

Clinico-Microbiological Study of Corneal Ulcer in Assam Medical College & Hospital, Dibrugarh

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I. Introduction:

Corneal ulcer is a common cause of consultation in ophthalmology and one of the major cause of high ocular morbidity especially in developing countries. Corneal ulceration results in 1.5-2 million new cases of corneal blindness annually, posing a major public health problem according to the World Health organization (WHO) reports¹. India being an agricultural country corneal trauma leading to corneal ulceration is very common. Fungi are the most common etiological agents which account for 30–40% whereas bacteria account for 13–48% of all cases of suppurative keratitis; this varies by geographical area.² The burden of corneal disease in our country is reflected by the fact that 90% of the global cases of ocular trauma and corneal ulceration leading to corneal blindness occur in developing countries.³ The microbial causes of suppurative keratitis vary considerably between continents and countries and also within countries. It is essential to determine the local aetiology within a given region when planning a corneal ulcer management strategy. Several studies have investigated the epidemiology of corneal ulceration, causative micro-organisms, and effective treatments, particularly in the Indian subcontinent.² So we are doing this study to find out the bacterial rate and fungal rate causing corneal ulcer of the patients coming to Department of Ophthalmology, Assam Medical College & Hospital, Dibrugarh. The purpose of this study is to evaluate the common etiological agents, predisposing factors, age, gender, occupational distribution, incidence and to study the clinical features and management of corneal ulcer cases in Department of Ophthalmology, Assam Medical College & Hospital during the period of 1 November 2018 to 30 June 2019.

II. Materials And Methods:

This a prospective nonrandomized study carried out in department of ophthalmology, Assam Medical College & Hospital, Dibrugarh over a period of 6 months from 1 nov,2018 to 30th April 2019. Cases of graft ulcers were excluded from this study.

Corneal ulcer was diagnosed as loss of corneal epithelium with underlying stromal infiltration with signs of inflammation with or without hypopyon.⁴ The ulcers were classified microbiologically into bacterial, fungal or mixed for the purpose of the study.⁵

A total of 60 cases with corneal ulcers attending the out-patient department of AMCH were included in this study. A standardized proforma was filled out on each patient documenting socio-demographic information as well as clinical database of each corneal ulcer patient.

All patients included in this study were subjected to ophthalmologic examinations like visual acuity recording and a detailed slit lamp bio-microscopic examination was done in each case along with fluorescent staining. The ulcer was examined for presence of any foreign body, hypopyon and any associated ocular condition like blepharitis, entropion, concretions etc. Syringing of nasolacrimal passage was done in each patient to look for patency as blockage may indicate infections in lacrimal sac which is one of the predisposing factors for corneal ulcer to happen.

Exclusion Criteria:

- Cases presenting as non-infectious keratitis were excluded from this study.
- Viral keratitis was excluded from this study.

Laboratory investigations: In every ulcer cases routine investigations like RE BLOOD, RBS, ESR were done. Corneal scrapings material was collected before giving antibiotic therapy. If the patient is using antibiotics eye drop then it was stopped for 24 hrs and after that corneal scraping was done. The ulcer was cleaned with sterile normal saline and preservative free lignocaine 4% was applied as a local anaesthetic agent. Corneal scrapping was performed under slit lamp microscope using a sterile Bard-Parker blade no 15. The material was directly inoculated into blood agar and Sabouraud’s Dextrose Agar (SDA) making multiple C shaped marks and stained for Gram stain and KOH wet mount. Identification of growth on SDA was done by lactophenol cotton blue stain, by pigment production and by the morphological appearance of hyphae and spores.⁶ If by microscopy, hyphae were observed in corneal scrapings, but failed to grow in culture, the causative organism was reported as fungal. If no organisms were found on scrapings, then on the basis of clinical signs or symptoms and improvement with treatment it was considered either as bacterial or fungal and if it improved with both antibacterial and antifungal medications it was considered as mixed infections. In diagnosed cases of bacterial corneal ulcer, patients were treated with 4th generation fluoroquinolone (0.3% Gatifloxacin) or fortified antibiotic drops (Vancomycin, Amikacin, Gentamicin) either as monotherapy or combination

