

ULCERATIVE KERATITIS A PROSPECTIVE HOSPITAL BASED CLINICAL AND MICROBIOLOGICAL STUDY

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ABSTRACT: A total of 150 patients with clinical diagnosis of ulcerative keratitis with or without hypopyon were enrolled in this study. A maximum of patients were from age group 21 to 40 years followed by patients in the age group of 41 to 60 years and there was male predominance. Seventy percent patients hailed from rural areas. Occupation profile mainly consisted of agricultural workers (50%), followed by industrial workers (20%), students (15%), and others (15%). The most common predisposing factor was trauma with vegetable matter (52%), followed by dry eye (10%), corneal xerosis (6%) and dacryocystitis. Microbial etiology was established in 50% of scrapings. 58% were fungal, mostly due to *Aspergillus*. 42% were bacterial mostly Gram positive cocci *Staphylococcus aureus*. In a majority of cases only one eye was involved (59% in the left eye and 41% in right eye). Many patients presented with multiple symptoms and most of them presented with Pain, redness, watering of eyes and decreased vision. Ulcer was central in 40%, Peripheral in 28% and in both areas in 32% of cases. 6.6% cases were diagnosed as viral keratitis. Fungal hyphae were observed in 16.66% of cases.

KEYWORDS: Corneal Ulcer, Keratitis, Fluorescein staining, Herpes Zoster Ophthalmicus.

INTRODUCTION: The present study was undertaken with the title 'ulcerative keratitis a prospective hospital based clinical and microbiological study', among the patients attending the outpatient department of ophthalmology, Katuri medical college and hospital, Chinakondrupadu Guntur, Andhra Pradesh.

AIM OF THE STUDY: To study and identify epidemiological characteristics, predisposing factors, clinical features, microbiological profile and treatment outcome of patients with ulcerative keratitis

MATERIALS AND METHODS: The material for present study was constituted by patients attending to the outpatient department of ophthalmology Katuri medical college and hospital, Chinakondrupadu, Guntur, who were diagnosed as ulcerative keratitis

PERIOD OF STUDY: This clinical study was done during the period from 2011 October to 2014 October for 36 months.

- **Selection of cases:** Out of 400 cases of corneal ulcers, 150 cases were selected for detailed study.
- **Inclusion criteria:** Ulcer cases having presence of corneal epithelial defect with stromal infiltrate seen upon slit lamp examination were included in the study.

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- **Exclusion criteria:** NON COMPLIANT PATIENTS AS REGARDS proper treatment schedule and regular follow up.
- **Detailed history:** A detailed case history including age, sex, occupation, and predisposing factors were recorded. A detailed interrogation was made to elicit other signs and symptoms to exclude other ocular conditions.
- **Ophthalmic examination:** Consists of external examination and slit lamp examination of anterior segment of eye. If possible posterior segment is also examined.
 - Fluorescein staining was done.
 - Visual acuity was recorded.
 - Detailed examination of ulcer and documentation was done
 - Grading of severity of ulcer was done taking in to consideration the DB Jones criteria and location of the ulcer.
- **The criteria for non-severe ulcer:** slowly progressive, small size, minimal infiltration less than 6mm, minimal necrosis, no hypopyon, perforation unlikely.

The criteria for severe ulcer:

- Rapidly progressive, large size infiltration >6mm, deep stromal involvement, central location of ulcer threatening visual acuity, marked stromal thinning with impending perforation, presence of hypopyon and scleral involvement.
- **Local investigation:** Syringing of nasolacrimal passages.
 - Laboratory investigations: Urine –albumine and sugar
 - Total leucocyte count, differential laeucocyte count.
 - Haemoglobin%.
- **Specific investigations:** Corneal scrapings: Procedure for corneal scrapings; Topical anaesthesia with 4% xylocaine used to anaesthetise the cornea. Under slit lamp with sterile No.15 size surgical blade corneal scrapings done. Multiple scrapings obtained were smeared on culture media.
- **Smear staining;** One slide was heat sterilised and smeared with corneal scrapings and heat fixed, later sent to microbiology department for Gram staining. On second slide corneal scrapings were smeared and a drop of 10% KOH SOLUTION WAS APPLIED AND OVER IT A COVER SLIP WAS APPLIED AND EXAMINED UNDER MICROSCOPE.
- **Culture:** corneal scrapings were directly smeared on the culture media in a C shaped manner.
 - For bacterial keratitis nutrient agar, blood agar was used.
 - For fungal keratitis Sabourauds dextrose agar was used.
 - First line of management: This was based on the interpretation of corneal smears and clinical assessment of severity of corneal ulcer.
 - Diagnosis of viral keratitis by clinical diagnosis. Scrapings were taken only when secondary infection was suspected.
 - In Herpes simplex keratitis acyclovir 3% eye ointment 5 times/day.
 - In Herpes ZOSTER Ophthalmic US ORAL ACYCLOVIR 800mg 5 times/day for 7 to 10 days, if cornea was involved topical acyclovir 3% eye ointment was used.

