Impact of the COVID-19 pandemic on uveitis patient care

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► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bjophthalmol-2021-320368).

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Received 1 September 2021
Accepted 11 January 2022
Published Online First 24 January 2022

To cite: Vu AF, Kodati S, Lin P, *et al*. *Br J Ophthalmol* 2023;**107**:790–794.

ABSTRACT

Background The COVID-19 pandemic has significantly changed practice of medicine and patient care worldwide. The impact of the pandemic on patients with uveitis is unknown. We developed the COVID-19 Practice Patterns Study Group to evaluate the effect of the pandemic on uveitis patient care.

Methods This is a multicentre, cross-sectional survey of uveitis specialists practising worldwide. A web-based survey was distributed through the mailing lists of international uveitis societies to assess modifications in patient care, and use of immunomodulatory therapies (IMTs),aswell as considerations regarding COVID-19 vaccination.

Results A diverse group consisting of 187 uveitis specialists from six continents participated in this survey. Most of these experts noted a disruption in clinical management of patients, including clinic closures or decrease in volume, patients missing in-person visits due to the fear of infection and difficulties obtaining laboratory testing. Most participants initiated (66.8%) and continued (93.3%) IMTs based on clinical presentation and did not modify their use of immunosuppressives. In cases of reported exposure to COVID-19 infection, most participants (65.3%) recommended no change in IMTs. However, 73.0% of the respondents did recommend holding all or select IMTs in case of COVID-19 infection. COVID-19 vaccine was recommended universally by almost all the specialists and 52% stated that they would counsel patients regarding the decreased immunogenicity and effectiveness of the vaccine in immunocompromised patients.

Conclusions Uveitis patient care has changed significantly since the beginning of the pandemic. The recommendations will continue to evolve as new data on IMTs and vaccination become available.

INTRODUCTION

On 30 January 2020, the WHO announced the COVID-19 outbreak as a 'public health emergency of international concern' and quickly escalated its characterisation of the disease as a 'pandemic' on 11 March 2020.[1] This unprecedented event has disrupted many facets of our society and continues to have an enormous impact on the economy, mental health and public health.[2] Ophthalmologists were significantly affected by lockdowns and curfews, shortage of personal protective equipment,[3] redeployments of physicians to inpatient units and emergency departments,[4] and the curtailing of non-emergent and elective visits and procedures.[5] Although ophthalmology clinics have largely reopened under loosening of restrictions on non-urgent visits and elective procedure, their practices have been partially or completely transformed.

Uveitis practice has particularly been affected by the pandemic. Non-infectious uveitis is a chronic condition in which timely diagnosis, prompt treatment and routine follow-up are crucial in preventing sight-threatening complications.[6] Decreased availability of routine, non-urgent ophthalmic care during the pandemic had unknown consequences on these patients. Moreover, control of inflammation in non-infectious uveitis often requires systemic treatment with systemic immunomodulatory therapy (IMT) including corticosteroids, conventional steroid-sparing IMTs and biological agents.[7] These medications suppress the immune system, therefore increasing patients' susceptibility to various infections. Treatment with these medications also requires routine monitoring of laboratory testing which may have been impacted by lockdowns and diversion of healthcare resources.

Due to the rapidly evolving nature of the pandemic and changing practice patterns, major uveitis societies and the American College of Rheumatology (ACR) have published ongoing recommendations on the use of IMTs.[8 9] On 11 December 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization for the first COVID-19 vaccine, and its distribution started soon afterwards.[10] This new development prompted discussions regarding modifications to treatment plans in patients receiving IMTs.[9] The aim of this study was to evaluate the uveitis patient care across the globe, to assess challenges specialists are facing in managing their patients within the evolving landscape of the pandemic, and to identify considerations and recommendations regarding COVID-19 vaccination in patients with uveitis.

METHODS

A questionnaire consisting of 30 questions was designed by the authors and used to create a web-based interactive survey (Qualtrics, Provo, Utah, USA). The questions are available and can be reviewed online (online supplemental appendix 1).

