



# Clinical profile of keratitis treated within 3 months of acute COVID-19 illness at a tertiary care eye centre

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## Abstract

**Purpose** To report the spectrum of keratitis treated within 3 months of acute COVID-19 infection.

**Methods** Retrospective, descriptive case series study of 19 eyes of 16 patients who presented at tertiary eye care centre in Southern India.

**Results** Median age of the patients was 43(IQR 35–55.5) years. Majority (15/16, 93.75%) were males. Unilateral affliction was predominant (13/16, 81.25% patients). Nine had a history of hospitalization, five had received oxygen supplementation and five had been treated with steroids during COVID-19 illness. The median duration between COVID-19 diagnosis and the ocular symptoms in the eye was 29 (IQR 22–57) days. Microbiological diagnosis consisted of microsporidia in nine eyes of seven patients, fungus in six patients, Pythium in one patient, and herpes

zoster ophthalmicus in one patient. One patient had neurotrophic keratitis. Therapeutic penetrating keratoplasty was performed in five patients, glue application in two patients and three were managed with tarsorrhaphy with/without amniotic membrane grafting or tenoplasty. There was medical and surgical cure in all patients.

**Conclusions** Microsporidia was the commonest cause of keratitis, followed by fungal infection. Majority of the microsporidia infections were keratoconjunctivitis. The fungal isolates identified were *Aspergillus* and *Mucor species*. All patients responded to conventional management guidelines with favourable outcomes.

**Keywords** COVID-19 · SARS-CoV-2 · Microbial keratitis · Microsporidia · Post-COVID conditions

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## Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) caused a global pandemic that caused mortality and morbidity of an alarming and unprecedented scale [1]. Each passing day in the year 2020 provided new evidence and information about the condition and its management. The acute COVID-19 usually lasts until 4 weeks from the onset of symptoms [2, 3]. An entity called post-COVID-19 condition has been recognized that refers to a wide range of health consequences that present four or more weeks

after the infection with SARS-CoV-2 [4, 5]. Existing literature describes the systemic features noted in survivors of coronavirus infection. The common conditions that have been described are related to pulmonary, haematologic, cardiovascular, neuropsychiatric, renal, endocrinal, dermatologic, gastrointestinal, and hepatobiliary organ systems [5]. Ophthalmic symptoms and associations have also been reported in association with acute COVID-19 illness [6].

The purpose of this study is to report the clinical and demographic profile of keratitis in patients who presented within 3 months of acute COVID-19 infection.

## Materials and methods

This was a retrospective study of 19 eyes of 16 patients who were treated at our clinics between September 2020 and September 2021, for keratitis occurring within 3 months of diagnosis of COVID-19 infection. The diagnosis of COVID-19 was ascertained from the history and confirmed from the medical records available with the patient. As per the medical records, the diagnosis of COVID-19 illness was made by the treating internists based on the symptomatology along with supporting investigations that included RT-PCR and chest CT scans. At the time of clinic presentation, the patients did not have active COVID illness. Except one patient (Patient 14), all other patients were evaluated after the onset of the second wave of COVID-19 infection (March–April 2021). The patient search was carried out using the key diagnosis ‘COVID-19 illness’ and ‘keratitis’ from electronic medical records (EyeSmart EMR). The diagnosis ‘COVID-19 illness’ has been adopted in the EMR to track the patients who have had COVID-19 illness. Those patients who had an unclear history and the duration between diagnosis of COVID-19 infection and ocular signs, and where symptoms of keratitis occurred more than 3 months later from the diagnosis of COVID-19 infection were excluded.

The data collected included demographic profile, duration of ocular symptoms, date of diagnosis of COVID-19 infection and time of recovery (as stated by the treating physicians in the medical records available with the patient at the time of initial clinic visit), duration of hospitalization (if any), details of medications, oxygen therapy, systemic comorbidities,

