JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

A Study on Corneal Ulceration in Bangladesh

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ABSTRACT

Corneal opacification has become the second most common cause of visual disability in the world.' Suppurative keratitis is an important preventable cause of blindness in the developing world. Most of the organisms cultured from corneal infections are of the same species that are normally present on the lids and periocular skin, in the conjunctival sac or in adjacent nasal passage. However, both gram-positive and gram-negative bacteria are responsible for causing suppurative corneal ulcers with Staphylococcus, Streptococcus and Pseudomonas are the most frequent isolates. While among the fungal causes of suppurative corneal ulcers, *Fusarium* and *Aspergillus* species are the predominant agents reported by many investigators. In Bangladesh corneal ulcer is also a problem for many patients. However the present study has conducted to explore the suppurative corneal ulceration in Bangladesh and to provide policy recommendations. The study was conducted at inpatients and outpatients at the Chittagong Eye Infirmary with the diagnosis of suppurative keratitis were studied. The study was descriptive cross sectional study. Purposive sampling method was used for the study. Data were collected from primary and secondary sources. Primary data were collected from the patients of the selected study area. Secondary data were collected from secondary sources. Patients of eye hospital of Chittangong are the sample population of the study. Total 142 patients were selected for the study. Patient information, clinical histories and clinical features of infection were recorded at presentation and updated during treatment. Representative areas of suppuration in the cornea were sampled using a sterile 'Kimura' platinum spatula or a scalpel blade. A local anaesthetic without preservative was used. Smears were fixed with 95% methanol before Gram staining by standard methods. The culture, identification and antibiotic sensitivity methods used were those described previously. Facilities for anaerobic, mycobacterial and acanthamoeba culture were not available. Some bacteria and all fungi were sent for identification and antifungal sensitivity testing was performed at eye hospitals in Chittagong city in Bangladesh. Questionnaire was used for data collection. Data were collected by observing the patients and face to face interview with the patients. Collected data were analyzed by using Computer Program Microsoft EXCEL. From the result it was found that suppurative keratitis is an important preventable cause of blindness, particularly in the developing world. The five most common pathogens were: *Pseudornonas* sp. 24%, Streptococcus pneumoniae 7%, *Aspergillus* sp. 13%, *Fusariurn* sp. 7% and *Curvularia* sp. 6%. Gram stain and culture results were consistent in 62.6% of cases. Previous antibiotic treatment was a significant factor for failure of culture isolation and less so for Gram stain failure. On Gram stain, 55.9% of pseudomonal cases were missed, but only 2% of fungal cases were missed. Over all, Gram stain had a sensitivity of 62% and positive predictive value of 84% for bacterial cases, and 98% and 94% for fungal cases, respectively. Fungal ulcers were typically filamentous, but an antecedent history of trauma was not common. The most frequent injury was due to rice grains, but the inoculum appeared to be introduced during eye washing with contaminated water. Pseudomonal ulcers occurred most frequently in the monsoon season, and Fusariurn cases were seen only in the hot, dry season.

Key words: *Corneal ulcer, Scarring, Microbial cause, Gram stain, Trauma, Intractable infection.*

INTRODUCTION

Corneal ulcer is one of the important ophthalmic conditions causing significant morbidity especially in the developing countries. Scarring of the cornea developed as a result of suppurative corneal ulcer is the second commonest cause of preventable blindness after unoperated cataract among people in Asia, Africa and in the Middle East. In Bangladesh, 33.55% of all cases of unilateral blindness were reported due to complication of corneal ulcer. Corneal ulcerations can be caused by different microbial agents. Although any organism can invade the corneal stroma if the corneal protective mechanisms such as blinking, tear dynamics and epithelial integrity are compromised but microbial causes of suppurative corneal ulcers vary considerably in different geographical areas. Bacteria and fungi are frequently responsible for suppurative corneal ulcers especially in the developing countries. The range of pathogens known to cause corneal ulcers is very broad

and shows geographic variation. The tropics are noted for the increased prevalence of Gram-negative isolates. Filamentous fungi may account for a third of all cases of suppurative keratitis in the tropics. Williams et al. established a low-cost microbiology laboratory in Chittagong Eye Infirmary and Training.

