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ORIGINAL RESEARCH

Impact of the COVID-19 Pandemic on the Incidence and Characteristics of Culture-Positive Microbial Keratitis at a Tertiary Eye Hospital in the UK

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Purpose: The COVID-19 pandemic has led to drastic changes to the daily lives of those living in the United Kingdom. We hypothesized that the effect of the imposed lockdown on both behaviour and social interaction has the potential to influence the characteristics of microbial keratitis presenting locally to Manchester Royal Eye Hospital — a major tertiary eye centre in the UK.
Methods: We conducted a retrospective case-note review of all positive corneal scrape cultures identified by our local microbiology laboratory during the year since the announcement of lockdown measures in the UK (23 March 2020 to 23 March 2021). Culture results were compared with previously collated, published "baseline" data from prior to the onset of the COVID-19 pandemic (2004–2019). Statistical analysis was undertaken, predominantly looking at the incidence of microbial keratitis and the variety of cultured pathogens.
Results: A total of 6243 corneal scrape results were reviewed. Comparison of data between the COVID-19 pandemic and subsequent lockdown did not show a significant change in the incidence of culture-positive microbial keratitis: mean annual positive samples during 2004–2019 were 128 (35%) vs 91 (29%) during lockdown (P=0.096). No statistically significant shifts in the incidence of organism subtypes — fungi, acanthamoeba, Gram-positive bacteria, or Gram negative bacteria — were identified (P=0.196, 1, 0.366, and 0.087, respectively).
Conclusion: Contrary to our hypothesis, our results suggest that the COVID-19 pandemic did not alter the incidence or characteristics of microbial keratitis presenting to Manchester Royal Eye Hospital in the year following the implementation of lockdown measures in the UK.
Keywords: COVID-19, keratitis, microbiology, microbial keratitis

Introduction

Microbial keratitis is a condition encountered across the world that can lead to irreversible sight loss.[1] The incidence of the condition and causative microbes have been shown to have geographic and seasonal variation as a result of differing risk factors across regions.[2,3] Previously identified risk factors include socioeconomic status, contact lens wear and hygiene practices, trauma, recent surgery, and a compromised ocular surface.[4,5] Environmental factors, such as humidity, climate, and pathogenic environments, have also been shown to play a role.[6–9]

As the COVID-19 pandemic evolves and with the near-global enforcement of measures to curb the spread of the SARS-COV-2 virus, the behaviours and activities of the general population have drastically changed. Lockdown measures and social distancing were introduced in the UK on 23 March 2020 with the aim of reducing contact between humans and to limit transmission of the virus. This strategy is widely accepted by multiple international bodies to be the most effective strategy in limiting virus transmission.[10]

One of the most significant measures in place to deter the spread of this airborne virus is the use of face masks to limit and capture the spread of infective respiratory droplets. In the earlier stages of the pandemic, it was hypothesized that face masks may redirect expiratory airflow upwards towards the eyes, resulting in dispersion of oral flora onto the ocular surface and increasing the risk of post-intravitreal injection endophthalmitis. Patel et al recently published a large

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multicentre retrospective study of 505,968 intravitreal injections performed in the US that did not suggest that patient face-mask use influenced the rate of presumed acute-onset bacterial endophthalmitis (OR 0.74, 95% CI 0.51–1.19; *P*=0.097), but in fact reduced the rate of culture-positive endophthalmitis (OR 0.46, 95% CI 0.22–0.99; *P*=0.041).[11] As the incidence of oral flora–related endophthalmitis is overall an extremely rare event, despite this study's large sample, the authors concluded that the study was underpowered and unable to demonstrate an effect of patient mask use on the incidence of oral flora–associated endophthalmitis.[11] Consequently, an association between mask use and oral flora–related endophthalmitis and other ocular infections, such as microbial keratitis, remains unestablished.

Beyond mask use, we also hypothesized that other behavioural factors related to the pandemic may have played a role in affecting patients' ocular surfaces and their exposure to pathogens. These included: infection-prevention measures, social distancing, social isolation, handwashing, disinfection protocols, widespread use of alcohol hand gels, change in lifestyle, indoor living, less traffic-related pollution, less contact lens wear at home, and increased screen time whilst working from home. The aim of this study was to assess what impact the COVID-19 pandemic has had on the incidence and characteristics of microbial keratitis presenting to Manchester Royal Eye hospital — a major tertiary eye hospital in the UK.

Methods

Ethics

Using the NHS Health Research Authority decision tool for ethics approval, this study was deemed not to require any ethics approval, as it employed anonymous unidentifiable retrospective patient data that was not generalisable and the study protocol did not involve any deviation from the expected standard of patient care.

Data Collection

Data were collected in the form of all corneal scrape specimens sampled in the year from the UK commencing its first national lockdown (23 March 2020). This period will be referred to as "lockdown" in the remainder of the text. Data were retrieved using our microbiology laboratory's established electronic database, and included date of the scrape with culture results and antimicrobial sensitivities. Equivalent data for 2004–2019 were also retrieved to use as our comparison control. Scrape data were categorised according to organism subtypes: fungi, acanthamoeba, and Gram-positive and Gram-negative bacteria.

