



Ocular Manifestations among Hospitalized COVID-19 Patients in the Southeast of Iran

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Abstract

Background: COVID-19 has a range of manifestations among different patients. Knowing the various manifestations of COVID-19 could help in better managing the infection. This study aimed to investigate the ocular manifestations of hospitalized COVID-19 patients.

Methods: In this study, 379 PCR-positive COVID-19 patients hospitalized in Afzalipour hospital, a tertiary care academic medical center in Kerman city, were recruited. Demographic variables (age and sex), history of systemic diseases (diabetes mellitus and arterial hypertension), systemic COVID-19 signs and symptoms (respiratory, gastrointestinal, neurologic, and sensory), and the severity of the disease were evaluated. Patients were asked about ophthalmic symptoms. If a patient had serious ocular complaints, such as ocular pain or vision loss, and needed specialized examination, an ophthalmologist examined the patient.

Results: The patients' mean (standard deviation) age was 54.2 (15.8) years. Overall, 46 patients (12.1%, 95% confidence interval: 9.0–15.8) showed at least one ocular manifestation. The most common signs and symptoms among those with ocular manifestations were redness (n=37, 80.4%), discharge (n=35, 76.1%), lacrimation (n=31, 67.4%), itching (n=15, 32.6%), and dry eye sensation (n=15, 32.6%). Ocular manifestations were more prevalent among those ≥60 years old, those with hospitalization days >7 days, those with more severe respiratory system involvement, and diabetic patients.

Conclusion: One out of eight COVID-19 inpatients showed at least one ocular manifestation. As tear and ocular secretions are considered a route for coronavirus transmission, it is essential to pay attention to the early detection of ocular manifestations.

Keywords: COVID-19, Ocular manifestations, Severity, Ocular surface, Inpatient

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Introduction

The last coronavirus pandemic, caused by COVID-19, began in Wuhan city, China, in December 2019 in clusters of patients with pneumonia. The novel coronavirus was detected in patient specimens by China's CDC (1,2). On February 1, 2022, there were more than 380 million cases of COVID-19 worldwide, and more than 5.6 million deaths had occurred (3). COVID-19 involves multiple organs in the human body with various manifestations, including other viral, infectious, and immunologic disorders (4,5). Different COVID-19 manifestations can develop at any stage of the disease (6).

Eye involvement has been observed in COVID-19 patients, and many manifestations occur after eye involvement (7). In some patients, ocular manifestations could be the first manifestation of the infection (8). Usually, ophthalmic manifestations, especially ocular surface

symptoms, are self-limiting, but more serious vision-threatening manifestations cannot be ignored (6,9,10). Isolation of coronavirus particles from the patients' tear secretions is another aspect of paying attention to ocular symptoms. Ocular surface manifestations are red flags for diagnosing contaminated individuals, and timely social isolation of these contaminated persons is necessary to prevent disease transmission through ocular secretions, even if they are asymptomatic (11-13). The manifestations of the disease can be a warning for more severe and fatal consequences.

As the signs and symptoms of COVID-19 are changing in different variants, it is necessary to follow the various manifestations of the infection through time. This study aimed to evaluate ocular manifestations in COVID-19 patients hospitalized in a selected referral center in Kerman, Iran, during the fourth and fifth wave of the



disease when the dominant variant in the country was the Delta variant.

Methods

Study design

This cross-sectional study included 379 COVID-19 patients hospitalized in Afzalipour hospital, a tertiary academic medical center in Kerman, southeast Iran, from July to August 2021. Hospitalized patients who had a PCR-positive nasopharyngeal swab test result (confirmed cases) and consented to participate were included in this study. Patients with negative PCR, those admitted due to another diagnosis or a superimposed process, and noncooperative persons were excluded.

