Case Series

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Ocular manifestations in COVID-19 infections: a case series

Naram Khalayli, MD[a], Ghina Haider, MD[a,*], Yara Hodifa, MD[a], Maysoun Kudsi, PhD, MD[a], Nada Naman, MD[b]

Introduction: The prevalence of ocular abnormalities of COVID-19 is different according to different reports. However, currently available evidence on the presence of this virus in ocular secretions and its association with conjunctivitis is not well established.
Objective: To reveal the ocular features among COVID-19 patients and to describe them with the findings of clinical data, inflammatory markers, and respiratory support therapy.
Methods: Ocular symptoms were evaluated and recorded in 494 COV19 patients through questionnaire-style interviews, and an ophthalmologic examination. Data including age, sex, disease severity, and nasopharyngeal swab results were collected. Laboratory test values were reviewed. Patients with COVID-19 infections were classified into severe cases and mild cases.
Results: The prevalence of ocular features was (2.83%). The most common features were conjunctival hyperaemia, epiphora, and foreign body sensation with itching. Patients with ocular manifestations on CPAP support therapy had higher rates of itching, lower rates of foreign body sensation. No differences were found in the levels of inflammatory marker. Meanwhile, patients used respiratory-aid therapy revealed higher values of white blood cells, platelet counts, erythrocyte sedimentation rate, C-reactive protein, ferritin, and lactate dehydrogenase.
Discussion: Ocular involvement in COVID-19 and possibility of disease transmission through ocular tissues and secretions, has been registered in some reports, with a prevalence of 2–32%. The external and internal ocular parts are involved.
Conclusion: Ocular features are not infrequent in COVID-19 patients.

Keywords: conjunctivitis, COVID-19, ocular manifestations, uveitis

Introduction

Coronavirus infections have been responsible for respiratory illnesses since 2019 with varying severity worldwide[1].

Extra-respiratory manifestations of this COVID-19 have been described, including a possible ocular involvement, usually at the onset of the illness[2]. The prevalence of ocular abnormalities ranges from 0.8 to 31.6%, according to different reports[3,4], and happens either as a prodromal manifestation of the disease or during hospitalization[5]. Moreover, some ophthalmologists were infected during clinical practice, prompting research on the possibility of COVID-19 transmission through eye contact[6]. However, currently available evidence on the presence of the COVID-19 virus in ocular secretions and its association with conjunctivitis is not well established.

Respiratory support therapy has been associated with ocular irritation symptoms, but its relationship with the development of ocular abnormalities in COVID-19 patients has not been investigated until now[7].

This report aimed to reveal the prevalence of ocular manifestations in a sample of Syrian patients with COVID-19 infections and to describe its relationship with clinical data, laboratory inflammatory markers, and respiratory support therapy in our sample of patients.

HIGHLIGHTS

- To reveal the ocular features among COVID-19 patients and to describe them with the findings of clinical data, inflammatory markers, and respiratory support therapy.
- Currently available evidence on the presence of this virus in ocular secretions and its association with conjunctivitis is not well established.
- In our cases the prevalence of ocular features was (2.83%). The most common features were conjunctival hyperaemia, epiphora, and foreign body sensation with itching. Patients with ocular manifestations on CPAP support therapy had higher rates of itching, lower rates of foreign body sensation.
- Patients used respiratory-aid therapy revealed higher values of white blood cells, platelet counts, erythrocyte sedimentation rate, C-reactive protein, ferritin, and lactate dehydrogenase.

[a]Damascus University and [b]DIS in Ophthalmology, Director of Sham Medical Complex, Damascus, Syrian Arab Republic

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article

*Corresponding author. Address: Al Mazzeh, Jalaa St., Faculty of Medicine. E-mail: gtghinahaidar@gmail.com (G. Hiader).

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Materials and methods

Sample size calculation and study design

A cross-sectional study, conducted on COVID-19-infected patients, Damascus, Syria, between November 2021 and November 2022.

The sample size was calculated via www.raosoft.com and it was 385 patients with a CI of 95% and a predictive value of 0.05. Our study sample size was 494 patients.

All procedures were compatible with the declaration of Helsinki

Inclusion criteria: COVID-19-infected patients, all above 18 years old who had ocular manifestations.

Exclusion criteria were any previous ocular complaints, ocular disease, ocular therapy or surgery, and any other cause of ocular surface alterations lasting more than 1 week before the COVID-19 infection.

