Clinico-microbiological perspective of corneal ulcer

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Abstract
Corneal ulcer is a major cause of mono-ocular blindness in developing countries. Clinical diagnosis and management of corneal ulcers is helped by microbiological diagnosis.
Purpose: To evaluate microbiological support for clinical diagnosis and management of corneal ulcers.
Materials and Methods: All the patients presenting with corneal ulceration underwent clinical evaluation and standard microbiological evaluation of their corneal scrapings.
Results: Out of 200 corneal ulcer cases, 127 were clinically diagnosed as bacterial and 73 as fungal.
On microscopy 65 were positive for Gram's staining, 49 were stained by KOH staining and rest 86 were negative for Gram's and KOH staining.
Further culture examination of total corneal cases identified 69 bacterial isolates and 50 fungal isolates.
Conclusion: A good clinical evaluation aided by microbiological support will help in better diagnosis and treatment of corneal ulcer.

Keywords: Clinically diagnosed, Corneal ulceration.

Introduction
Corneal ulcer is a major cause of mono-ocular blindness in developing countries. Surveys in Africa and Asia have confirmed this finding.[1-3] Corneal ulceration is second only to cataract as a major etiology of blindness and visual disability in many developing countries.[4] Annual incidence of corneal ulceration was as high as 10 times more than age and sex adjusted population in USA.[5]

Microbiological methods of confirmation of diagnosis of corneal ulcer has been found to be difficult due to sample collection, sample size, prior use of antibiotic eye drops at presentation etc.

Materials and Methods
All patients with corneal ulceration presenting to Ophthalmology OPD of SVS Medical College and Hospital, Mahabubnagar, Telangana between February 2013 and August 2014 were studied. A total number of 200 cases of corneal ulcerations were taken up for study. Cases presenting with typical viral ulcerations, shield ulcers, neurotrophic ulcers, neuroparalytic ulcers, phylectenular keratitis, Mooren's ulcer were excluded from the study.

Clinical diagnosis was based on severity of symptoms, nature of injuring agent, duration and findings under slit lamp examination, ulcer characteristics like site, size and depth of infiltrate, margins of ulcer, satellite lesions, immune ring and hypopyon.

The corneal scraping sample was taken using a slit lamp under aseptic conditions. Scrapings taken with the help of topical 0.5% proparacaine and sterile badparkers blade [no 15]. Scraping material was taken from the edge and base of the ulcer. The scraped material was examined using Gram's staining, 10% KOH mount and cultured in blood agar, chocolate agar, nutrient agar and Sabouraud's dextrose agar without antibiotics. Bacteria were identified by using routine biochemical tests. Filamentous fungi were identified on the basis of growth rate, colony characteristics and microscopy.

All corneal ulcers were grouped under bacterial and fungal based on clinical and microbiological results and were compared.

Results
A total of 200 patients of corneal ulcers without any history of preexisting ocular disease were included in present study and following observations were made:

Table 1: Clinical profile of corneal ulcers under study

History of injury with vegetative matter		82%(41%)
Nature of infiltrate	Dry	88(44%)
	Wet	112(56%)
Depth of infiltrate	<1/3rd corneal thickness	142[71%]
	>1/3rd corneal thickness	58 [29%]
Satellite lesions		19 [9.5%]
Hypopyon		46[23%]
Size of ulcers	<6mm	154{77%]
	>6mm	46(23%)

Taking into consideration the above clinical characteristics mentioned, in Table 1 we grouped the cases under study into clinically bacterial -127(63.5%) and clinically fungal-73(36.5%). Corneal ulcers with regular margins, wet exudative infiltrate and mobile hypopyon with more symptoms were grouped under bacterial ulcers. Those with irregular margins, dry leathery infiltrate/ thick immobile hypopyon, satellite lesions, predominantly having history of injury with vegetative matter and with more signs were grouped under fungal ulcers.

Microbiological Reports

Table 2A: Microscopy

Total cases	Gram staining	KOH mount	Microscopy negative
200	65(32.5%)	49(24.5%)	86(43%)

Total cases	Culture positive		Culture negative
200			

Table 2 B: Culture reports

Total cases	Culture positive		Culture negative
	119(59%)		
	Bacterial/Fungal		
200	69(34.5%)	50(25%)	81(40.5%)

Finally summarizing the clinical diagnosis and microbiological reports the following observations were made:

Table 3: Comparison of clinical and microbiological findings

		Grams staining	KOH mount	Bacterial culture positive	Fungal culture positive
Clinically Bacterial	127(63.5%)	60(47.24%)	4(3.14%)	60(47.24%)	4(3.14%)
Clinically Fungal	73(36.5%)	5(6.84%)	45(61.64%)	5(6.84%)	46(63.01%)

