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## Original Research Article

## A study of ophthalmic co-morbidities in mild to moderate cases of COVID-19 infection

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## ABSTRACT

**Aims:** To study the ophthalmic co-morbidities and post- COVID ophthalmic complications in mild to moderate COVID positive patients.

**Materials and Methods:** This was a questionnaire based prospective longitudinal study conducted between August 2020 and December 2020. In the first phase, an ophthalmologist in personal protective equipment (PPE) physically visited the patients and a pre-designed structured questionnaire regarding any ophthalmic complaints was filled and scoring was done later. In the second phase, the patients were telephonically interviewed after 3-6 months of their discharge from the hospital, regarding the development of ocular symptoms for which they needed to consult an ophthalmologist and the treatment taken was noted.

**Results:** 9% of the total 77 patients included in the study reported severe symptoms (scores between 17-24/24). On comparing the mean questionnaire scores (out of 24) it was seen that more severe ophthalmic complaints were seen in patients aged  $\geq 50$  years than  $<50$  years (11.35 vs 5.75,  $p<0.05$ ), moderate category than mild category patients (11.70 vs 3.63,  $p<0.05$ ), patients with systemic co-morbidities than those who had none (11.48 vs 4.04,  $p<0.05$ ) and in patients who later needed to consult an ophthalmologist due to development of one or more complications than those who did not. (13.27 vs 6.63,  $p<0.05$ ).

Post- COVID complications were seen in 27 patients (35%). They included progression of pre-existing ocular disease like cataract, glaucoma, diabetic and hypertensive retinopathy, and new diagnosis of diabetic and hypertensive retinopathy and HCQ- related maculopathy.

**Conclusion:** Ocular co-morbidities should be looked for in every COVID patient. Those at higher risk of developing complications, should undergo a detailed ophthalmic examination after they are discharged from the isolation wards. Hospitals need to work on capacity building and/or look for alternatives, like telemedicine, to ensure timely eye care to all patients.

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## 1. Introduction

The COVID-19 pandemic, caused by the highly contagious virus named SARS-CoV-2, spread turmoil in the year 2020 and the world is still battling this disease. The spectrum of illness ranged from asymptomatic infection to severe pneumonia with Acute Respiratory Distress Syndrome (ARDS), septic shock and death.<sup>1,2</sup> The entire spectrum of the disease is still not known, with multiple

presentations being reported involving multiple organs, including the eye. Studies conducted in China first reported conjunctivitis as a common manifestation of coronavirus disease.<sup>3,4</sup> Ever since many other ocular manifestations, though not so common, have been reported, including episcleritis, lid margin telangiectasia/hyperaemia, retinal venous and arterial occlusions, choroiditis, optic neuritis, orbital cellulitis and mucormycosis among many others.<sup>5-11</sup>

During the COVID pandemic and surge of cases in the first and second wave, the non-COVID morbidities,

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ophthalmic and non-ophthalmic, were put on the back burner and largely ignored. Ophthalmologists in many hospitals were also involved in COVID care. This can be combined with attention to other ophthalmic pathologies to prevent gross morbidity including blindness and need of exenteration.<sup>12</sup>

This study was conducted in a level 3 COVID hospital in western UP, India to assess the burden of ophthalmic co-morbidities and post-COVID ocular complications in COVID positive patients.

## 2. Aims

To study the ophthalmic co-morbidities and post-COVID ophthalmic complications in mild to moderate COVID positive patients.

## 3. Materials and Methods

The study was a questionnaire based prospective observational study conducted on 95 COVID positive patients while they were admitted in COVID isolation wards at a level 3 COVID hospital between August 2020 and December 2020. Patients who were confirmed positive for COVID-19 by Reverse Transcription Polymerase Chain Reaction (RT-PCR) from nasopharyngeal swabs and consented to participate were included in the study. Diagnosis and grading of COVID-19 cases into mild, moderate and severe were done based on guidelines provided by Ministry of Health and Family Welfare, Directorate General of Health Services, India on 17<sup>th</sup> March 2020.<sup>13</sup> Only mild and moderate category patients were included in final analysis and any patient, who at any time of the disease course progressed to be labelled as a severe case, was excluded. Also, patients who were lost to follow-up for assessment of post-COVID complications were excluded. Ultimately, 77 patients were considered for analysis. The study was performed after an approval from the Institutional Review Board and Ethical Committee was obtained and adhered to the tenets of the Declaration of Helsinki. An informed consent was taken from the patients and/or their attendants.

The study was conducted in two phases. The first phase was an interview mode that made use of a pre-designed structured questionnaire consisting of Likert scale questions. (Table 1) An ophthalmologist in proper personal protective equipment (PPE) physically visited the patients in the COVID isolation wards and asked the pre-designed questionnaire and filled each of their responses. Patients were asked regarding any ophthalmic symptoms they might have had during their stay in the hospital.