Methods

The diagnosis of COVID-19 infection was either by positive polymerase chain reaction assay from nasopharyngeal swabs and/or compatible findings with interstitial pneumonia in the course of COVID-19 infection on chest computerized tomography.

Patients were classified as severe cases if they need respiratory support, meanwhile, those without respiratory support and in the absence of severe disease criteria were classified as mild cases.

Medical history

Data including age, sex, disease severity, the findings of computed tomography-Scans, nasopharyngeal swab results were collected .

Ocular symptoms were recorded through questionnaire-style interviews, then the patients were examined by an ophthalmic consultant who had accepted all the risks of examining COVID-19-infected patient

Physical examination

Full clinical examination was performed for the patients, and all the positive clinical signs had been registered, in addition to ocular examination performed by the same ophthalmic consultant

Laboratory analysis

Blood samples were collected including, complete blood count, urea, creatinine, erythrocyte sedimentation rate, and C-reactive protein. The sample analysis was performed with an automatic analyzer (Mindray/Olympus). Nasopharyngeal swabs were performed for all patients.

Measurements

WHO guidelines

According to the WHO guidelines[8], patients were classified as severe cases if they need respiratory support, meanwhile, those without respiratory support and in the absence of severe disease criteria were classified as mild cases.

Ocular examination

- Dry eye evaluation was performed by Schirmer test , fluorescein staining, and Rose Bengal (RB) staining. A 5-min conventional Schirmer test without anaesthesia was performed by placing a Schirmer strips at the junction of the middle and lateral third of the lower lid margin and into the tear film, and less than 55 mm in 5 min was considered positive.

Fluorescein measurements was considered in the mean value of a 1% total of three measurements was recorded.

- RB staining was performed by touching the inferotemporal bulbar conjunctiva with a RB strip, using van Bijsterveld scoring to classify the reaction, considering the positivity by TBUT less than 10 s and RB score greater than 3.

Patients were diagnosed with sicca eye if two or more tests were abnormal and with probable if only one test was abnormal. The diagnosis of KCS in this study was made by Copenhagen criteria.

- The best-corrected visual acuity was assessed using the Snellen chart, and the near vision was assessed using Jaeger charts. After the vision assessment, cover test and ocular motility examination, biomicroscopy was performed.
- The posterior pole was further evaluated by slit-lamp biomicroscopy using a 78-D Volk lens.
- Intraocular pressure was measured by Goldmann applanation tonometry.
- Indirect ophthalmoscopy was performed with an indirect ophthalmoscope and a 20-dioptre lens after both pupils were dilated with 1% tropicamide.
- A gonioscopy and automated perimetry using a Humphrey field analyzer was underwent to patients with suspected glaucoma (IOP >21 mmHg in either eye or IOP difference > 5 mmHg between the two eyes or optic disc suspicious for glaucoma). The glaucoma definition that was adopted has been defined elsewhere.

Our Case Series is compliant with The PROCESS 2020 Guideline[9], and this work is submitted on the research registry dashboard

Statistical analysis

Counts and percentages expressed all values for categorical variables, and quantitative variables were expressed as means ± SDs.

Results

A total of 494 patients with confirmed COVID-19 infections were enroled. Four hundred sixty (93.11%) patients had positive nasopharyngeal swabs, while 34 (6.88%) were diagnosed with suggestive computed tomography lung imaging findings. 320 (64.97%) were male, and 174 (35%) were women; the mean age was 64.2 ± 13.4 years.

Ocular features were found in 14 out of 494 patients (2.83%). Our results showed that age and sex had no significant effect on the prevalence and/or type of ocular presentation because out of the 14 patients with ocular manifestations, 8 were males, and 6 were females. The mean age of males was 54 ± 12.3 years, meanwhile, the mean age of the females was 49.5 ± 15.8 years.

The most common features were conjunctival hyperaemia, epiphora, foreign body sensation with itching, lid swelling, and

mucopurulent discharge. There was 1 patient with uveitis, and another with pan-uveitis. Patients had complained of more than one symptoms (Table 1).

Six patients had a severe form of the disease, while eight patients had a mild form. No relation was found between the disease severity and the ocular symptoms. The two patients with uveitis and pan-uveitis were not hospitalized as they had mild diseases.

Patients with ocular manifestations that were using CPAP therapy had higher rates of itching, lower rates of foreign body sensation, and the same rate of conjunctival hyperaemia, and epiphora.