III. Results & Observations

Out of 60 cases with clinical diagnosis of corneal ulcer included in our study, 29(58) were males and 21(42) were females. The age range of 41-50 was the most affected group followed by age 51-60 and 21-30 in both groups. (Table 1 & Table 2)

Table 1: Age distribution

Age	No. of cases	Percentage
11-20	1(19 years)	1.7
21-30	12	20
31-40	6	10
41-50	18	30
51-60	12	20
61-70	8	13.33
>70	3	5

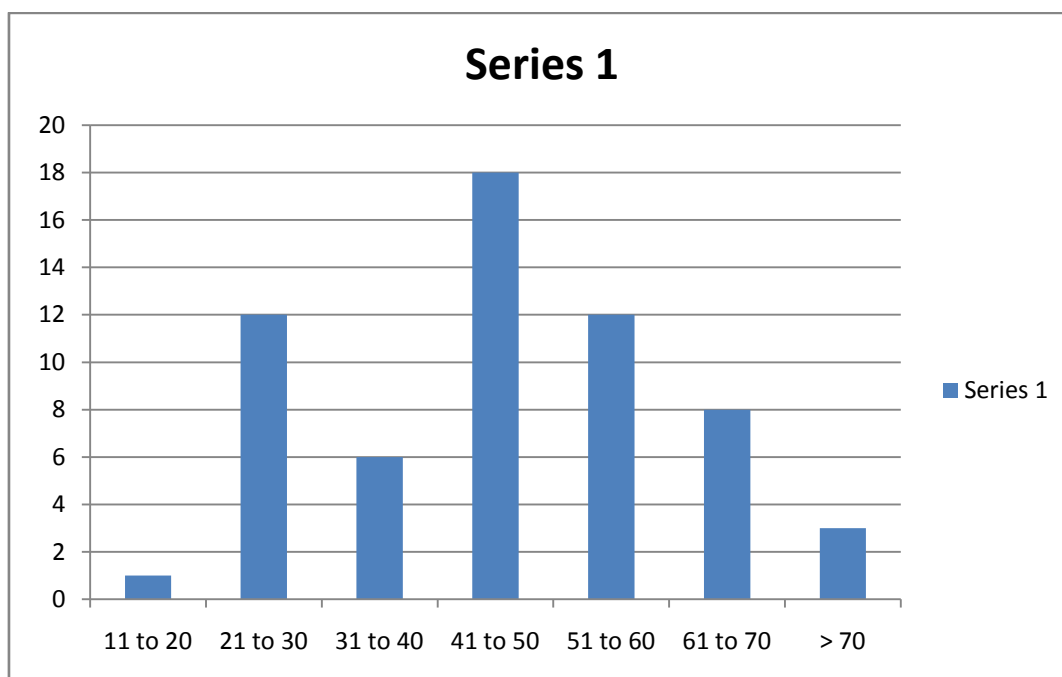


Table 2: Sex distribution

Sex	No of cases	Percentage
Males	34	56.67
Females	26	43.33

The predominance of corneal ulceration was most pronounced in the middle years with an overall ratio of male : female 1.3:1.

The majority of the cases were from rural population in Dibrugarh district or coming from nearby districts working as farmers or hired agricultural workers

