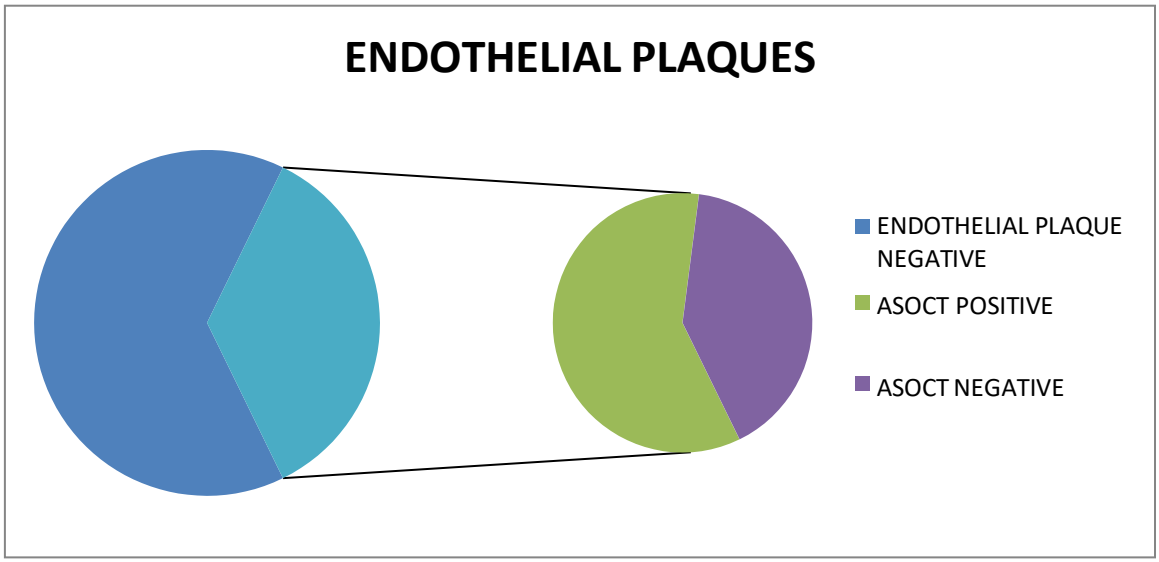
11) SYMPTOMS AND SIGNS

46 out of 52 cases complained of pain, 44.2% presented with symptoms of pain, pricking sensation, photophobia, blurring of vision, redness and watering. 32.7% presented with signs of lid edema, conjunvtival congestion, epithelial defect with infiltration and cataract. 10 out of 52 presented with perforation at consultation.

12) CORNEAL ULCER

The nature of the corneal ulcer was studied under slit lamp biomicroscopy. The common features noted were ciliary congestion (71.2%), irregular (69,2%), dry looking (84.6%), central corneal ulcer (61.5%) measuring 2-5mm (75%) extending 20-50% deep (78.8%), with mid stromal infiltration (51.9%) with feathery margins (71.2%) and satellite lesions (61.5%) and surrounding stromal edema (51.8%). 15.4% had a immune ring. 14 out of 52 had hypopyon. 51.9% had endothelial plaque.

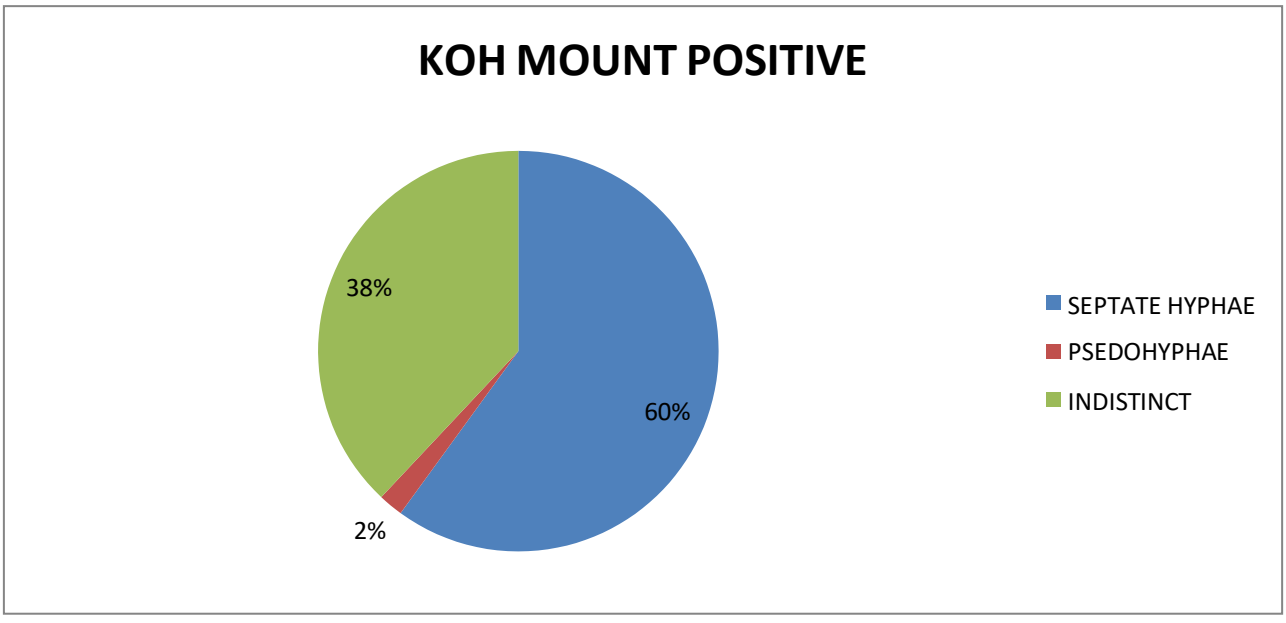
13) ASOCT



GRAPH 1O showing ASOCT association with endothelial plaque

Out of 27 cases of fungal keratitis with endothelial plaque , 16 cases were detected under anterior segment optical coherence tomography which proved to be statistically significant p(0.0001) thus showing that anterior segment optical coherence tomography can be used as an adjunct in monitoring the disease progression.