**Fig. 1** Clinical slit lamp photographs of 16 patients with keratitis: Both eyes of patient (Pt) 1 with stromal microsporidia keratitis. Slit lamp photographs of patient 2, 5, 9, 10, 12 and 15 showing microsporidia keratoconjunctivitis. Slit lamp photographs of the right eye patient 3, right eye of patient 4, left eye of patient 6, left eye of patient 7, right eye of patient 8, and left eye of patient 13 had fungal keratitis. The left eye of patient 3 had cyanoacrylate glue in place. The left eye of patient 11 showing *Pythium* keratitis. The left eye of patient 14 had dendritic keratitis and eyelid involvement (inset) secondary to Herpes zoster ophthalmicus. The left eye of patient 16 showing neurotrophic keratitis, inset shows abducens palsy

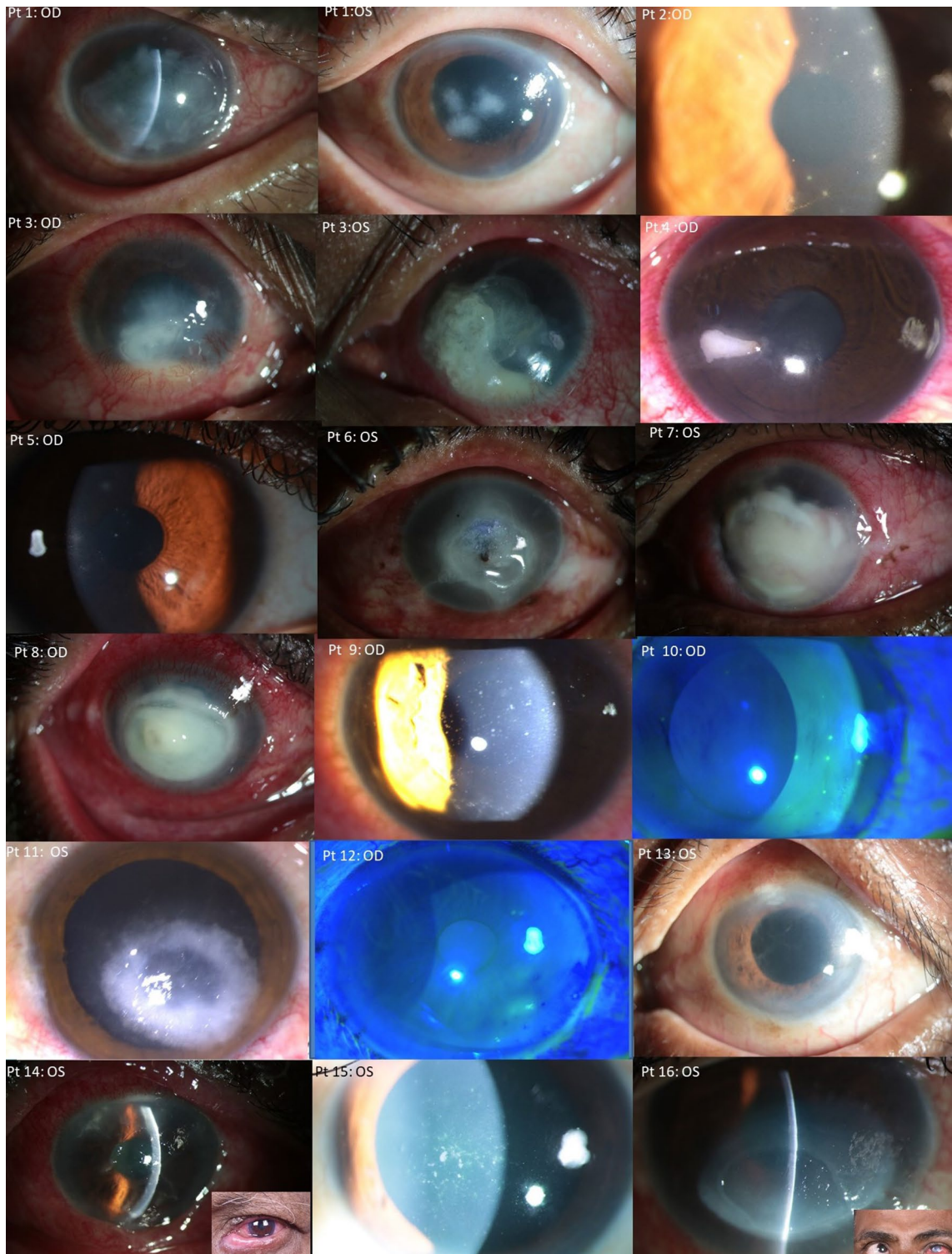
and management approach. The clinical characteristics of the corneal involvement were photo-documented. Diagnostic procedures such as corneal scrapings and biopsy along with microbiological work-up as described earlier [7] were undertaken when felt necessary for making a clinical diagnosis. The spectrum of microorganisms that caused infective keratitis was compared with those without the history of COVID-19 ( $N=3299$ ) during the same period of study.