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- If fungal hyphae were noticed 10%KOH wet mount –fungal corneal ulcer. natamycin5%eye suspension was used in most cases.
- In some cases Fluconazole 0.3% eye drops were used. In case of severe fungal keratitis with deep stromal involvement along with topical natamycin, oral fluconazole 200mg.bd for one week were used.
- In case of non-severe ulcers fluoroquinolone monotherapy with moxifloxacin 0.3% eye drops were used.
- **In case of severe ulcers:** combination therapy with fortified cephalosporin5%+fortified gentamycin1.4% eye drops was used. All cases were reviewed after 48hours i.e after culture and sensitivity report.
- **Second line of management:** After culture and sensitivity reports:
- **If culture is positive:** if ulcer shows signs of improvement, same initial therapy were continued irrespective of c/s reports. If the ulcer is stationary with-out improvement but not worsened same drug is continued for two more days. If it remained the same, sensitive antibiotic was used. If the ulcer worsens initial therapy was changed.
- Sensitive antibiotics were used, fortified drops considered if commercially available drops were used previously.
- If culture is negative: It is sterile ulcer(non-infective ulcer).it can be due to healing stage of infective ulcer or lack of adequate scrapings for culture media to grow or using antibiotic eyedrops prior to corneal scrapings
- In non-infective ulcer other associated clinical features help in making a diagnosis.
- If decreased corneal sensation it is neurotropic ulcer-treatment: artificial tears, prophylactic antibiotics, tarsorrhaphy.
- If associated facial nerve paralysis- it is neuroparalytic keratitis-treatment: artificial tears, prophylactic antibiotics, tarsorrhaphy
- If vernal keratoconjunctivitis(shield ulcer)-treatment steroids along with prophylactic antibiotic were used.
- If marginal infiltrates were found with meibominitis-it is marginal ulcer. treatment oral tetracycline, topical steroid, antibiotic eyedrops, lid hygiene.
- For phlyctenular keratitis, treatment: topical steroids, prophylactic antibiotics.
- Along with specific therapy:
- ATROPINE1%drops or ointment2times/day, local hygiene, warm compresses, eye shield, if raised intraocular pressure tablet diamox 250 mg. qid were used.
- If ulcer is progressive despite the above measures with marked stromal thinning descematocele is formed
- Treatment of descematocele:
- Bandage contact lens or pad and bandage was applied and referred to higher Centre for further management.
- If it is small perforation-bandage contact lens was applied and referred to higher Centre.
- If it is large perforation pad and bandage was applied and referred to higher Centre.
- Follow up and hospitalisation: Hospitalisation was advised in severe ulcers, paediatric cases, out of station patients.

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- Follow up after first visit: 2nd visit –after 2 days. later depending upon the state of ulcer daily, twice weekly.
- Later weekly follow up until ulcer is totally healed.
- Results:
- 150 patients with corneal ulcer were studied, with detailed recording of history, clinical examination, laboratory diagnosis, management and follow up. The following observations were made from this study.
- Incidence of corneal ulcer: during 2 year 10 months from october 2011 to october 2014, 50,000 new patients attended the ophthalmic outpatient department, Katuri medical college and hospital, Chinakondrupadu, Guntur. Out of them 400 cases corneal ulcers. 150 cases were selected for detailed study. $I = (400/50,000) = 0.8\%$.
- Epidemiological characters:
- Age distribution: The age of patients ranged from 8 yrs to 75 yrs.

Age in years	No. of cases	percentages
0-20	27	18%
21-40	75	50%
41-60	38	25%
Above 60 years	10	7%

Table 1: Age distribution

Incidence of corneal ulcer was more in age groups 21-40 and 41-60 yrs.

Sex	No. of cases	Percentage
Males	104	69%
Females	46	37%

Table 2: Distribution of sex

Incidence of corneal ulcer was more in males.