The survey consisted of a combination of multiple-choice questions with single and multiple response options; some of the questions allowed for additional free-text comments. Additional demographic questions were also included. The questions were divided into four categories looking at various modifications and adjustments made in specialists' clinical practice, use of systemic immunosuppressives, administration of local corticosteroids, and

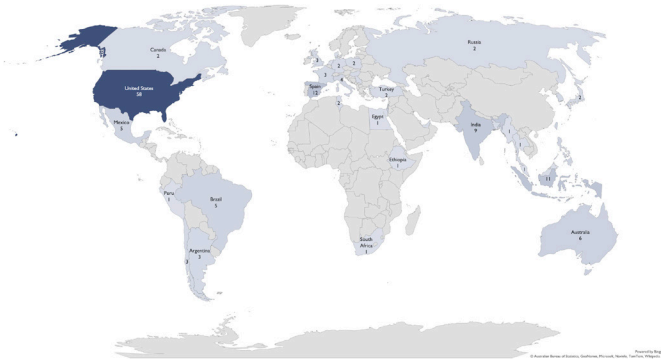

Figure 1 World map showing geographical distribution of specialists participating in this study (darker color shows more participants from each country). Map was generated using Microsoft Excel and Bing.

patient education regarding COVID-19 prevention and immunisation. Pilot testing was performed by the coauthors prior to final launch. The survey was then distributed among the members of the professional uveitis societies (the International Ocular Inflammation Society, the American Uveitis Society and the Young Uveitis Specialists) using the societies' listservs. Responses were completed between February and April 2021. Results were exported from the Qualtrics website to an Excel sheet and analysed using descriptive statistics.

RESULTS

Participants

A total of 187 uveitis specialists from 41 countries (51.6% female) participated in the survey (figure 1). These experts were at various stages of their professional career; most of them (n=127, 68.6%) were in practice for more than 5 years and 51% (n=95) had more than 10 years of experience managing patients with uveitis. Most of the participants were practising in an academic (n=97, 51.8%) or hybrid (n=62, 33.16%) setting. These specialists were leading their practice in various disciplines including retina and uveitis (n=86, 46.2%), primarily uveitis (n=44, 23.6%), cornea and uveitis (n=23, 12.3%), and comprehensive ophthalmology (n=19, 10.2%). Other practice types (n=14, 7.2%) included glaucoma, paediatric ophthalmology, ocular oncology, neuro-ophthalmology, ocular genetics and rheumatology. Demographics and other characteristics of the participants are summarised in table 1 (online supplemental appendix 2: the credit roster for the COVID-19 Practice Pattern Study Group).

Table 1 Demographics of the specialists participating in the survey

Characteristics	Number of respondents, n (%)
Gender, female	95 (51.6)
Years in practice following fellowship	
<3 years	25 (13.5)
3–5 years	33 (17.8)
6–10 years	32 (17.3)
11–20 years	50 (27.0)
>20 years	45 (24.3)
Type of practice	
Academic	97 (51.8)
Private	28 (14.9)
Hybrid	62 (33.1)
Subspecialty	
Retina and uveitis	86 (46.2)
Primarily uveitis	44 (23.6)
Cornea and uveitis	23 (12.3)
Comprehensive ophthalmology and uveitis	19 (10.2)
Glaucoma and uveitis	4 (2.1)
Paediatric ophthalmology and uveitis	3 (1.6)
Ocular oncology and uveitis	2 (1.0)
Ocular genetics	2 (1.0)
Rheumatology	2 (1.0)
Neuro-ophthalmology and uveitis	1 (0.5)
Geographical area of practice	
North America	60 (33.0)
Asia	52 (28.6)
Europe	40 (22.0)
Central/South America	19 (10.4)
Oceania	6 (3.3)
Africa	5 (2.7)

Clinical practice

During the initial phase of the pandemic (between March and June 2020), more than 90% of the specialists (n=173, 93.5%) experienced some disruption in outpatient visits; 31.3% (n=58) reported that the clinics were either completely closed or only accepting emergencies, and 48.6% (n=90) noted a decrease in clinical volume to <80% of the pre-pandemic volume. This decrease in volume lasted <3 months in most practices (n=122, 70.1%). Nineteen per cent (n=36) of participants reported that they volunteered or were redeployed to care for patients with non-eye disease.