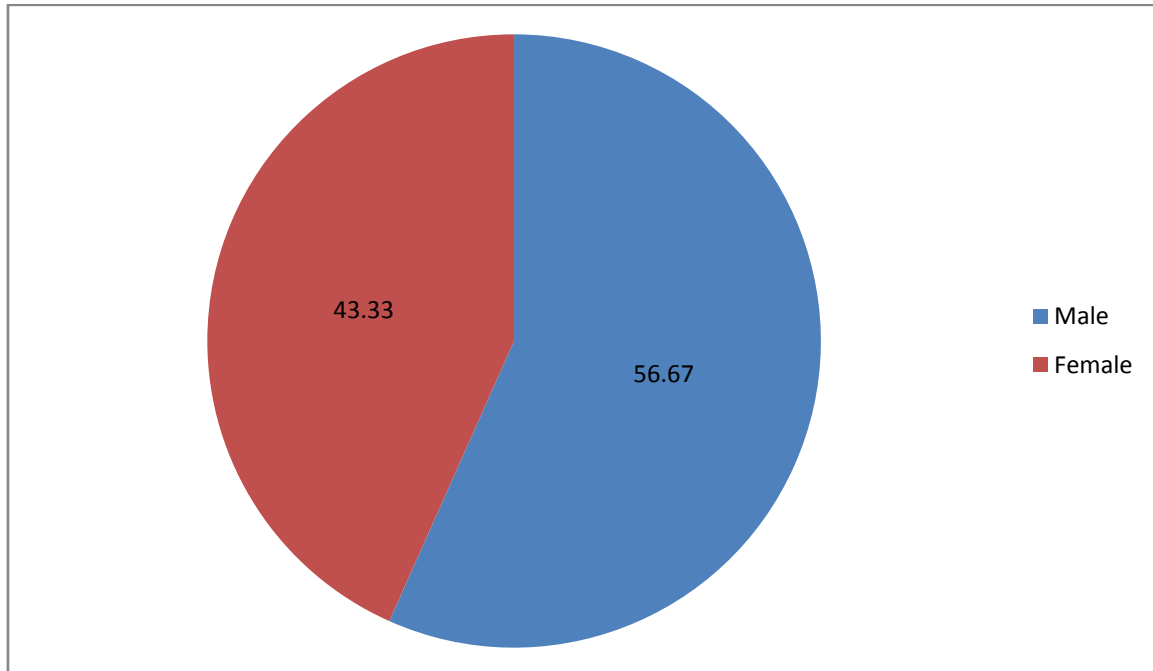
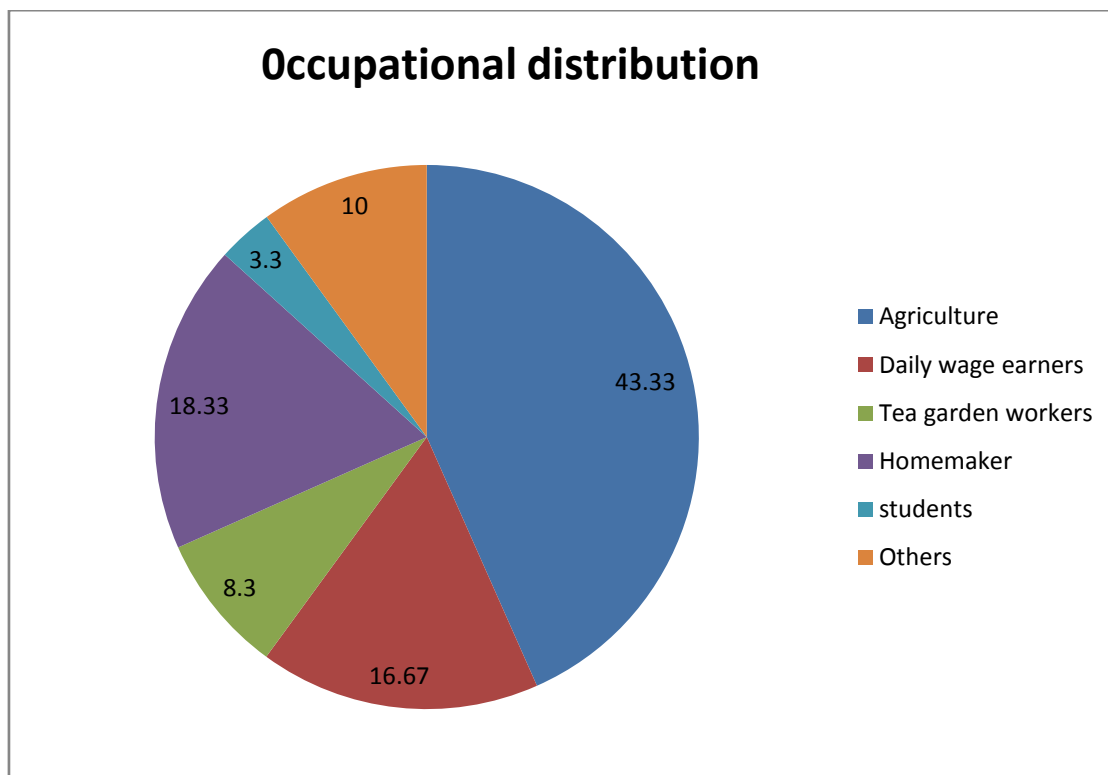


Table 3: Occupational distribution

Occupation	No. of cases	Percentage(%)
Agriculture	26	43.33
Daily wage earners	10	16.67
Tea garden workers	5	8.3
Homemaker	11	18.33
Students	2	3.3
Others (pond dwellers, fisherman etc.)	6	10



Out of 60 cases, 32 cases were found coming to Department of Ophthalmology, AMCH for seeking treatment within 7 days of onset of symptoms. But 9 patients (14.54) waited for more than 1 month before coming to hospital for evaluation.

