



# Challenges in management of microbial keratitis during COVID-19 pandemic related lockdown: a comparative analysis with pre pandemic data

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## Abstract

**Purpose** To study the challenges of managing microbial keratitis (MK) during the COVID-19 pandemic related lockdown and assess the outcomes of treatment at a tertiary cornea service.

**Methods** Retrospective, non-comparative study of electronic medical records of MK presenting to a network of four tertiary care cornea services. The medical history, presenting clinical features, microbiology work up and treatment outcomes were analyzed. The primary outcome measure was final outcome at last follow up. Secondary outcomes measures were

non-compliance to treatment due to travel restrictions, therapeutic PKP not done due to non-availability of corneal tissues. **Results** MK was noted in 330 eyes of 330 patients between April and May 2020. Of these 237 (71.8%) were males. Median age was 45 years (IQR, 33–56). Low socioeconomic status was noted in 102 (30.9%). Patients travelling beyond the district from where the hospital was located comprised of 64.9% (n=214). At a median follow up of 32 days (IQR, 9–54), 118 (35.8%) patients had resolved, with medical management, 73 (22.1%) patients were under active treatment, 139 (42.1%) were lost to follow up. Sixty-six patients (20%) were non-compliant to treatment of which 59 could not follow appointment schedule due to travel restrictions. Therapeutic PKP (TPK) was planned in 48/128 (37.5%) patients, but was performed in only 34/48 (70.8%) due to non-availability of donor corneas.

**Conclusions** Abnormal social circumstances due to the COVID pandemic and the ensuing impediments to travel for access to health care affected compliance to treatment of ocular emergencies such as microbial keratitis.

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## Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) outbreak was declared a pandemic by the World Health Organization (WHO) on 11th March 2020 [1]. This led to a series of control measures by governments across the globe. India enforced a nationwide lockdown commencing March 24th and extended until May 31st with sealed international borders, restricted travel and nationwide ban on gatherings [2]. While emergency health services were still available, access to health care was severely affected particularly for patients with non-communicable diseases [3]. The International Agency for the Prevention of Blindness (IAPB) reported an impact on eye care with widespread reduction in hospital visits, decrease in the number of outreach facilities and complete cessation of elective eye surgeries across the South East Asian countries [4]. This was further compounded by lack of public transport, loss of income and rising cost of health care [4, 5].

A review from the developing world suggests that microbial keratitis (MK) has reached epidemic proportions [6]. Whitcher and Srinivasan estimated over 800,000 cases of MK per annum in India [7]. During the COVID pandemic, MK was the most common ocular emergency (23.74%) reporting to our emergency services [8]. Considering the significant disruption in access to health care and medication coupled with the increase in COVID-19 cases in the community, we aimed to evaluate the challenges in the management of MK and outcome of therapy during the pandemic related lockdown in comparison to data from the pre pandemic period.

## Materials and methods

A retrospective, non-comparative study was conducted across cornea services of four tertiary eye care centers spread across 3 states in India. It was approved by the Institutional Review Boards of these centers (LEC-BHR-R-08-20-487) and adhered to the tenets of the declaration of Helsinki. We accessed the EyeSmart electronic medical records for all new cases of microbial keratitis presenting between April and May 2020 with four weeks follow-up. We validated this data from the records of the microbiology database of corneal scrapings performed during this

time period. We compared this data with cases of MK presenting to the tertiary centres during the months of April and May 2019.

We defined microbial keratitis as any clinically infectious looking corneal lesion with the presence of an epithelial defect with stromal infiltration and features of inflammation. Severe MK were defined as the presence of any one of the following clinical features: size > 6 mm in any meridian, posterior stromal involvement, presence of endothelial plaque, anterior chamber (AC) exudates, limbal or scleral involvement. The work-up of all patients was done based on the institute protocol [9]. Briefly, a detailed clinical history was elicited which included the duration of symptoms, local consultation, use of traditional medicines or over the counter medications or any local interventions prior to presentation. We examined patients weekly and noted the following ulcer characteristics: size, depth and involvement of endothelium or anterior chamber at every visit.