Clinic shutdowns and decrease in availability of non-urgent appointments prompted some specialists to use teleophthalmology. Eighty-seven per cent of the participants (n=163) reported that they had not used televisits prior to the pandemic. Since the beginning of the pandemic, 67.5% of the specialists (n=125) reported that they incorporated some level of teleophthalmology in their practice (figure 2).

Twenty per cent of the respondents (n=38) indicated that their patients experienced more flares, but 63% (n=116) did not report any increase in the rate of flare-ups. Most of the specialists (n=120, 65.2%) experienced patients' refusal to come to the clinic for an in-person evaluation due to fear of COVID-19 infection. The majority of respondents (n=62, 52.1%) approached the situation by reassuring patients and emphasising the importance of in-person eye examination, and 36.1% (n=43) offered televisits.

Systemic immunosuppression and local corticosteroids

Initiating or continuing systemic immunosuppressives in patients with uveitis has been challenging during the pandemic. Sixty-five per cent (n=120) of participants stated that they encountered patients who refused to start or continue immunosuppressives due to the fear of COVID-19 infection. Moreover, 47.5% of specialists (n=89) mentioned difficulties in obtaining screening or follow-up laboratory tests either due to patients' lack of follow-up (n=62, 33.1%) or lab facility closures (n=27, 14.4%).

Most respondents (62.3%, n=114) stated that, in general, they did not change their pharmacological management during the pandemic, but 32.2% (n=59) reported a preference to avoid systemic immunosuppressives. In patients requiring initiation of systemic immunosuppression, most respondents (n=119, 66.8%) approached patients solely based on the clinical indication, while

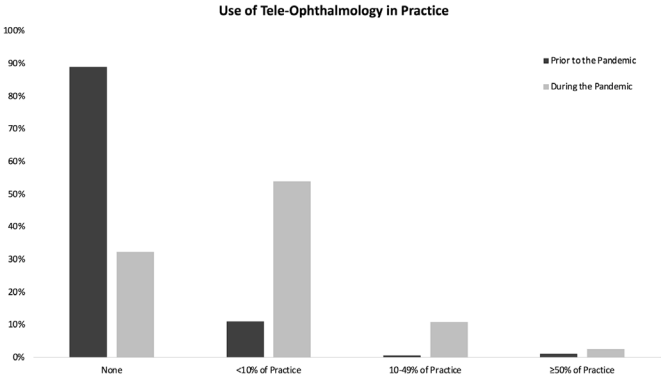

Figure 2 Bar graph comparing use of teleophthalmology in uveitis practice shows that most participants implemented remote visits in their practice during the pandemic.

others tried to avoid high-dose systemic steroids (n=33, 12.7%), rituximab (n=26, 10%) or cyclophosphamide (n=20, 7.7%) (table 2). In patients already on chronic IMTs, most respondents stated that they would continue low-dose systemic corticosteroids (n=163, 90%) and/or corticosteroid-sparing therapy (n=167, 93.3%) as clinically indicated and would not stop or change the dose of the medications.

In cases of reported exposure to COVID-19 infection, most participants (n=117, 65.36%) did not recommend any change in medications. However, 62 (34.6%) respondents reported that they would either hold all (n=23, 12.8%) or select immunosuppressives (n=39, 21.8%, table 2). Among these specialists, the majority reported that they would restart the medications 2 weeks after the exposure if patients did not develop any COVID-19 infection symptoms (n=28, 45.9%) or recommended that patients get tested for COVID-19 and restart after a negative test result (n=25, 40.9%).