## Results

Table 1 illustrates the demographics, clinical profile, management and outcomes of the 16 patients. Table 2 shows the correlation of presumed risk factors associated with the type of keratitis. Figure 1 shows the clinical photographs of the keratitis in the 16 patients. Figure 2 shows representative microbiological diagnosis of keratitis samples.

### Demographics

Median age of the patients was 43 (interquartile range 35–55.5) years. Majority (15/16, 93.75%) were males. Unilateral affliction was predominant (13/16, 81.25% patients). The 3 who had bilateral involvement, the microorganism causing keratitis was the same in 2 patients (patient 1 and 2) and could not be ascertained in one eye of one patient (patient 3). The mean presenting visual acuity was 1.12 Log MAR (range-Hand motions to 20/20). The median duration of ocular symptoms was 8.5 (interquartile range 7–14) days. The median duration between COVID-19 diagnosis and the ocular symptoms was 29 (interquartile range 22–57) days. The median duration of resolution from



**Table 1** Demographics, clinical profile, management and outcomes

Pt. no	Age/Sex	Eye affected	BCVA	Clinical features	Duration of ocular complaints (days)	Duration between COVID-19 diagnosis and ocular symptoms	Presumed risk factors/ Comorbid associations	Diagnostic work-up	Diagnosis of keratitis	Management	Time of resolution and outcomes
1	69/m	OD OS	HM CFCF	OU Deep stromal infiltrate, pigment clumps on endothelium	210	28 (OU)	Diabetes, Hypertension, coronary artery disease, s/post Stent Surgery	Confocal microscopy, AC Tap, Histopathology of Corneal sample	OU Microsporidia Stromal keratitis	OD Th PK OS Th PK	7 days, No recurrence till last follow up
2	60/m	OD OS	20/20 20/20	OU Punctate epithelial lesions	7	21 (OD) 31 (OS)	Diabetes, H/o Hospitalization	Corneal scraping	OU Microsporidia Keratoconjunctivitis	Medical Mx	10 days in both eyes
3	49/m	OD OS	20/500 CFCF	OD Infiltrate 2×3.5 mm OS status post Glue application(elsewhere)	10	25 (OU)	H/o hospitalization, Steroids	Corneal Scrapings	OD Aspergillus niger OS Microbial keratitis Microbiology unascertained, (S/post TA)	Medical Mx, OD TA and BCL, Amniotic membrane grafting, tarsorrhaphy Medical Mx	28 days in each eye
4	24/m	OD	20/40	Corneal infiltrate 4×2.5 mm with plaque	10	7	-	Corneal Scraping	Fungus	Medical Mx	7 days
5	32/m	OD	20/40	Punctate epithelial lesions, status post LASIK	14	30	H/o hospitalization, Oxygen therapy, Steroids	Corneal Scraping	Microsporidia keratoconjunctivitis	Medical Mx	7 days
6	44/m	OS	PL PR Inaccurate	Perforated corneal ulcer, OD Phthisical eye	15	23	H/o hospitalization, Oxygen therapy	Corneal Scraping	Fungus	Tissue adhesive and BCL Tenonplasty, tarsorrhaphy	70 days