A detailed microbiological work-up was done based on our protocol. Briefly, all new cases of MK were subjected to scraping and plating the specimens on slides for Gram's stain and 10% potassium hydroxide or calcofluor white wet mount. Samples were plated onto blood agar, chocolate agar, Sabouraud's dextrose agar, potato dextrose agar and non-nutrient agar and liquid media included brain heart infusion broth and thioglycolate broth. Treatment strategies were based on these results and as per our protocol. Broad spectrum empirical antibiotics include combination of 1% fortified vancomycin or 5% fortified cefuroxime with 0.3% ciprofloxacin in bacterial keratitis. Fungal keratitis were treated with 5% natamycin. For acanthamoeba, 0.02% polyhexabimethylguanide and 0.02% chlorhexidine eye drops was prescribed [9]. For pythium keratitis, 0.2% linezolid and 0.3% azithromycin eye drops were prescribed [10]. In case of negative smear, broad spectrum antibiotics were prescribed.

The clinical response was assessed before repeat scraping. Surgical management, where required, included tissue adhesive application, tenonplasty, conjunctival flap and therapeutic penetrating keratoplasty. Glycerol preserved corneal tissues from our network of eye banks were utilized for emergency tectonic transplants, determined by the priority. Data pertaining to causes of treatment failure, lack of availability of medications, difficulty in follow-up,

instances where keratoplasty could not be performed due to unavailability of corneas, alternatives to therapeutic keratoplasty and final outcome at last follow-up was collected.

Data was interpreted with descriptive statistical analysis using Microsoft excel version 16.16.27. Data with non-normal distribution was described as median and inter-quartile range (IQR). Categorical data were described in proportions. A mixed-effects model with maximum likelihood estimation was used and multifactorial analysis was performed using STATA v14.2 (StataCorp, College Station, TX, USA).

## Results

We examined 330 eyes of 330 patients with MK between April and May 2020. The demographics of the study population are summarized in Table 1. Briefly, a majority were males (237, 71.8%). Median age of patients was 45 years (IQR, 33–56 years). Patients belonging to the low socio-economic strata constituted 30.9% ( $n=102$ ). Nearly 2/3rd (234, 64.9%) of patients hailed from districts beyond which the tertiary care center was located. Median duration

of symptoms was 12 days (IQR, 5–21.8 days). Most patients (257, 77.9%) had a primary consultation with an ophthalmologist prior to presentation and 261 (79.1%) of them were on medications as prescribed by the treating ophthalmologist. Six patients had used over the counter medications and only 2 patients had used traditional medications.

The median best-corrected visual acuity (BCVA) at presentation, in logMAR, was 1.98 (IQR, 0.79–2.00). There were 161 (48.8%) eyes with features of severe MK at presentation. Microbiology report was unavailable or could not be performed at the initial visit in 43 patients (13%). Based on the results of the corneal scraping, broad spectrum antibiotics were administered in 187 patients (56.7%), antifungals in 148 patients (44.9%), anti-parasitic drugs in 7 patients (2.1%) and antivirals in 9 patients (2.73%). The remaining patients were administered combinations of antiviral drugs or antifungals with antibiotics as per the microbiologists' report.

