The impact of the COVID-19 pandemic on microbial keratitis presentation patterns

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Background, Aims and Methods

Background: Microbial keratitis (MK) is the most common non-surgical ophthalmic emergency, and can rapidly progress, causing irreversible sight-loss. Emergency Departments (EDs) across England experienced a significant decrease in activity during the national lockdown period [1] raising concerns about whether patients were seeking help appropriately. Concurrently, rising numbers of reports describe public apprehensions about attending hospital or seeking medical attention [2]. Our group previously characterised public perceptions of eye symptom severity and consequent health seeking behaviour (Butt, GF, ARVO-Abstract[3546115], 2021). The comparison of various clinical scenarios in normal and pandemic contexts revealed that respondents felt materially less of an impetus to seek in-person clinical help during the pandemic. For mild self-limiting disease, this study highlighted the potentially beneficial adaptive behaviours that may reduce the risk of COVID-19 exposure; however, this difference was also noted in response to serious conditions such as MK, raising concerns about potential delays in presentation and consequent poorer clinical outcomes.
Aim: This study explored whether the COVID-19 (C19) national lockdown impacted upon the clinical presentation and outcomes of MK at a UK tertiary-care centre.
Methods: This study was conducted in accordance with the Declaration of Helsinki, and approval was obtained from Sandwell and West Birmingham Hospitals NHS Trust Department of Clinical Effectiveness (registration #1512) to undertake this project as a service evaluation. Medical records were retrospectively reviewed for all patients with presumed MK requiring corneal scrapes, presenting between 23rd March and 30th June in 2020 (Y2020), and the equivalent time windows in 2017, 2018 and 2019 (pre-C19). Cases of viral keratitis were excluded. All data were recorded in an adaptation of a validated data collection proforma used in a previous study [3] using Research Electronic Data Capture (REDCap© v9.6.3 2020 Vanderbilt University, Nashville, TN, USA). Data collected included patient demographics (sex, age, ethnicity and Index of multiple deprivation [IMD]), clinical details (presenting features, underlying risk factors, past ocular history, medications) and microbiology results. All analyses were performed using IBM SPSS 26 (IBM Corp. Armonk, NY), with p<0.05 deemed to be indicative of statistical significance throughout.

Results

Table 1. Characteristics of patients presenting with microbial keratitis

	Pre-C19		Y2020		
	N	*Statistic*	*N*	*Statistic*	p-Value
Age (years, *mean ± SD*)	181	55.5 ± 21.1	49	53.3 ± 17.8	0.503
Sex - male (%)	181	95 (52.5%)	49	31 (63.3%)	0.198
Ethnicity	164		38		0.864
White		112 (68.3%)		27 (71.1%)	
Asian		38 (23.2%)		7 (18.4%)	
Black		9 (5.5%)		3 (7.9%)	
Mixed / Other		5 (3.0%)		1 (2.6%)	
IMD decile	178		49		0.839*
1-3		96 (53.9%)		26 (53.1%)	
4-7		58 (32.6%)		19 (38.8%)	
8-10		24 (13.5%)		4 (8.2%)	
Laterality - right (%)	181	89 (49.2%)	49	27 (55.1%)	0.521
Duration of symptoms at presentation (days; *median (IQR)*)	121	3 (1-6)	37	4 (2-7)	0.201
Risk factors					
Contact lens	181	60 (33.1%)	49	14 (28.6%)	0.608
Underlying OSD (active)**	181	80 (44.2%)	49	26 (53.1%)	0.333
Previous keratitis***	181	20 (11.0%)	49	7 (14.3%)	0.616
Previous surgery/trauma	181	31 (17.1%)	49	10 (20.4%)	0.674
Concurrent trauma	181	10 (5.5%)	49	8 (16.3%)	**0.030**
Foreign body	181	3 (1.7%)	49	2 (4.1%)	0.289
Diabetes mellitus	181	17 (9.4%)	49	7 (14.3%)	0.304
Rheumatoid arthritis	181	6 (3.3%)	49	1 (2.0%)	1.000
Systemic immunosuppression	181	3 (1.7%)	49	6 (12.2%)	**0.004**
Thyroid eye disease	181	1 (0.6%)	49	0 (0.0%)	1.000

Table 1. *Abbreviations: Pre-C19, Pre-COVID-19 Years (2017,2018,2019); Y2020, year 2020; OSD, ocular surface disease; IMD, index of multiple deprivation; MK, microbial keratitis, IQR, inter quartile range. Bold p-values are significant at p<0.05. For risk factors, "previous" denotes that the risk factor had healed prior to onset of MK. *p-Value from Mann-Whitney U test, as the factor is ordinal. **Ocular surface disease, such as dry eye, affecting the patient at the time of presentation. ***Viral/bacterial/fungal/parasitic/marginal disease.*