Place	No. of cases	Percentages
Rural	105	70%
Urban	45	30%

Table 3: Living conditions

Incidence was more among rural population.

Occupation	No. of cases	Percentage
Agriculture	75	50
Industrial	30	20
House wives	15	10

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Others	30	20
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Table 4: Occupational incidence

Agricultural laborers form major occupational groups associated with corneal ulcers

Predisposing factors	No. of cases	Percentage
Local:		
1. Ocular trauma including foreign body	72	48%
2. Ocular surface diseases	24	16%
3. Dacryocystitis	6	4%
4. Eyelid or lashes abnormality	3	2%
5. Decreased corneal sensation	6	4%
6. Exposure Keratopathy	3	2%
7. Contact lens wear	0	0%
8. After Ocular surgery	5	3%
SYSTEMIC:		
1. Diabetes Mellitus	9	6%
2. HIV	2	1.3%
3. Immunosuppressive drug Usage		0%
4. Allergy		0%
5. Psychiatric disturbances		0%
6. Hepatitis	2	1.3%
7. None	18	12%

Table 5: Predisposing factors

Ocular trauma and foreign body in the eye were associated with a majority of corneal ulcers

CLINICAL FEATURES: In all cases only one eye was involved. Right eye in 63 Patients (41%) and left eye in 82 patients (59%)

Symptoms	No. of cases	Percentage
1. Pain	123	82%
2. Redness	113	75%
3. Watering	90	60%
4. Diminution of Vision	68	45%
5. Photophobia	51	34%
6. Foreign Body sensation	30	20%

Table 6: Symptoms

Many patients presented with multiple symptoms and most of them presented with Pain, redness, watering of eyes and decreased vision.

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Location	No. of cases	Percentage
Central	60	40
Peripheral	42	28
Both areas	48	32

Table 7: Location of Ulcers

Ulcer is considered central if it is in central 5mm in diameter. Ulcer is considered peripheral if it is present within three mm from the limbus.

Area	No. of cases	Percentage
Less than 6mm in diameter	96	64%
More than 6 mm diameter	54	36%

Table 8: Size of infiltrate

Depth	No. of cases	Percentage
Less than two thirds of stroma	120	80%
More than two thirds	30	20%

Table 9: Depth of infiltrate

Microbiological characteristics and laboratory diagnosis.

Out of 150 cases corneal scrapings were taken from 100 cases, 10 eyes were diagnosed as viral keratitis clinically. 25 patients were already using topical antibiotic drops.

STAINING RESULTS:

- On 10%KOH wet mount 25 cases with fungal hyphae were observed.
- On gram staining, gram positive organisms in 25 smears, gram negative organisms in 3 smears.
- Both gram positive and gram negative organisms in smears were observed.

Culture results	N = 100	percentage
Culture positive	45	45%
Culture negative	55	55%

Table 10: Culture results: Out of 100 cases culture positivity was reported in 45 cases i.e. 45%

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	No. of cases	Percentages
Bacterial	20	20%
Fungal	25	25%
Sterile	55	55%

Table 11: Out of 45 culture positive cases bacterial isolates 20 and fungal isolates were 25.

Lab diagnosis was based on culture reports of 100 cases.

Bacteria	No. of cases=20	Percentage
Staphylococcus aureus	5	22%
Coagulase negative staphylococcus	10	47%
Streptococcus pneumoniae	2	10.5%
Other streptococcal species	2	10.5%
Gram negative bacteria		
pseudomonas	2	10.5%

Table 12: Culture positive bacterial isolates were found in 20 cases.

FUNGAL ISOLATES: Among 25 cases of fungal isolates 20 cases were (80%) Aspergillus species (20%) were Fusarium species.

Sterile (culture negative) corneal ulcers were 50 in number (33.33%). Depending on supportive clinical features 1 case of marginal ulcer, 1 case- of vernal keratoconjunctivitis, 3 cases of Neuroparalytic ulcer, 3 cases of Neurotrophic ulcer, 1 case of Phlyctenular ulcer, 1 case of Moorens ulcer were diagnosed Remaining 40 cases were sterile due to 1.some patients using antibiotic eyedrops prior to corneal scrapings. 2. Healing stage of infective corneal ulcer 3. Insufficient corneal scrapings.

TREATMENT AND CLINICAL OUTCOME:

Out of 150 cases, outpatient treatment has been initiated in 100 cases (66%)

In all cases atropine 1% eye ointment or homatropine 2% eyedrops, tablet vitamin c, eye shield were used along with specific treatment.