Data collection

The study's protocol was reviewed and approved by the Ethics Committee of Kerman University of Medical Sciences (IR.KMU.AH.REC.1400.112) and was in accordance with the ethical standards of the Declaration of Helsinki. One of the authors (a general practitioner) referred to the hospital and collected the necessary data. Demographic variables, including age (15–40, 41–59, or ≤ 60), gender (male or female), history of systemic diseases (diabetes mellitus and arterial hypertension), systemic COVID-19 signs and symptoms (respiratory, gastrointestinal (GI), neurologic, and sensory), and the severity of the disease were evaluated. The patients were divided into three categories in terms of disease severity: mild (fever, sore throat, cough, or myalgia without shortness of breath, no dyspnea, and no pneumonia on imaging), moderate (fever, dyspnea, shortness of breath, and suspected or localized pneumonia on imaging), and severe (shortness of breath, dyspnea, diffuse pneumonia on imaging, and hypoxemia without respiratory support). The subjects with cardiovascular or brain involvement were classified in the severe category.

Ocular evaluation

Patients were asked about ophthalmic symptoms, and then an ocular exam was done. The medical records of the included patients were evaluated, and the necessary data were extracted. If the patients could not answer the questions, the family members (in the hospital or by telephone) were asked about the signs and symptoms. External ocular examination was done for all the patients. The examination of the anterior parts was done using a penlight. If the patient had serious ocular complaints such as ocular pain or vision loss and needed specialized examination, an ophthalmologist examined the patient. This was done by visual acuity and intraocular pressure measurement and fundus examination.

Statistical analysis

Categorical variables were described using numbers

and percentages. Continuous variables were described using mean and standard deviation (SD). The chi-square test was used to compare the association of ocular manifestation with independent variables. Data were analyzed using Stata 17.

Results

Among the 379 recruited patients, 192 (50.7%) were male. The mean (SD) age of the patients was 54.2 (15.8) years (range 15–99 years). The mean (SD) duration of hospitalization was 6.3 (3.9) days before the ocular examination (range 1–23 days). The mean (SD) of the time the COVID-19 patients had ocular problems was 4.9 (2.5), with a range of 1–10 days. Most of them had respiratory system involvement ($n=346$, 91.3%); after that, gastrointestinal involvement was seen in 50 patients (13.2%) and ocular manifestations involvement in 46 (12.1%) patients. Diabetes and arterial hypertension were seen in 49 (12.9%) and 58 (15.3%) patients, respectively. The most prevalent of the signs or symptoms were cough (345, 91.0%), dyspnea (255, 69.9%), and myalgia (222, 58.6%). In total, 46 patients (12.1%; 95% CI: 9.0–15.9) had at least one ocular sign or symptom. [Table 1](#) compares the demographic characteristics, complications, signs, and symptoms in the total included patients with and without ocular manifestations.

Among those with an ocular manifestation (46 cases, 12.1%), the most common ocular manifestations were redness ($n=37$, 80.4%), discharge ($n=35$, 76.1%), lacrimation ($n=31$, 67.4%), itching ($n=15$, 32.6%), and dry eye sensation ($n=15$, 32.6%). The most common form of ocular discharge was watery ($n=23$, 50.0%) ([Table 2](#)). Redness was localized, perilimbal or generalized, unilateral or bilateral, from mild discoloration to prominent pink eye with tarsal and palpebral conjunctival tissue involvement. None of the patients had subconjunctival hemorrhage, lymphadenopathy, or keratitis. The mean (SD) time from the start of the ocular signs or symptoms was 4.91 (2.51) days.

The prevalence of ocular manifestations was higher among those who were 60 years or older ($P<0.05$), except photophobia ($P=0.123$), ocular pain ($P=0.072$), and tenderness ($P=0.9$). Moreover, the prevalence of ocular manifestations was higher among those with more hospitalization duration. Those hospitalized for seven days or more had a higher rate of ocular signs or symptoms ($P<0.05$). The prevalence of ocular manifestations was more common in more severe patients ($P<0.05$) ([Table 3](#)).

