

Study on Ocular Manifestation in COVID-19 Patients Admitted at Tertiary Care Centre**Simmy Prajapati¹, Crazy Bhandari², Radha I. Dass³**¹Senior Resident, Department of Ophthalmology, Shri M P Shah Government Medical College, Jamnagar, Gujarat²Senior Resident, Department of Ophthalmology, Shri M P Shah Government Medical College, Jamnagar, Gujarat³Associate Professor, Department of Ophthalmology, Shri M P Shah Government Medical College, Jamnagar, Gujarat

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Conflict of interest: Nil

Abstract:

Background and Aim: There were several reports of eye redness and irritation in COVID-19 patients, suggesting that conjunctivitis is an ocular manifestation of SARS-CoV-2 infection. Reports continue to emerge on further associations of COVID-19 with uveitic, retinovascular, and neuro-ophthalmic disease. The aim of this study was to determine the frequency and various types of ophthalmic manifestation of patients with COVID-19. With the accumulating evidence of ocular manifestations of the 2019 novel coronavirus disease (COVID-19), the study aimed to systematically summarize the ocular manifestations in COVID-19 patients.

Material and Methods: This study was carried out in 60 patients who were admitted for treatment of covid 19 infections at COVID building at GG Government Hospital, Jamnagar. A thorough history is regarding the onset, duration, and characteristics of symptoms. Measurement of visual acuity, Visual acuity was recorded as 6 MFC, 5MFC, 1MFC or close to face finger counting, depending on distance (in meters) at which the patient is able to count fingers. The patient symptoms, ocular manifestations, chest computed tomographic scans, MRI in case of mucor and results of blood tests and reverse transcriptase–polymerase chain reaction (RT-PCR) from nasopharyngeal for SARS-CoV-2 were noted and analyzed.

Results: Maximum numbers of the patients are of 51-60 year age group. Out of 60 patients 36 were male (60%) and 24 were female (40%). In our study we found redness as most common presenting symptoms, in 52 patients (87%). Second most common presenting symptom was watering in 30 patients (50%). Keratitis was present in 24 patients (40%), ptosis in 18 patients(30%), proptosis in 15 patients (25%) and ophthalmoplegia in 21 patients(35%). Out of 60 patients 34 (56.66%) patients develop retinal findings. Cotton wool spots and retinal hemorrhages were present in more in males compared to females.

Conclusion: Conjunctivitis and lid edema are most common ocular maifestaion of COVID-19. Mucor mycosis was present in patients with known case of diabetes and recently diagnosed with diabetes secondary to judicious use of systemic corticosteroids.

Keywords: Conjunctivitis, COVID-19, Keratitis, Proptosis.

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Introduction

The disease caused by SARS-CoV-2 has been named “COVID-19”. During December 2019, several cases of pneumonia of unknown origin were reported in Wuhan, the capital of Hubei Province in China. A young ophthalmologist, Dr. Li Wenliang, was the first physician to report similarities with severe acute respiratory syndrome (SARS). Dr. Wenliang himself contracted the virus after treating an infected glaucoma patient and subsequently passed away.[1,2] The first infected people were exposed to live animals being sold in a wet market in Wuhan. Transmission of the disease

from human to human mainly occurs via direct contact or droplets from an infected patient through coughing or sneezing. Coronaviruses (CoVs) affect a wide range of birds and mammals. Their ability to undergo mutations facilitates the transmission from animals to humans. Beyond SARS-CoV-2, two human CoVs previously emerged as capable of causing respiratory failure: SARS-CoV and Middle East Respiratory Syndrome (MERS)-CoV. CoVs are single-stranded positive-sense RNA viruses. [3,4] The genome codes for both structural and nonstructural proteins. Structural proteins permit

the viral infection and replication. Specifically, the surface spike glycoprotein (S-protein) enables the attachment between CoV and host cells. There is a structural similarity between the receptor-binding domain of SARS-CoV and SARS-CoV-2. The lung epithelial cells are their primary target. They bind to the same primary cellular receptor, which is human angiotensin-converting enzyme 2 (ACE-2), causing potentially severe infections in both the upper and lower respiratory tracts.

