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COVID-19: Update on Its Ocular Involvements, and Complications From Its Treatments and Vaccinations

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Abstract

The coronavirus disease 2019 (COVID-19) came under the attention of the international medical community when China first notified the World Health Organization of a pneumonia outbreak of then-unknown etiology in Wuhan in December 2019. Since then, COVID-19 caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has appalled the world by spreading at a pandemic speed. Although ophthalmologists do not directly engage in the clinical care of COVID-19 patients, the ophthalmology community has become aware of the close ties between its practice and the pandemic. Not only are ophthalmologists at heightened risk of SARS-CoV-2 exposure due to their physical proximity with patients in routine ophthalmic examinations, but SARS-CoV-2 possesses ocular tropism resulting in ocular complications beyond the respiratory tract after viral exposure. Furthermore, patients could potentially suffer from adverse ocular effects in the therapeutic process. This review summarized the latest literature to cover the ophthalmic manifestations, effects of treatments, and vaccinations on the eye to aid the frontline clinicians in providing effective ophthalmic care to COVID-19 patients as the pandemic continues to evolve.

Keywords: complications from treatment, COVID-19, ocular involvement, vaccine-related eye problems

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The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), one of the worst pandemics the world has witnessed, continues to evolve since its advent in December 2019 with the emergence of novel variants.[1] As of September 2021, the case count of the COVID-19 pandemic has surpassed 200 million, with a death toll of 5 million. Ophthalmology, like all other medical specialties, has been substantially impacted by the pandemic in its practice.[2,3] As the pandemic unfolded, the literature has consistently reported the tropism of the SAR-CoV-2 for the ocular surface and retina due to the extra-pulmonary expression of ACE2 and TMPRSS2 receptors.[4,5] This tropism renders the eye a potential portal of entry for SARS-CoV-2.[6]

Early in the course of the outbreak, it was reported that conjunctivitis could be the first and only clinical manifestation among COVID-19 patients.[4,7,8] The SARS-CoV-2 has also been isolated from ocular surface specimens such as tears and conjunctival swabs from patients with COVID-19.[9,10] As these initial observations raised cautions against the ocular involvement of COVID-19, there was a surge in reports of ophthalmic manifestations at additional anatomical locations of the eye beyond just the ocular surface directly exposed to the coronavirus in the environment.[11,12]

Given the devastating effect of the COVID-19 pandemic on public health and its disastrous socioeconomic impact, there has been a relentless search for effective treatment strategies and vaccines to contain the pandemic. Chloroquine (CQ) and hydroxychloroquine (HCQ), which are known to result in retinal toxicity, have initially been proposed as a treatment of COVID-19.[13] Steroids used in COVID-19 were also associated with different ocular side effects such as ocular hypertension and endogenous endophthalmitis.[14] With the emergency use authorization of novel vaccines, adverse ocular outcomes have also been reported in the latest literature. Although ophthalmologists are rarely directly engaged in the clinical management of COVID-19 patients, it remains crucial to promptly recognize the ocular findings in these contexts. This review summarized results and data from the latest literature regarding the ophthalmic manifestations of COVID-19 and the adverse ocular outcomes secondary to treatment and vaccination to update ophthalmologists in the face of such patients.

METHODS

A systematic search of the literature on PubMed for articles about ophthalmic manifestations of COVID-19, adverse ocular effects from COVID-19 treatment, and vaccination were conducted. The following key words were used for searching the database: ("coronavirus" OR "covid-19" OR "sars-cov-2") AND ("eye" OR "ocular" OR "ophthalmic" OR "ophthalmology" OR "eyelid" OR "conjunctiva" OR "cornea" OR "uvea" OR "lens" OR "retina" OR "orbit" OR "ophthalmoplegia"). The final search was performed on September 10, 2021. Only articles in English were included. The references of the retrieved full texts were also reviewed and the relevant articles were included.

RESULTS

A total of 3767 studies were initially identified after searching according to the search strategy above. After title and abstract screening, 295 studies were chosen for full-text evaluation. Finally, 88 studies were included in this study. The ophthalmic manifestations of

COVID-19 in different parts of the eye, and the adverse ocular effects resulting from COVID-19 treatment and vaccination were discussed in the following sections. The ocular findings, management, and outcomes in these cases were summarized in Tables 1 and 2.

TABLE 1.

Summary of Ophthalmic Manifestations in COVID-19

Site	Ophthalmic Manifestation/Diagnosis	Ocular Findings	Management	Outcome
Ocular Surface	Conjunctivitis[17,19–26,30]	Conjunctival hyperemia, epiphora, chemosis, foreign body sensation	Cold compresses, ocular lubricants	Self-limiting complete recovery af treatment
	Keratoconjunctivitis[31–33]	Ocular discomfort/pain, epiphora, mucus discharge, photophobia, foreign body sensation, erythema and edema of the eyelid, blepharospasm, corneal epithelial defects on fluorescence test	Artificial tears, cycloplegic eye drops, eye bandage, topical fluorometholone	Complete recovery af treatment
	Episcleritis[34,35]	Episcleral injection, epiphora, foreign body sensation, photophobia, positive phenylephrine blanching test	Artificial tears/ocular lubricants, topical fluorometholone	Complete recovery af treatment
	Acute corneal graft rejection[37]	Ocular pain, red eye, decreased visual acuity; the presence of keratic precipitates, and microcystic and stroma edema involving the corneal graft	Repeat corneal transplant (penetrating keratoplasty)	Best-correc visual acuit improved tc 20/40 (baseline: 20/80), anc the new corneal gra remained cl without sig of rejection
Orbit	Orbital cellulitis[38]	Periorbital edema and erythema, chemosis, proptosis, ophthalmoplegia; CT/MRI findings suggestive of	Broad-spectrum parenteral antibiotics, followed by endoscopic sinus surgery, and surgical drainage of orbital	Near resolution c orbital findi and ocular motility

Site	Ophthalmic Manifestation/Diagnosis	Ocular Findings	Management	Outcome
		paranasal/subperiosteal abscesses	and subperiosteal abscesses	
	Rhino-orbital mucormycosis[39–49]	Periorbital edema with soft tissue necrosis, complete ptosis, proptosis, conjunctival edema, exposure keratopathy, ophthalmoplegia, decreased visual acuity	Management of hyperglycemia; Systemic antifungal agents; Aggressive surgical interventions including endoscopic sinus debridement surgery and orbital exenteration	Usually poo fatal cases l been documente
Uvea	Uveitis[50]	Decreased visual acuity, presence of anterior chamber cells, posterior synechiae, vitritis, optic nerve swelling with peripapillary subretinal fluid and choroidal folds	High dose oral prednisone, topical steroid eyedrops and mydriatics	Severe opti atrophy
Retina	Abnormal OCT findings[51]	Hyper-reflective lesions at the level of retinal ganglion cells and inner plexiform layers	Not reported in the literature	Not reporte in the literature
	Abnormal fundus examination[51–53]	Ischemic changes (cotton wool spots, microhemorrhage along the retinal arcade), flame-shaped hemorrhage, macular hemorrhage with hard exudates	Not reported in the literature	Not reporte in the literature
	Atypical acute retinal necrosis due to Varicella-Zoster Virus[54]	Decreased visual acuity, panuveitis, necrotizing retinitis	Intravitreal foscarnet and oral valaciclovir	Significant visual improveme in one eye l residual vis impairment another eye
Neuro-ophthalmology	Miller Fisher Syndrome[56,57]	Ophthalmoplegia, ataxia, areflexia	Intravenous immunoglobulin	Complete recovery af treatment
	Cranial Nerve Palsy[58–63]	Palsy of the third, fourth or sixth nerve	Oral prednisone and intravenous immunoglobulin	Complete recovery af treatment is possible; residual neurologic deficit