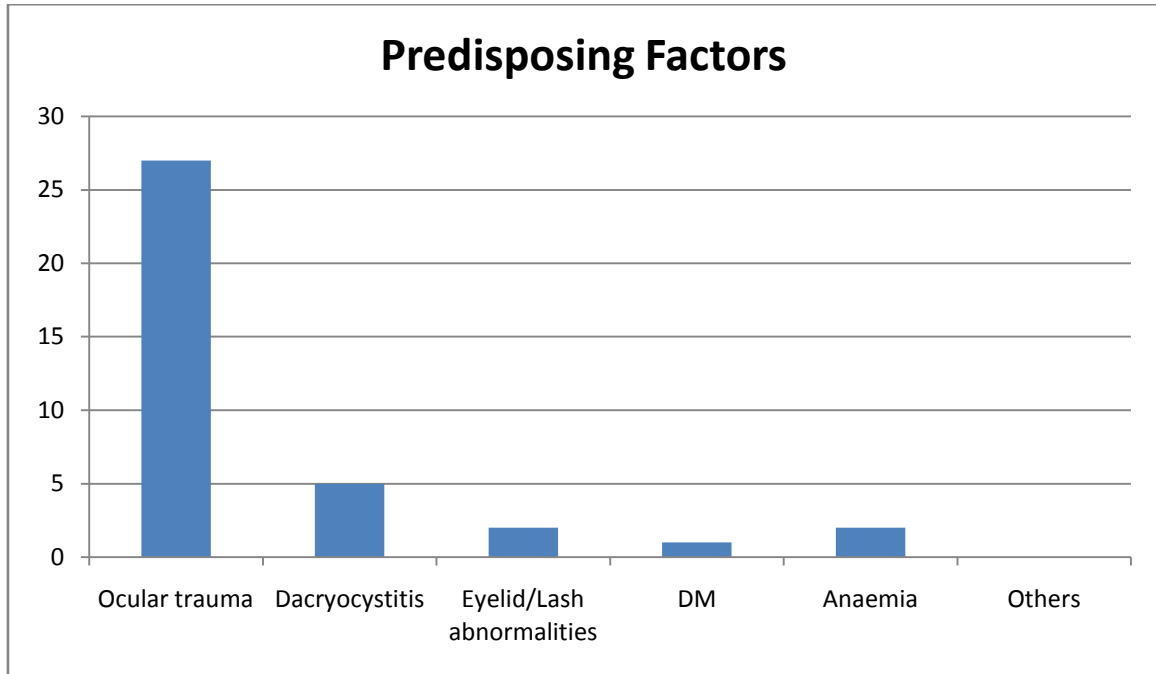
Duration of symptoms (interval up to first visit to OPD)	No. of cases	Percentage
1-3 days	10	16.67
4-7 days	22	36.67
8-14 days	12	20
15-29 days	7	11.67
>1 month	9	23.33
Total	60	100

Medical help was sought by 13(21.67%) of the 60 patients before coming to Department of Ophthalmology, AMCH. Out of 13 only 2 (15.3%) cases were seen by eye physicians of their local area. 5(38.4%) received advice from chemists or pharmacists and 6(46.1%) went to village healers. It is of interest that 7 (11.67%) of the total 60 cases were using some kind of herbal topical medications before coming to AMCH.

Table 5: Predisposing Factors

Predisposing factor	No. of cases	Percentage
Ocular trauma	27	45
Dacryocystitis	5	8.3
Eyelids or lash abnormalities	2	3.33
Diabetes Mellitus	1	1.67
Anemia	2	3.33

Out of 60 cases, 27 (45%) patients gave recent history of ocular trauma. Agents responsible for trauma were mainly agricultural (by paddy leaves 16 cases (59.2%), by rice grain 6 cases (22.22%) and 2 cases (7.4%) by soil products while harvesting) and animal products in 3 cases (11.11%). Co-existing ocular disease like dacryocystitis was present in 5 (8.3%) cases and entropion in 2 (3.33%) cases. Systemic factors like diabetes mellitus and anaemia were present in 1.67% and 3.33 % cases respectively.



