

## Original Article

# COVID-19 Ocular Manifestation: A Cross-Sectional Study

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**Abstract****Introduction**

The world is infected with a new strain of the coronavirus family known as COVID-19. This virus strain attacked several organs in the human body, causing symptoms ranging from mild to severe and, in some cases, life-threatening. Multiple organs, including the eye, can get infected.

**Methods**

The study was a single-center prospective cross-sectional study that included patients with a recent COVID-19 infection. The study was conducted in the ophthalmology department of Erbil Teaching Hospital in Erbil City from June 2021 to April 2022. The participants were recruited from the outpatient clinic in a non-probability convenience sampling way.

**Results**

The study included 75 patients. The most common ocular disease encountered in COVID-19 patients was posterior subcapsular cataract (12, 16.0%). Their ages are between 26 and 56 years old. The cataract developed in twelve patients (12, 16.0%) and was bilateral in nine cases (18 eyes) with varying 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 5 to 8 days after the prescription of topical anti-inflammatory medications.

**Conclusion**

COVID-19 infection is a multi-systemic disease that can cause various ocular clinical symptoms and complications. Blurred vision and conjunctivitis-like features are the most common ocular presentations of the infection.

## 1. Introduction

The SARS-CoV-2 virus, which causes COVID-19, is an enveloped RNA virus with a single strand. It has a high rate of transmission, particularly among the elderly and those with comorbidities such as immunological suppression, pulmonary disease, or diabetes mellitus [1,2]. Global casualties have been significant, impacting populations worldwide. Symptoms typically manifest within 2 to 14 days of virus exposure and may include coughing, shortness of breath (or difficulty in breathing), fever, chills, muscular or body pains, headache, sore throat, runny nose, nausea, vomiting, diarrhea, and the new-onset of a changed taste or odor [2,3]. In older people, tiredness and disorientation may be predominant. An early onset of illness with diarrhea appears common, based on anecdotal data, along with reports of conjunctivitis and severe eye discomfort. Severe cases can lead to complications such as encephalopathy, pneumonia, cardiomyopathy, stroke, and renal failure [1-3]. This study is important since it assesses the incidence of ocular findings following COVID-19 infection. This investigation was motivated by the observation that numerous patients had eye complications following the infection.

The study aims to report the ocular findings in patients who have the infection and how this has affected their vision.

## 2. Methods

### 2.1. Study design and setting

The study was a single-center prospective cross-sectional study that included patients who had recently been infected with COVID-19. From June 2021 to April 2022, the study was done in the ophthalmology department of Erbil Teaching Hospital in Erbil, Iraq. Non-probability convenience sampling was used to enroll individuals from the outpatient clinic. This study involved patients of any age who attended an eye clinic and had a verified COVID-19 infection. Reverse-transcriptase polymerase chain reaction (RT-PCR) studies on nasopharyngeal swab specimens at Erbil Central Laboratory confirmed the cases. We selected to recruit only patients who had been discharged from the hospital's isolation unit and had recovered sufficiently to return home for ethical and operational considerations.

### 2.2. Inclusion criteria

For a participant to be included in the study, they must meet the following requirements: Individuals who have recently contracted COVID-19 (for at least one month, up to three months), as determined by SARS and nasopharyngeal swap RT-PCR for SARS-COV-2.

### 2.3. Exclusion criteria

Participants with any of the following conditions were ruled out of the study: Participants had an ocular illness before the COVID-19 infection. Patients who were taking ocular or systemic drugs before infection with COVID-19, patients with a history of ocular trauma, patients who recovered from COVID-19 before three months from their initial presentation to the