**Table 1** (continued)

Pt. no	Age/Sex	Eye affected	BCVA	Clinical features	Duration of ocular complaints (days)	Duration between COVID-19 diagnosis and ocular symptoms	Presumed risk factors/Comorbid associations	Diagnostic work-up	Diagnosis of keratitis	Management	Time of resolution and outcomes
7	48/m	OS	HM	> 8X8mm infiltrate	10	80	–	Corneal Scraping	Fun-gus + Staphylococcus hominis	Th PK	10 days
8	39/m	OD	HM	Infiltrate 5 × 5.5 mm, vascularization	42	8	H/o hospitalization, Oxygen therapy, Steroids	Corneal Scraping	Aspergillus flavus	Th PK	35 days
9	14/f	OD	20/20	Punctate epithelial lesions, AC reaction and KP	7	21	–	Corneal Scraping	Microsporidia keratoconjunctivitis	Medical Mx	21 days
10	44/m	OD	20/30	Punctate epithelial lesions	7	55	H/o Hospitalization, Oxygen therapy	Corneal Scraping	Microsporidia keratoconjunctivitis	Medical Mx	14 days
11	42/m	OS	20/60	Ring infiltrate 4 × 4 mm	7	35	–	Corneal Scraping	Pythium spp.	Medical Mx	14 days
12	41/m	OD	20/25	Punctate epithelial lesions	5	60	–	Corneal Scraping	Microsporidia keratoconjunctivitis	Medical Mx	7 days
13	73/m	OS	PL PR Inac-curate	Side port infiltrate and endophthalmitis Status/Post Cataract surgery 1 month back, OD Absolute eye	14	90	H/o hospitalization, Oxygen therapy	Side port scraping, Vitreous biopsy	Mucor spp.	Th PK	42 days
14	71/m	OS	20/100	Lid margin excoriation, Dendritic epithelial keratitis	5	23	H/o hospitalization, Steroids	Nil	HZO	Medical Mx	56 days
15	41/m	OS	20/50	Punctate epithelial keratitis	5	47	H/o hospitalization	Corneal Scraping	Microsporidia KC	Medical Mx	21 days

**Table 1** (continued)

Pt. no	Age/Sex	Eye affected	BCVA	Clinical features	Duration of ocular complaints (days)	Duration between COVID-19 diagnosis and ocular symptoms	Presumed risk factors/Comorbid associations	Diagnostic work-up	Diagnosis of keratitis	Management	Time of resolution and outcomes
16	52/m	OS	20/600	Neurotrophic Keratitis, Abducens Palsy status/post ROCM	7	83	H/o hospitalization, Steroids	Nil	Neurotrophic Keratitis	Bandage Contact lens application, Tarsorrhaphy	7 days

(BCVA- best corrected visual acuity, AC- anterior chamber, TA- tissue adhesive, BCL- bandage contact lens, H/o- history of, ROCM- rhino-orbital-cerebral mucormycosis, ThPK- therapeutic penetrating keratoplasty, Mx- management)

the time of first diagnosis was 14 (interquartile range 7–31.5) days.

#### Microbiological spectrum

Microsporidia keratitis was diagnosed in 9 eyes of 7 patients (7/16, 43.75%), of which 2 eyes had bilateral stromal keratitis and rest 7 eyes had keratoconjunctivitis. One eye of one patient with microsporidia keratoconjunctivitis had endothelitis in association. Six eyes of six patients (6/16, 37.5%) had fungal keratitis, one eye of one patient (6.25%) had *Pythium* keratitis, one eye of one patient (6.25%) had herpes zoster ophthalmicus and one eye of one patient (6.25%) had neurotrophic keratitis. The fungal isolates identified included *Aspergillus* spp. (*Aspergillus niger* and *Aspergillus flavus*) in two eyes of two patients and *Mucor* spp. in one eye of one patient.

#### Management of COVID-19 illness

Of the 16 patients, 10 (62.5%) had a history of hospitalization during active COVID-19 illness, 5 (31.25%) had received oxygen therapy, and 5 (31.25%) had been treated with steroids.