No differences were found in levels of inflammatory markers based on the presence of ocular symptoms, meanwhile, patients with ocular symptoms and using CPAP machines (four patients), or ventilators (two patients) revealed higher values of white blood cells, platelet counts, erythrocyte sedimentation rate, and C-reactive protein.

Discussion

Ocular involvement in COVID-19 and the possibility of disease transmission through ocular tissues and secretions have been registered in some reports[2–5].

The prevalence and type of ocular manifestations differ according to the reports. The prevalence was found to be present in 2–32% of COVID-19-infected patients[10], 31.6% according to other reports[3], and 11.64% in another report[11]. Our study reported a (2.83%) prevalence of ocular manifestations in patients with a COVID-19 infection. We believe that this is important since only a minor percentage of infected patients require hospitalization and ocular symptoms related to COVID-19 may be more prevalent in the prodromal stages of the disease.

Conjunctival hyperaemia, unilateral and bilateral conjunctivitis, follicular conjunctivitis, chemosis, epiphora, red eye, foreign body sensation with itching, lid swelling, and mucopurulent discharge, are the most common outside-ocular involvement[3,10–13]. Haemorrhagic conjunctivitis with pseudomembranes was reported in one patient[14]. Daruich *et al.*[15] reported unilateral conjunctivitis as the first sign of COVID-19. Méndez Mangana *et al.*[16] reported the first case with episcleritis. The results of the above studies are compatible with ours.

The prevalence rate of acute conjunctivitis ranges from 1.1 to 31.6%[10,11,14], while its prevalence was higher in our cases, and this may be due to the small sample limited to one area, and to the lack of knowledge about COVID-19 infection in a low economic society.

Table 1

Ocular features

Ocular features	No. patients, *n* (%)
Conjunctival hyperaemia	11 (78.57)
Epiphora	11 (78.57)
Foreign body sensation with itching	13 (92.85)
Lid swelling	4 (28.57)
Mucopurulent discharge	2 (14.28)
Uveitis	1 (7.14)
Pan-uveitis	1 (7.14)

The tropism of COVID-19 for the conjunctival mucosa may differ among different virus isolates[4–7]. Moreover, ocular symptoms might occur in the presymptomatic phase, implying viral transfer through the conjunctiva,, so caution should be taken[1,3,10–12].

Intraocular involvement has also been mentioned like hyperreflective lesions at the inner plexiform level and ganglion cell layers on OCT scans, anterior uveitis, retinitis, optic neuritis, disk oedema, vascular tortuosity, acute macular neuroretinopathy, vasculitis, retinal artery occlusions, intraretinal haemorrhages, cotton wool spots, uveitis, and endogenous endophthalmitis[3,10,11,17,18]. Miller–Fisher syndrome or infarct-related central blindness is two neuro-ophthalmological consequences that might develop in extremely uncommon situations[19].

Other rare cases were bilateral intraretinal haemorrhage[20], blepharitis, and inferior scotoma[21,22], vascular occlusion with pan-uveitis[23], unilateral pan-uveitis and optic neuritis as the initial presentation[24], frosted branch angiitis in an HIV-infected patient, RVO as a result of COVID-19 and vision loss in the left eye 10 days after testing positive for SARS-CoV-2[25,26].

Infections such as endogenous endophthalmitis, candida retinitis, tubercular choroidal abscess, and bilateral pre-foveal haemorrhages were among the vision-threatening symptoms. Paracentral acute middle maculopathy, central serous chorioretinopathy, and voriconazole-induced visual complaints were among the milder signs[27]. We did not find any similar involvement in our patients.

All previous studies in adults concerning the ocular manifestations of COVID-19 infection are included in Table 2.

Our study also reported more prevalence among patients with ocular symptoms on CPAP, as air leaks from the CPAP mask, due to poorly fitting mask, resulted in quick drying of the eye surface and ocular discomfort[7], which may mimic the symptoms of viral conjunctivitis (red eye, watery discharge, burning, and itching)[15,18,28,29].

Higher inflammatory markers in patients with ocular symptoms were correlated with the advanced disease itself, and the use of CPAP respiratory support, as reported in many studies[40–42].