ophthalmology clinic, and patients who received the COVID-19 vaccination

### 2.4. Study Participant Assessment

Patients had been asked about ocular symptoms such as blurring of vision, ocular pain, irritation, diplopia, and other symptoms. The inquiry was also made about the onset and progression of those symptoms and whether they had such symptoms before getting an infection with COVID-19 or whether those symptoms appeared during or after being infected with the virus, and the diagnosis of COVID-19 had been made. Patients had also been asked about their systemic manifestation, the need for hospitalization, mechanical ventilation, and oxygen therapy, their past medical and surgical history, and their drug history. Full ophthalmological evaluations based on an examination, including best corrected visual acuity (BCVA) using Snellen charts, LogMAR chart intraocular pressure measurement using Goldmann tonometry, refraction using an auto-refractometer, slit lamp biomicroscope with a detailed lid and anterior segment exam, gonioscopy, and dilated fundus examination using condensing lenses, were performed. An ocular motility examination, along with a pupillary reflex and other cranial nerve examinations, had been performed. Ocular surface and tear status were evaluated by tear break-up time and fluorescence clearance tests. 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 were also taken to document the data. Visual field, MRI, and CT scans are used to figure out if there is any associated systemic disease.

### 2.5. Data 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 the form of frequencies and percentages.

## 3. Results

The total number of patients was 75. The mean age of the participants was  $39.59 \pm 14.54$  years. Most of the patients (45.3%) were aged between 26 and 40 years, followed by those aged between 11 and 25 years, as they represented 32% of the total participants. Those aged between 41 and 55 years represented 8% of the total participants. In terms of gender, 39 participants (52%) were female and 36 (48%) were male. 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, and another seven complained of red eyes. Epiphora and periorbital swelling were the next most common symptoms, in order of frequency. Reports of ocular pain and/or diplopia represented 8% of the total participants. Few patients presented with either frequent blinking or nystagmus. The most common ocular disease encountered in COVID-19 patients was posterior subcapsular

cataract (PSC) (Table 1). Their 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

**Table 1: Demographic and Ocular Manifestation**

Variables	N. patients (%)
<b>Demographics</b>	
Age (mean of means)	40.93 yrs.
11 – 25	24 (32%)
26 – 40	34 (45.3%)
41 – 55	6 (8%)
≥ 56	11 (14.7%)
<b>Sex</b>	
Male	36 (48%)
Female	39 (52%)
<b>Presentation</b>	
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%)
Ocular Pain	3 (4%)
Frequent blinking	1 (1.3%)
Nystagmus	1 (1.3%)
<b>Ocular Manifestation</b>	
Posterior sub capsular cataract	12 (16.0%)
Multiple punctate epitheliopathy	9 (12.0%)
Follicular conjunctivitis	8 (10.7%)
CRVO	8 (10.7%)
Optic neuritis	5 (6.7%)
Punctual stenosis	4 (4.0%)
Mucormycosis	4 (4.0%)
Fourth cranial nerve palsy	3 (4.0%)
CSCR	3 (4.0%)
Anterior uveitis	3 (4.0%)
Unresolved subconjunctival hemorrhage	2 (2.7%)
Orbital cellulitis	2 (2.7%)
BRVO	2 (2.7%)
Papilledema	2 (2.7%)
Multiple sclerosis	1 (1.3%)
Chronic dacryocystitis	1 (1.3%)
Vestibular neuritis	1 (1.3%)
VKH	1 (1.3%)
Valsalva retinopathy	1 (1.3%)
Multifocal choroiditis	1 (1.3%)
Anterior scleritis	1 (1.3%)
Anterior necrotizing scleritis	1 (1.3%)

vein occlusion (BRVO) developed in two patients. Central serous chorioretinopathy (CSCR) developed in three patients, and it was unilateral (3 eyes). In terms of neuroophthalmological manifestation, optic neuritis was the most common presentation, followed by fourth-cranial nerve palsy, papilledema, and multiple sclerosis (internuclear ophthalmoplegia and nystagmus, resulting in diplopia, oscillopsia, blurred visual, loss of stereopsis, and reading fatigue), which represented 5.3%, 4%, 2.7%, and 1.3% of the total number of patients, respectively. The ocular examination revealed 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 and neurological, auditory, and dermatological manifestations. (Table 1).