Out of 60 patients, 21 patients (35%) had hypopyon at presentation.

Table 6 : Seasonal distribution of patients in our study group

Seasons	No. of patients	Percentage(%)
Nov-Dec	10	16.67
Jan-Feb	21	35
March-April	18	30
May-June	11	18.33

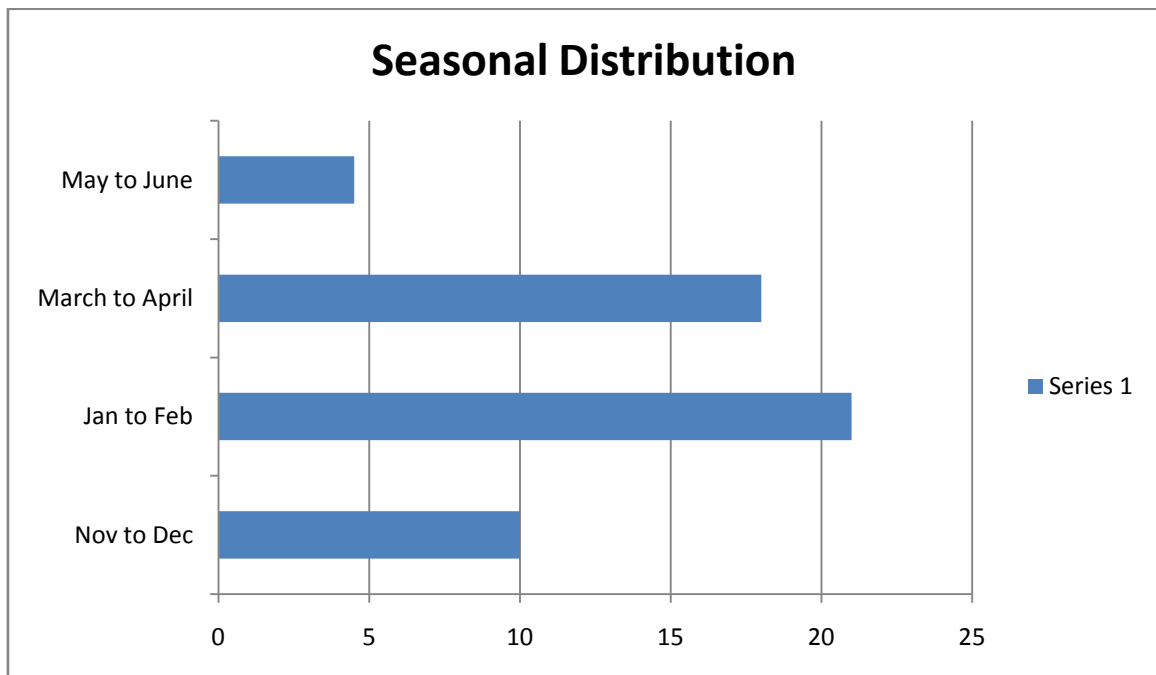
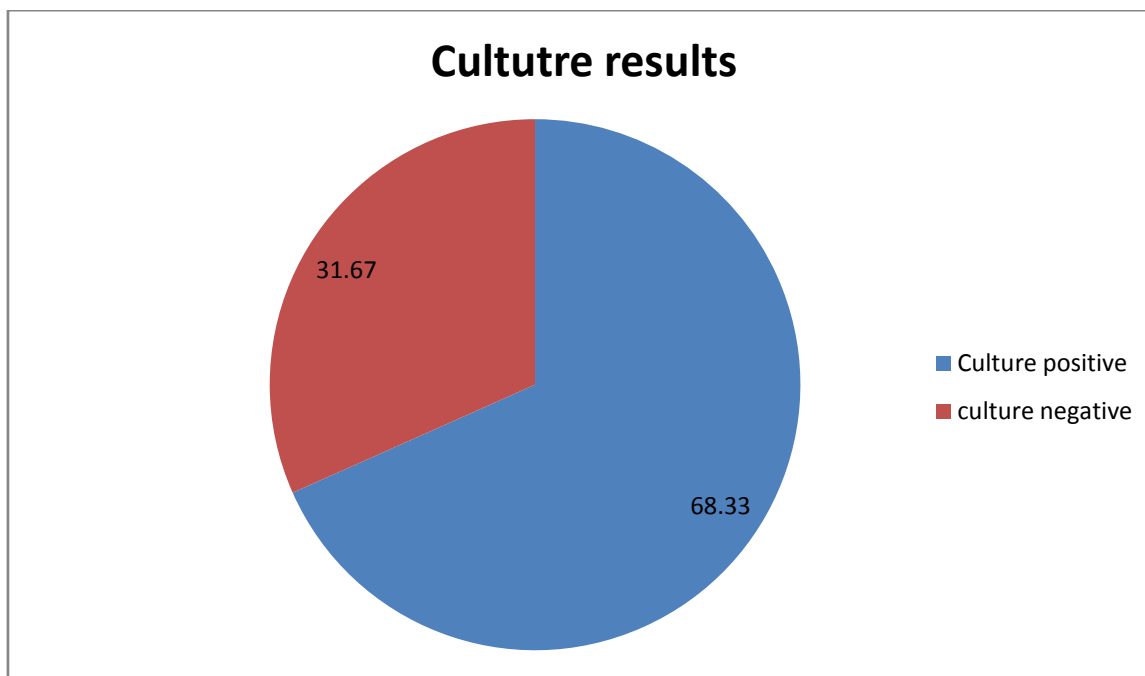