If patients developed COVID-19 infection confirmed by a positive test result, most specialists recommended holding all (n=60, 33.71%) or select immunosuppressives (n=70, 39.33%). Only 26.9% (n=48) of the participants recommended no change in regimen. Among the respondents who would only hold a select group of immunosuppressives, high-dose systemic corticosteroids were the most common (n=45, 15.5%), followed by tumour necrosis factor inhibitors (n=42, 14.5%), cyclophosphamide (n=41, 14.2%) and rituximab (n=36, 12.4%, table 2). Most respondents recommended restarting immunosuppressives either after a repeat negative COVID-19 test (n=68, 52.7%) or within 2–15 days of resolution of symptoms (n=50, 38.7%).

Many patients with uveitis require intraocular injections of steroid for sufficient control. However, there has been increased concern for post-injection endophthalmitis in patients improperly wearing face masks.[11] Most of the participants (n=123, 70.6%) stated that they did not have any concerns regarding the potential increase in risk of endophthalmitis. Among the 51 (29.3%) of the experts who did express concerns, 67.8% (n=31) recommended taping the mask to decrease this risk. Ninety per cent of the participants (n=154), however, stated that they did not encounter more cases of endophthalmitis compared with the pre-COVID-19 era.

Table 2 Immunomodulatory therapy and modifications at the time of COVID-19 pandemic

	No exposure	Positive exposure	Positive test
No change in IMTs	167 (93.3%)	117 (65.3%)	48 (26.9%)
Hold or stop select IMTs	12 (6.7%)	62 (34.6%)	130 (73.0%)
Modifications in select IMTs			
Systemic corticosteroids			
Low dose	1 (2.86%)	5 (3.4%)	5 (1.7%)
High dose	7 (20.0%)	23 (15.9%)	45 (15.5%)
Antimetabolites	6 (17.1%)	18 (12.5%)	35 (12.1%)
T-cell inhibitors	6 (17.1%)	17 (11.8%)	32 (11.0%)
Cyclophosphamide	4 (11.4%)	22 (15.2%)	41 (14.2%)
Anti-TNF-α	3 (8.5%)	22 (15.2%)	42 (14.5%)
IL-6 inhibitors	2 (5.7%)	8 (5.5%)	24 (8.3%)
Rituximab	3 (8.5%)	18 (12.5%)	36 (12.4%)
Interferon-α	3 (8.5%)	8 (5.5%)	23 (7.9%)

IL-6, interleukin 6; IMTs, immunomodulatory therapies; TNF-α, tumour necrosis factor alpha.

Prevention/immunisation

Ninety per cent (n=160) of the respondents recommended COVID-19 vaccination in immunosuppressed patients. Fifty-two per cent of these specialists stated that they would counsel the patients that the vaccine may be less effective due to IMT use necessitating booster shots. Fifty-nine per cent (n=101) did not recommend any modifications in immunosuppressives around the time of vaccination, but 29.8% (51) recommended holding medications for 1–2 weeks after each dose of the vaccine.

At the beginning of the pandemic and during the government-mandated shutdowns, schools were closed to in-person activities. With precautionary measures and guidelines and the advent of the COVID-19 vaccine, school districts are reopening which raises questions regarding immunocompromised children. Most of the specialists participating in this survey (n=120, 68.5%) recommended that children on IMTs can return to in-person school activities with precautionary measures and following guidelines of the school district. However, 55 (31.4%) of the respondents recommended continued distance learning in paediatric patients with uveitis receiving immunosuppressive therapy.

DISCUSSION

The COVID-19 pandemic has significantly impacted the practice of ophthalmology globally.[12] In this study, we evaluated the effect of the pandemic on uveitis patient care and practice patterns of specialists in regard to their day-to-day clinical practice, management of immunosuppressives, and recommendations and considerations for COVID-19 vaccination. Our study included a diverse group of uveitis specialists at various stages of practice in private, academic or hybrid settings. To date, this is the largest survey addressing the effect of the pandemic on the practice of uveitis worldwide with 187 participants from 43 countries and 6 continents.

