

Covid-19 Associated Ocular Manifestation; Presented in Tertiary Hospital Hyderabad

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ABSTRACT

OBJECTIVE: To explore the COVID-19 associated ocular manifestation in subjects visited tertiary hospital Hyderabad-Pakistan.

METHODOLOGY: This observational prospective study was conducted at the Institute of Ophthalmology, Liaquat University Medical and Health Sciences (LUMHS) Jamshoro from August 2020 to January 2021. All subjects' ages range from 18 to 65 years visiting the out-patient eye department and/ or admitted to the emergency ward of LUMHS Jamshoro having a positive nasopharyngeal PCR for COVID-19 with and without ocular signs and symptoms were included. The questionnaire proforma was designed to obtain related information. Social sciences of the statistical package, SPSS 22 version was used for results analysis.

RESULTS: Out of one hundred and eleven subjects, forty-nine (44.1%) subjects with ocular symptoms and Sixty-two (55.8%) without ocular symptoms had a fever and 7(14.2%) and 17(27.4%) had prior ocular history, respectively. Conjunctival secretion (57.1%) was found the most common abnormality of ocular surface manifestation followed by pain, redness, and burning sensation. Applying univariate analysis general characteristics exposed that gender, age, fever, ocular prior history, ventilation mechanical, state of disposition, and markers of inflammation were not associated significantly with ocular symptoms.

CONCLUSION: Conjunctival secretion was found the most common abnormality of ocular surface manifestation associated with COVID-19 infection. The increasing proportion of ocular COVID-19 signs and symptoms cannot be ignored. To obtain better outcomes, prompt and aggressive eye management is still necessary.

KEYWORDS: COVID 19; ocular manifestations; signs and symptoms; inflammatory markers.

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INTRODUCTION

The global pandemic pathogen causing the 2019 disease of coronavirus (COVID-19) has had far-reaching and lasting consequences. It is transmitted primarily with infectious respiratory droplets via mucous membranes contact. It was shown that in tissues of the conjunctiva, severe acute respiratory coronavirus 2 syndromes (CoV-2-SARS) replicate. For CoV-2-SARS RNA, the secretions of conjunctival by using reverse transcriptase-polymerase chain reaction (RT-PCR) have tested positive. Recent evidence also suggests that ocular transmission is possible. Conjunctival hyperemia, chemosis, and epiphora were also observed as the other most recurrent seen manifestation ocular in people with COVID-19. Ocular symptoms are reported as an initial COVID-19 manifestation infection. It highlights transmission that how eyes can be affected by COVID-19. In the world of Ophthalmologists, numerous infection manifestations in the eye are reported. The infection can affect almost every organ of the body. It varies asymptotically mild to life-threatening respiratory

distress. Recent evidence also indicates that people may have more severe diseases with ocular involvement. However, we lack such data that evaluate the COVID-19 hospitalized people with ocular manifestations at a tertiary medical care center in Pakistan.

Therefore, to understand the mode of transmission with signs and symptoms, this study was designed to inspect the COVID-19 associated ocular manifestation in subjects who visited tertiary hospital Hyderabad-Pakistan.

METHODOLOGY

It was a prospective observational study. The study was conducted at the Institute of Ophthalmology, Liaquat University of Medical and Health Sciences (LUMHS) Jamshoro. The duration of the study was from August 2020 to January 2021. Approval of the study for ethics was taken from the Institutional Review Board of LUMHS. Consent from each study participant was gained by informing before enrolling in the study.

All subjects' ages range from 18 to 65 years visiting

the out-patient eye department of the Institute of Ophthalmology and/ or admitted to the emergency ward of LUMHS Jamshoro for COVID-19 with and without signs and symptoms of ocular manifestation were included.

Only those subjects were included if they had nasopharyngeal positive RT-PCR for COVID-19 either reported instituting or admitted to the emergency department with ocular problems. Following Clinical Information was recorded in predesigned proforma.

1- For admitted patients.

- Duration of admission.
- Status of ventilation and disposition
- History of Fever
- Type of ocular symptoms.

2- For reported Patients.

- Time of reporting of ocular symptoms; before or after fever
- History of fever.
- Types of ocular symptoms.