The patients were required to grade the severity of each of the ocular symptoms, if any, like redness, eye pain or soreness, excessive tears or discharge, blurred or decreased vision, photophobia and itching, irritation and/or burning

sensation from 0 to 4. The score out of a maximum of 24 was calculated. The patients were also asked regarding any known pre-existing ocular condition or surgery.

The second phase of the study was carried out after 3-6 months on telemedicine basis. Patients were telephonically contacted after 3-6 months from their discharge from the hospital and were interviewed regarding the development of any ocular symptoms for which they needed to consult an ophthalmologist. If yes, the chief complaints were inquired about. The patients were asked to share their ophthalmologist's prescription as well. They were also asked about the course of the complaints that they had initially reported during phase 1 of the study.

### 3.1. Statistical analysis

The data was tabulated and analysed using the SPSS software (version 20; IBM Corp., New York, NY) and ANOVA test was applied. A p value of  $\leq 0.05$  was considered significant.

## 4. Results

This study included 77 COVID positive patients out of which 51 (66.2%) were males and 26 (33.8%) were females.

The mean age of the patients was 50.23 years with maximum number of patients in the age group of 61-70 years (n=21, 27.3%). The maximum mean questionnaire score (12.52 out of 24) was also of the patients between 61-70 years of age. For comparing the questionnaire scores with age, the patients were divided into two groups, one group comprising of patients aged less than and equal to 50 years and another group comprising of patients aged more than 50 years.

27 (35.1%) patients belonged to the mild category coronavirus disease and 50 (64.9%) patients to moderate category.

50 (64.9%) patients had systemic co-morbidities like diabetes mellitus, hypertension, coronary artery disease, chronic liver disease, hypothyroidism, etc.

A total of 21 (27.3%) patients were found to have one or more known ocular conditions like cataract, glaucoma, diabetic retinopathy, hypertensive retinopathy and refractive error. (Table 3)

8 patients (10.4%) reported no ocular symptoms. Mild ocular symptoms (score of 1-8/24) were reported by 28 (36.4%) patients. Moderate symptoms (scores between 9-16/24) were reported by 34 (44.1%) patients. Severe symptoms (scores between 17-24/24) were reported by 7 (9.1%) of patients. (Table 4) The maximum score reported was 19/24 by one patient.

Patients aged more than or equal to 50 years (n=43, 55.8%) had a mean score of 11.35, whereas those aged less than 50 years (n= 34, 44.2%) had a mean score of 5.74. This difference in scores was statistically highly significant. (p=

**Table 1:** Pre-designed questionnaire utilised for interviewing the patients in phase 1 of the study

Patient Name	Patient Number –				
Age/ Sex-					
I, hereby, consent to participate in this questionnaire-based study.					
A. Have you experienced any of the following ocular symptoms after being diagnosed with COVID-19?					
	All the time	Most of the time	Half of the time	Some of the time	None of the time
Eye redness	4	3	2	1	0
Eye pain or soreness	4	3	2	1	0
Excess tears or other discharge	4	3	2	1	0
Blurred vision/Decreased vision	4	3	2	1	0
Sensitivity to light (photophobia)	4	3	2	1	0
Itching, irritation, and/or burning	4	3	2	1	0
B. 1. Do you have any pre-existing ocular condition or disease or have undergone any ocular surgery?					
Yes					
No					
If yes, kindly specify					
2. Have you been on long-term treatment for the same?					
Yes					
No					
If yes, kindly specify					
3. Are you still taking the treatment?					
Yes					
No					
If not, specify the reason					
4. When did you last follow-up for the same?					
Before lockdown					
After lockdown					
C. Do you fall in any of the following category, you can tick more than one option:					
Have diabetes					
Have hypertension					
Age more than 60 years					
School-going					
Developed gradual/sudden diminution of vision post Covid-19					

**Table 2:** UBM findings

UBM Finding	No of cases, N=75
Zonular Dialysis	47 (61.8%)
Iridodialysis	17(22.6%)
Cyclodialysis	3(4%)
Traumatic Cataract	20(26.6%)
Posterior Chamber Cysts	4(5%)
Intraocular Foreign body	3(4%)
Angle recession	22(29.3%)

<0.001) (Table 5)

No significant difference in scores was seen with the gender of the patients ( $p=0.302$ ), with males ( $n=51$ , 66.2%) having an average score of 9.35 and females ( $n=26$ , 33.8%) having an average score of 7.92 out of 24. (Table 5)