Most of the participants in this survey reported a decrease in outpatient volume and clinic closures during the first few months of the pandemic which lasted <3 months for ~70% of the participants. This was in line with the guidelines from public health authorities as well as the American Academy of Ophthalmology, which recommended cessation of all non-urgent or emergent ophthalmological care.[5 12] Moreover, 19% of the respondents reported that they either volunteered or were redeployed to care for non-ophthalmology patients and to assist with physician shortages at the frontlines.[4 13] This number was lower than what was reported in another survey study of ophthalmologists which found that ~52% of the respondents were redeployed to other services.[4] This difference can be due to the fact that the majority

of their participants consisted of ophthalmologists in training, who were not included in our survey.

With outpatient appointments prioritised for emergent or urgent visits only, many physicians implemented virtual visits in their practices.[14] The new legislation and waiver passed in the USA during the early months of the pandemic broadened access and reduced the obstacles for more widespread implementation.[15 16] It has been estimated that virtual patient visits increased between 257% and 700% during the pandemic.[17 18] In our study, we found that use of televisits increased from 13% to 67.5% compared with prior to the pandemic. Despite this surge in utilisation, more extensive use of teleophthalmology has been hampered by logistical obstacles, technical challenges and limitations in examination.[16 19] This was noted in our study as well. Despite an increase in percentage of the specialists implementing virtual visits, teleophthalmology only compromised <10% of visits among most respondents and in case of uveitis flare-up, most providers preferred in-person evaluation. Future prospective studies are needed to compare outcomes of televisits with in-person consultations.

At the beginning of the pandemic, there were insufficient data on safety of IMTs in patients with uveitis. Some authors believe that patients on IMTs are at an increased risk of worse outcomes if they contract COVID-19.[20 21] There are reports of increased risk of severe COVID-19 infection in patients receiving high-dose glucocorticoids, rituximab and cyclophosphamide.[22 23] Conversely, other studies suggested that use of select immunosuppressives (including interleukin (IL)-6 inhibitors) might play a protective role against COVID-19 infection by dampening the severe inflammatory response and cytokine storm.[20 24 25] The ACR has published guidelines for management of patients with rheumatic disease during the pandemic.[26] These guidelines recommend that for asymptomatic patients with a reported exposure to COVID-19, IMTs (except for IL-6 inhibitors and methotrexate) should be temporarily held and restarted after 2 weeks of symptom-free observation. They suggest continuing IL-6 inhibitors in select circumstances, but no consensus was made regarding methotrexate.[26 27] In cases of confirmed or presumptive COVID-19 infection, all IMTs should be held or stopped, except for IL-6 inhibitors which may be continued in select patients. Medications can be restarted within 7–14 days of resolution of symptoms in patients with uncomplicated COVID-19 infection.[26]

In an effort to form consensus and expert opinion around the pharmacological treatment of non-infectious uveitis, the uveitis specialists formed the COVID-19 IMT Study Group.[28] The consensus guidelines from this group were published in June 2020 and suggested avoiding initiating IMTs in patients with suspected or confirmed COVID-19 and patients at a very high risk of severe COVID-19 infection.[28] In our study, we aimed to understand how uveitis specialists have been implementing these guidelines in management of their patients. We found that most respondents in our study would start or continue IMTs based on clinical indication and severity of ocular inflammation. In patients with a reported exposure to COVID-19 infection, most specialists favoured continuation of IMTs, and in cases of a positive COVID-19 test, most specialists held all or select IMTs, which was in line with recommendations from the ACR and the COVID-19 IMT Study Group.[27 28]

Considerations regarding systemic immunosuppressives prompted some specialists to use intraocular corticosteroids more frequently. However, concerns exist regarding an increased risk of endophthalmitis following intravitreal injection due to inappropriately worn face masks.[11] Experimental studies have shown an increase in air jets and bacterial dispersal from the superior edge of the mask towards the eye.[11 29] In our survey, most respondents (90%) did not see an increase in rates of post-injection endophthalmitis, and 70% did not express significant concern regarding an increased risk of endophthalmitis associated with patients' use of face masks. More studies are needed to evaluate real-world effect of face masks on risk of endophthalmitis.