A surgical intervention was performed in 170 patients (38.8%) either due to worsening despite medical management ( $n=34$ , 26.6%), thinning ( $n=67$ , 52.3%), corneal perforation ( $n=37$ , 28.9%) or a combination of these ( $n=32$ , 18.8%). The medical interventions and surgical procedures performed

**Table 1** Demographic data

| Particulars  | During COVID lockdown |      | Before lockdown |       | P        |
|--|-----------------------|------|-----------------|-------|----------|
|  | No. of patients       | (%)  | No. of patients | (%)   |          |
|  | N=330                 |      | N=436           |       |          |
| Male   | 237                   | 71.8 | 292             | 66.97 | 0.15     |
| Female   | 93                    | 28.2 | 144             | 33.03 | 0.15     |
| Age(Median)  | 45 years              |      | 48 years        |       | 0.27     |
| IQR1-3   | 33–56                 |      | 34.5–60         |       |          |
| Geographic location same as tertiary centre                                | 116                   | 35.1 | 138             | 31.65 | 0.30     |
| Duration of symptoms in days (Median)                                      | 12                    |      | 35              |       | 0.012    |
| IQR1-3   | 5–21.8                |      | 9–49            |       |          |
| Low Socioeconomic status   | 102                   | 30.9 | 192             | 44.04 | 0.00022  |
| Primary examination local ophthalmologist                                  | 257                   | 77.9 | 118             | 27.01 | <0.00001 |
| Use of prior medications   | 261                   | 79.1 | 115             | 26.37 | <0.00001 |
| One eyed   | 18                    | 5.5  | 35              | 8.02  | 0.16     |
| Severe Keratitis at presentation: > 6 mm, post stromal, limbal involvement | 161                   | 48.8 | 43              | 9.86  | <0.00001 |
| Significant Thinning   | 122                   | 37   | 4               | 0.92  |          |
| Perforation  | 28                    | 8.5  | 33              | 7.57  |          |
| Limbal involvement   | 27                    | 8.2  | 6               | 1.38  |          |

are summarized in Table 2. Therapeutic PKP (TPK) was planned in 48/170 (28.2%) patients but was performed in only 34 of the 48 eyes that were advised TPK ( $n=34/170$ , 20.0%) due to non-availability of donor corneas. Glycerol preserved corneas were used in 9/34 (26.5%) patients. Application of tissue adhesives was the most commonly performed procedure ( $n=90/170$ , 52.9%).

Median duration of follow-up was 32 days (IQR, 9–53.8 days). At last follow-up, 118 (35.8%) had resolved. Median BCVA at the last follow-up was 1.77 (IQR, 0.79–2.00) and was not significantly ( $p=0.55$ ) different from presenting BCVA. Sixty-six patients (20%) were non-compliant of which 59 (89.4%) were unable to adhere to the appointment schedule due to travel restrictions, 139 (42.1%) were lost to follow up, of these patients 95/139 (68.4%) were from a different district than the tertiary center. Eight patients could not access the medications locally and 4 patients lacked a caretaker for instillation of topical medications. In this cohort, 22/66 (33.3%) non-compliant patients had worsening ( $n=3$ ), thinning ( $n=16$ ) or perforation ( $n=3$ ). Eight were planned for TPK and three underwent TPK, while keratoplasty was deferred due to lack of corneal tissues in five patients. Loss-to-follow up was noted in 30/66 (45.5%) and one eye was eviscerated. Non-compliance to treatment was not found to be dependent on patient demographics and management variables on a multilevel mixed effects model.

A comparison of the differences in demographics, presenting features, management and outcome of microbial keratitis with a similar cohort of patients treated before the lockdown from the previous year (during the month of April and May 2019, 438 eyes of 436 patients) are shown in Table 1 and 2.

## Discussion

The SARS-COV-2 was declared as a global pandemic on 11th March 2020 by the WHO. During April to June 2020 COVID 19 has emerged as a serious threat to public health globally. The Indian government declared a nationwide lockdown from the last week of March 2020 as a measure to flatten the curve of the pandemic. This was done taking into consideration that case detection, isolation, contact tracing and quarantine activities could be effectively performed.