Table 2. *Abbreviations: Pre-C19, Pre-COVID-19 Years (2017,2018,2019); Y2020, year 2020. Data are reported as median (interquartile range), with p-values from Mann-Whitney U tests.*

Table 2. Clinical assessments and outcomes

	Pre-C19		Y2020		
	N	*Statistic*	*N*	*Statistic*	p-Value
All Patients (N=230)					
Visual acuity at presentation (LogMAR)	181	0.60 (0.18 - 2.10)	49	0.60 (0.18 - 2.40)	0.785
Final visual acuity (LogMAR)	181	0.30 (0.00 - 1.78)	49	0.30 (0.18 - 1.48)	0.990
Ulcer area at presentation (mm^2)	112	3.0 (1.0 - 9.5)	36	4.0 (1.7 - 9.7)	0.520
Corneal involvement score	72	2 (1 - 5)	29	5 (2 - 5)	0.120
Excluding patients with pre-existing visual impairment in affected eye (N=163)					
Visual acuity at presentation (LogMAR)	126	0.30 (0.18 - 1.00)	37	0.48 (0.18 - 1.00)	0.608
Final visual acuity (LogMAR)	126	0.18 (0.00 - 0.60)	37	0.18 (0.10 - 0.78)	0.458
Ulcer area at presentation (mm^2)	78	2.0 (1.0 - 6.3)	27	2.9 (0.8 - 12.0)	0.575
Corneal involvement score	54	2 (1 - 5)	23	5 (2 - 5)	0.167

Table 3. Clinical sequalae

	Pre-C19	Y2020	p-Value
Admissions	59 (32.6%)	4 (8.2%)	**<0.001**
Complications			
Re-admission*	1/59 (1.7%)	0/4 (0.0%)	1.000
Corneal perforation	12 (6.6%)	2 (4.1%)	0.740
Endophthalmitis	2 (1.1%)	1 (2.0%)	0.514
Phthisis	1 (0.6%)	1 (2.0%)	0.381
Other complication**	3 (1.7%)	1 (2.0%)	1.000
Interventions			
Therapeutic lens	11 (6.1%)	0 (0.0%)	0.126
Corneal biopsy	0 (0.0%)	1 (2.0%)	0.213
Botulinum toxin ptosis	2 (1.1%)	1 (2.0%)	0.514
Corneal gluing	11 (6.1%)	1 (2.0%)	0.469
Evisceration	1 (0.6%)	0 (0.0%)	1.000
Repeat scrape	5 (2.8%)	2 (4.1%)	0.643
Tectonic corneal transplant	2 (1.1%)	0 (0.0%)	1.000
Temporary surgical tarsorrhaphy	0 (0.0%)	1 (2.0%)	0.231
Amniotic membrane graft	2 (1.1%)	0 (0.0%)	1.000
Other intervention***	2 (1.1%)	3 (6.1%)	0.066

Figure 1 – Clinical assessments and microbiology by year of admission

Clinical assessments (Figure 1a) are summarised using boxplots, outliers indicated with circles or asterisks for those outside the box by 1.5- or 3-times the interquartile range, respectively. Microbiology is summarised as the total proportion of the cohort that were culture positive (Figure 1b), and the distribution of culture isolates from these positive cases (Figure 1c); unlabelled bars consist of <5% of cases. Definitions of the microbial cultures are in Table 4.

Table 3. *Abbreviations: Pre-C19, Pre-COVID-19 Years (2017,2018,2019); Y2020, year 2020.*
*All analyses are based on N=181/N=49 in the two groups, unless stated otherwise, with p-values from Fisher's exact tests. Bold p-values are significant at p<0.05. *In the subgroup of patients who were admitted on initial presentation.*
***Consisted of one retinal detachment, one case of corneal graft failure and one iatrogenic corneal perforation at the time of corneal scraping in the pre-C19 cohort, and a retinal detachment in the 2020 cohort.*
****Consisted of one count of suture removal and one count of anterior chamber reformation following persistent aqueous humour leakage in the pre-C19 cohort, and two counts of corneal suture removal and one retinal detachment surgery in the Y2020 cohort.*

