

## Ocular Manifestations in Symptomatic Covid-19 Patients

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### Abstract

**Background and objective:** As we are in the era of COVID-19 as which is new disease for our communities and we are responsible for what's new in our ophthalmology world, we want to report the new ocular finding in patients that got the infection and how this affected their vision.

**Methods:** The study was a hospital based prospective cross-sectional study which included patients with recent COVID-19 infection. The study was conducted in ophthalmology department of Erbil Teaching Hospital in Erbil city from June 2021 till April 2022. The participants were recruited from the outpatient clinic in a non-probability convenience sampling way.

**Results:** The most common ocular disease encountered in COVID-19 patients was posterior subcapsular cataract. Their ages were between 26->56. The cataract developed in twelve patients and it was bilateral in nine cases (18 eyes) with a varying degree of density. The next most common manifestation was multiple punctate epitheliopathy found in nine patients which was bilateral in all of them. Follicular conjunctivitis was encountered in eight patients; it resolved in a period of 5 to 8 days after the prescription of topical anti-inflammatory medications. Regarding the retina, eight patients had central retinal vein occlusion while branch retinal vein occlusion developed in two patients. Central serous chorioretinopathy developed in three patients and it was unilateral (3 eyes).

**Conclusion:** COVID-19 infection is a multi-systemic disease can cause a variety of ocular clinical symptoms and complications. Blurred vision and conjunctivitis like features are the most common ocular presentation of the infection.

**Keywords:** COVID-19; Posterior subcapsular cataract; Follicular conjunctivitis; Central serous chorioretinopathy.

### Introduction

The SARS-CoV-2 virus is an enveloped RNA virus with a single strand that is responsible for COVID-19. It has a high rate of transmission, especially among the elderly and those who suffer from comorbidities like immune suppression, respiratory disease, or diabetes mellitus, in particular.<sup>(1,2)</sup>

A large number of worldwide casualties have occurred, and the effect is being felt internationally. Usually, signs of COVID-19 occur within 2 to 14 days after virus

exposure. As was recently reported by the CDC, this may include symptoms such as coughing and shortness of breath (or trouble breathing), fever, chills, muscle or body aches, headache, sore throat, runny nose, nausea, vomiting, diarrhea, and new-onset of altered sensation of taste or odor.<sup>(2,3)</sup> Only lethargy and confusion can occur in elderly patients.

Anecdotal evidence suggests that an early infection with diarrhea is fairly typical; conjunctivitis and severe eye pain have also been reported.

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Some of the complications that can arise in severe cases include pneumonia, renal failure, cardiomyopathy, stroke, and encephalopathy.<sup>(1-3)</sup> The importance of this study is to evaluate the incidence of the ocular finding after COVID-19 infection. The rationale for this study is seeing many patients with ocular problems after infection.

The current understanding of the spread of COVID-19 is primarily focused on what is known about other related coronaviruses. There is a strong likelihood that the virus is transmitted from person to person primarily through the respiratory droplets that are produced when an infected person coughs or sneezes.<sup>(1,2)</sup> It is also possible for it to be spread when a person touches an object or surface that has been contaminated with the virus from an infected person, and then touches their own mouth, nose, or eyes.<sup>(3,4)</sup> In stool samples from infected patients, viral RNA was also detected, increasing the likelihood of transmission via the faecal/oral path. Current evidence suggests that asymptomatic and presymptomatic patients can transmit the disease.<sup>(2,4,5)</sup>

A research published on February 21 in JAMA reports a case of an asymptomatic carrier who, despite having regular chest computed tomography (CT) findings, may have infected five family members. In an outbreak at a long-term care skilled nursing facility in King County, Washington, 30% of patients tested positive for SARS-CoV-2; half of these were asymptomatic on the day of testing. In another study from China, the virus was found in 30% of patients.