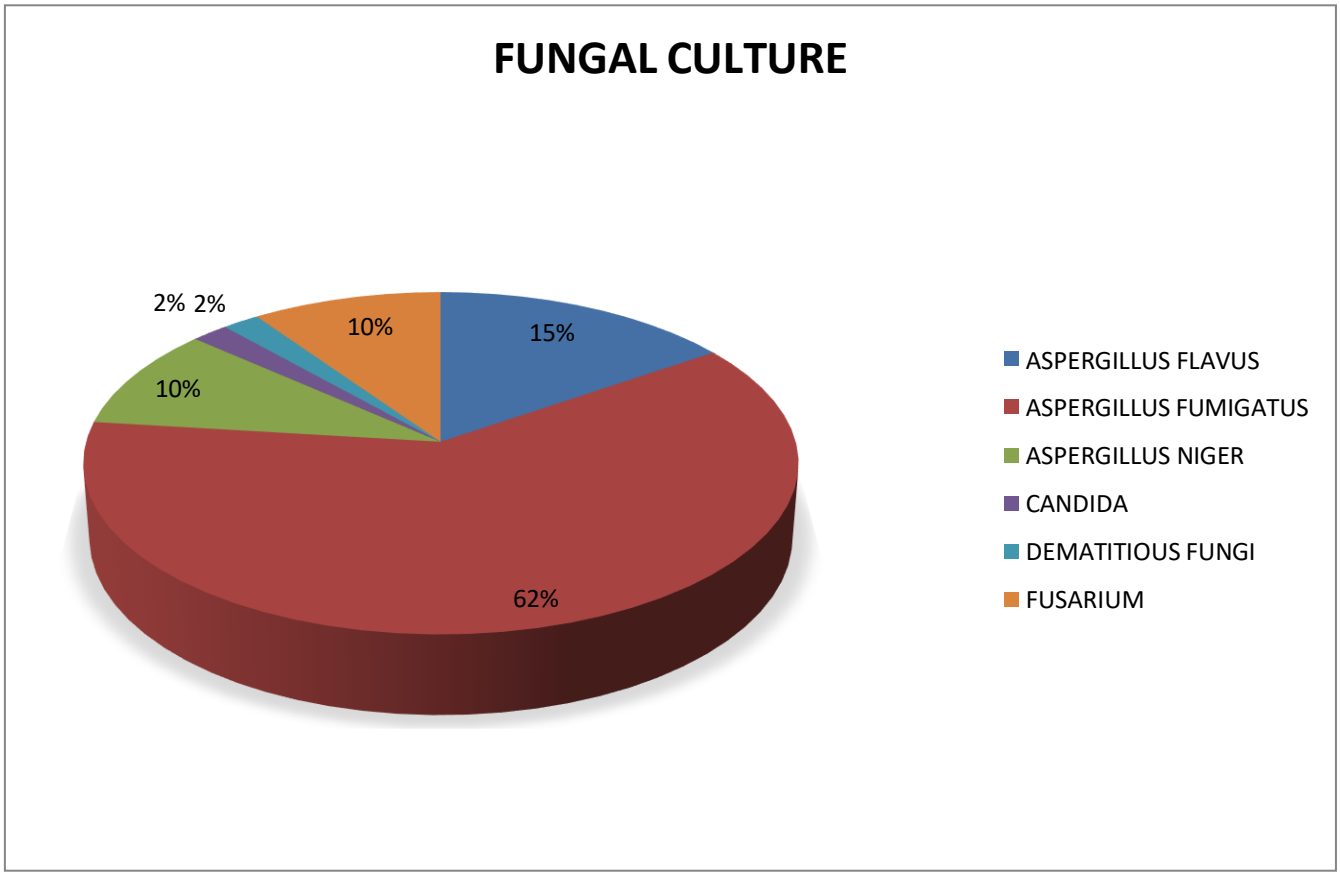
14) KOH mount



GRAPH 11 graph showing KOH mount positivity

147 patients were screened, out of which 69 samples were KOH mount positive ,making the sensitivity of KOH mount to be 46.9% .The 52 patients which were KOH mount and culture positive for fungal elements were included in the study, with majority showing septate hyphae (59.6%), (2%) showing pseudohyphae and the rest were indistinct (38%) .Out of 69 KOH mount positive 52 were culture positive therefore they were included in the study.

17) FUNGAL CULTURE



Graph 12: graph showing various fungal species obtained during the study

147 cases were screened, out of which 52 patients were fungal culture positive making its sensitivity 36.3%. Among the 52 culture positive cases, majority of fungi were aspergillus fumigatus (62%) followed by aspergillus flavus (15%). 2% cases were candida and dematitious fungi respectively. 10% were aspergillus niger and fusarium respectively.

DISCUSSION

One of the main reasons for vision loss in underdeveloped nations is fungal keratitis [45]. In these infections, treatment success may be lower resulting in poor visual outcomes due to challenges in mycological and clinical diagnosis and the ineffectiveness of antifungal medications [46]. The socioeconomic makeup, climate, and environmental factors influence the occurrence of fungal keratitis in different regions [47]. A significant number of cases of microbial keratitis are caused by fungi, particularly in hot, humid regions and in locations with large populations of agricultural workers [48].The incidence in this country ranges from 44% to 47%. Chittur. Y. Ranjini et al. on the microbial profile of corneal ulcers in south India found that (61.5%) were male. The age range of 41-60 years was the most affected group. In our study. we discovered that 57,7% of the patients were men and that the bulk of them were in the 50- to 59-year age range. This might be as a result of men contributing to the substantial agricultural labour force in society. The majority of them were farmers (53.8%) and illiterates (80.8%).

Al-Badriyeh et al. and Tabatabaei et al. discovered that concurrent ocular illnesses, extended use of corticosteroids, incorrect use of antifungal drugs, and corneal damage with vegetative matter were further risk factors for keratitis. According to Mravii et al., a corneal infection begins when the epithelial integrity is compromised, either as a result of trauma or an ocular surface condition, and fungi gain access to the tissues, multiply, and trigger a strong inflammatory response that may result in stromal necrosis [48, 49, and 50]. Similar to the above studies we found that 59.6% of patients were predisposed to trauma

majority of which had trauma with vegetable matter (55.8%) followed by animal matter (23.1%), insect (7.7%) and metallic piece (3.8%).

According to a study by W. Zbiba, in addition to ocular damage, other risk factors for fungal keratitis include diabetes, contact lens use, and corticosteroid use [(51)]. In our study we found that stye (11.5%), chronic dacryocystitis, (13.5%) were some of the predisposing factors associated with fungal keratitis. In Namperuvalsamy v prajna et al study, patients with fungal keratitis had vision worse than 20/400 [(19)].

Another study by Stine E Nielson et al also found that final visual outcome was poor in fungal keratitis [(52)]. The majority of the patients in our study (32.7%) had visual acuity of hand movements when they first arrived, followed by PL positive and PR accurate in all quadrants (30.8%). Overall the vision at presentation was poor. This is mainly because of late presentation, illiteracy and usage of occult vegetative oils.

The common symptoms presented in our study were pain, pricking sensation, photophobia, blurring of vision, redness and watering (44.2%). 32.7% presented with signs of lid edema, conjunvtival congestion, epithelial defect with infiltration and cataract. 10 out of 52 presented with perforation at consultation. According to a study by Mahmoudi, the earliest indications of fungal keratitis are a corneal infiltration with feathery borders, a dry, elevated necrotic surface, and maybe satellite lesions [(53,54)]. Infections closer to the limbus are typically less severe than infections in the centre of the cornea. Hypopyon, neovascularization, deteriorating corneal opacity, and corneal perforation are symptoms that may be seen if the infection is not treated [(55)]. In a study by jin min et al endothelial plaque occurs due to damage to the endothelium as the fungal

elements enters through the stromal layer into the (AC) anterior chamber, which is a crucial indicator in mycotic keratitis, which is associated with the diagnosis, surgical indications, and prognosis. They also found that endothelial plaques were associated with bacterial keratitis than mycotic keratitis [(21)]. According to Clemence Bonnet et al, Anterior segment optical coherence tomography can be instrumental in evaluating the range of reactions in the eye disorders in individuals with keratitis. Another study by Takezawa et al. documented 5 off 6 cases of fungal keratitis having an indistinct boundary of the plaque from endothelium, and they also noted that there was extension of hyper-reflective areas of plaque beyond corneal ulcer . They used ASOCT to identify endothelial plaques in individual diagnosed with mycotic keratitis [(56)]. The endothelial plaques were seen in 27 patients which were screened under ASOCT in our study. 16 of those cases revealed hyper-reflective lesions with a distinct separation of the plaque from the endothelial cells. In the rest of the 11 cases it was difficult to differentiate as the corneal ulcer was deeper and more aggressive in nature. Despite these disadvantages, the screening of endothelial plaque under anterior segment optical coherence tomography was proved to be statistically significant p(0.0001) thus showing that anterior segment optical coherence tomography can be used as an adjunct in monitoring the disease progression.