The clinical manifestations are variable. Patients with mild symptoms usually recover quickly, while severe cases may develop progressive respiratory failure, potentially leading to death. Currently, reverse transcriptase-polymerase chain reaction PCR (RT-PCR detection of the viral genome in the upper respiratory tract swabs is the most reliable diagnostic test.[5,6]

Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.[7,8] The best way to prevent and slow down transmission is to be well informed about the COVID-19 virus, the disease it causes and how it spreads. Protect yourself and others from infection by washing your hands or using an alcohol based rub frequently and not touching your face.

The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that you also practice respiratory etiquette. The earliest discovery of human coronavirus (HCoV) was reported in 1965 in patients with a common cold which was named as B814. Although most coronaviruses infections in human are associated with mild clinical symptoms, the notably pathogenic strains are SARS-CoV, Middle East respiratory syndrome Coronavirus (MERS-CoV) and the new SARS-CoV-2. [9,10] The mechanism of infectivity of SARS-CoV-2 in ocular tissue is still unknown.

In general, respiratory pathogens can manifest their ocular complications due to the anatomical conduit between the eyes and respiratory tissues, the immunological interdependence of ocular and respiratory tissues and the distributions of the cellular receptors in this system that contributes to the tropism of respiratory viruses. Initially, there were several reports of eye redness and irritation in COVID-19 patients, suggesting that conjunctivitis is an ocular manifestation of SARS-CoV-2 infection. Reports continue to emerge on further associations of COVID-19 with uveitic, retinovascular, and neuro-ophthalmic disease.[11]

The rare occurrence of conjunctivitis could be due to the protective effect accorded by the immune system of the ocular surface, in particular the antimicrobial agents in the tear film such as lactoferrin.[12] As seen in previous studies in SARS, cell surface molecules, heparan sulfate proteoglycans (HSPGs) provides early attachment sites for SARS-CoV invasion and lactoferrin was observed to bind to HSPGs thus preventing the preliminary interaction between SARS-CoV and the host cells.

The aim of this study was to determine the frequency and various types of ophthalmic manifestation of patients with COVID-19. With the accumulating evidence of ocular manifestations of the 2019 novel corona virus disease (COVID-19), the study aimed to systematically summarize the ocular manifestations in COVID-19 patients.

Material and Methods

This study was approved by ethical committee. Patient consent was obtained. All patient-protected health information remained confidential in this study. Study was conducted during period of 12 months from May 2020 to April 2021 on patients who were admitted to GG government hospital, Jamnagar.

Study Design: Cross sectional study

Inclusion Criteria:

To be included in the study patients had to:

1. Confirmed positive results for SARS-CoV-2 from nasopharyngeal or oropharyngeal swab testing at the time of the ophthalmological assessment.
2. Be able to understand the informed consent and agree to be part of the study.
3. Have symptoms onset during the period of hospital stay.
4. Age more than 18 years.

Exclusion Criteria:

1. RTPCR negative patients.
2. Covid suspect patients.

A thorough history is regarding the onset, duration, and characteristics of symptoms. Detailed anterior segment examination with a penlight at bedside. Measurement of visual acuity (6 meter finger counting at bedside), Visual acuity was recorded as 6 MFC, 5MFC 1MFC or close to face finger counting, depending on distance (in meters) at which the patient is able to count fingers. When patient fails to count fingers, visual acuity was taken by moving hand close to face; if patient can appreciate the hand movements, the VA was recorded as HM positive. When the patient cannot distinguish HM, perception of light present (PL +) or not was recorded. If PL +, then PR taken by

shining light in all was asked whether he/she is able to recognize the direction of light rays that is shown and recorded in all four quadrants.