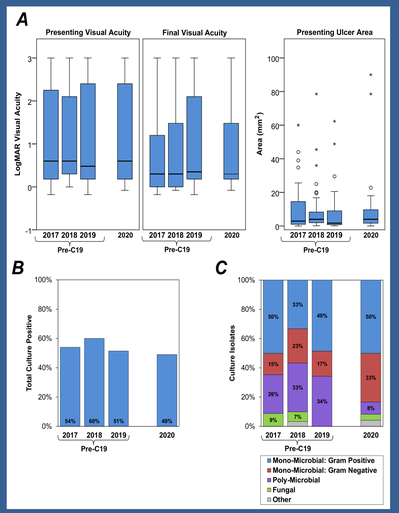


Table 4. Microbiology results summary

	Pre-C19	Y2020	p-Value
Total culture positive	99/181 (54.7%)	24/49 (49.0%)	0.520
Culture isolates			
Mono-microbial - gram positive	44/99 (44.4%)	12/24 (50.0%)	0.654
Mono-microbial - gram negative	18/99 (18.2%)	8/24 (33.3%)	0.160
Poly-microbial (bacterial only)	31/99 (31.3%)	2/24 (8.3%)	**0.022**
Fungal	5/99 (5.1%)	1/24 (4.2%)	1.000
Other*	1/99 (1.0%)	1/24 (4.2%)	0.353
Most frequent gram-positive isolates**			
Cutibacterium acnes	19/99 (19.2%)	1/24 (4.2%)	0.119
Staphylococcus epidermidis	18/99 (18.2%)	2/24 (8.3%)	0.359
Staphylococcus aureus	11/99 (11.1%)	6/24 (25.0%)	0.099
Streptococcus pneumoniae	10/99 (10.1%)	0/24 (0.0%)	0.207
Most frequent gram-negative isolates**			
All Moraxella species	17/99 (17.2%)	6/24 (25.0%)	0.389
Pseudomonas Aeruginosa	11/99 (11.1%)	0/24 (0.0%)	0.120
All Serratia species	5/99 (5.1%)	3/24 (12.5%)	0.187
Haemophilus influenzae	2/99 (2.0%)	1/24 (4.2%)	0.482

Table 4*. Abbreviations: Pre-C19, Pre-COVID-19 Years (2017,2018,2019); Y2020, year 2020. p-Values are from Fisher's exact tests and bold p-values are significant at p<0.05. Bacterial isolates are presented as the number of cases in which they were isolated, and as a percentage of the total number of culture positive cases in the respective group. Poly-microbial bacterial infections were defined as more than one pathogenic bacterial isolate. *Other cultures consisted of a mixed parasitic-bacterial case in the pre-C19 group, and a mixed fungal-bacterial infection in the Y2020 group. **Most frequent isolates are calculated as the total frequency of isolation of each species in all the samples, accounting for both mono- and poly-microbial isolates.*

Conclusions

- These results demonstrate the strong similarity between patients in the first UK lockdown and those from previous years, with respect to time-to-presentation, presenting VA and ulcer area, complications, interventions, and final VA, despite fewer patients being admitted for care.
- Concurrent trauma and use of systemic immunosuppression were greater in Y2020. The increase in ocular trauma during the lockdown is confirmed by other studies in the literature [4], which is a significant risk factor for MK. The reasons for increase in patients on immunosuppression is less apparent.
- Fewer poly-microbial infections occurred in 2020. Other changes in isolates were non-significant. These changes warrant further corroboration on a larger scale. Poor hand hygiene is a risk factor for MK and the increased handwashing during the pandemic may be contributing to the noted changes.
- Fewer ward admissions occurred in 2020 likely from clinicians wanting to limit patient exposure to hospital pathogens including COVID-19. The similarity between pre-C-19 and Y2020 groups, supports the notion that MK can be safely managed in the outpatient-dept.

References

1] NHS England Statistics. A&E Attendances and Emergency Admissions [Internet]. 2020. Available from: https://www.england.nhs.uk/statistics/statistical-work-areas/ae-waiting-times-and-activity/. **[2]** Pritchard R, Brady EM, Chudasama Y V, et al. Perceptions of Risk of Attending Hospital During The COVID-19 Pandemic: A UK Public Opinion Survey. (Under Rev BMC Public Heal [Internet]. 2020 Oct 6 [cited 2020 Oct 22]; Available from: https://doi.org/10.21203/rs.3.rs-76617/v1 **[3]** Moussa G, Hodson J, Gooch N, et al. Calculating the economic burden of presumed microbial keratitis admissions at a tertiary referral centre in the UK. Eye [Internet]. 2020 Dec 7 [cited 2021 Jan 2]; Available from: http://www.nature.com/articles/s41433-020-01333-9 **[4]** Pellegrini M, Roda M, Di Geronimo N, et al. Changing trends of ocular trauma in the time of COVID-19 pandemic [Internet]. Vol. 34, Eye (Basingstoke). Springer Nature; 2020 [cited 2021 Jan 11]. p. 1248–50. Available from: https://doi.org/10.1038/s41433-020-0933-x