The rationale for this study is seeing many patients with ocular problems after infection. As we are in the era of COVID-19 as which is new disease for our communities and we are responsible for what's new in our ophthalmology world, we want to report the new ocular finding in patients that got the infection and how this affected their vision. Does COVID-19 infection exert both direct and indirect effects on ocular issues

## Methods

### Study Design and Setting

The study was a hospital based prospective cross-sectional study which included patients with recent Covid 19 infection. The study was conducted in ophthalmology department of Erbil Teaching Hospital in Erbil city from June 2021 till April 2022. The participants were recruited from the outpatient clinic in a non-probability convenience sampling way. Patients of any age attended ophthalmology clinic with proven COVID-19 infection were enrolled in this study. The cases were confirmed by reverse-transcriptase polymerase-chain-reaction (RT-PCR) assays of nasopharyngeal swab specimens at Erbil Central Laboratory. For ethical and operational reasons, we chose to recruit only those patients who were discharged from the isolation ward of the hospital and had recovered well enough to return to their homes.

Participant should have the following criteria in order to be involved in the study: -Patients with recent COVID-19 infection (at least one month up to three months) diagnosed by nasopharyngeal swab and SARS-COV-2 RT-PCR. Any participant with any of the following settings has been excluded from the study: Participants with ocular disease prior to COVID-19 infection, patients on ocular or systemic medications prior to COVID-19 infection, history of ocular trauma, patients recovered from COVID-19 before three months from their initial presentation to ophthalmology clinic, and patients received COVID-19 vaccination.

### Study Participants Assessment

Patients had been inquired about ocular symptoms such as blurring of vision, ocular pain, irritation, diplopia, and other symptoms. Inquiry also made about the onset and progression of those symptoms and whether they had such symptoms before getting infection with COVID-19 or those symptoms appeared during or after being infected with the virus and the diagnosis of COVID-19 had been made.

Patients had also been inquired about their systemic manifestation, the need for hospitalization, mechanical ventilation and oxygen therapy, their past medical and surgical history, drug history. Full ophthalmological evaluations based on examination, including best corrected visual acuity (BCVA) using Snellen charts, LogMAR chart intraocular pressure measurement using Goldmann tonometry, refraction using autorefractometer, slit lamp biomicroscope with detailed lid and anterior segment exam, gonioscopy and dilated fundus examination using condensing lenses were performed. Ocular motility examination along with pupillary reflex and other cranial nerve examination had been performed.

Ocular surface and tear status had been evaluated by tear break up time and fluorescence clearance test. Ocular investigations had been tailored according to each specific patient's needs. Optical coherence tomography was performed to evaluate the macula, the optic disc and the ganglion cell complex in patients with retinal or disc involvement such as branch retinal vein occlusion or glaucoma. Color fundus pictures also taken in order to document the data. Visual field and MRI, CT scan used to figure out if there is any associate systemic disease.

### Statistical Analysis

Data analysis was performed through the Statistical Package for the Social Sciences (SPSS) version 26. Quantitative continuous variables were presented as mean, median and standard deviation. Categorical nominal and ordinal variables were

presented in form of frequencies and percentages.

### Ethical Consideration

All data will be anonymous and no personal, or identifiable information are required as a part of this study. Data from information will be stored with me and be kept until I publish my research results then I will discard them and I will ensure that no one will use them again.

An informed consent and information sheet will be given to patients according to his language, either English, Kurdish or Arabic before involving them into the research. Samples of information form, information sheet and informed consent are attached in the appendix.

### Results

Seventy-five patients who have been recruited from outpatient clinic with recent COVID-19 infection confirmed by nasal swap and PCR have been involved in this hospital based prospective cross-sectional study.

### Demographic Data of the Study Group

The demographic data of the study group are examined and illustrated in Table 1. The mean age of participants was  $39.59 \pm 14.54$  years. Most of the patients (45.3%) aged between 26 and 40 years followed by those aged between 11 to 25 years as they represented 32% of total participants. Those aged between 41 to 55 years represented 8% of total participants. In terms of gender, 39 participants were female and represented 52% of the study group while 36 male participants were about 48% of the study group.

**Table 1** Demographic data of the Study groups

Age (years)	Frequency	Percent %
11 – 25	24	32%
26 – 40	34	45.3%
41 – 55	6	8%
≥ 56	11	14.7%
<b>Gender</b>		
Male	36	48%
Female	39	52%
<b>Total</b>	100	100%

**Clinical presentation of study group participants**

In terms of the initial clinical symptoms and chief complaint, 44 patients (58.7%) reported a recent onset of blurring of vision. Seven patients reported a foreign body sensation with another seven had complained of red eye. Epiphora and periorbital swelling were the next common symptom in order of frequency. Reports of ocular pain and/or diplopia represented 8% of total participants. Few patients presented with either frequent blinking or nystagmus.