In this study we found that 10% KOH mount is and easy, faster and rapid modality to diagnose fungal culture. The sensitivity of it being 46.7% . Among the KOH mount positive 38% were found to have septate hyphaes pointing out the presence of filamentous fungi. It is rapid, requires less resources, therefore used in the peripheral primary health centres to diagnose fungal keratitis, making it easier for rural areas to get access to

treatment. These findings were similar and in sinc with a study conducted by jayashree et al. in the year 2020.[35]

A study by manisha acharya found that bacterial culture accounted for 60.6% (238/393) and fungal cultures were 143 (36.4%) [57].Another study conducted in America by menard et al found that fungal keratitis by yeast (27.4%) is less common than filamentous organisms (66.1%). The common filamentous organisms found in this study were Fusarium species 17.7% and Apergillus species 16.1%, whereas the most common yeast was Candida 24.2%. The use of contact lens was found to be the main predisposing factor in keratitis by filamentous fungi. Immunocompromised host and ocular surface disease were associated with keratitis by yeasts. (31) According to a 16-year study by Satpathy G, the most prevalent fungus was Aspergillus species, which made up 31.1% of the total. Fusarium species came in second with 24.5%, followed by species like alternaria (approximately10.5%) and Curvularia (10.2%)[58]. Another study by Misra et a found that fusarium species (33.2%) was the most predominant followed by Curvularia species (21.9%) and Aspergillus species (16.7%) [28]. In our study, we found that majority of fungal keratitis were culture positive for filamentous fungi like aspergillus fumigatus (62%) followed by aspergillus flavus (15%) 10% were aspergillus niger,10% fusarium and dematitious fungi (2%) respectively. 2% cases were candida. This highlighted that north Karnataka region, being densely populated by people who have agriculture as their source of income are predisposed to trauma, hence are more prone to develop fungal keratitis secondary to infection by filamentous fungi. Therefore it is of utmost necessity to create awareness among rural population especially farmers about this vision threatening

condition and they should be counseled about the need to wear protective glasses while working. They also counseled about the aggressive nature of the disease and adviced to report immediately following trauma and be compliant to the medications adviced by the ophthalmologists.

CONCLUSION

Fungal keratitis is a aggressive disease with poor visual prognosis. It is more prevalent in areas where agriculture is the source of livelihood. Thus farmer being the backbone of Indian economy are more prone to attain this disease. In this part of north Karnataka, filamentous fungi were found to be more prevalent with male preponderance and risk factors being older age, trauma to the eye with vegetative matter in the fields, illiteracy, chronic dacryocystitis. Anterior segment optical coherence tomography can be instrumental in monitoring the progression of the disease. 10% KOH Mount was found to be very useful in rapid diagnosis of fungal keratitis.

A corneal ulcer is a medical emergency of the eye. The effects of corneal blindness are profound in a developing nation like ours. It is essential to do a microbiological analysis by taking corneal scraping samples before starting the right course of treatment.Corneal blindness can be prevented in large part by raising public awareness of proper eye hygiene and use to protective glasses.

Therefore, it is important to to study the microbiological and clinical profile of fungal keratitis in every part of the country and together we can prevent blindness in the country.

SUMMARY.

This prospective, cross sectional study was conducted with the aim of assessing the clinical and microbiological profile of fungal keratitis in this part of north Karnataka where the population of farmers is larger in number. Our study noted that trauma with vegetable matter was the major cause of development of fungal keratitis. The major features peculiar to this diseases were dry looking, 2-5mm, irregular, epithelial defect with infiltration extending to mid periphery, feathery margins, satellite lesions and endothelial plaques. ASOCT was helpful in detecting endothelial plaques and can be used to further monitor the progression of the disease. 46.9% out of 147 patients screened were 10% KOH mount positive, can be used as a rapid method in diagnosing fungal keratitis. Filamentous fungi were responsible for the majority of fungal keratitis. 10 patients had presented with perforation at their first visit. This shows that the disease is aggressive in nature and can progress to blindness if not diagnosed and intervened early. This necessitates the need of counseling rural people who are illiterates, about the need for eye hygiene. They should also be advised to report early, be compliant with medications and follow ups.

THE LIMITATIONS OF THIS STUDY

- Small sample size
- Anterior segment optical coherence tomography cannot be used in cases where there is a dense infiltrates
- Follow up of the cases were not done to evaluate the progression of the disease.

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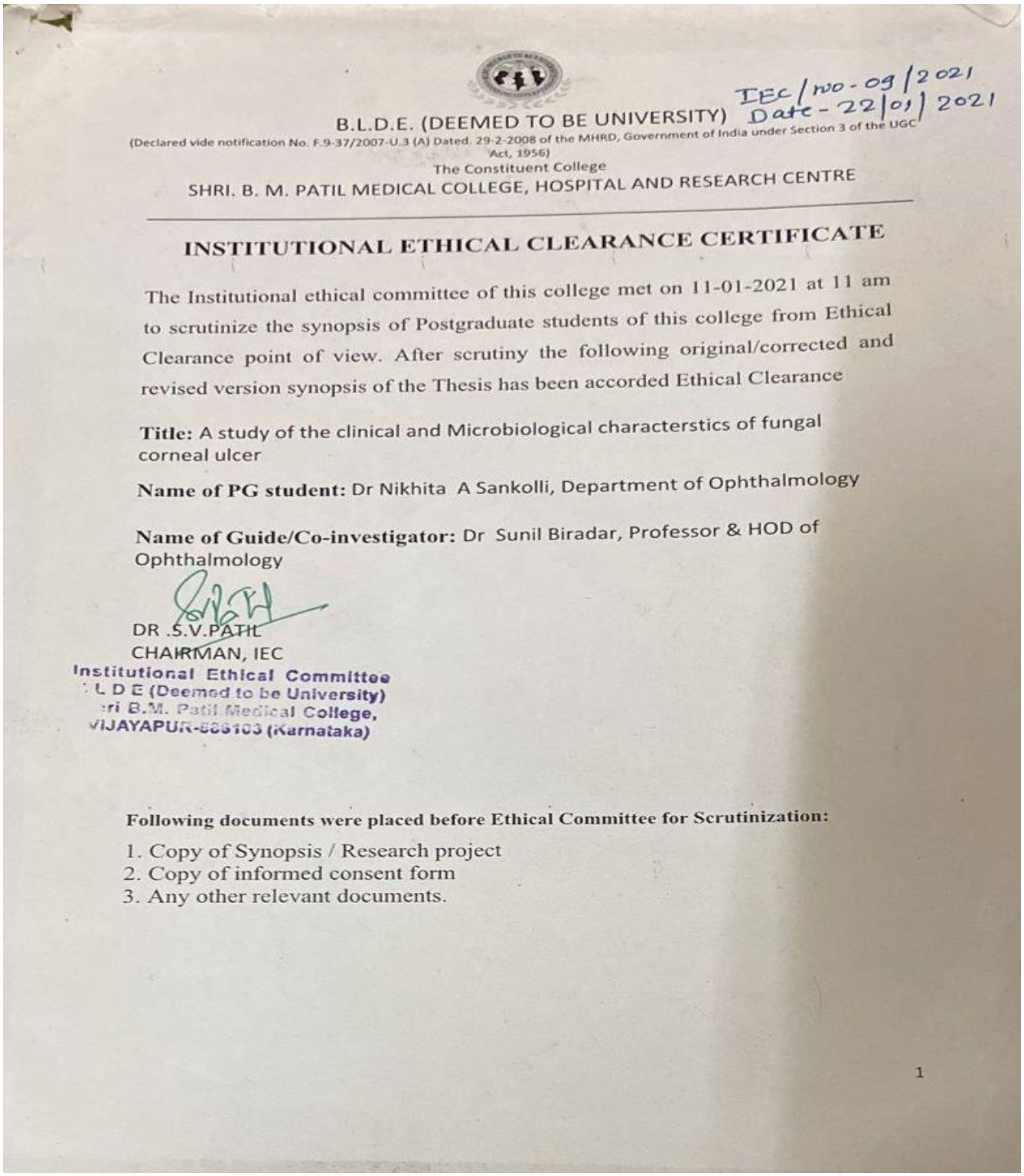
i. ANNEXURES