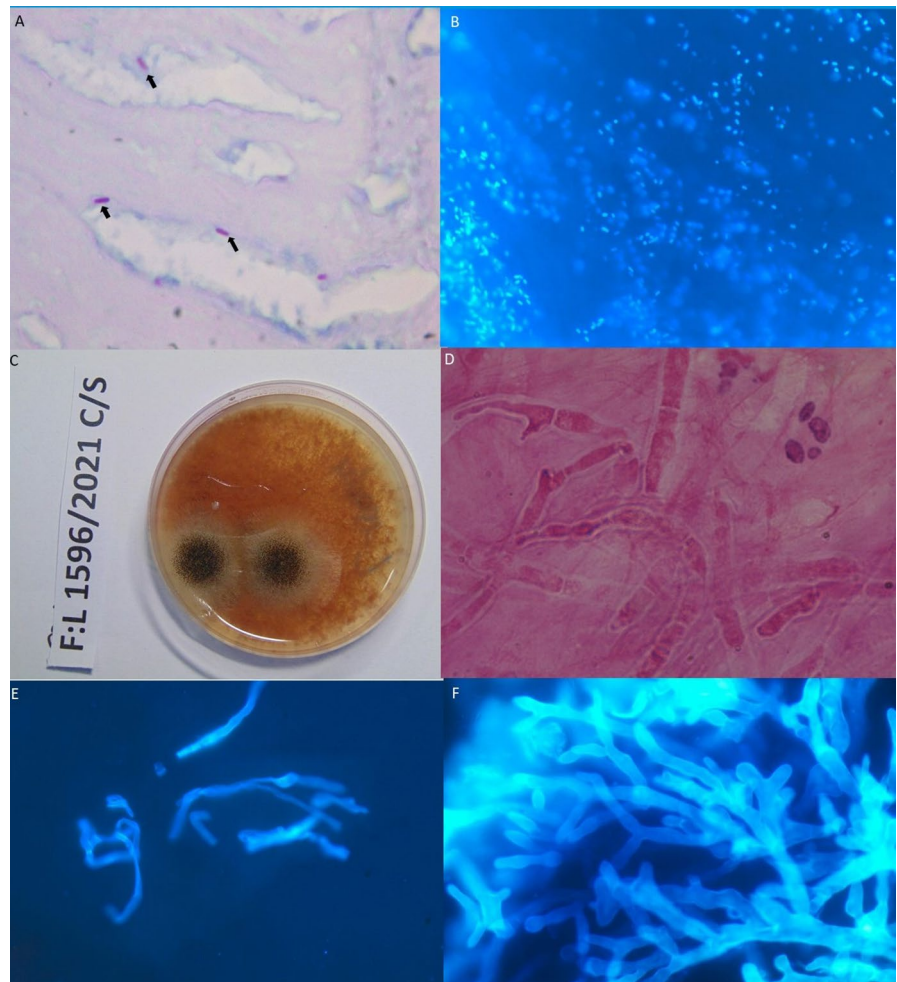
#### Corneal sensations

Corneal sensations were evaluated in eight eyes of six patients, and all eyes had either reduced or absent sensations (tested with a wisp of cotton). The documentation of corneal sensations was missing in ten patients.

#### Management and outcomes

Ten eyes of nine patients were managed with medical treatment alone, five eyes of four patients underwent therapeutic penetrating keratoplasty, two eyes of two patients were managed by glue application and three eyes of three patients required tarsorrhaphy along with amniotic membrane grafting/tenonplasty. The median duration of resolution of keratitis from the time of first visit was 14 days.

**Fig. 2** **A** Histopathology of the corneal sample of patient 1 after therapeutic penetrating keratoplasty, showing microsporidia (black arrows); **B** Smear from patient 2 showing plenty of microsporidia (Calcofluor white 40x); **C** Culture plates inoculated with corneal scrapings from the right eye of patient 3 showing colonies of *Aspergillus niger*; **D** Smear from the left eye of patient 6 showing fungal filaments (Gram stain 100x); **E** Smear examination from the left eye of patient 11 showing ribbon like filaments characteristic of *Pythium* spp. (Calcofluor white 40x); **F** Smears from the corneal scrapings of patient 13 showing fungus(*Mucor* spp.) (Calcofluor white fluorescence 40x)



**Table 2** Co-relation of presumed risk factors associated with the type of keratitis

Type of keratitis	No. of patients (No. of eyes)	Hypertension	Coronary artery disease	DM	Trauma/ Foreign body history	History of hospitalization	Oxygen therapy	Steroid Therapy	*Reduced/ Absent corneal sensations
Microsporidia Keratitis (Stromal + Keratoconjunctivitis)	7 (9 eyes)	1	1	2	-	4	2	1	2 (4 eyes)
Fungal Keratitis	6 (6 eyes)	-	-	-	1	4	3	2	2 (3 eyes)
Pythium	1 (1 eye)	-	-	-	-	-	-	-	-
HZO	1 (1 eye)	-	-	-	-	1	-	1	1
Neurotrophic Keratitis	1 (1 eye)	-	-	-	-	1	-	1	1

