RESEARCH ARTICLE

Risk factors, causative organisms and sensitivity patterns of infective keratitis in a tertiary care hospital in Rawalpindi

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Abstract

Objective: To determine the risk factors, causative organisms, sensitivity patterns and treatment outcomes of infective corneal ulcers.

Methods: The prospective cohort study was conducted from January 2018 to December 2019 at the Department of Ophthalmology, Fauji Foundation Hospital, Rawalpindi, Pakistan, and comprised eyes of patients with corneal ulcer. Corneal scrapes were sent for microbiological assessment. Variables studied were age, gender, risk factors, onset and duration of symptoms, best corrected visual acuity, treatment and complications. Data was analysed using SPSS 20.

Results: Of the 65 eyes of as many patients, 40(61.5%) were from female patients and 25(38.4%) from males. The most common local risk factor was ocular surgery 19(29.2%), followed by ocular trauma 15(23.1%). Diabetes was present in 29(44.6%) cases. Culture results after corneal scrapings were positive for 39(60%) samples, while 26(40%) had no growth. Bacterial growth was present in 20(51.3%) eyes, fungal in 11(28.2%) and polymicrobial organisms were present in 8(20.5%). The most common pathogens were pseudomonas 10(25.6%) that were most sensitive to ciprofloxacin. By the end of the follow-up, 40(61.5%) cases showed improvement.

Conclusion: Isolated pseudomonas was the most common pathogen. Prompt diagnosis with culture sensitivity tests are needed in developing countries to avoid blindness due to infective corneal ulcers.

Keywords: Infective keratitis, Risk factors, Corneal ulcer, Culture sensitivity. (JPMA 71: 2735; 2021)

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Introduction

Infective keratitis is the leading cause of blindness in the developing world. It may be caused by bacteria, viruses, fungi or acanthamoeba.[1] Infective keratitis affects about 1.5 million to 2 million individuals annually in the developing world with prevalence depending on factors, such as locality, type and causative factors.[2] It is the second most common cause of blindness in Pakistan after cataract.[3] As such, infective keratitis is a major clinical challenge, particularly in urban environments.[4]

Most of the organisms, apart from the fastidious organisms, invade the epithelium of the cornea first and then continue to penetrate the stroma and cause stromal necrosis, leading to perforation and endophthalmitis.[5]

The primary cause of infective keratitis is different in industrialised nations and the developing world. The most significant risk factor contributing to infective keratitis in the industrialised world is contact lens wear. However, in the developing world, the most common risk factors are ocular surface diseases and trauma. There is also a difference in the type of organism that most commonly causes infective keratitis globally. The cause is bacterial in industrial nations, whereas it is fungal in the developing world. This difference is attributable to a larger work-force in the agricultural sector in the developing world, exposing themselves to fungi sourced in vegetation.[6]

A diagnosis of infective keratitis via slit-lamp examination does not necessarily lead to an understanding of the causative agents. This determination is also essential for proper treatment and must be performed via microbiological investigation. Timely diagnosis of infective keratitis and the organism causing it is essential for good treatment outcome.[7] The primary cause for blindness resulting from infective keratitis is delayed medical treatment.[8] The success rate in public-sector medical facilities is low in infective keratitis cases compared to private clinics, primarily because of delays in patient presentation.[9] It is to be noted that the most significant factor contributing to poor recovery from infective keratitis is delayed presentation of patient, resulting in large size of ulcer and poor visual acuity (VA) at presentation.[10]

The aetiologies and causes of infective keratitis vary widely between different regions, and within a country they may be different for various demographics. It is, therefore, important to understand the causes and types

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of infective keratitis in a local hospital setting.

The current study was planned to understand the causes and types of infective keratitis, including the risk factors and sensitivity patterns of the offending organisms.