ETHICAL CLEARANCE CERTIFICATES



B.L.D.E. (DEEMED TO BE UNIVERSITY)

IEC/no-09/2021
Date-22/01/2021

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A study of the clinical and Microbiological characterstics of fungal corneal ulcer

Name of PG student: Dr Nikhita A Sankolli, Department of Ophthalmology

Name of Guide/Co-investigator: Dr Sunil Biradar, Professor & HOD of Ophthalmology

DR .S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
L D E (Deemed to be University)
ri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

1

STUDY SUBJECT CONSENT FORM

I confirm that Dr. NIKHITA ANIL SANKOLLI has explained to me the purpose of research, the study procedure and the possible discomforts as well as benefits that I may experience in my own language. I have been explained all the above in detail 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)

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomforts during the examination. The procedures of this study are not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation will help in the assessment of fungal keratitis.

I understand and accept the risks, benefits and costs involved. I willingly give consent to take part in the study.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more questions about the study to Dr. Sunil G Biradar in the Department of Ophthalmology who will be available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr. Nikhita Anil Sankolli may terminate my participation in the study after she has explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in the study, if such injury were reported promptly, the appropriate treatment would be available to me. But no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

_____ – _____

(participant) (date)

I have explained to_____the purpose of the research, the procedures required and the possible risks to the best of my ability.

_____ _____

Dr. NIKHITA ANIL SANKOLLI Date

(Investigator)

1. PROFORMA FOR CASE TAKING

PROFORMA FOR CASE TAKING

DEPARTMENT OF OPHTHALMOLOGY

B.L.D.E UNIVERSITY'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586103

CASE NO: DATE

OPD/IPD NO:

NAME:

AGE:

SEX: MALE O FEMALE O

LITERATE O ILLITERATE O

OCCUPATION: FARMER O LABOURER O DRIVER O MECHANIC O

ADDRESS:

COMPLAINTS:

25

HISTORY OF PRESENT ILLNESS:

	YES	NO
TRAUMA		
VEGETABLE MATTER O		
ANIMAL MATTER O		
INSECT O		
METAL O		
PAIN		
PRICKING SENSATION		
PHOTOPHOBIA		
BLURRING OF VISION		
DISCHARGE		

IF YES, WATERY

MUCOPURULENT

PAST HISTORY:	YES	NO
A) DIABETES MELLITUS		
B) HYPERTENSION		
C) TUBERCULOSIS		
D) CONTACT LENS		
E) SWIMMING		

PAST SURGERY:

PAST INFECTIONS:

- STYE
- SINUSITIS
- DACRYOCYSTITIS

FAMILY HISTORY:

26

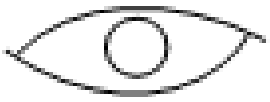
GENERAL PHYSICAL EXAMINATION

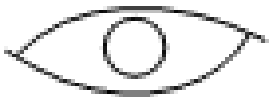
EXAMINATION OF THE EYE: **RIGHT EYE** **LEFT EYE**

UNAIDED VISION

AIDED VISION

EXTERNAL APPEARANCE



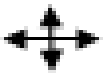


LIDS

1. BLEPHARITIS
2. MEIBOMITIS

LACRIMAL PASSAGE:

OCULAR MOTILITY



CONJUNCTIVA

CONGESTION:

a) Conjunctival
b) Circumciliary
c) Mixed

27

CORNEA

ULCER
1) SHAPE
2) SIZE
3) DEPTH
4) LOCATION
5) BASE
6) EDGE

IMMUNE RING

INVOLVING POSTERIOR STROMA

FEATHERY EDGE

SATELLITE LESIONS

ENDOTHELIAL PLAQUE

OTHER FINDINGS

ANTERIOR CHAMBER:

1) HYPOPYON
2) AC REACTION
   CELLS
   FLARE

PUPIL

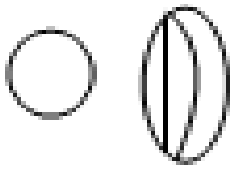
1. ROUND
2. REGULAR
3. REACTIVE

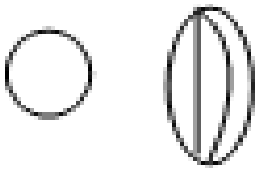
IRIS:

1. NORMAL
2. INFLAMED

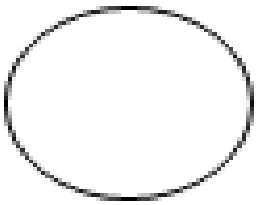
LENS

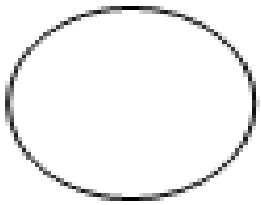
1. IMMATURE CATARACT
2. MATURE CATARACT
3. HYPERMATURE CATARACT
4. PSEUDOPHAKIA





FUNDUS EXAMINATION





A) MEDIA
B) DISC
C) BLOODVESSELS

D) BACKGROUND

E) MACULA

DIGITAL IOP:

SOFT

HARD

IMPRESSION:

INVESTIGATIONS:

SLIT LAMP EXAMINATION WITH PHOTOGRAPHY

RBS

CBC

1. TC
2. DC
    a. NEUTROPHIL
    b. EOSINOPHIL
    c. MONOCYTE
    d. LYMPHOCYTE

Gram stain

10%KOH mount

FUNGAL CULTURE USING SABOURAUD'S DEXTROSE AGAR (SDA)

AT ROOM TEMPERATURE

AT 37 DEGREE CELSIUS

ASOCT

COLOR PLATES

Figure 1: examining the corneal ulcer under slit lamp biomicroscopy

Figure 2: Observing the extent of corneal ulcer after fluorescent staining under cobalt blue filter

Figure 3: Corneal scraping of a patient using 11 number blade

Figure 4: Equisition of anterior segment optical coherence tomography of endothelial plaque