**Table 2** Types of Interventions (medical and surgical) and outcomes

| Medical interventions  | During COVID lockdown (n = 330) |        | Before lockdown (n = 438) |        | P       | Surgical interventions                 |    | During COVID lockdown (n = 170) |    | Before lockdown (n = 196) |          | P |
|--|---------------------------------|--------|---------------------------|--------|---------|--|----|---------------------------------|----|---------------------------|----------|---|
|  | N                               | %      | N                         | %      |         | N                                      | %  | N                               | %  | N                         | %        |   |
| Antibacterial  | 167                             | 50.61% | 240                       | 54.79% | 0.021   | Therapeutic PKP                        | 34 | 20.0%                           | 51 | 26.02%                    | 0.17     |   |
| Antifungal   | 130                             | 39.39% | 155                       | 35.39% | 0.25    | Tissue adhesive + Bandage contact lens | 90 | 52.9%                           | 28 | 14.28%                    | <0.00001 |   |
| Antiparasitic  | 7                               | 2.12%  | 5                         | 1.14%  | 0.28    | Tenonplasty                            | 2  | 1.17%                           | 0  | 0%                        | 0.13     |   |
| Misc. (Anti Viral agents, Combinations of antifungal/Antibacterial etc.) | 26                              | 7.87%  | 38                        | 8.67%  | 0.69    | Amniotic membrane                      | 2  | 1.17%                           | 2  | 1.02%                     | 0.89     |   |
| Resolution at last follow up   | 118                             | 35.8%  | 211                       | 48.4%  | 0.00046 | Intracamerai/Intrastromal              | 13 | 7.64%                           | 34 | 17.34%                    | 0.0056   |   |
|  |                                 |        |                           |        |         | Vit Biopsy/Intraocular Antibiotics     | 9  | 5.29%                           | 25 | 12.75%                    | 0.014    |   |
|  |                                 |        |                           |        |         | Tarsorrhaphy                           | 4  | 2.35%                           | 22 | 11.22%                    | 0.00096  |   |
|  |                                 |        |                           |        |         | AC Reformation                         | 15 | 8.82%                           | 14 | 7.14%                     | 0.55     |   |
|  |                                 |        |                           |        |         | AC Wash                                | 1  | 0.58%                           | 20 | 10.20%                    | 0.00008  |   |

The restriction on travel, social distancing, suspension of all social, mass and community activities led to socioeconomic burdens, health problems and emerging challenges in responding to healthcare issues in a safe and effective manner [11].

Microbial keratitis is an ocular emergency and a common cause of corneal blindness. In a review of triaging practices during the lockdown our group reported MK to be the most common ocular emergency (23.74%) [8]. MK needs immediate ophthalmic care, microbiology services, frequent follow up and if needed surgical intervention including keratoplasty. Several aspects of this multifactorial management was disrupted during the nationwide lockdown and hence it is relevant to understand challenges in management of MK during the lockdown period of the COVID 19 pandemic.

We noted that a third of our patients (30.92%) were from low socioeconomic background and majority of patients (63.29%) lived beyond the district from where the tertiary center was located. Similar trends were observed for ocular emergencies by Das et al. [8] These patterns are indicative of the challenges faced by patients when travel restrictions are imposed and all public modes of transport are suspended. We noted that 77.16% had a local consultation with ophthalmologist prior to presentation which was indicative of availability of basic eye care services locally. In a previous publication from our group 54.6% of microbial keratitis patients had consulted an ophthalmologist and 48.6% were on appropriate antibiotics at presentation [9]. The duration of symptoms at presentation for our patients presenting during lockdown was 12 days compared to 35 days prior to lockdown ( $p 0.012$ ) and primary examinations conducted locally were significantly more, Table 1 (257vs 118,  $p < 0.00001$ ). It may be interpreted as a significant reduction in the time to presentation compared to pre lockdown data, and a surrogate measure of severity of the keratitis needing referral to a tertiary cornea service in spite of primary management within the community. Rural populations are at particular disadvantage especially due to lack of access to health care. A study from North India reported that there is a 5 day delay for rural population in reaching a secondary center and 11 day delay in reaching a tertiary center [12].