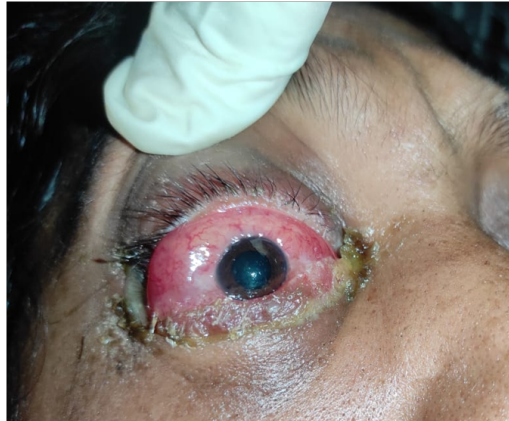


Figure 1: fixed and dilated pupil in case of mucormycosis. Lid edema with proptosis and chemosis also present

The patient symptoms, ocular manifestations, chest computed tomographic scans, MRI in case of mucor and results of blood tests and reverse transcriptase–polymerase chain reaction (RT-PCR) from nasopharyngeal for SARS-CoV-2 were noted and analyzed. For dilated fundus examination indirect ophthalmoscope and 20D lense were used. Tropicamide eye drops were used for pupil dilatation.

Patients were looked for lid edema, lagophthalmos, ptosis, conjunctival congestion, chemosis, exposure keratitis, papillary reaction, hyphema and exudation an anterior chamber(AC), ocular movement by torch light examination. (Figure) By

fundoscopic examination, patient was examined for retinal hemorrhages, cotton wool spots, dilated and tortuosity of vessels, drusens, retinal sectorial pallor. Patient’s comorbidity, ongoing treatment for covid like oxygen support or mechanical ventilatory support, systemic steroid, anticoagulants, immunosuppressants, antifungal also noted. Laboratory investigation, like crp, d-dimer, IL-6 level also noted. The ocular exam was not performed unless an ophthalmic evaluation was requested by the primary team. The ocular exam was not performed by an ophthalmologist unless an ophthalmic evaluation was requested by the primary team. During examination PPE were used.

Statistical Method:

The Frequencies procedure provides statistics and graphical displays that are useful for describing many types of variables. The Chi-Square Test procedure tabulates a variable into categories and computes a chi-square statistic.

This goodness-of-fit test compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values or that each category contains a user-specified proportion of values.

Results

In this cross sectional study total 60 patients of confirmed covid 19 infection were included in which ocular complains were observed.

All patients were primarily admitted for covid 19 infections and develop ocular symptoms. Following observations have been made regarding ocular manifestation in covid 19.

Table 1: Age Distribution of Patients

Age	No. Of Patients
≤18 - 30	3
31 -40	11
41-50	18
51-60	13
61-70	10
71-80	4
>81	1
Total	60

Maximum numbers of the patients are of 51-60 year age group, 18 patients.

Minimum number of patient i.e; only 1 patient is of >81 year has noted. In ≤ 18 - 30 years of age group 3 cases has noted.11 cases in 31-40 year age group has noted.51 -60 year age group 13 case has noted. In 61-70 year age group10 cases and in 71 -80 year

age group cases has noted. It shows that from gender distribution in our study, it was found that Out of 60 patients 36 were male (60%) and 24 were female (40%).

In 20(33%) cases complain was in right eye and in 26 cases (43%) complain was in left eye. Both eyes complain were found in 14 cases.