Case Photos

Figure A : slit lamp picture of corneal ulcers noted during the study

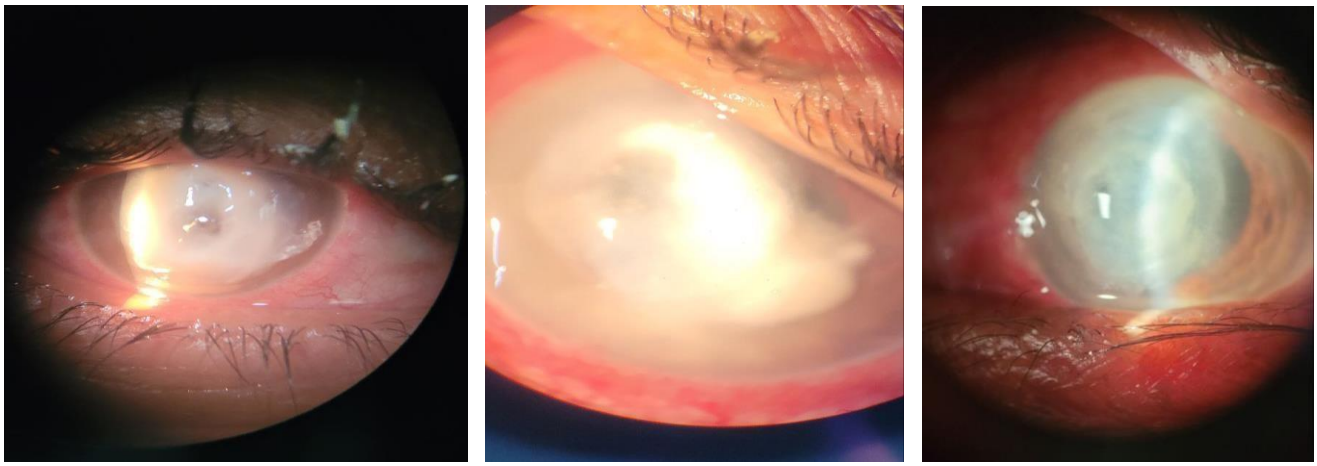


Figure B: Images of cornea ulcer after fluorescent staining

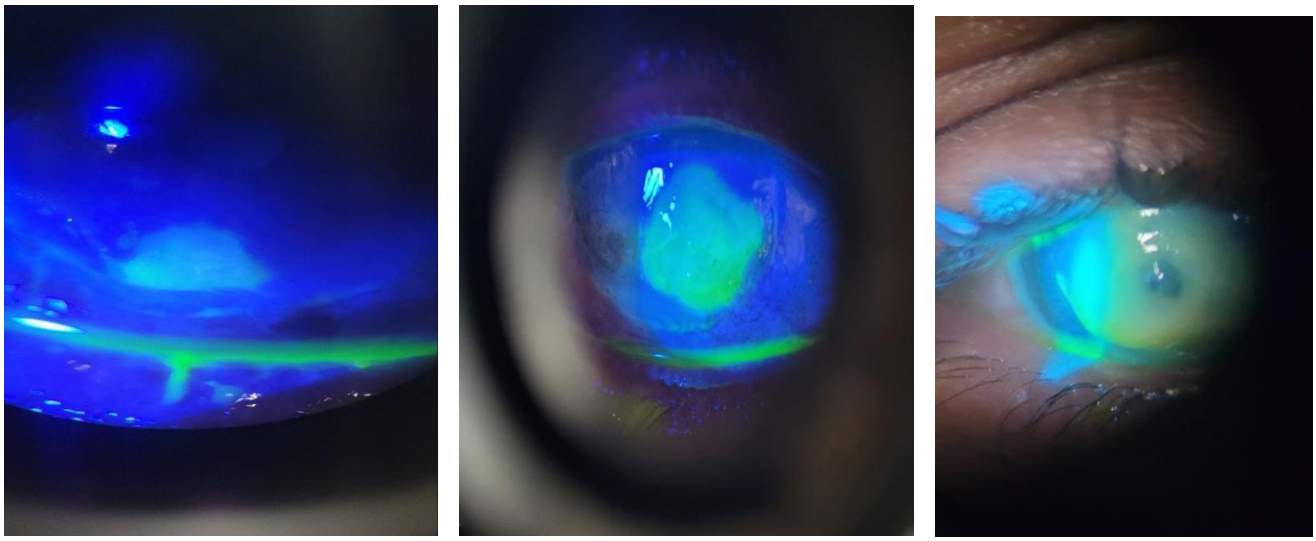


Figure C: KOH mount showing septated hyphaes and pseudohyphaes

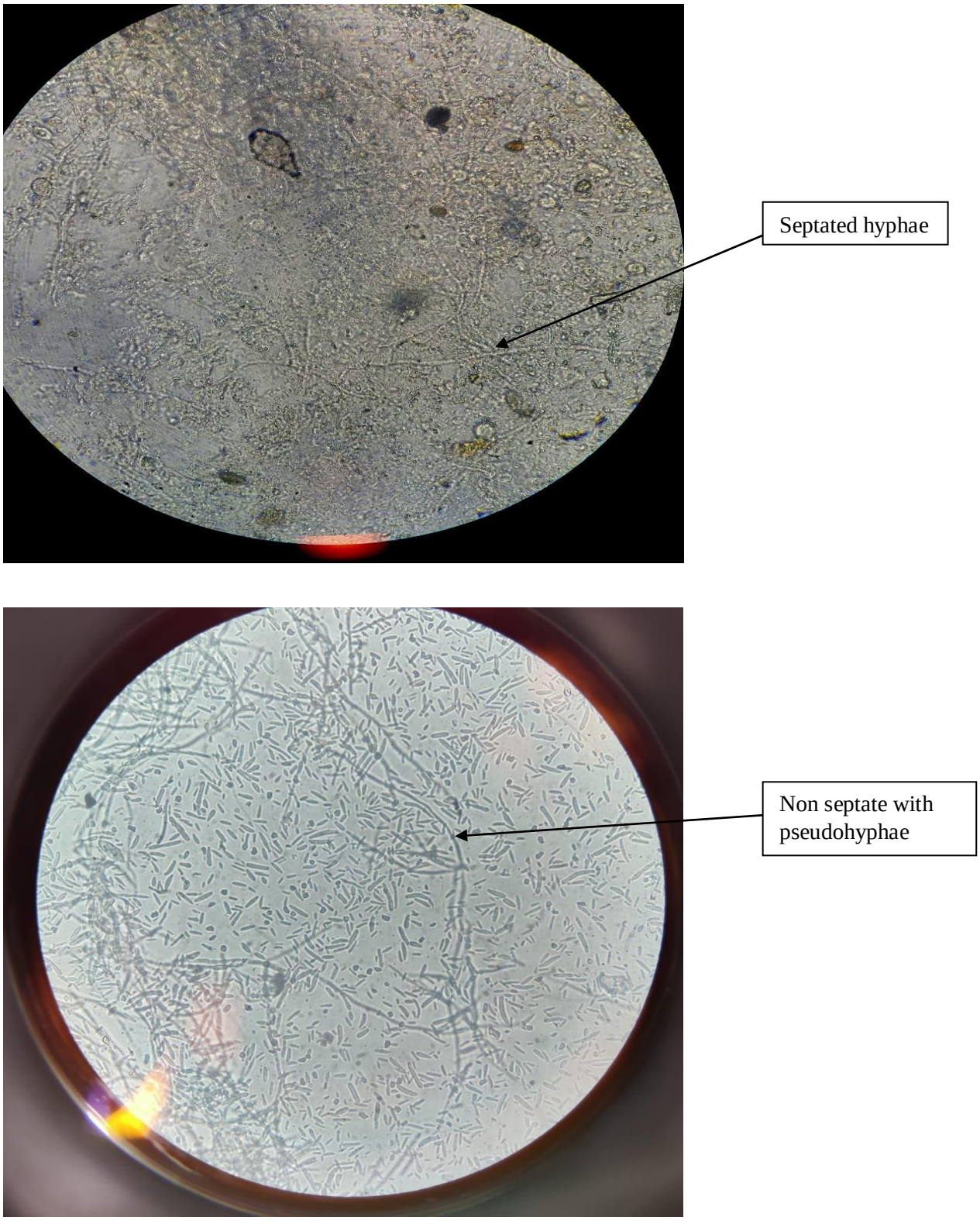
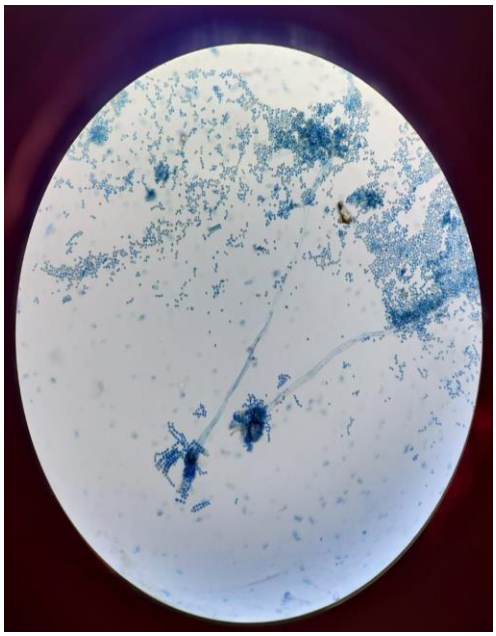
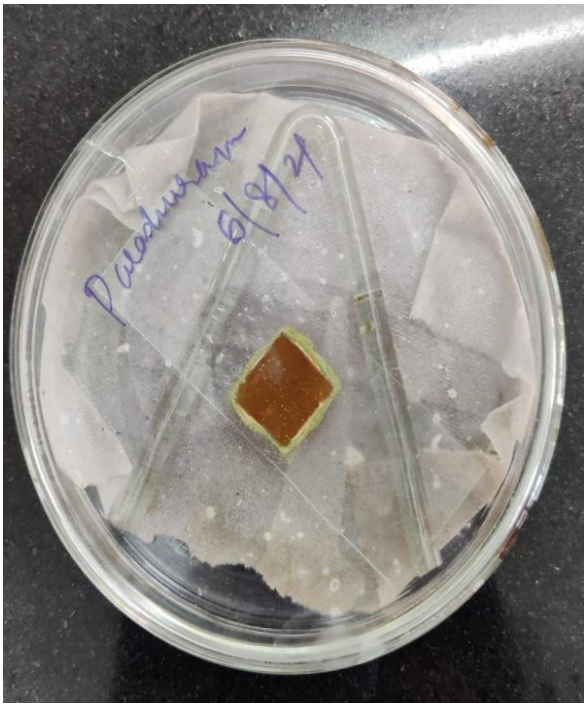