The management of microbial keratitis requires close and regular follow up over a couple of weeks

until signs of resolution are noted. During the lockdown, due to cessation of public transport and strict travel restrictions, access to the tertiary centers was severely affected. More than 1/3rd of our patients were lost to follow up and of these 63.29% were from districts beyond the one in which the tertiary center was located. In addition, 66 patients were non-compliant of which 59(89.4%) cited inability to travel as the reason for noncompliance. Analysis of outcomes of treatment at the last follow up of patients examined during the COVID lock down, showed a significant difference from pre COVID era (118/330(35.8%) vs.221/436(48.4%),  $p 0.00046$ ). This highlights the barriers to clinical care during lockdown. Tele consultation is an unexplored modality of reducing patient follow ups in management of microbial keratitis. It has several benefits in disasters and pandemics but in addition many barriers need to be overcome in order to provide robust care to patients [13].

The presenting BCVA and presence of deep keratitis and hypopyon was a predictor for poorer outcomes and need for TPK [14]. The mean BCVA was 1.67 LogMAR units and nearly half of our patients (48.55%) had severe keratitis at presentation.

Our study was similar to a similar experience reported from South India on the outcomes of infectious keratitis. Our rate of resolution was lower (35.8%) compared to Christy et al. (45.6%), this could be due to the higher incidence of severe keratitis in our study population (48.8% vs. 41.9%) [15].

Surgical management during lockdown was required ( $n=170/330$ ) 51.5% of our patients and amongst these ( $n=48/170$ ) 41.98% required TPK. However TPK could only be done in ( $n=34/170$ ) 20.0% due to unavailability of donor corneal tissue. Eye banking activities suffered tremendously during the pandemic[16, 17] and reduced to 3% compared to the previous year in an attempt to protect eye bank personnel and prevent transmission of Corona virus from donor to recipient. Following gradual cautious resumption of eye banking activities, 34 PKP were performed though almost 40% of patients advised surgery couldn't undergo the procedure due to non-availability of corneas. The travel restrictions also affected the transport of tissues therefore contributing to the scarcity of donor corneas [18]. Glycerol preserved corneas are a fall back measure during such times of crisis and a third of all TKP were performed using tissues preserved in glycerol. In a previous



paper from our group on corneal transplantation during the COVID-19 pandemic related lockdown, TPK with glycerol preserved corneas constituted 38% of all keratoplasty, as a viable alternative for maintaining globe integrity during times when corneal tissue is unavailable and eye banking services were limited [19].

Upon comparison with historical data from a cohort of patients with MK who were examined prior to lockdown in the previous year (Table 1 and 2); we found the following key differences in managing MK during the lockdown 1) Due to travel restrictions, lesser number of patients who were examined during the lockdown were from a low socioeconomic strata, suggesting that those who had the resources could travel and seek care at a tertiary eye care hospital 2) Most patients preferred to have a primary consultation with a local ophthalmologist due to limitations of access to specialized care 3) Majority of the patients who presented to the cornea service had severe keratitis that could not have been managed without a cornea specialist 4) Tissue adhesives were the commonest surgical intervention and was performed due to lack of availability of donor corneas.

## Conclusion

The COVID pandemic and ensuing lockdown posed major challenges to MK patients in accessing health care facilities and also crippled eye banking activities resulting in deferral of TKP in patients with severe keratitis. Tele-consultations with regular monitoring in consultation with a cornea specialist and use of long term corneal storage techniques like glycerol preservation may be used as fall back strategies for maintenance of tectonic integrity of the globe in emergency.

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## Declarations

**Conflict of interest** “The authors have no relevant financial or non-financial interests to disclose.”

**Consent to participate** “Informed consent was obtained from all individual participants included in the study.”

**Consent to publish** “The authors affirm that no individual data of human research participants were included that may in any manner disclose their personal identity and participants had provided consent to publish”

**Ethics approval** “This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of L V Prasad Eye Institute LEC-BHR-R-08-20-487”

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