\*Checked in 8 eyes of 6 patients, not evaluated in others

## Discussion

The patients infected with SARS-CoV-19 may develop of new or recurrent symptoms that occur after the symptoms of acute illness have resolved. Much has been described about systemic associations and findings in the convalescence phase of COVID-19 infection [5]. The reported incidence of ocular symptoms in temporal association with COVID-19 infection ranges from 2 to 32%, which includes conjunctival congestion, increased tearing, recurrent conjunctivitis, keratitis, scleritis, anterior uveitis, optic neuritis, and retinopathy [6]. Chen et al. [8] described acute conjunctivitis in most patients and a small percentage of keratitis (14/535, 2.6%) in their series on ocular symptoms in acute COVID-19 illness phase. A relapsing keratoconjunctivitis which was microbiologically sterile and had nonspecific corneal cellularity has been reported by Huatama et al. [9].

Herein, we report the clinical spectrum of keratitis that was treated within 3 months of diagnosis of acute COVID-19 infection. We chose the arbitrary time frame of 3 months, as a rough approximation to evaluate the concomitant and temporal association of acute COVID-19 illness and keratitis.

Bilateral involvement was noted in 3 patients, of which one was a patient with microsporidia stromal keratitis (Patient 1), one with microsporidia keratoconjunctivitis (Patient 2) and one patient (Patient 3) had fungal keratitis (*Aspergillus niger*) in one eye, and non-conclusive microbiological diagnosis (scrapings could not be sent from this eye due to cyanoacrylate glue in place at the time of initial visit, but infiltrate resolved on empirical treatment with anti-fungal and anti-bacterial). In the 3 patients (1, 2, and 3) with bilateral keratitis, the duration between acute COVID-19 diagnosis to first ocular symptom was 28, 21 and 25 days, respectively. In the patient 1 with microsporidia stromal keratitis, there were several systemic comorbidities that included diabetes, hypertension, coronary artery disease with stent surgery in the past. The patient 2, who had microsporidia keratoconjunctivitis, was diabetic and had history of hospitalization following initial diagnosis. In the patient 3, with proven fungal infection in one eye and non-conclusive microbiological diagnosis in the other eye, there were no systemic diseases, but he had a history of hospitalization and treatment with steroids following acute COVID-19 illness. In the rest other

patients, all of whom had unilateral involvement, there was no history of any prior systemic diseases. Amongst those with unilateral involvement, eight had a history of hospitalization, five had received oxygen therapy during hospitalization, and five had received steroid treatment during the illness. Patients 4 and 8 gave a history of ocular symptoms within 2 weeks of COVID-19 illness and were diagnosed to have fungal keratitis when they presented to the clinic.

We observed a preponderance of microsporidia keratitis, followed by fungus, *Pythium*, and herpes zoster. There were certain peculiarities in the clinical presentation of keratitis in some of these patients, which is described here. The clinical picture in one eye with fungal keratitis (OD of patient 3) was unusual, and at presentation resembled that which is typical of a neurotrophic keratitis (heaped up epithelial defect). One patient (Patient 13) had infection at the paracentesis/side port with *Mucor* spp that was associated with low-grade endophthalmitis. *Mucor* species is an extremely rare cause of keratitis, and only a few isolated cases of keratitis have been identified at our microbiology services (5 cases over a span of 5 years from 2016 to 2020, and/or 5 positive cases from a total of 12,719 keratitis samples evaluated in 5 years). This patient had undergone cataract surgery elsewhere, for a mature cataract that developed one month after recovery from COVID-19 infection. The uneventful cataract surgery was complicated by side port infection due to *Mucor* species and endophthalmitis probably secondary to spread of sinus mucormycosis which may not been recognized at the time of cataract surgery. One patient (Patient 14) had HZO following recovery from COVID-19 illness. The predisposing risk factor in this patient could be attributed to the usage of systemic steroids during management of acute COVID-19 illness. Another patient (Patient 16) had neurotrophic keratitis because of neurological complications following acute COVID-19 illness.