Table 2: Ocular Symptoms

Symptoms	Male	Female
Redness	30	22

Watering	16	14
Burning Sensation	18	7
Fb Sensation	10	11
Dov	14	8
Pain	14	9

In our study we found redness as most common presenting symptoms, in 52 patients (87%). The second most common presenting symptom was watering in 30 patients (50%). Other symptoms like burning in 25 patients (42%), foreign body sensation in 21 patients (35%) and diminish of vision or blurring of vision in 22 (37%) patients. 23 patients (38%) presented with complain of pain. Symptoms like redness, watering, burning, diminish of vision and pain were common in male as compared to females; while fb sensation almost same in male and females. Above table shows that conjunctivitis in 26 patients (43%) and lid edema 26 patients (43%) were most common presenting features in our study. Orbital Mucor was present in

17 cases (28%). Keratitis was present in 24 patients (40%), ptosis in 18 patients (30%), proptosis in 15 patients (25%) and ophthalmoplegia in 21 patients (35%).

Conjunctivitis was equally common in male and females. Proptosis was more in female as compared to males in our study. Other signs like lid edema, ptosis, keratitis, chemosis, ophthalmoplegia, and mucor were more commonly presented by males compared to females.

CRP was raised in 59 patients (98%) in our study. D-dimer was raised in 54 patients (90%). 6 patients (10%) had raised s. creat level. IL -6 was raised in 22 patients (37%).

Table 3: Retinal Manifestations of Covid 19

Retinal Findings	No. Of Patients	Male	Female	Crp	D-Dimer
Cws And Retinal Hemorrhage	18(30%)	11	7	Raised	Raised
Brvo/Crvo	7(11.66%)	5	2	Raised	Raised
Crao	1(1.66%)	0	1	Raised	Raised
Disc Pallor	8(13.33%)	4	4	Raised	Raised
Total	35(58.33%)	20	15	Raised	Raised

Out of 60 patients 34 (56.66%) patients develop retinal findings. Cotton wool spots and retinal hemorrhages were present in more in males compared to females. CRAO was only found in female in our study. Male female ratio was same for disc pallor in our study. All patients with retinal findings were have raised CRP and D-dimer level. It was found that 66.66% of the patients developed Other ocular symptoms while 33.33% developed conjunctivitis among those who needed oxygen support in covid infection while 83.33% and 16.66% developed conjunctivitis and other ocular symptoms respectively who were treated on room air. Observed difference oxygen use and conjunctivitis is statistically significant.

It was found that intraocular pressure, which was taken by digital method, was high in 11 cases (18%) and normal in 49 cases (87%). Normal pupillary reaction was present in maximum patients i.e; 40 patients (67%). In 16 patients (27%) fixed dilated pupil was present. RAPD was present in 4 patients (6%). The data collected showed that all patients (60 patients;100%) were on systemic steroids. Oxygen support was needed in 48 patients (80%). 15 patients (25%) was on systemic immunosuppressants. Inj. Amphotericine B was given to 17 patients. Tocilizumab or itollizumab was given as immunosuppressant. liposomal amphotericin-B was used as antifungal in mucor patient. In

patients with mucor mycosis there were sign and symptoms of orbital cellulitis was observed. Patients with ptosis, proptosis, conjunctival chemosis, fixed dilated pupil and total ophthalmoplegia were suspect of mucor. For confirmation of fungal etiolog histopathological examination of biopsy taken from mucosa was done. Suspect cases were undergone Radio imaging (MRI BRAIN OR CT BRAIN) for brain and paranasal sinuses to find out fungal invasion.

Data showed that 33% of patient develop mucor and 67% patients develop other symptoms among the patients who were on O₂ support while 8% patient develop mucor among patients who were not on O₂ requirement. Observed difference oxygen use and mucormycosis is statistically significant.

Mucor mycosis was more during the second wave of covid. The patients included in our study duration were during the initial phase of second wave of covid, so 17 patients of the mucor were noticed during this period. Total around 250 cases of mucor were admitted during second wave of covid in our institute.