Table 1: Microbiological results

(a) Corneal smear microscopy and culture both positive			
Bacterial pathogens		*Fungal pathogens*	
Streptococcus pneumoniae	22	*Aspergillus fumigatus*	16
Pseudomonas aeruginosa	10	*Aspergillus flavus*	3
Pseudomonas sp.	5	*Fusarium solani*	8
Streptococcus pyogenes GpA	1	*Fusarium dimerum*	1
Staphylococcus aureus	1	*Curvularia fallax*	7
Corynebacterium sp.	1	*Curvularia* sp.	2
Moraxella sp.	1	*Lasiodiplodia theobromae*	2
E. coli	1	*Scedosporium* sp.	1
Total	42	*Epicoccum* sp.	1
		Candida albicans	1
		Cylindrocarpon vaginae	1
		Dichotomophthoropsis nymphaearum	1
		Lost or not sent for identification	3
		Total	47
(b) Corneal smear microscopy negative but culture positive			
Bacterial pathogens		*Fungal pathogens*	
Pseudomonas sp.	11	*Fusarium solani*	1
Pseudomonas aeruginosa	8		
Streptococcus pneumoniae	2		
Staphylococcus aureus	1		
Corynebacterium sp.	1		
Enterobacter sp.	1		
'Coliform'	2		
Total	26		
(c) Corneal smear microscopy positive but culture negative			
Bacterial organisms seen		*Fungal hyphae seen*	3
Gram-positive diplococci	2		
Gram-positive cocci	1		
Gram-positive rods	1		
Gram-negative rods	2		
Gram-negative cocco bacilli	1		
Gram-negative diplobacilli	1		
Total	8		
(d) Corneal smear microscopy and culture both negative — Total 15			

Complex in 1983. A pilot study at this time and a later study of 127 cases has identified the prevalence of corneal pathogens in the region and demonstrated the value of Gram stain to allow rational selection of antimicrobial agent. This study from the same base hospital aims to investigate further the value of the Gram stain as a first line investigation, particularly for demonstrating fungal elements. It also aims to give epidemiological information (prevalence, associated history, seasonality and clinical features) that may aid the clinician successfully to treat suppurative keratitis when Gram stain or culture results are not available.

OBJECTIVES OF THE STUDY

The Objectives of the study are as follows:

1. To explore the suppurative corneal ulceration in Bangladesh.
2. To provide policy recommendations.

MATERIAL AND METHODS

Study place: The study was conducted at inpatients and outpatients at the Chittagong Eye Infirmary with the diagnosis of supportive keratitis were studied.

Design of the study: The study was descriptive cross sectional study.

Sampling method: Purposive sampling method was used for the study.

Sources of data: Data were collected from primary and secondary sources.

Sources of primary data: Primary data were collected from the patients of the selected study area.

Sources of secondary data: Secondary data were collected from secondary sources. Such as Books, Research report, Journal, Website of Ministry of Health and Family Welfare, Bangladesh, Internet, Other different websites etc.

Sample population: Patients of eye hospital of Chittangong are the sample population of the study.

Sample Size: Total 142 patients were selected for the study.

Patent information: Patient information, clinical histories and clinical features of infection were recorded at presentation and updated during treatment.

Exclusion criteria: The Exclusion criteria of the study were herpetic ulcers, neuroparalytic keratitis, interstitial keratitis, ulcers associated with autoimmune conditions (e.g., Mooren's ulcer) and of course patient refusal.

Microbiological methods: Representative areas of suppuration in the cornea were sampled using a sterile 'Kimura' platinum spatula or a scalpel blade. A local anaesthetic without preservative was used. Smears were fixed with 95% methanol before Gram staining by standard methods. The culture, identification and antibiotic sensitivity methods used were those described previously. Facilities for anaerobic, mycobacterial and acanthamoeba culture were not available. Some bacteria and all fungi were sent for identification and antifungal sensitivity testing was performed at eye hospitals in Chittagong city in Bangladesh.