In 10 cases of Herpes simplex keratitis—topical acyclovir 3% eye ointment was initiated. Four cases were diagnosed as Herpes Zoster Ophthalmicus with corneal ulcer-Topical acyclovir 3% eye ointment and acyclovir 800mg tablet 5 times/day was administered. Response was good in all cases.

Fungal corneal ulcer (25 cases): Among 25 cases natamycin 5% suspension alone was used in 14 cases. In 7 cases natamycin 5% suspension + oral fluconazole 200mg two times daily.

In four cases fluconazole 0.3% eye drops alone was used.

In two cases natamycin 5% was used.

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RESPONSE TO FUNGAL TREATMENT: 20 cases responded well. 5 cases were refractory to therapy. Out of them 3 cases developed perforation, descematocele occurred in 1 case.

All refractory cases were referred to higher ophthalmic Centres for further management.

Bacterial corneal ulcers were diagnosed in 20 cases. In 14 cases of bacterial corneal ulcers fluoroquinolone monotherapy was used. In 5 cases antibiotic was changed to fortified cephazoline. In 5 cases combination therapy with cephazoline 5% +gentamycin 1.4% was used.

Response to antibacterial treatment was good -Only one case was refractory to the above treatment modality.

In culture negative cases; The etiology of the ulcers was found out with supportive clinical findings and treated.

Remaining cases; most of them were clinically bacterial. 25 cases showed signs of healing with antibiotics. 8 cases not responding were treated with fortified eye drops.

8 cases showed clinically fungal, natamycin 5% suspension was used. 35 cases responded well to treatment, healed with residual corneal opacity.

6 cases were refractory. Perforation occurred in one case, descematocele in one case and these cases were referred to higher ophthalmic centres.

TREATMENT OUTCOME: 85 patients responded to treatment with varying corneal opacities. 15 cases were refractory to treatment. Many refractory cases were fungal corneal ulcers. Corneal perforation occurred in 5 cases. Descematocele in 2 cases.

Follow up: Mean followup period was one month. Viral and fungal ulcers were followed for long duration (2 to 3 months).

SUMMARY: A total of 150 patients with clinical diagnosis of ulcerative keratitis with or without hypopyon were enrolled in this study. A maximum of patients were from age group 21 to 40 years followed by patients in the age group of 41 to 60 years and there was male predominance. Seventy percent patients hailed from rural areas. Occupation profile mainly consisted of agricultural workers (50%), followed by industrial workers (20%), students (15%), and others (15%). The most common predisposing factor was trauma with vegetable matter (52%), followed by dry eye(10%), corneal xerosis (6%) and dacryocystitis.

Microbial etiology was established in 50% of scrapings. 58% were fungal, mostly due to *Aspergillus*. 42% were bacterial mostly Gram positive cocci *Staphylococcus aureus*. In a majority of cases only one eye was involved (59% in the left eye and 41% in right eye). Many patients presented with multiple symptoms and most of them presented with Pain, redness, watering of eyes and decreased vision. Ulcer was central in 40%, Peripheral in 28% and in both areas in 32% of cases. 6.6% cases were diagnosed as viral keratitis. Fungal hyphae were observed in 16.66% of cases.

DISCUSSION: Corneal ulcer is a major cause of monocular blindness in developing countries. The results of the current study were discussed under the following headings;

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- a. Incidence of corneal ulcer: In this study the incidence of corneal ulcer was 2% i.e. is 3 cases for 150 patients attending the ophthalmic clinic. According to Gonzales et. Al (ref 1) 1996 estimated incidence was over 1.3% of entire general population.
- b. Age distribution: majority of the patients were (80%) were in the age group 21-40 and 41-60 years. As s this group forms most of the working class who are exposed to risk factors more frequently.
- c. Sex distribution: male to female ratio was 2:1. Males form the majority of working class hence exposure to risk factors is more. The ratio of 1.6:1 was reported by Gonzales et. Al.1996'Srinivasan.Met. al;1997(16)
- d. Living conditions: Majority (70%) are from rural areas. The incidence in them were more because chance of exposure to injury, lack of awareness of problems, delay in consulting an ophthalmologist, using native modalities of treatment as application of some irritants in eye and other unsterile material.
- e. Occupation: 50% are agricultural labourers. Agriculture is the major occupation in this district. These patients are prone more for ocular trauma with organic material, hence fungal ulcers are common.
- f. Predisposing factors: Ocular trauma and foreign body in eye were the major predisposing factors. This was seen in 50% of patients. In developing world non-surgical ocular trauma accounted for 50 to 60%of all corneal ulcers (Srinvas et. Al. 1997 MadanP. Upadhyayet.al.).² Madanmohan et., al DOSTimes jan³. p5-16.9. In developed countries contact lens wear is the major risk factor.(Bounciert et. Al., 2003), Tongabay et al.⁴