Patients and Methods

The prospective cohort study was conducted at the Ophthalmology Department, Fauji Foundation Hospital (FFH), Rawalpindi, Pakistan, from January 2018 to December 2019. After approval from the institutional ethics review committee, the sample size was calculated using anticipated population 59%[11] with 12% precision and 95% confidence interval (CI). The sample was raised using non-probability convenience sampling technique from among patients of either gender with presumed diagnosis of infectious keratitis. Patients with Mooren's ulcer, marginal ulcer or ulcers due to peripheral ulcerative keratitis (PUK), and those who were lost to follow-up were excluded. Data was collected after taking written informed consent from all the subjects. Corneal scrapings were taken on day of presentation under topical anaesthesia using the standard protocol. Conjunctival swabs were also taken. Gram staining and potassium hydroxide (KOH) 10% preparation for fungal hyphae was done, then inoculated on blood agar, chocolate agar, MacConkey agar, Sabouraud agar and brain-heart infusion. Viral keratitis was diagnosed via clinical assessment on the basis of dendritic lesions on slit-lamp examination and loss of corneal sensations. Patients were divided into two groups; the exposed group consisting of patients who showed growth on culture, and the control group comprising patients who did not show growth or ulcers that were viral in origin. Treatment for bacterial infections began using moxifloxacin 0.5% eye drops and it was modified according to the culture report. For fungal infections, natamycin 5% eye drops were used. Ulcers were monitored for size and regression of symptoms in addition to VA of patients, and the final assessment was done at the end of the one-month follow-up. VA was measured using a Snellen's chart and it was converted into decimal acuity. The Freiburg visual acuity test[11] has established the decimal acuity values of counting finger (CF) and hand movement (HM) as 0.014 and 0.005, respectively, and they were analysed as such. Individuals having vision worse than HM were removed from analyses, as it cannot be quantified in such cases.

Age, gender, risk factors, onset and duration of symptoms, ulcer size, best corrected visual acuity (BCVA), culture results and their sensitivity were noted for each patient. Data was analysed using SPSS 20. $P<0.05$ was taken as significant.

Results

Of the 65 eyes of as many patients, 40(61.5%) were from female patients and 25(38.4%) were male. The overall age ranged between 0-80 years. Isolated risk factors were seen in 37(57%) cases, while 24(37%) individuals presented with compounded risk factors. The remaining 4(6%) subjects did not have any risk factor. The most common systemic risk factor was diabetes 29(44.6%), while local risk factor was ocular surgery 19(29.2%), followed by ocular trauma 15(23.1%) (Table-1).

Culture results after corneal scrapings were positive for 39(60%) samples, while 26(40%) had no growth. Bacterial growth was present in 20(51.3%) eyes, fungal in 11(28.2%) and polymicrobial organisms were present in 8(20.5%). The most common pathogens were pseudomonas 10(25.6%) that were most sensitive to ciprofloxacin (Figure).

Patients had presented on an average of 11.15 ± 13.80 days since the start of symptoms. Hypopyon was present in 22 eyes (33.80%). Deep ulcer was present in 46 (70.8%) eyes, while the rest had superficial erosions. The infiltrate was limited to the anterior stroma in 38(58.5%) eyes, while 7(10.8%) patients had infiltrates as far as the posterior stroma. Also 23(35.4%) eyes were associated with moderate lid oedema, while 6(9.2%)eyes, with severe

Table-1: Demographic data and risk factors of infective keratitis cases (n=65).

Gender	Age	Frequency of risk factors							
		Ocular Trauma	Dacrocystitis	Corneal Exposure	Contact Lens wear	Ocular Surgery	Ocular surface disease	Diabetes	Malignancy
Male	0-20	0	0	1	1	0	1	1	0
	21-40	5	0	1	2	0	2	1	0
	41-60	2	0	0	1	2	1	3	0
	61-80	0	1	1	0	3	0	4	0
Female	0-20	1	0	0	0	1	2	1	0
	21-40	1	0	0	1	0	1	0	0
	41-60	4	0	1	2	4	0	10	0
	61-80	2	0	2	1	9	3	9	1
Total (%)		15(23.1)	1 (1.5)	6 (9.2)	8 (12.3)	19(29.2)	10(15.3)	29(44.6)	1(1.5)

Table-2: Drug sensitivity with their causative organisms.

Drug sensitivity	*Pseudomonas* (n=12)*		*Streptococcus* (n=7)*		*Staphylococcus* (n=5)*		MRSA (n=5)*	
	S	R	S	R	S	R	S	R
Ciprofloxacin	12(100%)	0	1(14.3%)	6	1(20%)	4	2(40%)	3
Ceftazidime	11(91.7%)	1	0	7	0	5	0	5
Penicillin	0	12	6(85.7%)	1	3(60%)	2	0	5
Vancomycin	0	12	7(100%)	0	5(100%)	0	5(100%)	0
Doxycycline	0	12	0	7	5(100%)	0	3(60%)	2
Gentamicin	11(91.7%)	1	7(100%)	0	2(40%)	3	2(40%)	3
Cefepime	10(83.3%)	2	0	7	0	5	0	5
Cefazolin	0	12	6(85.7%)	1	3(60%)	2	1(20%)	4
Cefuroxime	0	12	0	7	3(60%)	2	1(20%)	4
Clindamycin	0	12	6(85.7%)	1	3(60%)	2	1(20%)	4
Cotrimoxazole	0	12	1(14.3%)	6	1(20%)	4	1(20%)	4
Chloramphenicol	0	12	0	7	2(40%)	3	2(40%)	3

*=isolated + polymicrobial. S: Sensitive, R: Resistant, MRSA: Methicillin-resistant staphylococcus aureus.