Tools for data collection: Questionnaire was used for data collection.

Method of data collection: Data were collected by observing the patients and face to face interview with the patients.

Data analysis: Collected data were analyzed by using Computer Program Microsoft EXCEL.

RESULTS

One hundred and fifty-one cases were referred over an 11-month period. Nine were excluded under the aforementioned criteria. Eighty-nine cases (63%) showed consistent microscopy and culture results, while 27 cases (19%) showed growth on culture but no organisms were seen on Gram stain. In 11 cases (8%), organisms were seen on Gram stain, but not isolated on culture. In I5 cases (1 I **YO),** no organisms were seen on Gram stain and culture was negative. Seventy-six patients (54%) had bacterial keratitis and 51 patients (36%) had fungal keratitis. In six patients both bacterial and fungal organisms were isolated. The bacteria isolated in these cases were ***Staphylococcus aureus*** (three cases) and ***Streptococcus pneumoniae*** (three cases). These bacteria may be components of the conjunctival flora. Their role in ulcer pathogenesis is unclear, but the fungal organisms were considered to be the major pathogens. These cases were therefore included with the other fungal cases for further analysis. The five most commonly encountered pathogens were: ***Pseudomonas*** sp. 34 cases (%YO), ***Streptococcus pneumoniae*** 24 cases (17%), ***Aspergillus*** sp. 19 cases (13%), ***Fusarium*** sp. 10 cases (7%) and ***Curvularia*** nine cases (6%). Note that of the 27 cases which showed growth on culture but no organisms on Gram stain, only one case was fungal, and 19 cases were pseudomonal (eight of these were *P.**aeruginosa).*** Table 2 evaluates microscopy by Gram stain as a diagnostic technique against the culture results as a standard. For fungal ulcers the sensitivity, specificity and predictive value of Gram stain microscopy is much higher than that for bacterial ulcers.

Comparison of the clinical features of bacterial and fungal corneal ulcers

The presenting features of bacterial and fungal ulcers were compared to identify characteristics which aid clinical differentiation. Table 3 shows eight features examined and the results obtained for each aetiological group. The main findings are:

1. Fungal ulcers had a significantly longer history compared with bacterial cases (mean durations 16.6 and 10.8 days respectively, P<O.Ol).
2. Pseudomonal ulcers had significantly larger mean epithelial defect and corneal infiltrate diameters (both *P*< 0.01) compared with those caused by *S.* ***pneumoniae*** although there was no sigdkant Herence between mean duration

Table 2. The evaluation of microscopy of Gram-stained corneal smears against culture of corneal material of symptoms of the two groups.

Element	Bacterial ulcers	Fungal ulcers	All
Sensitivity	62%	98%	77%
Specificity	65%	83%	60%
False-positive rate	8.7%	4.6%	8%
False-negative rate	28%	1.5%	19%
Predictive value of a positive microscopy result	84%	94%	89%
Predictive value of a negative microscopy result	37%	94%	36%

Pseudomonal ulcers also had a significantly larger mean defect diameter compared with that of the fungal group in total (P< 0.05). Pneumococcal ulcers had a significantly larger mean hypopyon height compared with the pseudomonal group: 1.9 mm and 1.3 mm respectively (P<O.Ol). Forty-six per cent of pneumococcal ulcers showed corneal thinning of greater than half its thickness compared with 26% in the pseudomonal group. Ulcers with a dry, raised, necrotic or fluffy surface were seen significantly more frequently in the fungal group compared with the bacterial group (23% v. 2.9%; P<O.Ol). Endothelial rings were also seen more frequently in the fungal group (13% o. 7.4%). Dacryocystitis in the affected eye was diagnosed in 33% of the patients with pneumococcal ulcers. This relationship is highly significant; the condition was seen in only four other cases in the series. Other features examined were endothelial plaques, corneal vascularisation, intraocular pressure and corneal satellite lesions. Endothelial plaques were seen in only eight cases with no obvious difference between the groups. Satellite lesions were seen in only two cases, one bacterial and one fungal. Increased vascularity was observed in severe infections and when the ulcer was more peripheral. Raised intraocular pressure was found in only seven cases, two bacterial and five fungal.