Distribution of Culture Positive Cases

Table 4 A: Bacterial isolates

Bacterial isolates	Number of cases	Percentage
Pseudomonas aeruginosa	31	44.92
Streptococcus pneumonia	19	27.53
Staphylococuus aureus	13	18.84
Micrococcus	6	8.69
Total	69	100

Table 4 B: Fungal isolates

Fungal isolates	Number of cases	Percentage
Aspergillus	26	52
Fusarium	16	32
Pencillin	3	6
Others	5	5
Total	50	100

Discussion

Corneal ulcer is the most common cause of monocular blindness in developing countries. Most of primary and secondary eye care centers rely on clinical characteristics of an ulcer for diagnosis and treatment. As of now only at tertiary institution based eye care centers have facility of microbiological support. The purpose of our study was to evaluate significance of microbiological support for clinical diagnosis and management of corneal ulcer.

In our study, 200 corneal ulcers based on clinical characteristics were grouped under clinically bacterial 127(63.5%) and clinically fungal 73(36.5%). All these cases were subjected to staining and culture. The initial line of treatment was started after microscopy reports.

Out of 127, clinically diagnosed bacterial keratitis, Gram's staining was positive in 60 cases (47.24%) and these were managed purely with anti-bacterial drugs. In non-severe cases (size less than 6mm, depth less than 1/3rd of corneal thickness) commercially available antibacterials were used (4th generation fluoroquinolones). In severe cases (size more than 6mm, more than 1/3rd corneal thickness) fortified antibiotics were started. In proven Gram's stain positive cases fortified Cephazoline was used. Out of 127, clinically diagnosed bacterial cases, 4 cases (3.14%) were KOH positive and treated with anti-fungals.

Remaining 63 cases where staining was negative but are clinically bacterial, were started with antimicrobial treatment depending on severity and reviewed for response. In few cases, line of management was changed according to culture and sensitivity reports. Over all out of 127 clinically diagnosed as bacterial corneal ulcers, culture positivity was seen in 64 cases (50.3%).Based on clinical response to

antimicrobial therapy in these cases, 113 cases (88%) were considered to be bacterial. 10 cases which did not respond to antimicrobial therapy were added with anti-fungals without any response and their clinical outcome progressively worsened.

In our study, out of 200 corneal ulcer cases seen, 73 cases were clinically diagnosed as fungal. Out of 73 cases, KOH staining was positive in 45 cases (61.64%) and these were managed purely with antifungal drugs. In non severe cases, topical Natamycin drops were prescribed and in severe cases, oral Fluconazole was given for two weeks duration. Out of 73 cases, clinically diagnosed as fungal ulcers, 5 cases (6.84%) were Gram's stain positive and hence treated with antibacterial drugs.

Remaining 23 cases where staining was negative but clinically fungal, were started with anti-fungal treatment depending on severity and reviewed for response. In few cases line of management was changed according to culture and sensitivity reports.Overall out of 73 clinically diagnosed as fungal corneal ulcers, culture positivity was in 46 cases (63.01%). Based on clinical response to antifungal therapy in these cases, 56 cases (76.7%) were considered to be fungal. 12 cases did not respond to any antifungal therapy and were added with anti-bacterials showing no response and they clinically worsened.

We isolated Pseudomonas aeruginosa in 31 cases (42.92%) as the predominant bacterial pathogen followed by Streptococcus in 19 cases (27.53%) among bacterial ulcer patients. Pseudomonas keratitis tends to progress rapidly if inadequately treated.[8] Basak SK et al. isolated Pseudomonas at 74% isolation rate.[9] In Ghana, more than 50% of bacterial isolates were Pseudomonas species.[10] Among fungal, Aspergillus was most common in isolates 26 cases(52%) followed by Fusarium 16 cases(32%). Basak SK el al. isolated Aspergillus at 59.8% isolation rate and Fusarium at 21.2% isolation rate.[9]

Out of 200 cases in 9 cases (4.5%) our clinical diagnosis proved to be wrong by microbiological reports. Culture positivity in most of the studies including ours was around 60%. So entirely relying on the microbiological support for the initial line of management of corneal ulcers is not mandatory. Microbiological reports definitely have a role in avoiding false positive diagnosis, to the change the line of management in refractive cases and for epidemiological purposes.

Conclusion

A good clinical evaluation aided by microbiological support will help in better diagnosis and treating the corneal ulcer. Most bacterial ulcers resolve with early and appropriate treatment. Few cases of Deep Stromal Fungal keratitis were refractory to treatment. Microbiology helped to change the line of management in significant number of cases.

Conflict of Interest: None.

Reference

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