Site	Ophthalmic Manifestation/Diagnosis	Ocular Findings	Management	Outcome
				suggestive o denervation has also bee reported[61]
	Myasthenia Gravis[64]	Fluctuating diplopia, ptosis, positive Cogan lid twitch test	Intravenous immunoglobulin and oral pyridostigmine	Significant recovery af treatment
	Neuromyelitis optica[65]	Bilateral optic neuritis (subacute vision loss, painful extraocular movement, papilloedema, relative afferent pupillary defect)	Intravenous methylprednisolone followed by oral prednisone taper	Rapid improveme after treatm
	Ophthalmic artery occlusion (OAO); central retinal artery/vein occlusion (CRAO/CRVO)[67–72,74,75]	Acute painless vision loss, relative afferent pupillary defect, absent accommodation reflex; Also in OAO: Retinal edema, attenuated retinal vessels, papilloedema Also in CRAO: cherry-red spot, retinal whitening, retinal arterial narrowing Also in CRVO: dilated and tortuous retinal veins, macular edema, retinal hemorrhage, papilloedema; areas of hypofluorescence, vessel wall staining and leakage in fluorescein angiogram	OAO: not reported in the literature CRAO: not reported in the literature CRVO: intravitreal anti-VEGF injection, systemic anticoagulation, systemic steroid	Ophthalmic artery occlusion: n reported in literature CRAO: not reported in literature CRVO: significant improveme after treatm
	Ischemic optic neuropathy[73]	Acute painless vision loss	Aspirin and statin for secondary prevention	Spontaneou improveme
	Cortical visual impairment[76]	Bilateral acute painless vision loss	Systemic anticoagulation followed by dual antiplatelet therapy	No significa improveme in vision
	Adie pupil[77–79]	Enlarged tonic pupil with poor response to light, cholinergic hypersensitivity	Oral prednisone	Full recover

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CT indicates computated tomography; MRI, magnetic resonance imaging; OCT, optical coherence tomography.

TABLE 2.

Summary of Adverse Ocular Outcomes of Interventions and Vaccinations in COVID-19

Intervention/Vaccine	Adverse Ocular Outcomes	Ocular Findings	Management
Pharmacological Treatment			
Remdesivir	Not reported in the literature	/	/
Anti–SARS-CoV-2 monoclonal antibodies	Not reported in the literature	/	/
Steroid[83–85]	Ocular hypertension	Elevated intraocular pressure	Topical glaucoma therapy

Intervention/Vaccine	Adverse Ocular Outcomes	Ocular Findings	Management
	Central serous chorioretinopathy	Decreased visual acuity, absent foveal reflex with serous elevation of the retina with ring reflex at the macula; hyper-reflective dots in the posterior vitreous and altered foveal contour with serous detachment in the macular and with pigment epithelial detachment on OCT; hyperfluorescent spots in macular which increased in size and intensity in later films in an inkblot pattern on fluorescein angiography	Cessation of steroid therapy
	Endogenous endophthalmitis	Ophthalmoplegia, chemosis, exposure keratopathy, Descemet membrane folds, scleral abscess, anterior chamber cells, vitritis	Pars plana vitrector with intravitreal antifungal injection, followed by systemi antimicrobial agents
Hydroxychloroquine/Chloroquine[13,82,86–89]	Unlikely to produce retinal toxicity with short term use in COVID-19; no longer supported by the latest evidence and treatment guidelines for use in COVID-19	/	/
Nonpharmacological Intervention			
Mechanical ventilation[26,90–93]	Orbital emphysema	Subcutaneous emphysema involving the	Nil

Intervention/Vaccine	Adverse Ocular Outcomes	Ocular Findings	Management
		conjunctiva and eyelids, palpable crepitus in periocular region	
	Exposure keratopathy	Lagophthalmos, chemosis, corneal epithelial changes (punctate epithelial erosions, macroepithelial defects, stromal whitening in the presence of epithelial defects, stromal scar, microbial keratitis)	Not reported in the literature
Mask[94,95]	Nontraumatic orbital hemorrhage	Ophthalmoplegia, diplopia, orbital-conjunctival hemorrhage-hematoma	Conservative treatment
	Dry eye	Ocular irritation and discomfort, exacerbation of pre-existing dry eye disease	Proper use of appropriate face masks, ocular lubricants
Inappropriate ingestion of sanitizer[96]	Methanol-induced toxic optic neuropathy	Bilateral acute painless loss of vision, mid-dilated and nonreactive pupils, optic disc pallor; thinning of the retinal nerve fiber layer in both eyes on OCT; extinguished visual evoked potentials (VEP) in both eyes	Not reported in the literature
Vaccination			
Pfizer-BioNTech vaccine[100–107]	Acute abducens nerve palsy	Horizontal diplopia, esotropia, abduction deficit	Not reported in the literature
	Uveitis	Decreased visual acuity, ocular pain, red eye, photophobia, cells	Systemic and topica steroid

Intervention/Vaccine	Adverse Ocular Outcomes	Ocular Findings	Management
		in the anterior chamber and vitreous	
	Vogt-Koyanagi-Harada (VKH) disease	Anterior chamber inflammation, cells in the vitreous; retinal folds and subretinal fluid on OCT; Exudative retinal detachment on fluorescein angiography; hypofluorescent dark dots on indocyanine angiography	Aggressive immunosuppressio (intravenous methylprednisolone followed by oral prednisone with concomitant cyclosporine, mycophenolic acid, and infliximab)
	Arteritic anterior ischemic optic neuropathy	Acute loss of vision, relative afferent pupillary defect, optic disc pallor	Systemic steroid an subcutaneous tocilizumab
	Acute corneal graft rejection	Decreased visual acuity, ocular pain, red eye, photophobia, thickened cornea, Descemet folds	Systemic and topica steroid
Moderna vaccine[104]	Bilateral acute zonal occult outer retinopathy (AZOOR)	Nonspecific nasal field defect, photopsia; Outer retinal layer segmental disruption on OCT	Intravitreal dexamethasone implant
AstraZeneca vaccine[108–110]	Acute macular neuroretinopathy	Paracentral scotoma; Oval prarafoveal hyporeflective lesions on infrared reflectance imaging	Not reported in the literature
	Bilateral immune-mediated keratolysis	Progressive bilateral corneal melting, decreased visual acuity	Tetonic penetrating keratoplasty
	Vogt-Koyanagi-Harada (VKH) disease	Bilateral acute vision loss, cells in the anterior chamber and	Systemic steroid

Intervention/Vaccine	Adverse Ocular Outcomes	Ocular Findings	Management
		vitreous, serous retinal detachment, optic disc hyperemia	
Johnson & Johnson vaccine	Not reported in the literature	/	/
SinoPharm vaccine[111]	Anterior scleritis	Scleral hyperemia, ocular pain, positive phenylephrine test	Topical steroid
	Acute macular neuroretinopathy	Acute vision loss; hyperreflectivity of the outer plexiform layer, Henle fiber layer, and outer nuclear layer on OCT nasal to the unchanged pigment epithelium detachment	Conservative treatment
	Paracentral acute middle maculopathy	Inferior scotoma, dot hemorrhage superior to the fovea; superior enlargement of the foveal avascular zone on OCT angiography	Not reported in the literature
	Episcleritis	Details not provided in the literature	/
	Subretinal fluid	Details not provided in the literature	/
Sinovac vaccine[112]	Bilateral transient visual field defect	Left congruous hemianopia	Nil

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IOP indicates intraocular pressure; OCT, optical coherence tomography; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Ocular Manifestations

Ocular Surface

The ocular surface was postulated to be a portal of entry and potential route of transmission of SARS-CoV-2 early in the course of the pandemic. Notably, the expression of ACE2 and TMPRSS2 was observed in conjunctival and cornea tissues.[4] ACE2 serves as the key cell-surface receptor which binds the viral spike protein of SARS-CoV-2,[15] and the subsequent viral entry involves TMPRSS2, a cell surface-associated protease.[16] In view of the ocular surface susceptibility to the virus, it was hypothesized that primary viral infection of the ocular surface could induce local immune or inflammatory responses and resulting in the reported spectrum manifestations such as conjunctival hyperemia, tearing, and chemosis.[17]