For those patients with an 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 2. 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 most common, followed by posterior subcapsular cataract and follicular conjunctivitis (Table 2).

#### 4. Discussion

Covid-19, a novel coronavirus (nCoV) virus, was initially detected in Wuhan, China, in 2019 and quickly evolved into the fifth documented flu pandemic since 1918. Within two years of its discovery, the pandemic has led to more than 200 million confirmed cases and 4.6 million deaths worldwide [4]. This study evaluates the ocular manifestations of COVID-19 disease in the Kurdistan region, to the best of our knowledge, marking the first such investigation in the region [5].

CoV, a single-strand positive-strand RNA virus, primarily causes severe respiratory problems in humans while also affecting the gastrointestinal and central neurological systems, posing a significant risk to human life [6]. Human-to-human transmission of COVID-19 primarily occurs through respiratory droplets expelled by an infected individual while coughing or sneezing. Additionally, contact with contaminated objects by infected individuals poses a risk through fomite transfer. When this virus enters the body, it utilizes human angiotensin II (ACE2) as a cell entry receptor, infiltrating respiratory and lung epithelial cells via the spike (S) protein [7]. However, recent research suggests that COVID-19 transmission might not be limited to spreading droplets and fomites alone. There is growing evidence that the eye may be a potential transmission route with the use of eye drops as a means of entering the respiratory tract. As droplets infect the conjunctiva, the virus enters tears via the lacrimal duct before spreading to the nasal and nasopharyngeal mucosa, contributing to respiratory tract infections [8]. Recent studies and meta-analyses have found a higher prevalence of ocular signs and symptoms, ranging from 2% to 32% [9].

Patients typically report symptoms such as conjunctivitis, ocular discomfort, redness, swelling, and discharge. Follicular conjunctivitis is frequently the first symptom of COVID-19 [10]. The most common symptom reported by patients in this study (58.7%) was blurred vision, followed by conjunctivitis-like symptoms such as foreign body sensation, redness, and excessive tearing. Other less common symptoms include periorbital swelling, double vision, and ocular pain. Other reports worldwide revealed a wide and significant heterogeneity

in all the presenting ocular symptoms. Perlman et al. [11] reported 29.1% dry eyes and 19.1% ocular pain. Guemes-Villahoz et al. found that 50% of cases had red eyes, 8.3% had subconjunctival hemorrhage, and 5.5% had pterygium. [12] Rokohl et al. discovered that 34.26% of patients had a burning sensation, 31.4% had epiphora, and 20.2% had photophobia [13]. This study found that posterior subcapsular cataract is the most common ocular manifestation (16%) in COVID-19 patients. Abrishami et al. reported 7.7% of cataract cases [14].

cranial nerve paresis [28-31]. Zhou et al. also described an optic neuritis case [32]. The presence of the ACE2 receptor on the nerve ending, which the virus uses to enter the tissue, makes the nerves a desirable target for the virus [33]. This investigation also discovered orbital cellulitis and mucormycosis, both of which are potentially fatal. Turbin et al. and Shires et al. both reported orbital involvement. Again, immune system suppression and dysregulation, as well as the use of systemic corticosteroids, may contribute to the development of such

**Table 2:** Ocular manifestation according to age varying by age

Variable	Age				P-value
	11-25	26-40	41-55	≥ 56	
Ocular manifestations					
Follicular conjunctivitis	4 (5.3%)	2 (2.7%)	0 (0.0%)	2 (2.7%)	0.168
CRVO	3 (4.0%)	1 (1.3%)	2 (2.7%)	2 (2.7%)	0.168
Multiple punctate epitheliopathy	3 (4.0%)	6 (8.0%)	0 (0.0%)	0 (0.0%)	0.331
PSC	2 (2.7%)	5 (6.7%)	2 (2.7%)	3 (4.0%)	0.669
Optic neuritis	0 (0.0%)	4 (5.3%)	1 (1.3%)	0 (0.0%)	0.494
Mucormycosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (5.3%)	0.506

Cataract development occurs due to three factors: increased oxidative stress on the lens caused by viral infection, increased use of systemic corticosteroids, and the development of uveitis secondary to COVID-19 as this and many other studies report [15].