Figure D: Culture growth on sabourauds dextrose agar

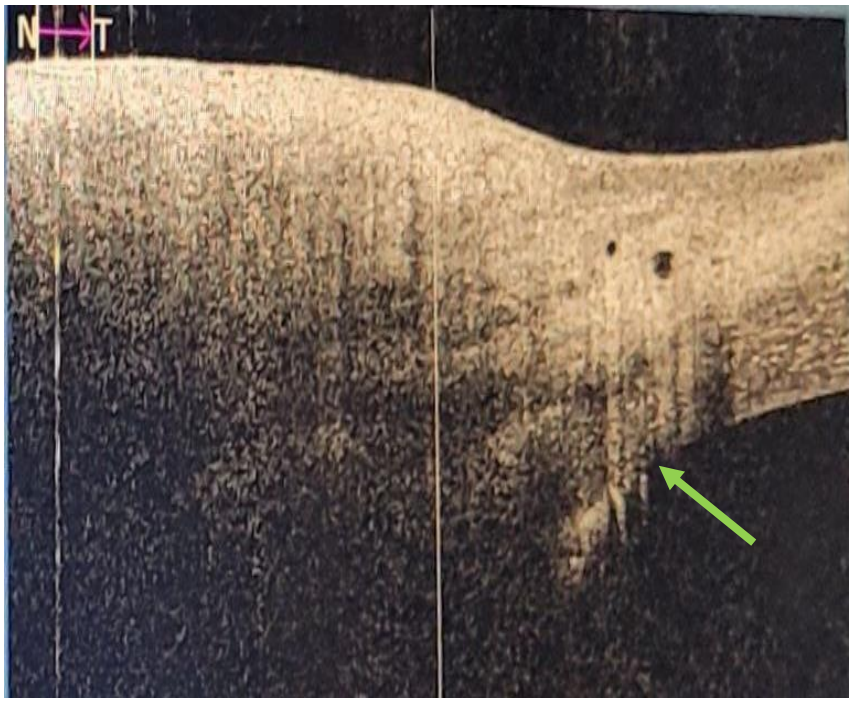


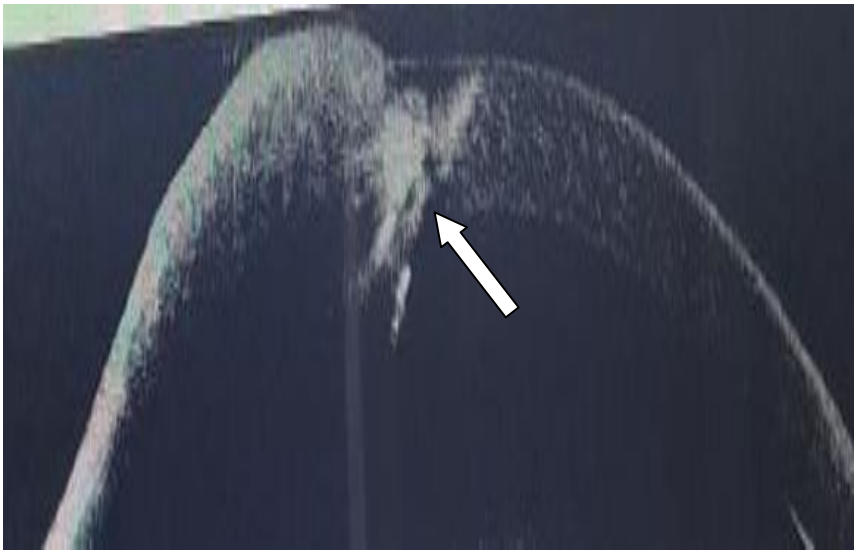
Aspergillus fumigatus



fusarium

Figure F: Anterior segment optical coherence tomography showing endothelial plaque