Coronavirus is known to cause conjunctivitis in humans,[18] and conjunctivitis was the most commonly reported ophthalmic manifestation of COVID-19.[19] The prevalence of conjunctivitis varied from <1% to 63.6%.[20,21] Although conjunctivitis were the initial presenting symptoms of mild COVID-19 cases which were otherwise asymptomatic,[22] it was also reported as a late manifestation and on the more severe spectrum of the disease.[23,24] A meta-analysis concluded that the overall rate of conjunctivitis in COVID-19 was 1.1%, and it was 3% and 0.7% in severe and nonsevere COVID-19 patients, respectively.[25]

The common symptoms of conjunctivitis associated with COVID-19 infection included conjunctival hyperemia, foreign body sensation, hypersecretion, chemosis, and epiphora.[17] The differential diagnosis of conjunctivitis associated with COVID-19 includes all causes of red eye before the COVID-19 era. In the current context, it may also reflect either the direct viral or immune response to SARS-CoV-2, or ocular surface disturbances in the setting of COVID-19 patients admitted to the intensive care unit (ICU).[26] As many cases of conjunctivitis in COVID-19 were the initial or sole clinical feature of the infection, it presents a diagnostic challenge for frontline clinicians to ascertain a diagnosis of COVID-19–associated conjunctivitis. Although it is possible to perform real-time polymerase chain reaction (RT-PCR) of tears and conjunctival secretions, the detection rate of SARS-CoV-2 from ocular surface specimens was low. Wu et al reported that the detection rate of conjunctival SARS-CoV-2 was only 16.7%, as compared with 91.7% from nasopharyngeal swabs in COVID-19 patients with ocular abnormalities.[17] Similar findings were confirmed by Zhou et al.[27] The low yield of SARS-CoV-2 detection in ocular surface specimens could be attributed to the inclusion of patients with asymptomatic or mild diseases.[27] Alternatively, in a recent study that included only patients with moderate to severe COVID-19 without ocular involvement, it has reported a SARS-CoV-2 detection rate of up to 24%.[28] This implied the presence of SARS-CoV-2 in the ocular surface was likely related to the disease severity, and the absence of ocular manifestations does not safely exclude the possibility of viral shedding from tears. Therefore, clinicians ought to maintain a high index of suspicion for patients presenting with conjunctivitis or signs of ocular surface inflammation and exercise contact precaution during ocular examination in the COVID-19 era.[29] Almost all cases of conjunctivitis related to COVID-19 were self-limiting in nature, which resolved with conservative management without subsequent ocular or systemic sequelae.[30]

Besides conjunctivitis, ocular surface manifestations of COVID-19 reported in the literature also include keratoconjunctivitis[31–33] and episcleritis.[34,35] It is notable that as SARS-CoV-2 infection of the ocular surface induces immune and inflammatory dysregulations and can potentially compromise the ocular immune privilege,[36] cases of acute corneal graft rejection in patients with COVID-19 have also been reported in the literature.[37]

Orbit

Although orbital involvement in COVID-19 infection remained uncommon, cases of orbital cellulitis as the presenting clinical feature of COVID-19 in pediatric patients have been reported.[38] More severe orbital complications could occur in COVID-19 patients with coexisting systemic comorbidities and the use of immunosuppressive agents such as steroids. Various cases of development of rhino-orbital mucormycosis were reported in COVID-19 patients with pre-existing diabetes mellitus (DM) and subjected to parenteral broad-spectrum antibiotics and steroids.[39–46] In these patients, ophthalmic examination revealed extensive edema of the periorbital region with soft tissue necrosis along the eyelids, proptosis, conjunctival edema, exposure keratopathy, decreased visual acuity, and restricted extraocular movement.[47] Fatal cases resulting from rhino-orbital cerebral mucormycosis in COVID-19 have also been documented.[48] Of note, there was a case series of 13 previously immunocompetent and nondiabetic patients developing new-onset DM complicated by rhino-orbial mucormycosis following COVID-19 infection, in which aggressive surgical intervention including orbital exenteration was necessary.[49] Among these 13 cases, 6 received no steroids or immunomodulators.[49] Therefore, ophthalmologists and clinicians involved in the care of COVID-19 patients ought to be aware of the possibility of recent-onset diabetes and its potentially devastating orbital consequences.

Uvea

As the ACE2 receptors which bind the SARS-CoV-2 viral spike proteins are also found in other anatomical locations of the eye besides the ocular surface, it is also possible for the virus to produce ophthalmic manifestations at these sites. Following an initial episode of conjunctivitis, panuveitis with the presence of decreased visual acuity, anterior chamber cells, posterior synechiae, vitritis, optic nerve swelling with peripapillary subretinal fluid and choroidal folds was reported as a presenting clinical feature in a patient who was subsequently diagnosed with COVID-19.[50]

Retina

OCT changes of the retina were also reported in COVID-19 with hyper-reflective lesions at the level of retinal ganglion cells and inner plexiform layers.[51] Fundus examination revealed cotton wool spots and microhemorrhages along the retinal arcade suggestive of ischaemic changes, flame-shaped hemorrhage, and macular hemorrhage with hard exudates.[51–53] Despite the presence of retinal manifestations, these patients have no visual symptoms. There was also a report of sight-threatening atypical acute retinal necrosis due to Varicella-Zoster Virus occurring concomitantly in COVID-19 patients who had received immunosuppressive agents.[54]

Neuro-ophthalmology

Neuro-ophthalmic manifestations of COVID-19 have also been reported in the literature.[55] COVID-19 could result in ophthalmoplegia, diplopia, cranial nerve palsies, acute vision loss, and defective pupillary responses as described in the cases below.

Miller Fisher syndrome (MFS), characterized by a triad of ophthalmoplegia, ataxia, and areflexia, may also be associated with COVID-19 infection. MFS is a variant of Guillain-Barre syndrome, defined as an acute peripheral neuropathy after exposure to various viral, bacterial, or fungal pathogens. Classical development of MFS with bilateral ophthalmoplegia, ataxia, and hyporeflexia subsequently improved upon treatment with intravenous immunoglobulin have been reported in COVID-19 patients.[56,57]

Diplopia and ophthalmoplegia due to cranial nerve palsies in COVID-19 patients have also been reported. Dinkin et al[58] reported a case of unilateral oculomotor nerve palsy with magnetic resonance imaging (MRI) demonstrating T2 hyperintensity and enlargement of the left oculomotor nerve following COVID-19 development. Falcone et al reported a case of unilateral abducens nerve palsy with MRI findings of lateral rectus muscle atrophy in a middle-aged patient 5 weeks after COVID-19 development.[59] Similar findings of ophthalmoplegia due to cranial nerve palsies were reported in later studies,[60–63] and complete recovery was possible upon treatment and recovery from COVID-19.[61] Alternatively, COVID-19 infection could also result in diplopia due to the development of postinfectious myasthenia gravis. In such case, acetylcholine receptor antibodies were detected serologically alongside antibodies against SARS-CoV-2 one month following COVID-19; the patient showed improvement with the administration of intravenous immunoglobulin and pyridostigmine.[64] Bilateral subacute vision loss secondary to neuromyelitis optica were present in a young patient simultaneously positive for SARS-CoV-2 and myelin oligodendrocyte glycoprotein (MOG) IgG antibodies.[65] The patient's visual acuity improved rapidly after administration of intravenous methylprednisolone followed by oral prednisolone taper.