Discussion

COVID-19 is a novel disease caused by SARS CoV 2 RNA virus. COVID-19 is known to affect various organ systems in the human body with

clinical presentations ranging from asymptomatic disease to severe respiratory failure and death. Thus, eye involvement can be expected in the spectrum of COVID-19 manifestations.[13,14]

Patients included in our study were primarily admitted for covid 19, secondarily ocular symptoms were developed. 60 patients were included in our study who had ocular complaints. Maximum number of patients 30% was in 41-50 year age group. 60% male and 40% female was part of our study. 23% patients complain in both the eyes while 43% of left eye and 33% of right eye.

A retrospective, cross-sectional study was conducted by Yilin Feng et al. on individuals aged 18 and over who were hospitalized for COVID-19; 400 patients were included. The mean patient age was 61.7 years (SD 15.5) and 233 (58.3%) were males. Ocular signs and symptoms were noted in 38 (9.5%) patients. In our study 60 patient with ocular complaint with covid 19 infection was included. Mean age was 51 year with SD 13, which is not similar to our study.[14]

The ocular manifestations of SARS-CoV-2 as reported previously by various authors are conjunctival hyperaemia, chemosis, follicular conjunctivitis, epiphora, watery discharge, eyelid oedema, and enlarged preauricular and submaxillary lymph nodes. Epiphora as a presenting symptom of COVID-19 has also been previously reported. Study by Sindhuja et al. shows that conjunctival congestion is one of the major ocular manifestation in covid positive. In their study they concluded that Mild conjunctivitis manifesting as conjunctival congestion is common and is one of the major ocular manifestations in COVID-19 positive patients even with milder disease. This is similar to our study in which redness (conjunctival congestion) was most common ocular symptom in 86.66% patients, which is similar to our study.[15,16]

Study by Babak Sayad et al. shows high incidence of mucormycosis among COVID-19 patients. Diabetes mellitus and corticosteroid use were the dominant predisposing factor of mucormycosis. In their study twelve patients with COVID-19-associated rhino-orbital mucormycosis were identified from 12 October to 18 November 2020. All cases reported as proven mucormycosis had a history of hospitalisation due to COVID-19. Comorbidities mainly included diabetes mellitus (83.33%) and hypertension (58.33%). Seventy-five per cent of patients received corticosteroids for COVID-19 treatment. The sites of involvement were rhino-sino-orbital (83%) and rhino-sino (17%). Amphotericin B/liposomal amphotericin B alone or in combination with surgical debridement or orbital exenteration was used as the first-line

therapy. The overall mortality rate was 66.7% (8/12).

In our study out of 60 patients 17(28.33%) developed ROCM, all patients had comorbidities, out of which 46% patient were recently diagnosed for DM 2 after getting covid infection and its treatment. All patients in our study were on systemic steroids either inj. Dexamethasone or inj MPS.

Pirraglia et al. studied retinal involvement in covid 19 patients. They observed absence of retinal manifestations in SARS-CoV-2 pneumonia patients. That found cotton-wool-like lesions and microhemorrhages in 4 out of 12 patients and inner retinal OCT hyperreflective spots in the whole sample. However, apart from "normal blood parameters", the authors did not provide any specific information enabling the clinical characterization of their patients.[17]

Indeed, no data regarding the presence of systemic comorbidities as well as no details regarding the patients' ongoing therapy were given. Hence, it cannot be excluded that their findings may be ascribed to pre-existing non-COVID-19-related systemic diseases affecting the retina, such as hypertensive or diabetic retinopathy or other infectious diseases. In our study retinal findings like CWS and retinal hemorrhages were found in 18.33% patients. But in maximum patients (66%) there was no any retinal findings present.

Most patients requiring mechanical ventilation and oxygen mask may experience disorders of the eye surface, with a variable degree of severity. It may be difficult to treat these occurrences while the patient remains in the ICU; however, they may lead to sight-threatening complications, like bacterial superinfection and corneal abrasions.

Conclusion

In our study, result showed, conjunctivitis and lid edema are most common ocular manifestation of COVID-19. Mucor mycosis was present in patients with known case of diabetes and recently diagnosed with diabetes secondary to judicious use of systemic corticosteroids.

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