Discussion

In this study, one out of each eight confirmed PCR-positive hospitalized COVID-19 patients had at least one ocular manifestation during their disease. The ocular manifestations were in the third order of prevalence after respiratory and GI manifestations. Red eye, ocular

Table 1. Demographic characteristics, complications, signs, and symptoms in COVID-19 patients admitted to a hospital in southeast Iran

Variable	Total	Ocular manifestation (Yes)	Ocular manifestation (No)
Total, No. (%)	379 (100.0)	46 (100.0)	333 (100.0)
Gender, No. (%)			
Male	192 (50.7)	18 (39.1)	175 (52.6)
Female	187 (49.3)	28 (60.9)	158 (47.4)
Age group, No. (%)			
15–40	82 (21.6)	7 (15.2)	75 (22.5)
41–59	158 (41.7)	24 (52.2)	134 (40.3)
≥60	139 (36.7)	15 (32.6)	124 (37.2)
Complications, No. (%)			
Respiratory system	346 (91.3)	46 (100.0)	300 (90.1)
Gastrointestinal system	50 (13.2)	5 (10.9)	45 (13.5)
Central nervous system	15 (4.0)	1 (2.2)	14 (4.2)
Urinary system	15 (4.0)	4 (8.7)	11 (3.3)
Underlying disease, No. (%)			
Diabetes mellitus	49 (12.9)	8 (17.4)	41 (12.3)
Arterial hypertension	58 (15.3)	6 (13.0)	52 (15.6)
Signs or symptoms, No. (%)			
Cough	345 (91.0)	39 (84.4)	306 (91.9)
Dyspnea	265 (69.9)	32 (69.6)	233 (70.0)
Myalgia	222 (58.6)	25 (54.3)	197 (59.2)
Chest pain	181(47.8)	21 (45.7)	160 (48.0)
Sore throat	107 (28.2)	16 (34.8)	91 (27.3)
Headache	87 (23.0)	8 (17.4)	79 (23.7)
Fever	82 (21.6)	6 (13.0)	76 (22.8)
Diarrhea	59 (15.6)	4 (8.7)	55 (16.5)
Dysgeusia (Taste disturbance)	43 (11.3)	7 (15.2)	36 (10.8)
Dyssomnia (Smell disturbance)	42 (11.1)	7 (15.2)	35 (10.5)
Abdominal pain	36 (9.5)	4 (8.7)	32 (9.6)
Nausea	23 (6.1)	3 (6.5)	20 (6.0)
Vomiting	21 (5.5)	3 (6.5)	18 (5.4)
Duration of admission, No. (%)			
<7	236 (62.3)	31 (67.4)	205 (61.6)
7	143 (37.7)	15 (32.6)	128 (38.4)
Disease severity, No. (%)			
Mild	259 (68.3)	16 (34.78)	244 (73.3)
Moderate	100 (26.4)	19 (41.30)	80 (24.02)
Sever	20 (5.3)	11 (23.91)	9 (2.7)
Hospitalization time (day), Mean ± SD	6.27 ± 3.86	9.24 ± 5.01	5.87 ± 3.50
Laboratory test			
WBC	7306.5 ± 3941.8	7190.2 ± 3386.4	7322.6 ± 4016.7
Creatinine	1.0 ± 0.6	0.9 ± 0.4	1.1 ± 0.6
Blood urea	36.9 ± 20.6	35.9 ± 20.7	37.1 ± 20.6

SD, standard deviation; WBC, white blood cell.

discharge, and lacrimation were the most common manifestations in PCR-confirmed subjects. However, other ocular findings such as itching, photophobia, ocular

and periorbital pain or tenderness, conjunctival chemosis, foreign body sensation, dry eye sensation, and visual impairment must also be noted. Ocular manifestations

were not associated with gender but were more common in patients aged 60 years and above. Ocular manifestations can present at any time in the course of the disease. These presentations are more prevalent in the more prolonged course of the disease. However, they may present early during the disease and even as heralding manifestations days before more severe problems are evident.