Infection of SARS-CoV-2 was also associated with systemic inflammatory response and coagulation activation. The binding of SARS-CoV-2 to ACE2 receptors within vascular endothelial cells was hypothesized to result in systemic endothelial dysfunction and a state of hypercoagulability. The state of hypercoagulability has important implications to the eye as occlusion of retinal blood vessels by thromboembolism could result in serious ophthalmic complications.[66] Acute vision loss in COVID-19 patients attributed to vascular complications of COVID-19 has been reported in the literature. These could manifest as an ophthalmic artery or central retinal artery/vein occlusion and ischemic optic neuropathy.[67–75] Furthermore, hypercoagulability can also result in vascular occlusion beyond the retina at the central nervous system and manifest as bilateral acute vision loss due to infarct of the visual cortices in bilateral occipital territories.[76]

Finally, pupillary involvement such as Adie pupil was also documented as a complication following COVID-19 infections.[77–79]

Ocular Side Effects Arising From Treatment and Prevention

As frontline clinicians directly involved in the care of patients, besides promptly recognizing ophthalmic manifestations of COVID-19 so that timely diagnosis and interventions can be arranged, ophthalmologists need to be aware of the potential side effects that may arise from treatments or preventive measures of COVID-19.[80,81] Currently, therapeutic strategies for COVID-19 patients depend on the disease severity. General management of nonhospitalized patients with mild to moderate disease involves supportive care, isolation, and serial follow-up. In hospitalized patients, among patients with severe COVID-19 requiring supplemental oxygen for respiratory support, there is evidence supporting the use of the antiviral remdesivir, dexamethasone, and monoclonal antibodies.[82] Bamlanivimab, etesevimab, casirivimab, imdevimab, and sotrovimab are anti–SARS-CoV-2 monoclonal antibodies that have received emergency use authorizations from the Food and Drug Administration of the United States.[82]

At the time of review, there have been no reports on adverse ocular effects of remdisivir and anti–SARS-CoV-2 monoclonal antibodies in the literature. Steroid is well known to produce ocular hypertension, which may necessitate glaucoma therapy to reduce the intraocular pressure (IOP) to eliminate the symptoms associated with the acute surge in IOP and prevent potential visual field loss.[83] The administration of steroids for treatment of COVID-19 was also reported to result in central serous chorioretinopathy.[84] In a series of 7 COVID-19 cases complicated by endogenous endophthalmitis, 6 cases were secondary to mucormycosis-associated sinusitis or systemic fungal infections, and all had received intravenous corticosteroid for COVID-19.[85] As prolonged use of systemic steroids creates an immunocompromised state and predisposes patients to such sight-threatening complications, ophthalmologists ought to have a high index of suspicion in their evaluation of these patients.

The use of HCQ and CQ during the early COVID-19 period sparked heated debates within and beyond the ophthalmology community. There were initial concerns regarding its potential retinal toxicity and the development of Bull's eye maculopathy associated with its use.[13] Nevertheless, it is uncommon to develop retinopathy before 10 or more years of using such medications at the American Academy of Ophthalmology's recommended dosage of <5 mg/kg real weight.[86] As HCQ and CQ use in COVID-19 is only within a short period, it is extremely unlikely to produce such ocular complications.[13,87] However, most of the evidence has shown no benefit of HCQ as compared to the standard of care across the different severities of COVID-19, and both drugs are no longer recommended by the latest evidence and treatment guidelines.[82,88,89]

Complications from nonpharmacological interventions for COVID-19 patients have also been reported in the literature. Patients who developed severe pneumonia and respiratory failure related to COVID-19 often required intensive care and ventilatory support. The development of orbital emphysema extending from the chest to the face and periocular crepitus has been documented in COVID-19 patients placed on positive end-expiratory pressure ventilation.[90,91] Furthermore, in patients who require advanced ventilatory support in the intensive care unit, exposure keratopathy was previously reported to develop in >50% of mechanically ventilated patients.[92] This can be attributed to the use of sedation and neuromuscular blocking agents which reduces the orbicularis muscle tone and prone positioning of the patients, both of which increase the risk of exposure keratopathy.[26,93]

The World Health Organization (WHO) has endorsed face masks to prevent transmission of COVID-19. Nevertheless, inappropriate use of masks can result in ocular complications. Nontraumatic orbital hemorrhage presented as sudden orbital-subconjunctival-eyelid cutaneous hemorrhage-hematoma with conjunctival protrusion from the palpebral fissure has been reported in the improper fitting of face mask whereby excessive pressure was exerted on the nasal bridge and lower eyelid.[94] Alternatively, unsuitable fitting with face masks in which exhaled air flows across the ocular surface could exacerbate tear film evaporation and predispose patients to the development of dry eye.[95]

At the beginning of the rapidly evolving pandemic, public fear and confusion regarding appropriate public health measures and behaviors to eliminate COVID-19 transmission have fuelled the dissemination of erroneous information and false beliefs. A patient developed bilateral complete vision loss within 24 hours following intentional ingestion of alcohol-based sanitizer solution.[96] Alcohol-based sanitizers usually contain ethanol, isopropyl alcohol, n-propyl alcohol, or their combinations as the major component. These agents had not been previously reported to result in vision loss. Retrospective investigation revealed that the patient in this case likely ingested a sanitizer that contained methyl alcohol (methanol), which is rapidly absorbed and metabolized into formaldehyde to produce ocular toxicity.

Adverse Effects From Vaccination

Currently, 6 commonly used vaccines in the Asia-Pacific region and the western world were granted the emergency use authorization (EUA) from WHO. The currently EUA qualified COVID-19 vaccines include mRNA vaccines (Pfizer-BioNTech, Moderna), adenovirus vector vaccines (AstraZeneca, Johnson & Johnson), and whole inactivated coronavirus vaccines (SinoPharm, Sinovac), and various systemic and ocular adverse effects have been reported in the literature. For instance, vaccine-induced immune thrombotic thrombocytopenia (VITT) and thrombosis resulting in potentially lethal thrombotic events have been reported after the administration of the AstraZeneca vaccine.[97–99] Therefore, ophthalmologists ought to be aware of potential ocular adverse effects that may arise subsequent to COVID-19 vaccination.

The Pfizer-BioNTech vaccine was reported to be associated with various ocular adverse effects. Reyes-Capo et al[100] reported a case of acute abducens nerve palsy following a febrile illness 2 days after vaccination in a patient without significant comorbidities. Various authors also reported cases of uveitis and Vogt-Koyanagi-Harada (VKH) disease following vaccination; most cases resolve or significantly improve following both steroidal and nonsteroidal immunosuppression.[101–103] A case of arteritic anterior ischemic optic neuropathy (AAION) manifesting as acute loss of vision following vaccination was also reported in the literature.[104] Finally, there were also recent reports of corneal graft rejection following vaccination in patients who received endothelial keratoplasty or penetrating keratoplasty.[105–107] As another mRNA vaccine, there is currently 1 report of bilateral acute zonal occult outer retinopathy (AZOOR) manifesting as progressive nasal field defect following Moderna vaccination.[104]

Various adverse ocular effects have been reported after immunization by the AstraZeneca adenovirus vector vaccine. Acute macular neuroretinopathy, bilateral immune-mediated keratolysis, and VKH disease were all reported as potential adverse ocular events following vaccination.[108–110] Meanwhile, we did not identify reports of ocular adverse events following immunization by the Johnson & Johnson vaccine vaccine in the current literature.

A few adverse ocular effects were noted in the whole inactivated coronavirus vaccines. Following immunization, acute uveitis has been reported by the SinoPharm vaccine, which resolved with topical steroid treatment without recurrence. In a recent study, Pichi et al reported the presence of episcleritis, anterior scleritis, acute macular neuroretinopathy, paracentral acute middle maculopathy, and subretinal fluid from studying 7 patients who presented with ocular complaints following SinoPharm vaccination.[111] There was a report of bilateral transient visual field defect with spontaneous resolution in an ophthalmologist following Sinovac vaccination.[112]

It should nonetheless be emphasized that with more than 1.5 billion doses of COVID-19 vaccinations administered worldwide, determining the causal relationship in every case of the potential adverse event becomes a daunting, if at all possible, challenge. With the enormous number of vaccinations administered, it may be natural for these events to be coincidental.[113] The astute clinician shall evaluate these events with scientific rigor based on all evidence, and bear in mind the vast number of lives and benefits vaccination and herd immunity would bring to the society overall.