2. MASTER CHART

S. No – Serial Number

F – Female

M – Male

DM – Diabetes Mellitus

RBS – Random Blood Sugar

HIV – Human immunodeficiency

HbsAg – hepatitis B antigen

RE – Right Eye

LE – Left Eye

BE – Both eyes

CF – Counting fingers

HM – Hand movements

NI – No improvement

PL – Perception of light

S.NO	NAME	SEX1-male 2-female	AGE in years	OCCUPATION 1- FARMER 2- HOUSEWIFE 3- LABOURER 4- DRIVER 5- MECHANIC 6 STUDENTS	LITERACY 1-LITERATE 2- ILLITERATE	DIABETES 1- PRESENT 2-ABSENT	TRAUMA 1- PRESENT 2- ABSENT	TRAUMATIC AGENTS 1- PLANT 2- ANIMAL 3- INSECTS4- METALLIC PIECE 5- STONE	SYMPTOMS 1- PAIN 2- PRICKING SENSATION 3- PHOTOPHOBIA 4-BLURRING OF VISION 5- DISCHARGE 6- REDNESS 7- WATERING	SIGNS -LID EDEMA 2- RESTRICTED OCULAR MOVEMENT 3- CONJUNCTIVAL CONGESTION 4- epithelial defect with infiltration 5-HYPOPYON 6- PUPILLARY DEFECT 7- CATARACT 8- pseudophakia
1	SAYAMMA	2	30	2	1	1	2	2	1,4,6,7	3,4,5
2	SOMALABAI RATHOD	2	50	1	1	2	1	1	1,3,4,6,7	1,3,4,5,7
3	PAJWAL R	1	22	1	1	2	2	2	2,6,7	3,4
4	PARVATHI	2	45	2	1	2	1	1	1,3,4,6,7	3,4,1
5	LAXMAN HARJAN	1	58	1	1	1	2	1	1,2,3,4,5,6	1,3,4,5,
6	AMBAVVA	2	45	2	2	2	1	1	2,4,5,6,7	1,3,4,
7	KOLLEPPA	1	60	1	1	2	1	2	1,2,3,4,5,6	1,3,4,5,7
8	SUNIL	1	13	6	2	2	2	2	2,3,4,6,7	1,3,4,
9	MALLAPA BAJANTRI	1	75	1	1	1	1	1	1,2,3,4,5,6	1,3,4,5,7
10	Bapu majagi	1	70	1	1	1	1	1	1,2,3,4,5,6	1,3,4,
11	RAJKUMAR	1	45	1	1	2	2	2	1,2,3,4,6,7	1,3,4,5,7
12	RANGUBAI PATIL	2	35	3	2	2	1	5	2,6,7	1,3,4,
13	BHIMSHI BAJANTRI	1	50	1	1	1	1	1	1,2,3,4,5,6,7	1,2,3,4,5,7
14	HANAMANTH NAGANUR	1	21	3	2	2	2	1	1,2,3,4,6,7	1,3,4
15	ASHOK KOTTALAGI	1	41	1	1	2	1	1	2,4,6,7	1,3,4,
16	YALLAWWA	2	48	2	1	1	1	2	1,2,3,4,5,6,7	1,3,4,7
17	LAXMIBAI MASUTI	2	50	3	1	1	2	4	1,4,6,7	3,4,5
18	Amasidd salagar	1	45	1	1	2	1	2	2,4,5,7	3,4
19	Channabasu nijagond	1	35	5	2	2	1	1	1,2,4,6	1,3,4
20	Lalitha savadkar	2	56	2	1	2	2	2	1,2,3,6,7	1,2,3,4,5,7
21	Shivamma joji	2	60	2	1	2	1	2	1,2,3,4,5,6	1,3,4,7
22	Shiv Shankar patil	2	56	1	1	2	1	1	1.2,3,4,6,7	1,3,4,7
23	Shanta alur	2	45	1	1	2	1	5	1,2,3,4,5,6,7	1,3,4,7
24	Biranna	1	52	1	1	2	1	1	1,2,3,4,5,6,7	1,3,4,7
25	Shivanagonda	1	51	4	1	2	2	1	1,2,3,4,6,7	1,3,4
26	Renuka anagawadi	2	55	2	1	2	2	1	1,2,3,4,6,7	1,3,4,7
27	Irayya hiremath	1	45	1	2	2	1	5	1,2,3,4,5,6,7	1,3,4

28	Nanda bistagond	1	59	1	1	2	1	1	1,2,3,4,6,7	1,3,4
29	Gangabai chatarki	2	65	1	1	2	1	3	1,2,3,4,6,7	1,2,3,4,5,7
30	Venu	1	54	2	1	2	2	1	1,2,3,4,6,7	1,3,4
31	Sonapadashetti	2	13	2	2	2	2	1	1,2,3,4,6,7	1,3,4,7
32	Shrishail kumbar	2	67	3	1	2	2	1	1,2,3,4,5,6,7	1,3,4,7
33	Parashuram	1	65	2	1	2	2	3	1,2,3,4,6,7	1,3,4,7
34	Babu jadhav	1	69	4	1	2	1	1	1,2,3,4,6,7	1,3,4
35	Bhimangouda biradar	2	8	6	2	2	1	5	1,2,3,4,5,6,7	1,2,3,4,5,7
36	Shivappa chalawadi	1	68	1	1	1	1	1	1,2,3,4,6,7	1,3,4,7
37	Shashidhar	1	56	1	1	2	1	1	1,2,3,4,6,7	1,3,4
38	Khubu rathod	1	52	1	1	2	1	1	1,2,3,4,6,7	1,3,4,7
39	Basappa natikar	1	53	2	1	2	1	3	1,2,3,4,6,7	1,3,4
40	Sharanappa	2	64	1	1	2	2	2	1,2,3,4,5,6,7	1,3,4,7
41	Mallamma vouvare	2	58	2	1	2	2	1	1,2,3,4,6,7	1,3,4
42	Shankareppa hypur	1	60	1	1	1	1	1	1,2,3,4,6,7	1,3,4,7
43	Hanamanth natikar	1	62	2	1	2	1	4	1,2,3,4,6,7	1,3,4,7
44	Sunitha chavan	2	56	1	1	2	1	2	1,2,3,4,5,6,7	1,2,3,4,5,7
45	Sunita balakond	2	36	1	2	2	1	3	1,2,3,4,6,7	1,3,4
46	Sakshi Santhosh	2	52	1	1	2	1	2	1,2,3,4,6,7	1,3,4,7
47	Siddappa aliband	1	60	1	1	2	2	5	1,2,3,4,5,6,7	1,3,4
48	Kadappa Mali	1	62	3	1	1	2	1	1,2,3,4,6,7	1,2,3,4,5,7
49	Jyoteppa walikar	1	46	5	2	2	2	1	1,2,3,4,6,7	1,3,4,7
50	Sharadha irasangi	2	60	1	1	2	2	1	1,2,3,4,5,6,7	1,3,4
51	Shivanand	1	63	1	1	2	2	1	1,2,3,4,6,7	1,3,4,7
52	Siddappa badiger	1	80	1	1	2	1	1	1,2,3,4,6,7	1,3,4

S.NO	NAME	VISUAL ACUITYBCVA 1= PL -, 2= PL+ PR ACCURATE, 3=HM+4- CF-cf ,5-20/200-20/100, 6-20/40 - 20/100	CORNEAL ULCER SIZE 1-<2MM 2-2-5MM 3->5MM	CORNEAL ULCER - LOCATION1-CENTRAL 2-PARACENTRAL 3-PERIPHERY	CORNEAL ULCER DEPTH 1-<20%, 2-20-50% 3->50%	CORNEAL ULCER BASE 1-DRY LOOKING 2-NECROTIC	SATELLITE LESIONS 1-PRESENT 2- ABSENT	FEATHERY MARGIN 1-YES 2-NO	IMMUNE RING 1-PRESENT 2-ABSENT
1	SAYAMMA	6	2	1	2	1	2	2	1
2	SOMALABAI RATHOD	5	2	1	2	2	1	1	1
3	PAJWAL R	6	1	2	1	1	2	2	2
4	PARVATHI	5	1	2	2	1	1	2	1
5	LAXMAN HARJAN	3	3	1	2	1	2	1	1
6	AMBAVVA	6	2	1	2	1	2	1	2
7	KOLLEPPA	4	2	1	2	1	2	1	2
8	SUNIL	4	2	1	2	1	1	1	2
9	MALLAPA BAJANTRI	4	3	1	2	2	1	1	1
10	Bapu majagi	2	2	2	2	1	1	1	2
11	RAJKUMAR	3	3	1	3	1	1	1	2
12	RANGUBAI PATIL	5	1	2	1	1	1	1	1
13	BHIMSHI BAJANTRI	4	2	2	2	1	1	1	2
14	HANAMANTH NAGANUR	5	2	1	2	1	1	1	2
15	ASHOK KOTTALAGI	4	2	2	2	1	1	1	2
16	YALLAWWA	3	3	1	3	2	1	1	1
17	LAXMIBAI MASUTI	6	2	1	2	1	2	2	2
18	Amasidd salagar	6	2	2	1	1	1	1	2
19	Channabasu nijagond	6	2	2	2	1	2	1	2
20	Lalitha savadkar	5	1	2	2	1	2	2	2
21	Shivamma joji	4	3	1	3	1	2	1	2
22	Shiv Shankar patil	3	2	1	2	1	2	2	2
23	Shanta alur	2	2	1	2	1	2	2	2
24	Biranna	1	2	1	2	1	2	2	2
25	Shivanagonda	2	2	1	2	1	1	1	2
26	Renuka anagawadi	2	2	1	2	1	1	1	2
27	Irayya hiremath	2	2	1	2	1	1	1	2
28	Nanda bistagond	3	2	2	2	1	1	1	2