In a systematic review, included 38 studies with a total of 8219 COVID-19 patients, the prevalence of ocular manifestations was estimated to be 11.03%. The most common ocular manifestations were dry eye or foreign body sensation(16%), redness (13.3%), tearing (12.8%), itching (12.6%), eye pain (9.6%), and discharge (8.8%). Conjunctivitis had the highest rate (88.8)[11]

Conjunctivitis, or inflammation of the eyelid, is the primary ocular complication reported in individuals with confirmed influenza virus infection, in addition to limited cases of subconjunctival haemorrhage, uveitis, retinopathy, and optic neuritis[43].

Keratitis, conjunctivitis, retinopathy and corneal ulcers are the frequent ocular manifestations of the measles virus[44].

Coronavirus are consists of three kinds which are: COV19, Severe Acute Respiratory Syndrome, and Middle East Respiratory Syndrome[1,45].

A study did not demonstrate any ocular manifestations in patients with Severe Acute Respiratory Syndrome[45].

Conjunctivitis was the only ocular manifestation noted in Middle East Respiratory Syndrome[46].

From the previous reports, we noticed that COV19 infection had no specific ocular manifestations than some other kinds of viruses including coronavirus.

Table 2

The studies concerning the ocular manifestations of COVID-19 infection

Ocular manifestations	The study
Conjunctivitis	Colavita *et al.*[28]
	Daruich *et al.*[15]
	Drozd *et al.*[29]
	Karimi *et al.*[30]
	Lai *et al.*[31]
	Liu *et al.*[32]
	Salducci and La Torre[32]
	Wu *et al.*[3]
	Xia *et al.*[33]
	Zhang *et al.*[5]
Haemorrhagic conjunctivitis	Rokohl *et al.*[19]
Conjunctival hyperaemia	Chen *et al.*[14]
	Drozd *et al.*[34]
	Lai *et al.*[2]
	Wu *et al.*[3]
Follicular conjunctivitis	Benito-Pascual *et al.*[24]
	Wu *et al.*[3]
Fibrin pseudo-membranes and inflammatory cells on tarsal conjunctiva	Salducci and La Torre[32]
Chemosis	Salducci and La Torre[32]
	Wu *et al*[3]
Mucopurulent discharge	Drozd *et al.*[34]
	Lai *et al.*[2]
	Wu *et al.*[3]
Epiphora	Drozd *et al.*[34]
	Lai *et al.*[2]
	Wu *et al.*[3]
Foreign body sensations	Karimi *et al.*[30]
Dryness	Lim *et al.*[31]
Eye redness	Lim *et al.*[31]
Episcleritis	Méndez Mangana, et al.[16]
Reading impairment	Ortiz-Seller *et al.*[35]
Vertical diplopia	Vasanthapuram and Badakere.[36]
Retro-ocular pain	Ortiz-Seller *et al.*[37]
Disk oedema	Sharma *et al.*[22]
Optic neuritis	Sharma *et al*[22]
Multifocal chorioretinitis	Ortiz-Seller *et al*[37]
Adie's syndrome	Ortiz-Seller *et al.*[37]
Acute macular neuroretinopathy	Preti *et al.*[25]
Vacuities retinal vein occlusion	Sheth *et al.*[26]
Retinal artery occlusions and haemorrhages	Rokohl *et al.*[19]
Bilateral intraretinal haemorrhage	Monferrer-Adsuara *et al.*[20]
Pan-uveitis	Benito-Pascual *et al.*[23]
	Sanjay *et al.*[24]
Anterior uveitis	Alonso, *et al.*[38]
Bilateral pre-foveal haemorrhages	Shah *et al.*[39]
Central serous chorioretinopathy	Sanjay *et al.*[24]

Limitations of our report include the small sample size, the cross-sectional study design, and a large number of mild or asymptomatic patients, which do not seek medical aid.

Conclusion

Further research is warranted in order to understand the possible intraocular involvement of COVID-19.

Ethical approval and consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Consent for publication

Not applicable.

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Author contribution

N.K. wrote the discussion, G.H. wrote the abstract and the results, Y.H. wrote the discussion, N.N. examined the patients, and M.K. rewrite and reviewed the study.

Conflicts of interest disclosure

None of the authors have reported a competing interest.

Research registration unique identifying number (UIN)

1. Name of the registry: Maysoun Kudsi.
2. Unique Identifying number or registration ID: research-registry9182.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the-registry.

Guarantor

Dr. Maysoun Kudsi is the guarantor.

Data availability statement

Datasets generated during and/or analyzed during the current study are publicly available, available upon reasonable request, but some data sharing is not applicable to this article. The data supporting the results of this article is included within the article's references.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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