CONCLUSIONS

The SARS-CoV-2 emerged in late 2019 when the entire world knew little of it. As the pandemic continues to evolve with the advent of new viral variants, the medical community also witnesses a boom in knowledge and information covering all facets of the pathogen. This review summarized the ophthalmic manifestations and adverse ocular effects resulting from therapeutic and preventive measures of COVID-19, which can guide ophthalmologists in their clinical encounters of COVID-19 patients in the battle ahead.

Footnotes

The authors have no conflicts of interest to declare.

REFERENCES

1. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. *N Engl J Med* 2021; 385:585–594. [DOI] [PMC free article] [PubMed] [Google Scholar]

2. Wan KH, Lin TPH, Ko CN, Lam DSC. Impact of COVID-19 on ophthalmology and future practice of medicine. *Asia Pac J Ophthalmol (Phila)* 2020; 9:279–280. [DOI] [PubMed] [Google Scholar]

3. Khor WB, Yip L, Zhao P, et al. Evolving practice patterns in Singapore's public sector ophthalmology centers during the COVID-19 pandemic. *Asia Pac J Ophthalmol (Phila)* 2020; 9:285–290. [DOI] [PMC free article] [PubMed] [Google Scholar]

4. Zhou L, Xu Z, Castiglione GM, et al. ACE2 and TMPRSS2 are expressed on the human ocular surface, suggesting susceptibility to SARS-CoV-2 infection. *Ocul Surf* 2020; 18:537–544. [DOI] [PMC free article] [PubMed] [Google Scholar]

5. Zhou L, Xu Z, Guerra J, et al. Expression of the SARS-CoV-2 receptor ACE2 in human retina and diabetes-implications for retinopathy. *Invest Ophthalmol Vis Sci* 2021; 62:6.doi:10.1167/iovs.62.7.6. [DOI] [PMC free article] [PubMed] [Google Scholar]

6. Sun CB, Wang YY, Liu GH, Liu Z. Role of the eye in transmitting human coronavirus: what we know and what we do not know. *Front Public Health* 2020; 8:155.doi:10.3389/fpubh.2020.00155. [DOI] [PMC free article] [PubMed] [Google Scholar]

7. Scalinci SZ, Trovato Battagliola E. Conjunctivitis can be the only presenting sign and symptom of COVID-19. *IDCases* 2020; 20:e00774.doi:10.1016/j.idcr.2020.e00774. [DOI] [PMC free article] [PubMed] [Google Scholar]

8. Chen L, Deng C, Chen X, et al. Ocular manifestations and clinical characteristics of 535 cases of COVID-19 in Wuhan, China: a cross-sectional study. *Acta Ophthalmol* 2020; 98:e951–e959. [DOI] [PMC free article] [PubMed] [Google Scholar]

9. Seah IYJ, Anderson DE, Kang AEZ, et al. Assessing viral shedding and infectivity of tears in coronavirus disease 2019 (COVID-19) patients. *Ophthalmology* 2020; 127:977–979. [DOI] [PMC free article] [PubMed] [Google Scholar]

10. Zhang X, Chen X, Chen L, et al. The evidence of SARS-CoV-2 infection on ocular surface. *Ocul Surf* 2020; 18:360–362. [DOI] [PMC free article] [PubMed] [Google Scholar]

11. Gangaputra SS, Patel SN. Ocular Symptoms among nonhospitalized patients who underwent COVID-19 testing. *Ophthalmology* 2020; 127:1425–1427. [DOI] [PMC free article] [PubMed] [Google Scholar]

12. Wan KH, Chow VWS, Lam DSC. Risk of SARS-CoV-2 transmission via corneal transplant from donors with COVID-19. *JAMA Ophthalmol* 2021; 139:922–923. [DOI] [PubMed] [Google Scholar]

13. Ruamviboonsuk P, Lai TYY, Chang A, et al. Chloroquine and hydroxychloroquine retinal toxicity consideration in the treatment of COVID-19. *Asia Pac J Ophthalmol (Phila)* 2020; 9:85–87. [DOI] [PMC free article] [PubMed] [Google Scholar]

14. Bilgic A, Sudhalkar A, Gonzalez-Cortes JH, et al. Endogenous endophthalmitis in the setting of COVID-19 infection: a case series. *Retina* 2021; 41:1709–1714. [DOI] [PubMed] [Google Scholar]

15. Lan J, Ge J, Yu J, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. *Nature* 2020; 581:215–220. [DOI] [PubMed] [Google Scholar]

16. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 2020; 181:271–280. [DOI]

[PMC free article] [PubMed] [Google Scholar]

17. Wu P, Duan F, Luo C, et al. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020; 138:575–578. [DOI] [PMC free article] [PubMed] [Google Scholar]

18. Li JO, Lam DSC, Chen Y, Ting DSW. Novel coronavirus disease 2019 (COVID-19): the importance of recognising possible early ocular manifestation and using protective eyewear. *Br J Ophthalmol* 2020; 104:297–298. [DOI] [PubMed] [Google Scholar]

19. Al-Namaeh M. COVID-19 and conjunctivitis: a meta-analysis. *Ther Adv Ophthalmol* 2021; 13:25158414211003368.doi:10.1177/25158414211003368. [DOI] [PMC free article] [PubMed] [Google Scholar]

20. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382:1708–1720. [DOI] [PMC free article] [PubMed] [Google Scholar]

21. D'Amico Ricci G, Del Turco C, Belcastro E, et al. COVID-19 and acute conjunctivitis: controversial data from a tertiary refferral Italian center. *Eur J Ophthalmol* 2021; 1120672121991049.doi:10.1177/1120672121991049. [DOI] [PubMed] [Google Scholar]

22. Liu M, Dai C, Lv X, Li B. Letter to the editor: are severe COVID-19 patients more susceptible to conjunctivitis? *J Med Virol* 2020; 92:2394–2395. [DOI] [PMC free article] [PubMed] [Google Scholar]

23. Nayak B, Poddar C, Panigrahi MK, et al. Late manifestation of follicular conjunctivitis in ventilated patient following COVID-19 positive severe pneumonia. *Indian J Ophthalmol* 2020; 68:1675–1677. [DOI] [PMC free article] [PubMed] [Google Scholar]

24. Navel V, Chiambaretta F, Dutheil F. Haemorrhagic conjunctivitis with pseudomembranous related to SARS-CoV-2. *Am J Ophthalmol Case Rep* 2020; 19:100735.doi:10.1016/j.ajoc.2020.100735. [DOI] [PMC free article] [PubMed] [Google Scholar]

25. Loffredo L, Pacella F, Pacella E, et al. Conjunctivitis and COVID-19: a meta-analysis. *J Med Virol* 2020; 92:1413–1414. [DOI] [PMC free article] [PubMed] [Google Scholar]

26. Wan KH, Huang SS, Lam DSC. Conjunctival findings in patients with coronavirus disease 2019. *JAMA Ophthalmol* 2021; 139:254–255. [DOI] [PubMed] [Google Scholar]

27. Zhou Y, Duan C, Zeng Y, et al. Ocular findings and proportion with conjunctival SARS-COV-2 in COVID-19 patients. *Ophthalmology* 2020; 127:982–983. [DOI] [PMC free article] [PubMed] [Google Scholar]

28. Arora R, Goel R, Kumar S, et al. Evaluation of SARS-CoV-2 in tears of patients with moderate to severe COVID-19. *Ophthalmology* 2021; 128:494–503. [DOI] [PMC free article] [PubMed] [Google Scholar]