Epidemiology

Table 4 shows the mean age of patients in each group, sex ratios, occupations and history of antecedant eye injury. Few children were seen; 23 patients were under 18 years and only two were under 10 years.

Table 3. Clinical features

Feature	*Pseudomonas* $n=34$	*Pneumococcus* $n=24$	Other bacterial $n=10$	*Aspergillus* $n=19$	*Fusarium* $n=10$	*Curvularia* $n=6$*	Other fungal $n=13$	All bacterial $n=68$	All fungal $n=48$
Mean duration of symptoms in days	10.1	10.5	13.8	13.5	12.4	24.7	21.0	10.8	16.6
Mean diameter of epithelial defect (mm)	4.9	3.5	4.1	4.3	4.6	3.7	4.1	4.3	4.2
Mean diameter of corneal infiltrate (mm)	6.6	4.4	7.5	5.5	5.9	4.9	5.6	6.0	5.5
Mean height of hypopyon (mm)	1.3	1.9	2.0	1.6	1.8	0.9	1.2	1.6	1.5
Percentage of eyes with corneal thinning > 1/2 thickness	26%	46%	50%	42%	30%	50%	38.5%	37%	40%
Percentage of eyes with dry, raised or fluffy ulcer surface	6%	0	0	26%	20%	33%	15%	2.9%	23%
Percentage of eyes with dacryocystitis	0	33%	0	0	0	16.5%	7.7%	11.8%	4.2%
Percentage of eyes with endothelial ring	6%	13%	0	26%	0	0	7.7%	7.4%	12.5%

*No information for three cases hence, $n=6$.

The main epidemiological findings are:

1. Patients with pneumococcal ulcers tended to be older than those with pseudomonal infections (mean ages 52.5 and 29.8 years respectively; P<O.Ol).

2. The sex ratio for the series of 142 cases was 2.2 males to one female. The M:F ratio was higher in the pneumococcal group, 7M:lF.

3. No clear association between aetiology and agricultural occupation was found, but those with hngal ulcers were more likely to perform domestic work, e.g., housewives and servants (46% compared with 26% for bacterial cases).

4. A high percentage of patients gave no history of eye injury. Sixteen of those with pseudomonal ulcers (47%) had been injured with rice grains or leaves; 14 involved only grains. Three patients with Curvuluriu sp. infections reported injuries with vegetation, but more cases are needed to assess the significance of this finding.

5. The relationship between aetiology and date of onset was explored: 65% of the pseudomonal cases occurred during the monsoon period, July to September; and all of the Fusarium cases occurred in the first six months of the year, the hot-dry season. The other groups were evenly distributed throughout the 11 month study period.

Table 4. Epidemiology

Feature	*Pseudomonas* $n=34$	*Pneumococcus* $n=24$	Other bacterial $n=10$	*Aspergillus* $n=19$	*Fusarium* $n=10$	*Curvularia* $n=6$*	Other fungal $n=13$	All bacterial $n=68$	All fungal $n=48$
Mean age in years	29.8	52.5	44.2	40.0	40.2	53.6	38.8	39.9	41.4
Sex ratio M:F	1.8:1	7:1	2:1	1.1:1	2.3:1	0.5:1	12:1	2.6:1	1.8:1
Occupation									
Agriculture	27%	29%	20%	26%	30%	16.5%	38%	28%	29%
Domestic	33%	22%	20%	53%	20%	67%	46%	26%	46%
Labourer	9%	8%	10%	11%	10%	0	0	9%	6%
Student	19%	8%	10%	0	0	0	0	13%	0
Other	9%	4%	0	5%	20%	0	16%	6%	10.5%
Unemployed/unknown/ children	3%	29%	40%	5%	20%	16.5%	0	18%	8.5%
History of injury									
None	32%	63%	70%	48%	90%	50%	76%	48%	65%
Rice grain/leaf	47%	12%	20%	26%	0	0	8%	31%	13%
Bamboo	3%	0	0	5%	0	16.5%	8%	1.5%	6%
Other vegetable matter	3%	17%	0	5%	0	33.5%	8%	7.5%	8%
Mineral	9%	8%	10%	11%	10%	0	0	9%	6%
Other/unknown	6%	0	0	5%	0	0	0	3%	2%

*No information for three cases hence, $n=6$.