The temperature of each patient was recorded with a Celsius scale. The samples of tears/conjunctival secretions for RT-PCR testing were collected from the lower fornix with the cotton tip from each patient without anesthesia and nasopharyngeal samples were collected from reported patients with ocular problems either having fever or not for RT-PCR testing than all samples were sent to the clinical laboratory. Protein-C-reactive (CRP) and D-dimer were also recorded. A physical ocular examination was performed with a slit lamp biomicroscope to record the signs of ocular surface problems of Covid 19 patients.

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Analysis of results:

Social sciences of the statistical package, SPSS 22 version was used for results analysis. Variables (categorical) were analyzed using Chi-square or Fisher exact test, and for variables (continuous), Wilcoxon rank-sum test was applied. Data in the form of mean ± standard deviation (SD) and number (percentage, %) was reported. Association between ocular symptoms outcome and factors of interest was assessed, logistic regression univariate models were applied. Odds ratios, 95% intervals confidence were reported. P-value <0.05 was used as statistical significance indicative.

RESULTS

One hundred-one total subjects were included, 49 with ocular symptoms and 62 without ocular symptoms. Out of 49 patients, 35 were visited and 14 were admitted and out of 62 patients 40 were visited and 22 were admitted. Males and females' ratio was 21(42.8%)/28(57.1%) in subjects with ocular symptoms and 33(53.2%)/29(46.7%) without ocular symptoms. The mean age (years) was 60.2±11.56 and 57.7±9.13 in subjects with and without ocular symptoms respectively. 67.3% of subjects with ocular symptoms and 47.7% without ocular symptoms had a history of fever and 7(14.2%) and 17(27.4%) had prior ocular history, respectively. Subjects who visited the outpatient department were 18(36.7%) with ocular symptoms and 54(87.1%) without symptoms, while subjects who admitted to the emergency ward were 31(62.3%) and 8(12.9%) with and without ocular symptoms respectively (**Table I**). We observed a non-significant difference for mechanical ventilation and disposition status between groups. CRP levels were observed significantly high in subjects with ocular symptoms. D-dimer was observed non-significantly high between subjects with and without ocular symptoms and signs.

Symptoms and signs in subjects with ocular surface manifestations of COVID-19 are shown in **Table II**. Conjunctival secretion 28(57.1%) was found the most common abnormality of ocular surface manifestation followed by pain, redness, and burning sensation. More than 40% of patients have more than one sign and symptoms like conjunctival secretion, redness, and pain. Other ocular manifestation abnormalities were observed such as tearing, dryness, blurred vision, discharge, itchiness, crusted eyelashes, and scleral hemorrhage.

Applying univariate analysis general characteristics exposed that gender, age, fever, ocular prior history, ventilation mechanical, state of disposition, and markers of inflammation were not associated significantly with ocular symptoms (**Table III**). Due to the non-significant association of covariate with univariate analysis no multivariable logistic regression was applied.

TABLE I: BASELINE CHARACTERISTICS OF STUDY SUBJECTS OF COVID-19

Characteristics	Ocular Symptoms (Present) N=49 (%)	Ocular Symptoms (Absent) N=62 (%)	P-value
Male /Female	21(43.8)/28(57.1)	33(53.2)/29(47.7)	0.253
Age	60.2±11.56	57.7±9.13	0.002
Fever	33(67.3)	29(47.7)	0.157
Subjects Visited the outpatient department	18(36.7%)	54(87.1%)	0.321

Subjects admitted to the emergency ward	31(62.3%)	8(12.9%)	0.073
Prior ocular history	07(14.2)	17(27.4)	0.043
Mechanical ventilation	11(22.4)	09(14.5)	0.192
Disposition			
Home	41(83.6)	54(87.0)	
Facility	06(12.2)	08(12.9)	0.340
Hospice/Deceased	02(4.0)	00(00)	
CRP, mg/dL	11.1±4.31	8.9±5.46	0.026
D-Dimer, mg/L	01.9±3.32	1.8±2.19	0.591

Data presented as mean ± SD and N=numbers, percentage= (%), CRP= C-reactive protein.