29. Lam DSC, Wong RLM, Lai KHW, et al. COVID-19: special precautions in ophthalmic practice and FAQs on personal protection and mask selection. *Asia Pac J Ophthalmol (Phila)* 2020; 9:67–77. [DOI] [PMC free article] [PubMed] [Google Scholar]

30. American Academy of Ophthalmology. COVID Conjunctivitis. 2021. https://eyewiki.aao.org/COVID_Conjunctivitis#General_treatment. Accessed September 16, 2021. [Google Scholar]

31. Guo D, Xia J, Wang Y, et al. Relapsing viral keratoconjunctivitis in COVID-19: a case report. *Virol J* 2020; 17:97.doi:10.1186/s12985-020-01370-6. [DOI] [PMC free article] [PubMed] [Google Scholar]

32. Cheema M, Aghazadeh H, Nazarali S, et al. Keratoconjunctivitis as the initial medical presentation of the novel coronavirus disease 2019 (COVID-19). *Can J Ophthalmol* 2020; 55:e125–e129. [DOI] [PMC free article] [PubMed] [Google Scholar]

33. Hutama SA, Alkaff FF, Intan RE, et al. Recurrent keratoconjunctivitis as the sole manifestation of COVID-19 infection: A case report. *Eur J Ophthalmol* 2021; doi:10.1177/11206721211006583. [Epub ahead of print]. [DOI] [PMC free article] [PubMed] [Google Scholar]

34. Mendez Mangana C, Barraquer Kargacin A, Barraquer RI. Episcleritis as an ocular manifestation in a patient with COVID-19. *Acta Ophthalmol* 2020; 98:e1056–e1057. [DOI] [PMC free article] [PubMed] [Google Scholar]

35. Otaif W, Al Somali AI, Al Habash A. Episcleritis as a possible presenting sign of the novel coronavirus disease: A case report. *Am J Ophthalmol Case Rep* 2020; 20:100917.doi:10.1016/j.ajoc.2020.100917. [DOI] [PMC free article] [PubMed] [Google Scholar]

36. Shi Y, Wang Y, Shao C, et al. COVID-19 infection: the perspectives on immune responses. *Cell Death Differ* 2020; 27:1451–1454. [DOI] [PMC free article] [PubMed] [Google Scholar]

37. Jin SX, Juthani VV. Acute corneal endothelial graft rejection with coinciding COVID-19 infection. *Cornea* 2021; 40:123–124. [DOI] [PMC free article] [PubMed] [Google Scholar]

38. Turbin RE, Wawrzusin PJ, Sakla NM, et al. Orbital cellulitis, sinusitis and intracranial abnormalities in two adolescents with COVID-19. *Orbit* 2020; 39:305–310. [DOI] [PubMed] [Google Scholar]

39. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. *Cureus* 2020; 12:e10726.doi:10.7759/cureus.10726. [DOI] [PMC free article] [PubMed] [Google Scholar]

40. Veisi A, Bagheri A, Eshaghi M, et al. Rhino-orbital mucormycosis during steroid therapy in COVID-19 patients: A case report. *Eur J Ophthalmol* 2021; doi:10.1177/11206721211009450. [Epub ahead of print]. [DOI] [PMC free article] [PubMed] [Google Scholar]

41. Thanthoni RR, Warrier M, AS. COVID-19 coinfection with mucormycosis in a diabetic patient. *Cureus* 2021; 13:e15820.doi:10.7759/cureus.15820. [DOI] [PMC free article] [PubMed] [Google Scholar]

42. Garg R, Bharangar S, Gupta S, Bhardwaj S. Post COVID-19 Infection presenting as rhino-orbital mycosis. *Indian J Otolaryngol Head Neck Surg* 2021; doi: 10.1007/s12070-021-02722-6. [Epub ahead of print]. [DOI] [PMC free article] [PubMed] [Google Scholar]

43. Mitra S, Janweja M, Sengupta A. Post-COVID-19 rhino-orbito-cerebral mucormycosis: a new addition to challenges in pandemic control. *Eur Arch Otorhinolaryngol* 2021; 1–6. [DOI] [PMC free article] [PubMed] [Google Scholar]

44. Shakir M, Maan MHA, Waheed S. Mucormycosis in a patient with COVID-19 with uncontrolled diabetes. *BMJ Case Rep* 2021; 14.doi:10.1136/bcr-2021-245343. [DOI] [PMC free article] [PubMed] [Google Scholar]

45. Wadhwa L, Khurana S. Rhino-orbital mucormycosis in a COVID-19 patient co-infected with klebsiella pneumoniae. *Cureus* 2021; 13:e17249.doi:10.7759/cureus.17249. [DOI] [PMC free article] [PubMed] [Google Scholar]

46. Chauhan K, Soni D, Sarkar D, et al. Mucormycosis after COVID-19 in a patient with diabetes. *Lancet* 2021; 398:e10.doi:10.1016/S0140-6736(21)01641-X. [DOI] [PMC free article] [PubMed] [Google Scholar]

47. Maini A, Tomar G, Khanna D, et al. Sino-orbital mucormycosis in a COVID-19 patient: A case report. *Int J Surg Case Rep* 2021; 82:105957.doi:10.1016/j.ijscr.2021.105957. [DOI] [PMC free article] [PubMed] [Google Scholar]

48. Dallalzadeh LO, Ozzello DJ, Liu CY, et al. Secondary infection with rhino-orbital cerebral mucormycosis associated with COVID-19. *Orbit* 2021; 1–4. [DOI] [PubMed] [Google Scholar]

49. Nair AG, Adulkar NG, D'Cunha L, et al. Rhino-orbital mucormycosis following COVID-19 in previously non-diabetic, immunocompetent patients. *Orbit* 2021; 40:499–504. [DOI] [PubMed] [Google Scholar]

50. Benito-Pascual B, Gegundez JA, Diaz-Valle D, et al. Panuveitis and optic neuritis as a possible initial presentation of the novel coronavirus disease 2019 (COVID-19). *Ocul Immunol Inflamm* 2020; 28:922–925. [DOI] [PubMed] [Google Scholar]

51. Marinho PM, Marcos AAA, Romano AC, et al. Retinal findings in patients with COVID-19. *Lancet* 2020; 395:1610.doi:10.1016/S0140-6736(20)31014-X. [DOI] [PMC free article] [PubMed] [Google Scholar]

52. Pereira LA, Soares LCM, Nascimento PA, et al. Retinal findings in hospitalised patients with severe COVID-19. *Br J Ophthalmol* 2020; bjophthalmol-2020-317576. doi:10.1136/bjophthalmol-2020-317576. [DOI] [PubMed] [Google Scholar]

53. Gascon P, Briantais A, Bertrand E, et al. COVID-19-associated retinopathy: a case report. *Ocul Immunol Inflamm* 2020; 28:1293–1297. [DOI] [PubMed] [Google Scholar]

54. Gupta A, Dixit B, Stamoulas K, Akshikar R. Atypical bilateral acute retinal necrosis in a coronavirus disease 2019 positive immunosuppressed patient. *Eur J Ophthalmol* 2020; 1120672120974941.doi:10.1177/1120672120974941. [DOI] [PubMed] [Google Scholar]

55. Chwalisz BK, Dinkin MJ. Disease of the year: COVID-19 and its neuro-ophthalmic complications. *J Neuroophthalmol* 2020; 40:283–284. [DOI] [PMC free article] [PubMed] [Google Scholar]

56. Lantos JE, Strauss SB, Lin E. COVID-19-associated Miller Fisher syndrome: MRI findings. *AJNR Am J Neuroradiol* 2020; 41:1184–1186. [DOI] [PMC free article] [PubMed] [Google Scholar]

57. Gutierrez-Ortiz C, Mendez-Guerrero A, Rodrigo-Rey S, et al. Miller Fisher syndrome and polyneuritis cranialis in COVID-19. *Neurology* 2020; 95:e601–e605. [DOI] [PubMed] [Google Scholar]