Statistical Analysis

Statistical analysis was performed using SPSS 25.0 and χ^2, two-sample *t*, and Mann–Whitney *U* tests between pre-COVID and post-COVID groups where applicable. $P \leq 0.05$ was considered statistically significant.

Corneal Scrape Protocol

The methodology for corneal scrape specimen sampling was standardised as per departmental policy. This policy, as well as the microbiological methods utilised for organism identification and antibiotic-sensitivity testing at Manchester Royal Eye hospital, was described by Tan et al in 2017.[12]

Results

A total of 6243 scrape results were included in this study. During the lockdown period, 312 scrapes were sent for analysis, with 91 (29%) producing a positive culture result. This is comparable with pre-lockdown figures of an average of 364 scrapes per annum with a culture-positive result of 128 (35%, *P*=0.096 using χ^2 testing (Table 1). We did note that there was a suggestion that the rate of positive scrape results was reduced, perhaps alluding to a decreased infection rate overall; however, these results did not achieve statistical significance. As such, the null hypothesis remains true, i.e., the incidence of microbial keratitis was not significantly influenced by the COVID-19 pandemic or measures implemented during the lockdown period. Table 2 shows the raw-data trends of scrape organisms grown from 2004 to the lockdown period. Table 3 compares the mean number of organism subtypes prior to lockdown and also during the lockdown period.

Table 1 Cross-tabulation of scrape positivity for pre-lockdown vs lockdown

			Outcome		
			Culture positivity		
			Positive	Negative	Total
P=0.096*	Intervention	Pre-lockdown	128 (35%)	236 (65%)	364
		Lockdown	91 (29%)	221 (71%)	312

Note: *χ^2 test.

Discussion

The aim of this study was to assess the effect of the COVID-19 pandemic and the resultant national lockdown on the incidence and microbiological characteristics of microbial keratitis presenting to a major tertiary eye hospital in Manchester in the UK. Research in the early stages of the pandemic focused on identifying the systemic implications of a new virus. Whilst the literature suggests that dry eyes, conjunctivitis, keratitis and vein/cavernous sinus thrombosis, and other ocular pathology may be associated with COVID-19 infection, overall ocular morbidity from this viral infection is accepted to be minimal.[13–19]

With the awareness of changing antimicrobial trends and contact lens usage, the authors have previously discussed the importance of understanding local pathogenic variations, with other units also examining their own data.[3,12,20–25] Large-scale societal and behavioural changes, such as social distancing and mask wearing, have the potential to have profound effects on certain diseases and can aid our understanding of disease pathogenesis. Our knowledge of the SARS-COV-2 virus is increasing as we see and treat more cases of the disease. However, the longer-term effects of the virus are likely to be more subtle, both in terms of any future morbidity from the disease itself but also the implications of trying to manage future waves of the pandemic, with long-term mask usage likely to continue for the foreseeable future.

With the widespread introduction of infection-prevention protocols and the enforced usage of personal protective equipment, reports regarding the increased incidence of dry-eye symptoms started to emerge from the literature.[13,26–29] It has been postulated that personal protective equipment and mask use may lead to a compromised tear film as a result of increased evaporation or even mechanical processes that lead to malposition of the eyelids, e.g., mask tape leading to ectropion, in addition to altered airflow surrounding the periocular area.[26,29] A compromised tear film is known to result in reduced precorneal tear-film corneal coverage and epithelial microbreaks, which can increase the risk of ocular infections due to a reduction in the innate host ability of pathogen clearance when in contact with the ocular surface.[26,30] Exacerbations in dermatological conditions in health-care workers and the general population have also been reported.[31] Rosacea and other facial manifestations of dermatological disease are known to influence the ocular surface.[32] The above theories led us to our hypothesis that COVID-19 or associated change in behaviours in our local population may have influenced the local incidence and characteristics of microbial keratitis.

Tan et al conducted a 12-year analysis of microbial keratitis presenting to Manchester Royal Eye Hospital.[12] To the authors' knowledge, this is the largest study of microbial keratitis trends in the UK to date.[22–25] Using an expanded dataset, we did not find any particular deviation from the baseline incidence of organisms when compared with those encountered during the lockdown period. We do however note that there are potential flaws with our statistical methodology, although conclusions may still be drawn from the results. This is in part due to the necessity to compare an average of 16 years' worth of data with that of only 1 year of lockdown data. As this was a real-world study, examining a real world pandemic scenario, this is impossible to avoid. It is thus important to continue to examine the microbial trends, as continued mask wearing and social distancing may well play an evolving role into the future. As such, when comparing the statistical means from the pre-lockdown data to the results of the lockdown period, one does note that the values for the lockdown dataset are lower in numbers for all cases, particularly notable for the fungal keratitis subset. This may thus be unmasking an inherent and unavoidable type 2 error, which could only be corrected were the pandemic to continue in its current form for several years longer — which, hopefully for everyone involved, will not happen.