DISCUSSION

In this series, the Gram stain recovery rate of 70.4% (100 of 142) of cases is consistent with previous studies, range 57% to 7OYoy4-' as is the culture recovery rate of 81.7% (1 16 of 142), range 60% to 84C70.4-6.8-10I n 11 cases (7.770) organisms were seen on Gram stain, but not isolated on subsequent culturing. Possible reasons for this include previous antibiotic treatment, inadequate specimens or insufficient microbiological investigations. Five of the eight bacterial cases in this category (Table lc) had received antibiotics, a high percentage (63Yo) compared with prior antibiotic usage in the whole bacterial group (18%). In two of the three fungal cases (Table Ic) insufficient material was obtained for culture. A higher prior antibiotic usage (73%) was also reported in the 15 cases in which no pathogen was found on Gram stain or culture. Of the 27 cases which showed growth on culture but no organisms on the original Gram stain, 19 cases (70.4%) were pseudomonal. In fact, more *Pseudomonus* sp. were seen in this mode (Table lb) than when consistent with microscopy and culture (Table la; 15 cases). In this series, Gram stain is therefore a poor predictor of pseudomonal infection and we would advise appropriate antibiotic cover if the clinical history is suggestive and/or culture results are pending. With reference to Table 2, however, it can be seen that most cases will be guided reliably by their Gram stain results if culture facilities are not available. This is not to say that culture investigations are not warranted. Williams et al. highlighted the usefulness of culture for the monitoring of the prevalence and antibiotic sensitivities of corneal pathogen.

More significant is the fact that only one known case of fungal keratitis (2%) was missed on Gram stain, later to be identified on culture. A recovery rate of 98% is much more than predicted by Jones (78!70), or Upadhyay et al. (55.4%).'O The value of the Gram stain, in our hands, to identify fungi cannot be overstressed, particularly as antifungals are expensive and in short supply and therefore cannot be used in a broad-spectrum treatment protocol, despite the high incidence of fungal keratitis. Over 20 years ago, Jones observed that each geographic region has a differing prevalence of corneal pathogens." In accord, Asbell and Stenson recorded the changing prevalence of pathogens across America and also noted the change of prevalence within a region, with a change of socioeconomic status of the referral population. The observed trend is an increased incidence of Gram-negative and fungal isolates in the southern parts on America. This series shows that fungal keratitis accounts for 35.9% of presentations of suppurative keratitis against 53.5% of bacterial cases. The most common isolate was the Gram-negative organism Pseudomonas sp. (24%). Eighteen of the 34 Pseudomonal isolates were identified as *P. aeruginosa*. Other Suppurative corneal ulceration in Bangladesh studies in the tropics - Bangladesh,4,13 India,14 and South have shown *S. pneumoniae* and *S. aureus* to predominate. The association of pseudomonal infection with rice grain injuries

in the wet, rice-growing season may account for this difference. There is also a high concentration of Gram-negative rods isolated from pond and canal water in this region. This water may be used to wash foreign bodies from eyes, or be used as initial local treatment (holy water). Keratomycosis in tropical and subtropical regions is predominantly caused by filamentous fungi rather than yeast specie. The three major fungal pathogens in this study were filamentous species; *Aspergillus* sp. 37% (19 of 51)) *Fusarium* sp. 20% (10 of 51), and *Curvularia* sp. 18% (nine of 51). There was only one case of Candida keratitis. Lasiodiplodia and Scedosporium have been reported to cause keratomycosis. Dichotomophthoropsis nyrnphaearurn has been reported as a corneal pathogen only in this region, and only in one case.