The first COVID-19 vaccine was approved for emergency use in the USA in December 2020,[10] and since then, other vaccines have been approved and vaccination has started worldwide.[30] These vaccines confer 66%–95% protection against COVID-19 infection. However, the clinical trials excluded patients receiving immunosuppressive therapy.[31–33] Hence, limited data are available regarding the safety and efficacy of the vaccines in patients receiving IMTs. The guidelines published by the ACR specified no safety concerns regarding COVID-19 vaccination in patients on IMTs and recommended that these patients should receive the vaccine consistent with the Emergency Use Authorization or FDA. Moreover, there exists a theoretical risk of recurrence of inflammation in autoimmune diseases following vaccination with molecular mimicry being the possible mechanism.[30 34] However, data on the effects of vaccine on flare-up of autoimmune disease are very limited. In a paper recently published, flare-up of rheumatoid arthritis has been reported in a patient after each dose of COVID-19 vaccine.[30] So far, no data are available for patients with uveitis. Despite this and given the high risk of mortality and morbidity associated with COVID-19 infection, most experts agree that the benefits of vaccination outweigh the risks.[30]

In February 2021, the ACR put forth guidelines regarding IMT use and timing of vaccination to enhance vaccine immunogenicity.[34] They recommended that IMTs can be continued with no modification at the time of vaccination except for methotrexate (holding for 1 week after each dose of vaccine is recommended). If possible and depending on patients' risk factors and disease severity, vaccination is recommended to occur ~1 week prior to cyclophosphamide infusions and ~4 weeks prior to the next rituximab cycle.[34] No specific guideline is available for patients with uveitis. Along with the ACR guidelines, most of the participants in our survey recommended vaccination in immunosuppressed patients with no significant modification of IMTs and ~30% recommended holding IMTs for 1–2 weeks after each dose of the vaccine.

This study has a number of limitations. Most of the practitioners who participated in the survey practised in North America, Asia and Europe; and although these areas encompass early COVID-19 hotspots,[35] our study was not able to fully capture the status of uveitis practices in some other parts of the world with lower number of respondents. Moreover, the number of the COVID-19 cases and public health effect of the pandemic was different in various parts of the world, especially at the beginning of the pandemic, which might have had variable effect on the practice patterns of specialists in various parts of the world. To mitigate these limitations, we distributed the survey widely through three major international uveitis societies' listservs and was able to include a high number of uveitis specialists from six continents, but a non-response bias may still exist. This study was conducted more than a year after the beginning of the pandemic; thus, we may not have captured all aspects of practice patterns of the participants that may have continued evolving over time. Moreover, at the time of this survey, the COVID-19 vaccine eligibility and rollout were limited and varied significantly among different countries and geographical areas. Hence, our understanding of the efficacy of the vaccine and need for modification of IMTs will continue to change over time as more data become available.

In conclusion, this is the first and largest study looking at the effect of the COVID-19 pandemic on uveitis patient care and

practice patterns of uveitis specialists worldwide. The results of this survey suggest that the pandemic has significantly affected the practice of uveitis. These changes include a decrease in outpatient visits, increased use of virtual visits, concerns about the use of IMTs and discussion regarding the COVID-19 vaccination. Management of IMTs during the pandemic should be guided by a multidisciplinary approach, with case-by-case decision-making based on disease severity and possible exposure to COVID-19 infection. Most specialists recommend COVID-19 vaccination in patients on IMTs. However, more data are needed to determine optimal timing of vaccination in regard to the IMTs and vaccine efficacy.

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Contributors AFV drafted and critically reviewed the manuscript. SK critically reviewed study concept, collected data, edited and finalised the manuscript. PL critically reviewed study concept, collected data, edited and finalised the manuscript. BB critically reviewed study concept, collected data, edited and finalised the manuscript. PEN conceptualised the study, collected data, generated graphs and tables, drafted and edited the manuscript. PEN accepts full responsibility for the finished work and the conduct of the study, had access to the data, and controlled the decision to publish. The group listed in the online supplemental appendix 2 participated in administering the survey.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol and questionnaire were reviewed and approved by the Institutional Review Board of the University of California Davis (ID: 1694807-2). The study was conducted in adherence to the tenets of the Declaration of Helsinki.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Available upon request.

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