Table 7: Culture results in study

Culture	No of patients	Percentage
Culture positive	41	68.33
Culture negative	19	31.67



Among the culture positive cases 17 cases were reported fungal and the rest 24 cases were reported bacterial. Out of 19 culture negative cases those responded with antibacterial treatment we considered them as bacterial and it was found to be 8 cases. Those responded with antifungal treatment we considered them as fungal and a total of 6 cases responded with antifungal treatment. Out of the rest 5 cases 3cases responded both with antifungal and antibacterial treatment, so we considered them as mixed infections.

Table 8: Pathogens isolated from the culture positive cases

Fungal(17 cases)		Bacterial(24cases)	
Pathogen	Percentage	Pathogen	Percentage
Fusarium	11(64.7%)	Streptococcus pneumoniae	14(58.33%)
Aspergillus	2(11.7%)	Gram+ve cocci (staphylococcus)	7(29.1%)
Unidentified	4(23.5%)	Gram –ve cocci	2(8.33%)
		Gram –ve bacilli (diphtheroids)	1(4.2%)

Table 9: Treatment It includes all culture positive and culture negative cases. As described above culture negative cases were on the basis of signs and symptoms and treatment susceptibility we put them in bacterial or fungal or mixed infections if responded to both antibacterial and antifungal medications. All patients were given cycloplegics and IOP lowering medications.

Bacterial (both culture +ve & culture –ve cases)(32 cases)(53.33%)	Fungal (both culture +ve & culture –ve cases)(23 cases)(38.33%)	Mixed infections(3 cases) (5%)
Fortified vancomycin 11(culture+ve)(45.8%)	Natamycin 5% 20(86.9%)	Fortified vancomycin+Gatifloxacin0.3%+natamycin 5% 2 (66.67%)
Fortified amikacin 7(culture+ve)(29.2%)	Voriconazole 2 % 3(13.0%)	Fortified Amikacin+Gatifloxacin0.3%+Natamycin 5% 1 (33.33%)
Fortified Gentamycin 6(culture+ve)(25%)		
Fortified vancomycin+fortified amikacin 8(Culture –ve)(42.1%)		
Gatifloxacin 0.3% 25(both in culture +ve &-ve cases)(78.1%)		
Moxifloxacin 0.3% 7(both in culture +ve & -ve cases) (21.9%)		

Table 10 : We have been following up the patients for 1 month and during this period 27 cases(54%) we have lost to follow because patients did not want to stay in hospital for so long time and after discharged also they did not come for checkup when they are called.5 cases showed resolution of symptoms ,8 cases totally improved and they became stain negative when stained later on.7 cases showed slow improvement and during the period of 1 month. 2 cases showed no improvement and 1 case got perforated who came for first time with some amount of impending perforation.