Table 2 Data trends of scrape organisms 2004–2019 and for lockdown (2020)

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Mean (SE) pre-lockdown	Lockdown (2020)
Fungi	8	3	6	2	4	14	15	7	3	15	5	9	19	12	5	5	7.8 (1.3)	1
Acanthamoeba	2	1	0	0	1	2	0	5	8	5	2	8	5	6	1	5	3.1 (0.7)	2
Gram-positive	79	84	94	85	101	100	69	87	57	73	44	73	72	65	74	105	77.9 (4.0)	63
Gram-negative	33	31	38	33	40	31	44	36	36	34	26	45	51	47	47	44	37.7 (1.9)	25

Table 3 Mean number of keratitis subtypes prior to lockdown with number of cases during lockdown

Organism	Mean (SE) pre-lockdown	Lockdown	*P*
Fungi	7.8 (1.3)	1	0.196*
Acanthamoeba	3.1 (0.7)	2	1**
Gram Positive	77.9 (4.0)	63	0.366*
Gram Negative	37.7 (1.9)	25	0.087*

Notes: *Two-sample *t* test; **Mann–Whitney *U* test.

Another limitation of this study was the inability to directly identify any causative factors that may influence the incidence and characteristics of microbial keratitis. One accepted limitation of our large sample is the lack of patient demographic data. The primary aim of this paper was to look at the causative pathogens of the microbial infections, rather than specific patient demographics. This has been done in detail for specific pathogens in other publications.[21] Further to this, we note that the COVID-19 status of patients producing positive culture results was not assessed. Given the COVID-19 protocols at our hospital, only patients admitted for severe keratitis received a COVID-19 PCR test. We encouraged as many patients as possible to be treated on an outpatient basis, resulting in these patients not having their COVID-19 status assessed. These data are thus unobtainable. Whilst all our inpatients were screened as negative for COVID-19 (n=13), the selection bias of screening out milder presentations of keratitis does not allow for any further reliable and generalizable conclusions. Multiple factors may influence the annual incidence of microbial keratitis, and thus we opted to use a 16-year (as far as our electronic microbiological records extend) control period to allow for any expected annual confounding factors that may have influenced trends in keratitis rates.[12]

Lockdown measures in the UK were linked with a marked decrease in emergency department presentations.[33] This effect was also identified in our own eye emergency department.[34] This raised the concern that patients requiring urgent treatment for ocular conditions, such as microbial keratitis, may not seek appropriate urgent care.[35] Sight-threatening conditions, such as retinal detachment, were found to be reduced compared to pre-lockdown figures.[34] We are somewhat reassured that there was no significant fluctuation in the number of corneal scrape samples, suggesting that the number of presentations of microbial keratitis has not reduced dramatically, although the painful nature of the condition is likely to play a part in ensuring patients present to ophthalmic services, which may well be the determining factor for why patients present to the emergency department ahead of other painless forms of sight loss. A non-significant decrease in the incidence of samples for microbial keratitis may suggest that patients with milder infections have been able to access and receive treatment by other health-care providers specifically set up as part of the NHS response to the pandemic.[36] Another potentially confounding factor may be that measures introduced in order to reduce patient–doctor contact time may have resulted in some less severe cases not receiving microbiological sampling. However, despite this, the standard protocol within our unit is to sample any ulcer with an associated infiltrate >1 mm in size. This may have inherently "screened" out more mild cases that were not sampled.

With all of the aforementioned being considered, our dataset would suggest that the use of widespread infection-prevention measures have not had a negative impact on our local population's corneal health. Whilst the results are not generalizable, these findings could be used to inform infection-control measures and protocols for patients with microbial keratitis presenting to similar tertiary ophthalmic services in the UK. Our local arrangements for the delivery of emergency eye care for microbial keratitis, infection-prevention practices, and encouraging changes in behaviour of our local population do not appear to have significantly affected the incidence or characteristics of microbial keratitis. We would encourage other units to assess their local incidence and characteristics of microbial keratitis so that the full impact of infection-prevention protocols on ocular health can be ascertained.

In conclusion, this retrospective study reviewed and compared all corneal scrapes undertaken at Manchester Royal Eye Hospital between 2004 and until 1 year following the enforcement of lockdown measures in the UK. We analysed the rates of culture-positive cases of infectious keratitis and characterised infections into subgroups. Overall, no statistically significant differences were identified in the incidence of microbial keratitis or the rates of causative pathogens. We did note that there was perhaps a small trend towards a reduced incidence of cases, in particular in the fungal subgroup. However, given data limitations and multiple confounding variables, the significance of this is uncertain. It is our hope that these findings may be useful in informing ophthalmic health-care providers assessing and treating patients with microbial keratitis in their own local populations and that it adds to an emerging body of evidence as we continue to recover from the COVID-19 pandemic.

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