**Ocular manifestations of study group:**

The most common ocular disease encountered in COVID-19 patients was posterior subcapsular cataract (PSC) as

shown in Table 3 and Figure 1. There ages are between 26->56. The cataract developed in 12 patients and it was bilateral in 9 cases (18 eyes) with a varying degree of density. The next most common manifestation was multiple punctate epitheliopathy (9 patients) which was bilateral in all of them.

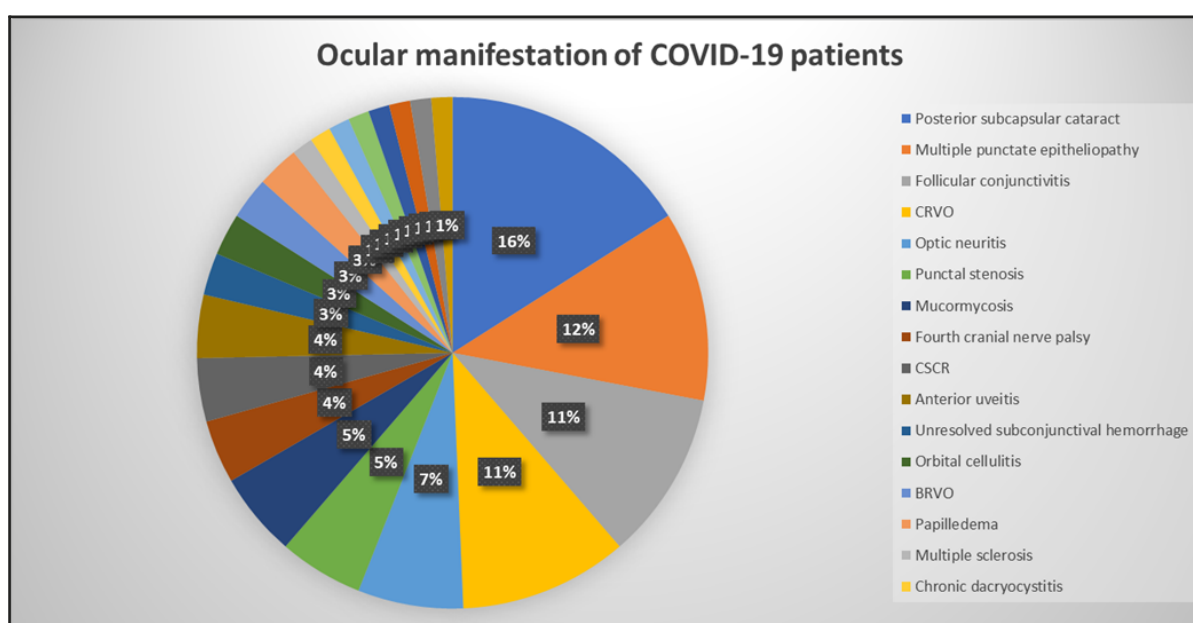
Follicular conjunctivitis was encountered in 8 patients; it resolved in a period of 5 to 8 days after the prescription of topical anti-inflammatory medications. Regarding the retina, eight patients had central retinal vein occlusion (CRVO) while branch retinal vein occlusion (BRVO) developed in 2 patients. Central serous chorioretinopathy (CSCR) developed in three patients and it was unilateral (3 eyes).

**Table 2** Chief complaints of study group participants

Chief complaint	Frequency	Percent %
Blurred vision	44	58.7%
Foreign body sensation	7	9.3%
Red eye	7	9.3%
Lacrimation	5	6.7%
Periorbital swelling	4	5.3%
Diplopia	3	4.0%
Ocular Pain	3	4.0%
Frequent blinking	1	1.3%
Nystagmus	1	1.3%
Total	75	100%