This study found that one out of each eight patients

Table 2. Ocular manifestations of COVID-19 patients admitted to a hospital in southeast Iran (n=46)

Variable	No. (%)
Ocular manifestation	
Redness	37 (80.4)
Discharge	35 (76.1)
Lacrimation	31 (67.4)
Itching	15 (32.6)
Dry eye sensation	15 (32.6)
Sore eye	12 (26.1)
Vision impairment	12 (26.1)
Photophobia	11 (23.9)
Eyelid edema	11 (23.9)
Periorbital pain	9 (19.6)
Chemosis	9 (19.6)
Foreign-body sensation	7 (15.2)
Blurred vision	5 (10.9)
Ocular tenderness	2 (4.3)
Discharge form	
Watery	23 (50.0)
Mucoid	9 (19.6)
Mucopurulent	3 (6.5)

showed at least one ocular manifestation. The most prevalent ocular manifestations were red eye, ocular discharge, and lacrimation. The ocular manifestations in different studies vary between 9.5% to 69.4% (7,12-16). In a study on 142 hospitalized COVID-19 patients in Mashhad, Iran, Abrishami et al reported a prevalence of ocular manifestations in more than half. The most common findings were conjunctival hyperemia (redness) and chemosis (14). In a meta-analysis on 8219 patients, Nasiri et al described the prevalence of ocular manifestations and the most common ocular findings. In their study, the prevalence of ocular manifestations was 11.03%, and the most common presentations were dry eye, foreign body sensation, and red eye, followed by tearing, itching, ocular pain, and discharge (7). In a study by Feng et al in Michigan, US, ophthalmic presentations were noted in 9.5% of the 400 included patients; the most common results were conjunctival injection (redness) and visual disturbances, followed by discharge and itching. In their study, the severity of systemic coronavirus disease was not associated with ocular manifestations (15).

In contrast, our study showed that most ocular presentations were related to the severity of the systemic disease; in more severe systemic diseases, ocular findings were more common. In their study on 108 COVID-19 European non-hospitalized patients, Rokohl et al concluded that ocular involvement is underestimated in these patients, with 69.4% of their patients showing at least one ocular symptom, including burning sensation, epiphora, and redness. A minority of the patients showed ocular findings before the systemic manifestations (16).

In our study, ocular manifestations were not associated with gender but were more common in patients aged 60 years and above and in subjects hospitalized for seven days

Table 3. Prevalence of ocular manifestations according to the age of patients, duration of hospitalization, and severity of the disease

Variable	< 60 (n=240)		P value	Hospitalized <7 days (n=236)		P value	Hospitalized ≥7 days (n=143)		P value	Mild (n=259)		P value	Moderate (n=100)		P value	severe (n=20)		P value
	No. (%)	No. (%)		No. (%)	No. (%)		No. (%)	No. (%)		No. (%)	No. (%)		No. (%)	No. (%)				
Discharge	7 (3.1)	23 (15.2)	0.001	8 (3.4)	22 (15.4)	0.001	8 (3.1)	15 (15.2)	7 (35.0)	<0.001								
Red eye	10 (4.4)	18 (11.9)	0.001	12 (5.1)	16 (11.2)	0.028	10 (3.8)	12 (12.1)	6 (30.0)	<0.001								
lacrimation	8 (3.5)	23 (15.2)	0.006	9 (3.8)	22 (15.4)	0.001	9 (3.5)	15 (15.2)	7 (35.0)	<0.001								
Itching	3 (1.3)	12 (7.9)	0.002	4 (1.7)	11 (7.7)	0.005	4 (1.5)	6 (6.1)	5 (25.0)	<0.001								
Dryness sensation	1 (0.4)	14 (9.3)	0.001	4 (1.7)	11 (7.7)	0.005	5 (1.9)	6 (6.1)	4 (20.0)	<0.001								
photophobia	4 (1.8)	7 (4.6)	0.123	4 (1.7)	7 (4.9)	0.111	4 (1.5)	5 (5.1)	2 (10.0)	0.032								
Ocular pain	4 (1.7)	8 (5.7)	0.072	3 (1.3)	9 (6.3)	0.012	6 (2.3)	3 (3.0)	3 (15.0)	0.008								
Visual disturbance	3 (1.3)	14 (9.3)	0.01	6 (2.5)	11 (7.7)	0.06	5 (1.9)	7 (7.0)	5 (25.0)	<0.001								
Foreign body sensation	0 (0.0)	7 (4.6)	0.001	2 (0.8)	5 (3.5)	0.109	1 (0.4)	3 (3.0)	3 (15.0)	<0.001								
Periorbital pain	1 (0.4)	8 (5.4)	0.003	3 (1.3)	6 (4.2)	0.089	1 (0.4)	6 (6.1)	2 (10.0)	<0.001								
Lid edema	2 (0.9)	9 (6.0)	0.009	3 (1.3)	8 (5.6)	0.024	3 (1.2)	3 (3.0)	5 (25.0)	<0.001								
Tenderness	1 (0.4)	1 (0.7)	0.90	0 (0.0)	2 (1.4)	0.142	1 (0.4)	1 (1.0)	0 (0.0)	0.724								
At least one sign or symptom	14 (6.14)	32 (21.19)	<0.001	17 (7.20)	29 (20.28)	<0.001	16 (6.20)	19 (19.9)	11 (55.0)	<0.001								