Follow up	No. of cases	Percentage
Lost to follow up	18	30%
Resolution of symptoms with minimal signs	6	10%
Improved	22	36.67%
Slow improvement	11	18.3%
No improvement	2	3.33%
Thinning with perforation	1	1.67%

IV. Discussion:

Corneal ulcer is a major health problem in developing world causing prolonged ocular morbidity often leading to blindness if early management is not instituted.⁷ Even with appropriate treatment, there is a high incidence of visual loss due to the development of dense corneal scar.⁸

In our present study, male subjects were more affected than female patients with a male :female ratio **1.3:1** which is in agreement with the study done by Titiyal et al.⁹ The age range more affected was **41-50(30%)** followed by **21-30(20%)** and **51-60(20%)**. This can conclude increase outdoor activity by this working age group and as Assam is highly dependent on agricultural field, most of male persons affected found here were working in agricultural area (**43.33%**) following which the homemaker (**18.33%**), daily wage earners (**16.67%**) and labourer groups come.

Similar results were also found in the studies by Jatoi et al. and Gopinathan et al., thus suggesting that corneal ulcers are more prevalent in farmers and other outdoor workers.^{10,11} Homemaker groups are mainly females .As these people belong to rural population many of them are still using fire woods for cooking and all, instead of LPG cylinder. So from their history we can conclude that constant rubbing of the eyes because of the smoke, abrasion of cornea occurred unwillingly and finally ulcer developed and secondly, because of ocular trauma in their day to day activities. Among the labourer group most of them were working in the industrial factories, many of them were associated with welding and grinding works.

Out of 60 cases in our study, 32 cases (53.33%) were found coming to Department of Ophthalmology, AMCH for seeking treatment within 7 days of onset of symptoms. The symptoms were mainly sudden onset of pain, redness, foreign body sensation, watering from the affected eye etc. Many of them gave a history of ocular trauma .So after getting injured only most of them reported to AMCH. Out of the rest of the cases 9 patients (15.0%) reported to AMCH after or more than 1 month. This can attribute to the ignorance of this group of patients to their health ,many of them were illiterate as they were belonging to very poor family so they were unaware of their conditions. We found that out these 9 cases 5(55.5%) were tea garden workers. The rest 4(44.4%) cases gave history of transport problems to Dibrugarh. 13 cases(21.67%)out of 60 cases sought medical help before they came to Department of Ophthalmology, AMCH and before starting their initial examinations. As described above out of 13 cases only 2 cases (15.4%)were seen by eye physicians of their local area. **5 (38.4%)** received advice from chemists or pharmacists, **6 (46.1%)** went to village healers. **7 (11.67%)** of total 60 Cases were using herbal medications before coming to AMCH.

The most common predisposing factors in our study were ocular trauma (45%) followed by dacryocystitis (**8.3%**).Trauma was also found to be the major predisposing cause in the studies by Assudani et al., Sethi et al., and Ranjini and Waddepally.^{12,13,14} A history of injury by agricultural product such as by paddy leaves (**59.2%**),by rice grain(**22.2%**)and by soil products (**7.4%**) were seen. Injury by animal products was seen in 11.1% cases. A similar high incidence of vegetative injury was seen in the study by Chhangte et al. done in Kumaon region of Uttarakhand, where 23.7% patients reported injury with vegetative matter.¹⁵ Eyelids abnormality like entropion found only in 2 cases (3.33%) one of which is associated with blepharitis. Systemic factors like diabetes mellitus and anaemia found in only 1(1.67%) and 2 cases (3.33%) respectively. And the number of cases of contact lens users found in our study which is similar to the study done by Basak et al.¹⁶

In our study, 68.33% cases were found culture positive and 31.67% cases were found culture negative. This is similar to the study done by Tiwari et al¹⁷ where they got 60% culture positive cases. Bacterial isolates were 58.5% whereas fungal isolates were 41.46%. Incidence of fungal isolates found in a study done by Dutta et al was (32%) conducted in Assam.¹⁸ Whether another study conducted in upper Assam by Nath et al found 60.6% incidence of fungal corneal ulcer.¹⁹ **Srinivasan et al** isolated equal numbers of bacteria(47.1%)and fungal(46.8%)agents causing infectious keratitis with 5.1% cases having mixed infections²⁰, which is similar to

our study, where 5% cases showed mixed infections. This change in shift of organisms can be attributed to changes in present climatic conditions, occupational exposures and individuals' risk factors.