**Table 3** Ocular manifestations of COVID-19 patients

Ocular Manifestation	Frequency	Percent %	Ocular Manifestation	Frequency	Percent %
Posterior subcapsular cataract	12	16.0%	Orbital cellulitis	2	2.7%
Multiple punctate epitheliopathy	9	12.0%	BRVO	2	2.7%
Follicular conjunctivitis	8	10.7%	Papilledema	2	2.7%
CRVO	8	10.7%	Multiple sclerosis	1	1.3%
Optic neuritis	5	6.7%	Chronic dacryocystitis	1	1.3%
Punctal stenosis	4	5.3%	Vestibular neuritis	1	1.3%
Mucormycosis	4	5.3%	VKH	1	1.3%
Fourth cranial nerve palsy	3	4.0%	Valsalva retinopathy	1	1.3%
CSCR	3	4.0%	Multifocal choroiditis	1	1.3%
Anterior uveitis	3	4.0%	Anterior scleritis	1	1.3%
Unresolved subconjunctival hemorrhage	2	2.7%	Anterior necrotizing scleritis	1	1.3%

**Figure 1** Ocular manifestations of COVID-19 patients

In terms of neuroophthalmological manifestation; optic neuritis was the most common presentation followed by fourth cranial nerve palsy, papilledema, and multiple sclerosis and it represented 5.3%, 4%, 2.7%, and 1.3% of the total number of patients respectively. Ocular examination has revealed in a group of five patients' intraocular inflammation; three of them had anterior non granulomatous uveitis with one case of multifocal choroiditis and another of Vogt-Koyanagi-Harada disease (VKH).

The case with VKH had a complete diagnostic criterion with bilateral ocular involvement with neurological/auditory and

dermatological manifestation.

For those patients with age range between 11 and 25 years old, follicular conjunctivitis was the most common presentation followed by central retinal vein occlusion and multiple punctate epitheliopathy as illustrated in Table 4.

multiple punctate epitheliopathy was the most common manifestation in patients with an age between 26 and 40 years followed by posterior subcapsular cataract and optic neuritis. For those patients who were older than 56 years old, mucormycosis was the commonest followed by posterior subcapsular cataract and follicular conjunctivitis.

**Table 4** Ocular manifestations relation with age.

	11-25	26-40	41-55	≥ 56	
Ocular manifestations	No. (%)	No. (%)	No. (%)	No. (%)	P value
Follicular conjunctivitis	4 (5.3%)	2 (2.7%)	0	2 (2.7%)	0.168
CRVO	3 (4.0%)	1 (1.3%)	2 (2.7%)	2 (2.7%)	0.412
Multiple punctate epitheliopathy	3 (4.0%)	6 (8.0%)	0	0	0.331
PSC	2 (2.7%)	5 (6.7%)	2 (2.7%)	3 (4.0%)	0.669
Optic neuritis	0	4 (5.3%)	1 (1.3%)	0	0.494
Mucormycosis	0	0	0	4 (5.3%)	0.506



## Discussion

In 2022, after the outbreak of coronavirus disease, SARS-CoV-2 virus has reached six continent and is responsible for the death of more than 6 million human beings till now.<sup>(1)</sup> It is mainly a disease of the respiratory system but it may affect many other organs including the ocular system as reported in many studies.<sup>(2)</sup> This study evaluates the ocular manifestations of COVID-19 disease in Kurdistan region, Iraq as the first study to see the light in this particular area of the world.

This study has found that the blurring of vision was the most common symptoms among the patients (58.7%). Conjunctivitis-like symptoms such as foreign body sensation, red eye and lacrimation comes next in line in order of frequency. Periorbital swelling, diplopia and ocular pain had been reported less frequently by the patients. Other reports worldwide showed a wide and significant heterogeneity for all the presenting ocular symptoms. Chen *et al.* reported that 12.7% had blurred vision, 20.9% with dry eye and 11.7% with foreign body sensation.<sup>(3)</sup> Perlman *et al.* has reported 29.1% with dry eye and 19.1% with ocular pain.<sup>(8)</sup>

On the other hand, GuemesVillahoz *et al.* had reported 50% of cases had red eye, 8.3% subconjunctival hemorrhage, and pterygium in 5.5%.<sup>(9)</sup> Rokohl *et al.* found that 34.26% of patients had burning sensation, 31.4% had epiphora and 20.2 % had photophobia.<sup>(10)</sup> This study has shown that posterior subcapsular cataract is the most common ocular complication (16%) in COVID-19 patients. Chen *et al.* reported 1.6% cases presented with cataract while Abrishami *et al.* reported 7.7% cases of cataract.<sup>(11)</sup> Cataract development due to three points; the increase of oxidative stress on the lens by the viral infection, increase in use of systemic corticosteroids, and the development of uveitis secondary to COVID-19 as this and many other studies reported.<sup>(12)</sup>

This study has shown ocular surface problems that represent the next most

common diagnosis after cataract.