We documented impaired corneal sensations in eight eyes of six patients (Patient 1, 2, 3, 13, 14 and 16). Corneal sensations were not documented in the rest others. Reduced corneal sensations or hypoesthesia is a risk factor for epithelial breakdown and can predispose to microbial keratitis. A confocal microscopy-based study found that patients who have recovered from COVID-19 illness tend to have decreased nerve density, nerve fibre length with increase in dendritic cells. The neural changes are notable in



COVID-19 survivors typically at  $3.7 \pm 1.5$  months after diagnosis and with neurologic symptoms compared to healthy controls [10]. In our series, those with bilateral keratitis had absent sensations noted in both eyes. In one patient, patient (Patient 3), the clinical appearance was noteworthy of neurotrophic keratitis with fungal infection.

Medical management alone was effective in nine eyes of eight patients. Therapeutic penetrating keratoplasty was required in five eyes of four patients, of which one also needed a pars plana vitrectomy (Patient 13) due to posterior segment spread of infection. Supportive management therapy (Glue application, amniotic membrane grafting and tarsorrhaphy) was needed in three eyes of three patients. All patients had a resolution of infection either on medical treatment or surgical management with no recurrences in the follow-up period.

Although the direct causal association of keratitis with COVID-19 infection cannot be concluded from this study, the temporal association of keratitis with the acute illness and convalescence phase is noteworthy. On analyzing the profile of microorganisms that caused infective keratitis in those without history of COVID-19 ( $N=3299$ ), 2939 (89%) had fungal keratitis, 27(0.8%) had *Pythium* keratitis, 330 (10%) had bacterial, 5 had *Nocardia* and 10 had *Acanthamoeba* keratitis. None in this group had microsporidia and *Mucor* spp. as a cause of keratitis in the study period. Majority of the patients (15/16) in this study were seen following the second wave of COVID-19 pandemic. In India, the second wave of COVID-19 was much more devastating than the first wave. Ours is a tertiary referral eye care centre, and hence, only those patients with stable systemic condition after COVID -19 infection would have visited the hospital for their eye complaints. The association of keratitis could be purely coincidental, but it is also possible that altered host immune responses and neurological alterations following acute illness could be implicated in the pathogenesis of the keratitis following COVID-19 infection.

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#### Declarations

**Conflict of interest** The authors declares that they have no conflict of interest.

#### References

1. Dong E, Du H, Gardner L (2020) An interactive web-based dashboard to track COVID-19 in real time. *Lancet Inf Dis* 20:533–534
2. Del Rio C, Collins LF, Malani P (2020) Long-term health consequences of COVID-19. *JAMA* 324(17):1723–1724
3. Michelen M, Manoharan L, Elkheir N et al (2021) Characterising long COVID: a living systematic review. *BMJ Glob Health* 6(9):e005427
4. Desforges M, Gurdasani D, Hamdy A et al (2021) Uncertainty around the long-term implications of COVID-19. *Pathogens* 10(10):1267
5. Nalbandian A, Sehgal K, Gupta A et al (2021) Post-acute COVID-19 syndrome. *Nat Med* 27(4):601–615
6. Hu K, Patel J, Swiston C, Patel BC Ophthalmic manifestations of coronavirus (COVID-19). *NCBI Bookshelf*
7. Mundra J, Dhakal R, Mohamed A et al (2019) Outcomes of therapeutic penetrating keratoplasty in 198 eyes with fungal keratitis. *Indian J Ophthalmol* 67(10):1599–1605
8. Chen L, Deng C, Chen X et al (2020) Ocular manifestations and clinical characteristics of 535 cases of COVID-19 in Wuhan, China: a cross-sectional study. *Acta Ophthalmol* 98(8):e951–e959
9. Hutama SA, Alkaff FF, Intan RE et al (2021) Recurrent keratoconjunctivitis as the sole manifestation of COVID-19 infection: a case report. *Eur J Ophthalmol*. <https://doi.org/10.1177/11206721211006583>
10. Bitirgen G, Korkmaz C, Zamani A et al (2021) Corneal confocal microscopy identifies corneal nerve fibre loss and increased dendritic cells in patients with long COVID. *Br J Ophthalmol*. <https://doi.org/10.1136/bjophthalmol-2021-319450>

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