Bacterial culture showed 58.33% cases of streptococcus pneumonia followed by staphylococcus 29.1%, gram -ve cocci which were diplococci mainly and gram -ve bacilli (diphtheroids) 8.33% and 5.2% respectively. Bacteria account for 65–90% of corneal infections with *Staphylococcus aureus*, *S. pneumoniae* and *Pseudomonas aeruginosa* accounting for more than 80% of bacterial keratitis.²¹ In our study, bacterial isolates were predominated by gram+ve bacteria similar to studies done by Gopinathan et al and Das et al.^{11,20} Among the fungal isolates, *Fusarium* accounts for 64.7% cases followed by *Aspergillus* 11.7% which all are filamentous fungi and unidentified hyaline fungi were 24.5%. A study done by Nath et al in upper Assam on mycotic corneal ulcer *Fusarium* species accounts for 25% culture positive cases followed by other fungal species.¹⁹ From our study, we found that these fungal corneal ulcer cases mostly come during January to February months which are mainly the harvesting periods in Assam and most of them are farmers. It is similar to the study done in Bellary by Krishna et al who reported maximum incidence of fungal keratitis during harvest months of January, February and June.²¹ A study conducted in Nepal by Suwal et al. found bacterial isolates (56%) outnumbering the fungal isolates (44%). Moreover, in their study, *S. pneumoniae* (31.1%) was the commonest among the bacteria, while *Fusarium* (13.4%) was the most common fungus isolated which is almost similar to our study in terms of prevalence of organisms.²²

In our study, 35 % and 30% patients were found coming to Department of Ophthalmology, AMCH, Dibrugarh during Jan- Feb and March-April months respectively. As these seasons are the harvesting seasons for Assamese people and many of them came with injury by vegetative matters while working in fields. From previous report from upper Assam, study done by Nath et al in AMCH, Dibrugarh also showed 21.9% cases which accounted for maximum number of cases coming and January to February months only.¹⁹

The standard protocol for treatment of corneal ulcer in our patients was topical instillation of antimicrobial drugs. We have considered the improvement on the basis of antibiotic sensitivity in cases of bacterial corneal ulcer and also on clinical improvement. Cases of bacterial corneal ulcer were treated with 4th generation fluoroquinolones like 0.3% Gatifloxacin in 25 cases (78.1%) followed by 0.3% Moxifloxacin in 7 cases (21.9%) and fortified antibiotic eyedrops like Vancomycin, Amikacin and Gentamycin. Vancomycin sensitivity was reported in 11 cases (45.8%) in our study followed by Amikacin 7 cases (29.2%) and Gentamycin 6 cases (25.0%). We gave combination therapy in the form of fortified Vancomycin+fortified Amikacin in 8 cases (42.1%) whose culture report showed no organisms and with this combination therapy we have seen a very good results in those culture negative cases also. Most of the fungal corneal ulcer cases were treated with Natamycin 5% almost in 86.9 % cases even in those culture negative cases who gave similar conditions like fungal ulcer. Voriconazole was given in only 13% cases who did not show improve with Natamycin. Both fortified antibiotic and antifungal were given in 3 cases (5%) out of 60 cases which we considered them as mixed infections.

Out of 60 cases 18 cases (30%) we have lost to follow as described above. 36.67% cases showed total improvement which became stain -ve although opacity remained. 18.3% cases showed slow improvement. We considered them as slow improvement because of their fluctuating signs and symptoms & as they mostly belonged to lower socio economic group as most of them were daily wage earners, some of them were tea garden workers also so nutritionally they were below average and immunity status was poor. Also the environmental factor we could consider as reason of their slow improvement. Similarly 10 % cases showed resolution of symptoms with minimal signs and in most of cases we found chronic alcoholism. 3.33% cases showed no improvement & 1.67% cases showed thinning with perforation and we considered bandage contact lens (BCL) for these patients as they had tendency of impending perforation.

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