Most commonly reported is follicular conjunctivitis, multiple punctate epitheliopathy and punctal stenosis. The prevalence of conjunctivitis varied from <1% to 63.6%.<sup>(13,14)</sup> This agrees with Bostanci *et al.* and Oncul *et al.*<sup>(15,16)</sup> Conjunctivitis has been reported to be the first clinical manifestation of COVID-19 infection.

In terms of retinal pathology, this study revealed eight cases of central retinal vein occlusion with three cases in the age range between 11 and 25 years. CRVO was followed by CSCR and BRVO in order of frequency. Walinjar *et al.*, Sheth *et al.*, Invernizzi *et al.*, and Gaba *et al.* have reported CRVO as a sequelae to COVID-19 patients with varying severity and outcome.<sup>(17-19)</sup> The development of CRVO can be explained by the fact the COVID-19 infection is a procoagulant state with elevation of cytokine, prothrombin and D-Dimer. Added to that, the involvement of respiratory tract results in hypoxia which is an important risk factor for CRVO development.<sup>(20,21)</sup>

On the other hand, Sanjay *et al.* has reported a case of CSCR after COVID-19 infection; the status of stress due to illness and the use of corticosteroid may justify the development of CSCR. Various forms of uveitis had been reported by this study; mostly anterior non granulomatous uveitis, a case of VKH and one case of multifocal choroiditis. Collange *et al.* presented a patient with posterior uveitis, Mazzotta *et al.* described a patient with anterior uveitis, and Pascual *et al.* reported a case of pan uveitis. There is one reported case of multifocal choroiditis by Providencia *et al.*<sup>(22-24)</sup> The deregulation of the immune and inflammatory status of the eye caused by COVID-19 may explain the development of various types of uveitis.<sup>(24)</sup>

Optic neuritis, fourth cranial nerve palsy, and papilledema were the most common neuroophthalmological manifestation in this study. There has been reports by Dinkin *et al.*, Falcone *et al.*, Pascual-Goni *et al.*,

and Belghmaidi *et al.* on multiple ocular cranial nerve paresis.<sup>(25-28)</sup> Zhou *et al.* also reported a case of optic neuritis.<sup>(29)</sup> The presence of ACE2 receptor on the nerve ending and it is being used by the virus in order to enter the tissue makes the nerves a favorable target to the virus.<sup>(30)</sup> Orbital cellulitis and Mucormycosis, which is life threatening, has also being reported by this study. Such orbital involvement had been reported by Turbin *et al.* and Shires *et al.* Again, the decrease and deregulation of the immune system and the use of systemic corticosteroid may contribute to the development of such complications.<sup>(31,32)</sup> One of the limitations of this study is that it was conducted in one city with a small size and non-diverse; so, we should not draw the inference that those results can be applied on greater population.

To the best of our knowledge, this is the first study in Kurdistan region that studied the ocular manifestation of COVID-19 disease.

## Conclusion

COVID-19 infection is a multi-systemic can cause a variety of ocular clinical symptoms and complications. Blurred vision and conjunctivitis like features are the most common ocular presentation of the infection. Posterior subcapsular cataract was the most common ocular diagnosis made in patients post COVID-19 infection and may be due to the drugs that are used for treatment of covid, as you know most patient who suffer from covid take steroids to decrease inflammation of the lung.

We recommend that the issue at hand necessitates further research with a larger sample size. The ocular manifestations that manifest during the initial stages of COVID-19 infection, The long-term repercussions of the virus's ocular manifestations and complications. The current availability of a variety of vaccines may lead to an adverse influence on the eyes as a result.

## Competing interests

The authors declare that they have no competing interests.

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