Clinical features

The microbial cause of corneal ulceration cannot generally be diagnosed clinically. Conclusions from this study must be tempered by the small number of cases observed for each pathogen, but the following are features we believe are worthy of mention. The fungal cases showed a longer history before presentation. The high prevalence of filamentous fungi meant that the ulcers took on the clinical appearance typical of the genera; a dry, raised, necrotic or fluffy surface, with an endothelial ring surrounding the ulcer, as opposed to the 'collarbutton' configuration typical of a yeast keratitis. Of the two most prevalent bacterial pathogens, the pneumococcal ulcers had smaller epithelial defect and infiltrate diameters, larger hypopyons and more severe corneal thinning than pseudomonal ulcers. Both had equal duration of symptoms before presentation. The association of pneumococcal ulcers with dacryocystitis is well recognized" and reemphasized in this series. This study confirms that in the tropics, corneal ulcers tend to occur in adult males working outdoors. Interestingly, fungal ulcers were seen frequently in domestic workers and Curvularia showed a female predominance. Of patients with fungal ulcers, 65% reported no history of trauma. This is contrary to what was predicted, as the fungal inoculum has been thought to be due to a injury with vegetable matter. The most frequent injury in this series was due to rice grains or leaves. These have been shown to carry Bacillus sp. and fungi of the Mucorales family. The rice grain injuries caused more bacterial ulcers (31%) than fungal (13%) and the most frequent pathogen was *Pseudomonas* sp., indicating that the inoculum more likely occurred during the washing of the injured eye with contaminated water carrying the Gram-negative rod. The implications for population education are obvious.

This study also indicates that the absence of trauma (e.g., with vegetation) does not exclude a fungal pathogen. Practitioners should also be aware of the increased incidence of pseudomonal cases during the monsoon period and the increased incidence of *Fusarium* during the dry-hot beginning of the year. Suppurative keratitis is relatively uncommon in the United Kingdom; 67 (only two fungal) over 20 months were reported in Moorfields by Coster in 1981.6 In the same year, Rahman saw 508 cases (22.6% fungal) at the Islamia Eye Hospital, Bang1adesh. Mmany areas of the developing world trachoma, onchoceriasis, leprosy and other infectious causes of ocular disease are endemic. It is well recognized that normal commensals can become pathogens in the compromised cornea. This may explain the increased incidence of suppurative keratitis, but other significant factors include the use of contaminated local remedies after minor trauma, uncontrolled medicines including steroids, poor availability of medical care and late referral to specialist care. In the early 2020, 200 to 300 cases of corneal ulcers were seen annually at the Chittagong Eye Infirmary. Intractable infection was responsible for about 60% of all eyes enucleated. Williams et al. have shown that the establishment of a low-cost microbiology laboratory to identify corneal pathogens and their antibiotic sensitivity has reduced this enucleation rate significantly. It is hoped that, using information from this laboratory to define the prevalence of pathogens and the pattern of disease in the region, we may be able to help medics in the region, without access to these facilities, to initiate early and effective treatment for suppurative keratitis.

CONCLUSION

Suppurative keratitis is an important preventable cause of blindness, particularly in the developing world. The five most common pathogens were: *Pseudornonas* sp. 24%, Streptococcus pneumoniae 7%, *Aspergillus* sp. 13%, *Fusariurn* sp. 7% and *Curvularia* sp. 6%. Gram stain and culture results were consistent in 62.6% of cases. Previous antibiotic treatment was a significant factor for failure of culture isolation and less so for Gram stain failure. On Gram stain, 55.9% of pseudomonal cases were missed, but only 2% of fungal cases were missed. Over all, Gram stain had a sensitivity of 62% and positive predictive value of 84% for bacterial cases, and 98% and 94% for fungal cases, respectively. Fungal ulcers were typically filamentous, but an antecedent history of trauma was not common. The most frequent injury was due to rice grains, but the inoculum appeared to be introduced during eye washing with contaminated water. Pseudomonal ulcers occurred most frequently in the monsoon season, and Fusariurn cases were seen only in the hot, dry season.

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