58. Dinkin M, Gao V, Kahan J, et al. COVID-19 presenting with ophthalmoparesis from cranial nerve palsy. *Neurology* 2020; 95:221–223. [DOI] [PubMed] [Google Scholar]

59. Falcone MM, Rong AJ, Salazar H, et al. Acute abducens nerve palsy in a patient with the novel coronavirus disease (COVID-19). *J AAPOS* 2020; 24:216–217. [DOI] [PMC free article] [PubMed] [Google Scholar]

60. Pascual-Goni E, Fortea J, Martinez-Domeno A, et al. COVID-19-associated ophthalmoparesis and hypothalamic involvement. *Neurol Neuroimmunol Neuroinflamm* 2020; 7.doi:10.1212/NXI.0000000000000823. [DOI] [PMC free article] [PubMed] [Google Scholar]

61. Belghmaidi S, Nassih H, Boutgayout S, et al. Third cranial nerve palsy presenting with unilateral diplopia and strabismus in a 24-year-old woman with COVID-19. *Am J Case Rep* 2020; 21:e925897.doi:10.12659/AJCR.925897. [DOI] [PMC free article] [PubMed] [Google Scholar]

62. Greer CE, Bhatt JM, Oliveira CA, Dinkin MJ. Isolated cranial nerve 6 palsy in 6 patients with COVID-19 infection. *J Neuroophthalmol* 2020; 40:520–522. [DOI] [PubMed] [Google Scholar]

63. Ordas CM, Villacieros-Alvarez J, Pastor-Vivas AI, Corrales-Benitez A. Concurrent tonic pupil and trochlear nerve palsy in COVID-19. *J Neurovirol* 2020; 26:970–972. [DOI] [PMC free article] [PubMed] [Google Scholar]

64. Huber M, Rogozinski S, Puppe W, et al. Postinfectious onset of myasthenia gravis in a COVID-19 patient. *Front Neurol* 2020; 11:576153.doi:10.3389/fneur.2020.576153. [DOI] [PMC free article] [PubMed] [Google Scholar]

65. Zhou S, Jones-Lopez EC, Soneji DJ, et al. Myelin oligodendrocyte glycoprotein antibody-associated optic neuritis and myelitis in COVID-19. *J Neuroophthalmol* 2020; 40:398–402. [DOI] [PMC free article] [PubMed] [Google Scholar]

66. Jager MJ, Seddon JM. Eye diseases direct interest to complement pathway and macrophages as regulators of inflammation in COVID-19. *Asia Pac J Ophthalmol (Phila)* 2020; 10:114–120. [DOI] [PMC free article] [PubMed] [Google Scholar]

67. Insausti-Garcia A, Reche-Sainz JA, Ruiz-Arranz C, et al. Papillophlebitis in a COVID-19 patient: inflammation and hypercoagulable state. *Eur J Ophthalmol* 2020; doi:10.1177/1120672120947591. [Epub ahead of print]. [DOI] [PMC free article] [PubMed] [Google Scholar]

68. Dumitrascu OM, Volod O, Bose S, et al. Acute ophthalmic artery occlusion in a COVID-19 patient on apixaban. *J Stroke Cerebrovasc Dis* 2020; 29:104982.doi:10.1016/j.jstrokecerebrovasdis.2020.104982. [DOI] [PMC free article] [PubMed] [Google Scholar]

69. Sheth JU, Narayanan R, Goyal J, Goyal V. Retinal vein occlusion in COVID-19: a novel entity. *Indian J Ophthalmol* 2020; 68:2291–2293. [DOI] [PMC free article] [PubMed] [Google Scholar]

70. Gaba WH, Ahmed D, Al Nuaimi RK, et al. Bilateral central retinal vein occlusion in a 40-year-old man with severe coronavirus disease 2019 (COVID-19) pneumonia. *Am J Case Rep* 2020; 21:e927691.doi:10.12659/AJCR.927691. [DOI] [PMC free article] [PubMed] [Google Scholar]

71. Walinjkar JA, Makhija SC, Sharma HR, et al. Central retinal vein occlusion with COVID-19 infection as the presumptive etiology. *Indian J Ophthalmol* 2020; 68:2572–2574. [DOI] [PMC free article] [PubMed] [Google Scholar]

72. Invernizzi A, Pellegrini M, Messenio D, et al. Impending central retinal vein occlusion in a patient with coronavirus disease 2019 (COVID-19). *Ocul Immunol Inflamm* 2020; 28:1290–1292. [DOI] [PubMed] [Google Scholar]

73. Selvaraj V, Sacchetti D, Finn A, Dapaah-Afriyie K. Acute vision loss in a patient with COVID-19. *R I Med J (2013)* 2020; 103:37–38. [PubMed] [Google Scholar]

74. Acharya S, Diamond M, Anwar S, et al. Unique case of central retinal artery occlusion secondary to COVID-19 disease. *IDCases* 2020; 21:e00867.doi:10.1016/j.idcr.2020.e00867. [DOI] [PMC free article] [PubMed] [Google Scholar]

75. Montesel A, Bucolo C, Mouvet V, et al. Case report: central retinal artery occlusion in a COVID-19 patient. *Front Pharmacol* 2020; 11:588384.doi:10.3389/fphar.2020.588384. [DOI] [PMC free article] [PubMed] [Google Scholar]

76. Cyr DG, Vicidomini CM, Siu NY, Elmann SE. Severe bilateral vision loss in 2 patients with coronavirus disease 2019. *J Neuroophthalmol* 2020; 40:403–405. [DOI] [PMC free article] [PubMed] [Google Scholar]

77. Ortiz-Seller A, Martinez Costa L, Hernandez-Pons A, et al. Ophthalmic and neuro-ophthalmic manifestations of coronavirus disease 2019 (COVID-19). *Ocul Immunol Inflamm* 2020; 28:1285–1289. [DOI] [PubMed] [Google Scholar]

78. Kaya Tutar N, Kale N, Tugcu B. Adie-Holmes syndrome associated with COVID-19 infection: a case report. *Indian J Ophthalmol* 2021; 69:773–774. [DOI] [PMC free article] [PubMed] [Google Scholar]

79. Gopal M, Ambika S, Padmalakshmi K. Tonic pupil following COVID 19. *J Neuroophthalmol* 2021; doi:10.1097/WNO.0000000000001221. [Epub ahead of print]. [DOI] [PMC free article] [PubMed] [Google Scholar]

80. Wong RLM, Ting DSW, Wan KH. COVID-19: ocular manifestations and the APAO prevention guidelines for ophthalmic practices. *Asia Pac J Ophthalmol (Phila)* 2020; 9:281–284. [DOI] [PMC free article] [PubMed] [Google Scholar]

81. Wan KH, Huang SS, Young AL, et al. Precautionary measures needed for ophthalmologists during pandemic of the coronavirus disease 2019 (COVID-19). *Acta Ophthalmol* 2020; 98:221–222. [DOI] [PMC free article] [PubMed] [Google Scholar]

82. National Institute of Health. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. https://www.covid19treatmentguidelines.nih.gov/%20management/clinical-management/clinical-management-summary/. Accessed September 24, 2021. [Google Scholar]

83. Tasaki A. Case report: steroid-induced ocular hypertension in a 6-year-old boy. *Optom Vis Sci* 2021; 98:867–869. [DOI] [PubMed] [Google Scholar]

84. Sanjay S, Gowda PB, Rao B, et al. Old wine in a new bottle" - post COVID-19 infection, central serous chorioretinopathy and the steroids. *J Ophthalmic Inflamm Infect* 2021; 11:14.doi:10.1186/s12348-021-00244-4. [DOI] [PMC free article] [PubMed] [Google Scholar]

85. Khatwani PR, Goel NP, Trivedi KY, Aggarwal SV. Unveiling endophthalmitis post COVID-19 - a case series. *Indian J Ophthalmol* 2021; 69:2869–2871. [DOI] [PMC free article] [PubMed] [Google Scholar]