or more. Rokohl et al found no significant association between ocular symptoms and gender, age, or many non-ocular manifestations, including rhinorrhea, nasal itching, sneezing, nasal congestion, cough, headache, sore throat, or fever (16). We found a significant association between ocular manifestations and symptoms, including myalgia, fever, chest pain, and headache. Sore throat was not significantly correlated to any ocular findings. Coughing was only correlated to dry eye sensation and no other ocular symptoms. Dyspnea was associated with ocular discharge and lacrimation. Taste and smell disturbances had no significant association with ocular symptoms. Moreover, systemic arterial hypertension was not significantly associated with ocular symptoms, but there was a significant association between diabetes mellitus and ophthalmic manifestations.

Most of the ocular findings in our study and other studies are presentations of ocular surface involvement. They are manifestations of conjunctivitis, either infectious or noninfectious, or dry eye symptoms. Conjunctival hyperemia, eye discharge, lacrimation, and chemosis are symptoms of conjunctival involvement. As tear and ocular secretions are considered a route for transmission of coronavirus disease (12,13,17-19), it is essential to pay attention to the early detection of ocular manifestations. Furthermore, ocular findings are more common in those with extended hospital stays. Therefore, more severe coronavirus disease and a longer duration of hospitalization can be expected in subjects with ophthalmic presentations. Ranzenigo et al in a study on 53 hospitalized COVID-19 patients, found that ocular signs and symptoms were more common and were predictors for more severe cases. They also found that subjects with ocular manifestations had older age and longer duration of hospitalization (20).

Limitations

This study had three limitations. First, the patients were selected among hospitalized subjects only in one center. As the prevalence of ocular manifestations may differ among outpatient cases, the results of this study may not be generalizable to all COVID-19 patients. Second, although data collection was done using a standard questionnaire, examination of all patients by an ophthalmologist was not feasible. Only those with severe symptoms (vision loss or severe ocular pain) were referred to an ophthalmologist. Finally, this was a cross-sectional study; therefore, we could not infer the causality of the included variables due to reverse causation.

Conclusion

Ocular manifestations are common among COVID-19 patients. One out of eight COVID-19 inpatients showed at least one ocular manifestation. Most ocular manifestations were presentations of ocular surface involvement.

Since tear and ocular secretions are considered a route for transmission of coronavirus, it is essential to pay attention to the early detection of ocular manifestations to protect people, especially ophthalmologists who are in close contact with the ocular secretions of the patients.

Authors' Contribution

Conceptualization: Ali Sharifi, Paria Mashayeshkhi.

Data curation: Ali Sharifi, Paria Mashayeshkhi.

Formal analysis: Naser Nasiri, Hamid Sharifi.

Funding acquisition: Naser Nasiri, Ali Sharifi.

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Software: Naser Nasiri, Ali Sharifi.

Supervision: Naser Nasiri, Ali Sharifi.

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Writing—original draft: Ali Sharifi.

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Competing Interests

The authors declare there are no conflicts of interest.

Ethical Approval

The study was approved by the Research Ethics Committee of the Kerman University of Medical Sciences (IR.KMU.AH.REC.1400.112).

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