This study showed that ocular surface issues are the second most common diagnosis after cataracts. The most commonly reported conditions are follicular conjunctivitis, multiple punctate epitheliopathy, and punctual stenosis. Individuals experience conjunctivitis at rates ranging from 1% to 63.6% [16,17], which is consistent with the findings of Bostanci et al. and Oncul et al. [18,19]. Intriguingly, conjunctivitis has been identified as the first clinical sign of COVID-19 infection.

Regarding retinal diseases, this investigation focuses on eight cases of central retinal vein occlusion (CRVO), three of which occurred in people aged 11 to 25. CRVO emerges as a common sequela in COVID-19 patients, with varying severity and prognosis [20,21,22]. COVID-19 induces a procoagulant condition characterized by elevated D-dimer, prothrombin, and cytokine levels, which is likely to contribute to the development of CRVO. Additionally, respiratory tract-induced hypoxia is a significant risk factor for CRVO [23,24]. In contrast, Sanjay et al. reported a case of central serous chorioretinopathy (CSCR) following COVID-19 infection, implying a link between corticosteroid use and illness-related stress.

Furthermore, this study distinguishes between various types of uveitis, the majority of which are anterior non-granulomatous uveitis, with some cases of Vogt-Koyanagi-Harada disease (VKH) and multifocal choroiditis. Collange et al., Mazzotta et al., Pascual et al., and Providencia et al. have published studies on various types of uveitis [25-26]. COVID-19-induced dysregulation of the eye's immunological and inflammatory conditions is most likely responsible for the development of these uveitis types [27].

The most common neuroophthalmological manifestations in this investigation were optic neuritis, fourth cranial nerve palsy, and papilledema. Dinkin et al., Falcone et al., Pascual-Goni et al., and Belghmaidi et al. have published studies of numerous ocular

problems [34,35]. However, it is important to note one limitation of this study: it was conducted in a small, non-diverse city. Therefore, caution should be exercised when extending these results to larger populations.

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

## 5. Conclusion

The COVID-19 infection is multi-systemic and can cause various ocular clinical symptoms and complications. Blurred vision and conjunctivitis-like features are the most common ocular presentations of the infection. Posterior subcapsular cataract was the most common ocular diagnosis made in patients post-COVID-19 infection.

## Declarations

**Conflicts of interest:** The author(s) have no conflicts of interest to disclose.

**Ethical approval:** was obtained from the ethical committee of the University of Sulaimani.

**Patient consent** (participation and publication): Written informed consent was obtained from the patient for participation in the present study and the publication of the study along with any accompanying images.

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**Role of Funder:** The funder remained independent, refraining from involvement in data collection, analysis, or result formulation, ensuring unbiased research free from external influence.

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**Authors' contributions:** HAR was a major contributor to the conception of the study, as well as in the literature search for

related studies. KKM, SHM, SJH, and IJH were Involved in the literature review, the writing of the manuscript, and data analysis and interpretation. BAA and FA Literature review, final approval of the manuscript, and processing of the tables. FHK and AAQ were involved in the literature review and the writing of the manuscript. REM and HKA were involved in the literature review, the design of the study, and the critical revision of the manuscript. SHM and KKH Confirmation of the authenticity of all the raw data All authors approved the final version of the manuscript.

**Use of AI:** AI was not used in the drafting of the manuscript, the production of graphical elements, or the collection and analysis of data.

**Data availability statement:** Not applicable.

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