CLINICAL FEATURES:

Symptoms: Majority of patients presented with complex symptoms mostly with pain, redness' watering and diminution of vision.25 cases were using topical antibiotic drops at presentation.

Location: In majority of cases central area was involved. In 45 cases only central area was involved. In 50 cases both centre and periphery were involved.

Size of infiltrate in majority cases the infiltrate was <6mm diameter. Depth of infiltrate in majority of cases was <2/3 of stroma.

In a majority of cases where symptoms were less Satellite lesions, thick,large hypopyon, irregular infiltrate margins, endothelial infiltrate, fungal culture were positive.

Microbiological characteristics-laboratory diagnosis: In the current study culture positive rate is 50%. In studies by Bouncier et.al.2003(70%):LeckA.K.et.al.2002,in SouthIndia68.71%. (Ref5)The culture positive rate in the current study is slightly less than the above figures.

BACTERIAL ISOLATES: Majority were gram positive organisms. Gram negative was pseudomonas.

Fungal isolates: In a majority Aspergillus was isolated and in a few Fusarium.

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Treatment and clinical outcome: Fluoroquinolone was used in less severe cases. Combination therapy of cephazoline 5% +gentamycin 1.4% is reserved for severe ulcers which cover 95% of commonly causing Gram positive and negative organisms.

In all cases cyclopegic (Atropine 1% eye ointment or Homatropine 2% eye drops), eye shield, tab. Vit C were given.

Acyclovir 3% eye ointment was superior in treating HSV Dendritic ulcers. Healing is faster and epithelial toxicity is less. common. CollUMn L.M. et. al. 1980⁷

Fungal ulcers were treated with 5% Natamycin.

Fluconazole 0.3% eye drops and oral fluconazole tablets 200mg. twice daily is also used. (Rao S.K. et.al., 1997⁸

Natamycin 5% suspension is the drug of choice in filamentous fungi (O'Day D.M.1987⁹).

In Marginal ulcers steroids were used along with antibiotics. Lid hygiene was advised and response was good.

Vernal keratoconjunctivitis with shield ulcer was treated with steroid and sodium chromoglycate 2% and response was good.

Phlyctenular ulcer was treated with steroid and antibiotic combination. Response was good.

Neuroparalytic ulcers were treated with artificial tears, antibiotic eye drops, lacryl gel eye ointment, eye shield, lateral tarsorrhaphy was done. Same treatment was given for neurotropic ulcers.

Moorens ulcer was treated with topical steroids and artificial tears and response was good.

Final treatment outcome: Out of 150 cases 95 patients responded to treatment with varying degree of corneal opacity. 25 cases were refractory to treatment. Mostly they were fungal ulcers. In 6 cases corneal perforation was observed and descematocele in 4 cases.

CONCLUSION: The conclusions drawn from this study are Incidence of corneal ulcer is 2% Corneal ulcer is more common in males. Corneal ulcers were more common in age group 20 to 60 years. Corneal ulcer is more common in rural population. Corneal ulcer was commonly observed in agricultural labourers. Ocular trauma was predisposing in a majority of cases.

Etiological agents: Among Fungi, filamentous fungi was common etiological agent of which Aspergillus was more common. In viral cases Herpes simplex was more common. 10% KOH wet mount and Gram stain were helpful in lab diagnosis and in the initiation of antimicrobial therapy.

In viral keratitis, acyclovir 3% eye ointment was very effective. In Fungal keratitis Natamycin 5% was effective. In bacterial keratitis for less severe ulcers Fluoroquinolone (Ciprofloxacin) 0.3% was effective. In severe ulcers Fortified eyedrops (cephazoline 5%+ gentamycin 1.4%) as initial therapy was very effective. 20 cases were refractory to treatment. Most of them were fungal ulcers. 15 cases were refractory to treatment, most of them were fungal ulcers.

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Corneal ulcer is a treatable condition. Early intervention in the hands of a specialist can prevent serious opacity.

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