29	Gangabai chatarki	3	3	1	3	2	1	1	2
30	Venu	3	2	2	2	1	1	1	2
31	Sonapadashetti	3	2	1	2	1	1	2	1
32	Shrishail kumbar	3	2	3	3	2	1	2	2
33	Parashuram	3	2	1	2	1	1	1	2
34	Babu jadhav	2	2	1	2	1	2	1	2
35	Bhimangouda biradar	2	3	1	3	2	2	1	2
36	Shivappa chalawadi	2	2	2	2	1	1	1	2
37	Shashidhar	3	2	2	2	1	1	1	2
38	Khubu rathod	3	2	2	2	1	2	1	2
39	Basappa natikar	3	2	2	2	1	1	2	2
40	Sharanappa	3	2	2	2	1	2	1	2
41	Mallamma vouvare	3	2	1	2	1	1	1	2
42	Shankareppa hypur	3	2	1	2	1	2	1	2
43	Hanamanth natikar	3	2	1	2	1	1	2	2
44	Sunitha chavan	2	3	1	3	2	2	1	2
45	Sunita balakond	2	2	1	2	1	1	1	2
46	Sakshi Santhosh	2	2	2	2	1	1	2	2
47	Siddappa aliband	2	2	3	2	1	2	1	2
48	Kadappa Mali	1	3	2	3	2	1	1	2
49	Jyoteppa walikar	2	2	1	2	1	1	1	2
50	Sharadha irasangi	2	2	1	2	1	1	1	2
51	Shivanand	2	2	1	2	1	1	2	2
52	Siddappa badiger	2	2	1	2	1	2	2	2

S.NO	NAME	HYPOPYON 1-PRESENT 2-ABSENT	PERFORATION 1-PRESENT 2- ABSENT	ENDOTHELIAL PLAQUE 1- PRESENT 2-ABSENT	ASOCT DETECTION OF ENDOTHELIAL PLAQUE 1-PRESENT 2-ABSENT	KOH MOUNT 1- POSITIVE 2-NEGATIVE	KOH MOUNT 1- SEPTATE HYPHAE2-PSEUDOHYPHAE3-INDISTINCT	FUNGAL CULTURE
1	SAYAMMA	1	2	1	0	1	1	ASPERGILLUS fumigatus
2	SOMALABAI RATHOD	1	2	2	0	1	1	ASPERGILLUS fumigatus
3	PAJWAL R	2	2	1	1	1	1	ASPERGILLUS niger
4	PARVATHI	2	1	2	0	1	1	ASPERGILLUS flavus
5	LAXMAN HARJAN	1	2	2	0	1	3	ASPERGILLUS flavus
6	AMBAVVA	2	2	1	1	1	1	ASPERGILLUS fumigatus
7	KOLLEPPA	1	2	2	0	1	1	ASPERGILLUS fumigatus
8	SUNIL	1	2	1	0	1	1	ASPERGILLUS fumigatus
9	MALLAPA BAJANTRI	2	2	2	0	1	3	ASPERGILLUS flavus
10	Bapu majagi	2	2	1	1	1	1	ASPERGILLUS fumigatus
11	RAJKUMAR	1	2	2	0	1	3	ASPERGILLUS flavus
12	RANGUBAI PATIL	2	2	1	1	1	1	ASPERGILLUS fumigatus
13	BHIMSHI BAJANTRI	1	2	2	0	1	1	ASPERGILLUS fumigatus
14	HANAMANTH NAGANUR	2	2	1	0	1	3	ASPERGILLUS fumigatus
15	ASHOK KOTTALAGI	2	2	2	0	1	1	ASPERGILLUS fumigatus
16	YALLAWWA	1	1	1	1	1	1	Fusarium
17	LAXMIBAI MASUTI	1	1	1	0	1	3	ASPERGILLUS flavus
18	Amasidd salagar	2	2	2	0	1	3	ASPERGILLUS fumigatus
19	Channabasu nijagond	2	2	2	0	1	1	ASPERGILLUS niger
20	Lalitha savadkar	2	2	1	1	1	1	ASPERGILLUS fumigatus
21	Shivamma joji	2	1	1	0	1	3	Fusarium
22	Shiv Shankar patil	2	2	1	0	1	1	Fusarium

23	Shanta alur	2	2	2	1	1	1	ASPERGILLUS fumigatus
24	Biranna	2	1	1	1	1	3	ASPERGILLUS niger
25	Shivanagonda	2	2	1	1	1	1	ASPERGILLUS fumigatus
26	Renuka anagawadi	2	1	1	1	1	1	ASPERGILLUS fumigatus
27	Irayya hiremath	2	1	2	0	1	3	ASPERGILLUS fumigatus
28	Nanda bistagond	2	2	2	0	1	1	Fusarium
29	Gangabai chatarki	1	2	1	0	1	3	ASPERGILLUS fumigatus
30	Venu	2	2	2	0	1	1	ASPERGILLUS fumigatus
31	Sonapadashetti	1	1	1	0	1	3	ASPERGILLUS flavus
32	Shrishail kumbar	2	2	2	1	1	1	ASPERGILLUS fumigatus
33	Parashuram	2	2	2	1	1	1	ASPERGILLUS fumigatus
34	Babu jadhav	2	1	2	1	1	1	ASPERGILLUS fumigatus
35	Bhimangouda biradar	1	2	1	0	1	3	Fusarium
36	Shivappa chalawadi	2	2	1	0	1	1	ASPERGILLUS fumigatus
37	Shashidhar	2	2	1	0	1	3	ASPERGILLUS fumigatus
38	Khubu rathod	2	2	2	0	1	3	ASPERGILLUS fumigatus
39	Basappa natikar	2	2	1	0	1	1	ASPERGILLUS fumigatus
40	Sharanappa	2	2	2	0	1	3	ASPERGILLUS fumigatus
41	Mallamma vouvare	2	2	1	0	1	1	ASPERGILLUS niger
42	Shankarepa hypur	2	2	2	1	1	1	ASPERGILLUS fumigatus
43	Hanamanth natikar	2	2	1	0	1	1	ASPERGILLUS fumigatus
44	Sunitha chavan	1	2	2	0	1	3	ASPERGILLUS flavus
45	Sunita balakond	2	2	1	1	1	1	ASPERGILLUS fumigatus
46	Sakshi Santhosh	2	2	2	0	1	3	ASPERGILLUS fumigatus
47	Siddappa aliband	2	2	1	0	1	1	ASPERGILLUS fumigatus
48	Kadappa Mali	1	2	1	1	1	1	ASPERGILLUS flavus

49	Jyoteppa walikar	2	2	2	0	1	1	ASPERGILLUS fumigatus
50	Sharadha irasangi	2	2	2	1	1	3	ASPERGILLUS fumigatus
51	Shivanand	2	1	1	0	1	1	ASPERGILLUS niger
52	Siddappa badiger	2	1	2	1	1	2	dematitious fungi