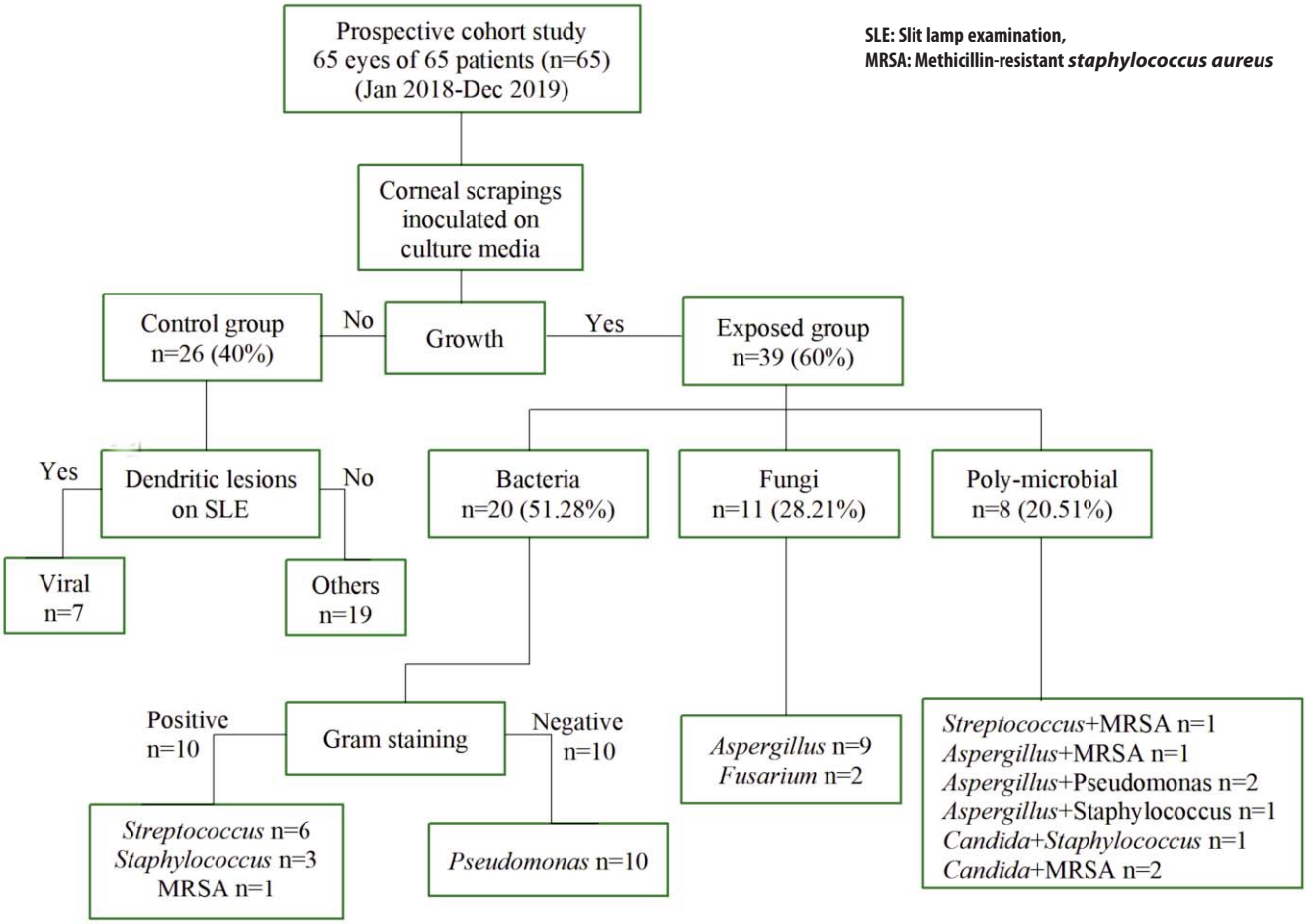

Figure: Study flowchart showing parameters and aetiological basis of corneal ulcers (n=65).

lid oedema. Corneal sensation was reduced in eight (12.3%) eyes, seven with viral ulcers (87.5%), and one with fungal ulcer (12.50%).

In terms of VA, the mean decimal acuity at presentation was 0.13 (SD: 0.122), which, when converted to Snellen's fraction, was 6/46 or 0.88 LogMAR acuity. The mean

decimal VA improved to 0.257 (SD: 0.244).