TABLE II: PRESENTATION OF OCULAR SURFACE PROBLEMS IN PATIENTS OF COVID-19

Symptoms and signs	N =49(%)
Dryness	17(34.7)
Pain	26(53.0)
Discharge	13(26.5)
Redness	23(46.9)
Tearing	19(38.7)
Itchiness	09(18.3)
Blurred vision	15(30.6)
Burning sensation	21(42.8)
Crusted eyelashes	07(14.2)
Conjunctival secretion	28(57.1)
Scleral hemorrhage	01(02.0)
Others include: Lower lid swelling & mild keratitis	02(04.0)

Data presented as numbers=N, percentage= (%)

TABLE III: ASSOCIATED FACTORS OF OCULAR EYE SYMPTOMS USING UNIVARIATE ANALYSIS

Characteristics	OR (95% CI)
Age	0.89 (0.55, 1.23)
Female	0.73 (0.48, 1.37)
Fever	1.98 (0.75, 3.38)
Ocular prior history	1.76 (0.75, 3.69)
Ventilation mechanical	1.73 (0.63, 2.58)
Disposition	
Facility vs home	0.68 (0.41, 1.78)
Hospice/Deceased vs home	0.82 (0.36, 1.86)
CRP (mg/dL)	1.20 (0.84, 1.46)
D-Dimer (mg/L)	1.04 (0.71, 1.13)

Data presented as odds ratio=OR, 95% confidence interval=(90%CI)

FIGURE I: CONJUNCTIVITIS WITH SECRETIONS



FIGURE II: RED EYE



DISCUSSION

Conjunctivitis was found the most common abnormality of ocular surface manifestation associated with COVID-19 infection. A recent study documented the conjunctivitis as most communal COVID-19 ophthalmic manifestation in patients.

Sindhuja et al., in cases of large series also stated that with COVID-19 mild infection 8.66% of patients had conjunctivitis. Chen et al., reported that manifestations ocular are rare more on basis of finding acute bilateral conjunctivitis follicular in the middle phase of the disease. Overall, our results show a non-significant association of covariate suggesting very low transmission risk through the surface of ocular. It is because although receptors of ACE-2 and others are found on conjunctival and corneal epithelia, however, in contrast to respiratory tissues the number of these receptors is very low. In a recent study, it was also found that the ocular surface binding capacity of the virus to the receptors is low. It is because lactoferrin in tea prevents the virus attachment to proteoglycans heparan sulfate which is involved in its binding to receptors of ACE-2 subsequently. A recent study found serum IgA to play a protective role.

The human eye has a unique structure and direct exposure to the environment. It can be affected by several uncommon infectious diseases. We found signs defiantly increase age in subjects with ocular symptoms. Although, non-significant associations using univariate analysis for demographic variables such as age and gender were observed showing that these variables do not have any association with ocular manifestation abnormality. However, our results support the recent findings that older are more prone to infection. We also observed the significantly high inflammatory marker (CRP) in subjects with ocular symptoms in comparison to those without ocular symptoms similar to Wu et al., and Ceran et al., study. Another inflammatory marker of D-dimer showed an insignificant association in subjects with and without symptoms of ocular in our study similar to Feng et al. Besides, the severity of another disease marker such as fever and mechanical ventilation was also observed non-significantly higher in subjects with ocular symptoms in comparison to without ocular symptoms.

Subjects admitted to the ward were not followed up is our limitation. Performa was filled by an internal medicine physician not directly by an ophthalmologist is also a limitation small sample size limited our study to determine the association with clinical factors. We lack information regarding COVID-19 associated diseases as diabetes mellitus and others that are beyond the scope of the study. However, our data in this region add clinical importance and suggest that with ocular direct manifestations ocular indirect symptoms in subjects with COVID-19 can also occur. Our data also help ophthalmologists to better understand ocular manifestations with COVID-19 and may enable e in the prevention of transmission and diagnosis of disease.

CONCLUSION

Conjunctival secretion was found the most common abnormality of ocular surface manifestation associated with COVID-19 infection. Although, our results show a non-significant association of covariate with univariate analysis. But the, increasing rate of ocular COVID-19 symptoms and signs cannot be ignored. To obtain better outcomes, prompt and aggressive management is still necessary.

Ethical permission: Institute of Ophthalmology Liaquat University of Medical & Health Sciences ERC letter No. LUMHS/REC/IOL/-05, Dated 20-07-2020.

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AUTHORS CONTRIBUTIONS

Khazada MA: Substantial contributions to conception & design, data analysis & interpretation of data.

Sultan S: Drafting the article and revising it critically for important intellectual content for final approval.

Gilal IA: Study design, data gathering, and analysis.

Sahito GH: Basic examination of all study patients and gathered basic clinical data.

Mahesar ML: Concept, Study design, manuscript writing, final review.

Shakeel A: Manuscript writing, final proofreading

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