86. Marmor MF, Kellner U, Lai TY, et al. Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision). *Ophthalmology* 2016; 123:1386–1394. [DOI] [PubMed] [Google Scholar]

87. Marmor MF. COVID-19 and chloroquine/hydroxychloroquine: is there ophthalmological concern? *Am J Ophthalmol* 2020; 213:A3–A4. [DOI] [PMC free article] [PubMed] [Google Scholar]

88. Mitja O, Corbacho-Monne M, Ubals M, et al. A cluster-randomized trial of hydroxychloroquine for prevention of COVID-19. *N Engl J Med* 2021; 384:417–427. [DOI] [PMC free article] [PubMed] [Google Scholar]

89. Geleris J, Sun Y, Platt J, et al. Observational study of hydroxychloroquine in hospitalized patients with COVID-19. *N Engl J Med* 2020; 382:2411–2418. [DOI] [PMC free article] [PubMed] [Google Scholar]

90. Stevens DV, Tran AQ, Kim E. Complications of orbital emphysema in a COVID-19 patient. *Ophthalmology* 2020; 127:990.doi:10.1016/j.ophtha.2020.05.011. [DOI] [PMC free article] [PubMed] [Google Scholar]

91. Das D, Anwer Z, Kumari N, Gupta S. Unilateral orbital emphysema in a COVID-19 patient. *Indian J Ophthalmol* 2020; 68:2535.doi:10.4103/ijo.IJO_2385_20. [DOI] [PMC free article] [PubMed] [Google Scholar]

92. Jammal H, Khader Y, Shihadeh W, et al. Exposure keratopathy in sedated and ventilated patients. *J Crit Care* 2012; 27:537–541. [DOI] [PubMed] [Google Scholar]

93. Soare C, Nowak VA, Osborne S. Eye Care in Intensive Care Group. Eye care in the intensive care unit during the COVID-19 pandemic and beyond. *Anaesthesia* 2020; 75:1118–1119. [DOI] [PMC free article] [PubMed] [Google Scholar]

94. Ruiz-Arranz C, Mencia-Gutierrez E, Bengoa-Gonzalez A, et al. Orbital-conjunctival-eyelid hemorrhage-hematoma due to inappropriate use of FFP2/NK95 facial mask in COVID-19. *Cureus* 2020; 12:e11273.doi:10.7759/cureus.11273. [DOI] [PMC free article] [PubMed] [Google Scholar]

95. Pandey SK, Sharma V. Mask-associated dry eye disease and dry eye due to prolonged screen time: are we heading towards a new dry eye epidemic during the COVID-19 era? *Indian J Ophthalmol* 2021; 69:448–449. [DOI] [PMC free article] [PubMed] [Google Scholar]

96. Kochgaway L, Nair AG, Mitra A, et al. COVID casualty: bilateral blindness due to ingestion of spurious sanitizer. *Oman J Ophthalmol* 2020; 13:164–166. [DOI] [PMC free article] [PubMed] [Google Scholar]

97. Greinacher A, Thiele T, Warkentin TE, et al. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. *N Engl J Med* 2021; 384:2092–2101. [DOI] [PMC free article] [PubMed] [Google Scholar]

98. Scully M, Singh D, Lown R, et al. Pathologic antibodies to platelet factor 4 after ChAdOx1 nCoV-19 vaccination. *N Engl J Med* 2021; 384:2202–2211. [DOI] [PMC free article] [PubMed] [Google Scholar]

99. Cines DB, Bussel JB. SARS-CoV-2 vaccine-induced immune thrombotic thrombocytopenia. *N Engl J Med* 2021; 384:2254–2256. [DOI] [PMC free article] [PubMed] [Google Scholar]

100. Reyes-Capo DP, Stevens SM, Cavuoto KM. Acute abducens nerve palsy following COVID-19 vaccination. *J AAPOS* 2021; doi:10.1016/j.jaapos.2021.05.003. [Epub ahead of print]. [DOI] [PMC free article] [PubMed] [Google Scholar]

101. Papasavvas I, Herbort CP, Jr. Reactivation of Vogt-Koyanagi-Harada disease under control for more than 6years, following anti-SARS-CoV-2 vaccination. *J Ophthalmic Inflamm Infect* 2021; 11:21.doi:10.1186/s12348-021-00251-5. [DOI] [PMC free article] [PubMed] [Google Scholar]

102. Rabinovitch T, Ben-Arie-Weintrob Y, Hareuveni-Blum T, et al. Uveitis following the BNT162b2 mRNA vaccination against SARS-CoV-2 infection: a possible association. *Retina* 2021; doi:10.1097/IAE.0000000000003277. [DOI] [PubMed] [Google Scholar]

103. Mudie LI, Zick JD, Dacey MS, Palestine AG. Panuveitis following vaccination for COVID-19. *Ocul Immunol Inflamm* 2021; 1–2. [DOI] [PubMed] [Google Scholar]

104. Maleki A, Look-Why S, Manhapra A, Foster CS. COVID-19 recombinant mrna vaccines and serious ocular inflammatory side effects: real or coincidence? *J Ophthal Vision Res* 2021; 16:490–501. [DOI] [PMC free article] [PubMed] [Google Scholar]

105. Wasser LM, Roditi E, Zadok D, et al. Keratoplasty rejection after the BNT162b2 messenger RNA vaccine. *Cornea* 2021; 40:1070–1072. [DOI] [PMC free article] [PubMed] [Google Scholar]

106. Phylactou M, Li JO, Larkin DFP. Characteristics of endothelial corneal transplant rejection following immunisation with SARS-CoV-2 messenger RNA vaccine. *Br J Ophthalmol* 2021; 105:893–896. [DOI] [PubMed] [Google Scholar]

107. Rallis KI, Ting DSJ, Said DG, et al. Corneal graft rejection following COVID-19 vaccine. *Eye (Lond)* 2021; 1–2. [DOI] [PMC free article] [PubMed] [Google Scholar]

108. Bohler AD, Strom ME, Sandvig KU, et al. Acute macular neuroretinopathy following COVID-19 vaccination. *Eye (Lond)* 2021; 1–2. [DOI] [PMC free article] [PubMed] [Google Scholar]

109. Khan TA, Sidhu N, Khan L, et al. Bilateral immune-mediated keratolysis after immunization with SARS-CoV-2 recombinant viral vector vaccine. *Cornea* 2021; 40:1629–1632. [DOI] [PubMed] [Google Scholar]

110. Saraceno JJF, Souza GM, Dos Santos Finamor LP, et al. Vogt-Koyanagi-Harada Syndrome following COVID-19 and ChAdOx1 nCoV-19 (AZD1222) vaccine. *Int J Retina Vitreous* 2021; 7:49.doi:10.1186/s40942-021-00319-3. [DOI] [PMC free article] [PubMed] [Google Scholar]

111. Pichi F, Aljneibi S, Neri P, et al. Association of ocular adverse events with inactivated COVID-19 vaccination in patients in Abu Dhabi. *JAMA Ophthalmol* 2021;

e213477.doi:10.1001/jamaophthalmol.2021.3477. [DOI] [PMC free article] [PubMed] [Google Scholar]

112. Jumroendararasame C, Panyakorn S, Othong R, et al. Transient visual field loss after COVID-19 vaccination: experienced by ophthalmologist, case report. *Am J Ophthalmol Case Rep* 2021; 24:101212.doi:10.1016/j.ajoc.2021.101212. [DOI] [PMC free article] [PubMed] [Google Scholar]

113. Jampol LM, Tauscher R Schwarz, HCOVID-L 19. COVID-19 vaccinations, and subsequent abnormalities in the retina: causation or coincidence? *JAMA Ophthalmol* 2021; 139:1135–1136. [DOI] [PubMed] [Google Scholar]