Improvement in VA was seen in 32(49.2%) eyes and it remained the same in 32(49.2%) eyes. In three cases (4.6 %), VA worsened.

According to sensitivity reports, more pseudomonas infections were sensitive to ciprofloxacin. Methicillin-resistant staphylococcus aureus (MRSA) were most sensitive to vancomycin, while streptococcus species were susceptible to vancomycin and gentamicin (Table-2).

By the end of the one-month follow-up, 40(61.5%) cases showed clinical improvement in terms of pain, infiltrate size, epithelial defect size or amount of hypopyon, while 6(9.2%) ulcers got perforated, 1(1.5%) developed endophthalmitis and 18(27.7%) showed no sign of improvement.

Discussion

Infective keratitis is one of the ophthalmic emergencies. Prompt diagnosis, culture and immediate treatment is required to minimise the sight-threatening elements. In the current study, out of 65 patients, there were 40 females (61.5%) and 25 males (38.4%). High prevalence of females is in accordance with a study in Nepal.[12] However, a study in Larkana showed high prevalence of males having keratitis.[13] High prevalence of females in the current study might be due to the fact that families of ex-serviceman are entitled to receive treatment at the FFH.

In the current study, majority of the patients were 40-60 years of age. This is due to factors like ocular surgery, ocular surface disorders, lid deformities and, above all, diabetes in this age group. This result is consistent with another study.[14]

The most common local risk factor in the current study was previous ocular surgery (29.2%). Other studies have noted various risk factors, like contact lens wear (31.4%),[15] while only 8 individuals in the current study used contact lenses. This may be due to the socioeconomic status of individuals as not many people may be able to afford or find it feasible to use contact lenses, among other factors. Ocular trauma has also been reported as the leading risk factor of corneal ulcer.[16,17]

Diabetes was the most common systemic risk factor (44.6%) in the current study. A large cohort study concluded that diabetes was the predictor of corneal ulcer.[18]

Among isolated organisms, pseudomonas was found to be the most common organism (25.6%) in the current study. The finding is consistent with another study.[19] Aspergillus was found to be the second most common (23%) organism in the current study. This is likely due to the hot and humid climate of the region and also because of the higher risk of vegetative injury as Pakistan is an agrarian country. These results are similar to an earlier study.[20]

It is important to note that in the current study, anti-fungal drops were being used by only 2 patients at presentation, which could highlight the need for more effective detection at the primary level care before referral.

In the current study, 40(61.5%) patients showed signs of healing in their ulcers, while 25 did not. These findings are consistent with medical literature that demonstrates healing rates of bacterial keratitis in excess of 60%.[21,22] Four perforated corneal ulcers were treated through tarsorrhaphy and 2 by Gundersen flap. Endophthalmitis was treated by injecting intravitreal vancomycin and ceftazidime injections.

Culture results were analysed for sensitivity and pseudomonas was found to be most sensitive to ciprofloxacin, followed by ceftazidime and gentamicin. These results are consistent with some studies,[23] and in contrast with some others.[24] Streptococcus was found to be most sensitive to vancomycin (100%) and gentamicin (100%), while it was least sensitive to ceftazidime, doxycycline and chloramphenicol. These findings are generally consistent with earlier reports[25] except that others found streptococcus to be sensitive to chloramphenicol in addition to the other antibiotics in the current study.

The current findings suggest that increased duration of symptoms, VA of CF or less at presentation, lid oedema, increased depth of infiltrate, increased size of ulcer, presence of hypopyon, and MRSA infection were associated with corneal perforation. However, logistic regression analysis using these covariates led to statistically non-significant findings.

The average VA improved in the current study after 1 month. It is important to mention that VA may improve even further after a few months for which data is not available in the current study.

The current study has limitations related to small sample size and short follow-up.

On the basis of the findings, however, it is strongly recommended that standard operating procedures (SOPs) should be formulated in every hospital to have microbiological testing at the time of presentation of

keratitis. Ophthalmologists need to be cognizant of the procedures for proper identification of the microbes causing keratitis. It is vital to do culture and sensitivity analysis in all keratitis patients.

Finally, awareness of patients about the use of topical antibiotics and corticosteroids after cataract surgery is imperative for reducing the risk of infection. Having said that, these medications should not be overused. In order to prevent the misuse, these drops should not be given without ophthalmologists' prescription.

Conclusion

The most common systemic risk factor was found to be diabetes, while the local risk factor was ocular surgery. Pseudomonas, aspergillus and streptococcus accounted for the bulk of infective keratitis cases. According to sensitivity reports, pseudomonas infections were most sensitive to ciprofloxacin, while streptococcus were sensitive to vancomycin and gentamycin.

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