Patients belonging to the moderate category of COVID infection ( $n=50$ , 64.9%) had an average score of 11.70, whereas those belonging to the mild category ( $n=27$ , 35.1%) had an average of only 3.63. This difference was statistically highly. ( $p<0.001$ ) (Table 3)

Patients with co-morbidities, ( $n=50$ , 64.9%) like Diabetes mellitus, Hypertension, Coronary artery disease, Chronic liver disease, Bronchial asthma and Hypothyroidism also had significantly higher mean score than those without any co-morbidities i.e., 11.48 vs. 4.04. ( $p<0.001$ ) (Table 5)

A strikingly high number of patients ( $n=27$ , 35.1%) needed to consult an ophthalmologist within 3-6 months from discharge. The average scores of these patients who later had the need to consult an ophthalmologist was 13.27, while that of those patients who did not need any ophthalmic consultation was 6.63. The difference was found to be statistically significant ( $p<0.001$ ). (Table 5)

The patients who visited an ophthalmologist after being discharged were asked to send their respective ophthalmologist's prescription and also their past records via online platforms.

Post COVID ophthalmic complications were seen in 27 (35.1%) patients. They included an aggravation of pre-existing diabetic retinopathy (in 6 out of 12 patients with diabetic retinopathy), progression of hypertensive retinopathy (in 3 out of 7 patients with hypertensive retinopathy), progression of cataract (in 8 out of the 12 known patients with cataract) and progression of glaucoma (in 2 out of 3 glaucoma patients). 10 patients were newly diagnosed with diabetic retinopathy and 7 patients with hypertensive retinopathy. All of these were already known cases of diabetes and/or hypertension. 3 patients developed HCQ related maculopathy. (Table 6)

## 5. Discussion

Mild conjunctivitis, manifesting as conjunctival congestion, is common in COVID patients. In a study conducted by Sindhuja et al. it was seen that patients who developed conjunctivitis had onset of ocular complaints even before the manifestation of definite systemic COVID-19 symptoms.<sup>12</sup>

Ocular manifestations of lesser to greater degrees were seen in 89.7% patients included in the study with scores ranging between 1-19/24. Some of these low scores could be non-significant and might not actually result from a conjunctivitis-like condition in these patients. Maximum number of patients ( $n=28$ , 36.4%) reported mild symptoms with scores ranging between 0-8/24. Moderate symptoms

with scores ranging between 9-16/24 were reported by 34 (44.1%) patients. Severe symptoms with scores between 17-24/24 were reported by 7 (9.1%) patients. With 9.1% patients reporting a severe score, it becomes vital to pay attention to the ocular status of every COVID patient. Every corona positive patient should be asked regarding any ocular complaints and if a detailed ocular examination is not possible in the isolation ward, then at least a torch light examination should be performed and the patient may be followed up after he/she turns negative for a detailed examination.

Patients aged more than or equal to 50 years ( $n=43$ ) had a mean score of 11.35, whereas patients aged less than 50 years ( $n=34$ ) had a mean score of 5.74. This difference in scores was statistically highly significant. ( $p<0.001$ ), implying that older COVID- positive had chances of a more frequent and more severe involvement of the eye.

Studies suggest that SARS-CoV-2 affects more men than women and with greater severity.<sup>14</sup> However, in our study no significant difference in the ophthalmic manifestations during COVID infection was seen between males and females. ( $p>0.05$ )

Patients belonging to the moderate category of COVID infection ( $n=50$ ) had an average score of 11.70 whereas those belonging to the mild category ( $n=27$ ) had an average of only 3.63. With this marked difference ( $p<0.05$ ) what can be inferred is the probable presence of a more widespread disease involving more organ systems in moderate/severe category patients as compared to a more localised lung infection in mild category. Moderate/ severe category patients were also on oxygen therapy and few were given sedation in the ICU, all of which are notorious causes of ocular surface diseases.

Patients with co-morbidities, like Diabetes mellitus, Hypertension, Coronary artery disease, Chronic liver disease, Bronchial asthma and Hypothyroidism also had statistically significant ( $p<0.05$ ) higher scores than those without any co-morbidities indicating a probably weaker immune- mechanism leading to more severe coronavirus disease. These systemic co-morbidities can themselves contribute to ophthalmic issues and require specialist consultation, treatment and follow-up. However, in our study we did not measure the contribution of each of the systemic illnesses individually.

A remarkably high number of patients (35.1%) needed to consult an ophthalmologist within 3-6 months from discharge. Many of these patients were follow up patients of cataract, glaucoma and diabetic or hypertensive retinopathy who could not visit the doctor due to the lockdown or their COVID disease. When the scores of these patients who later had the need to consult an ophthalmologist were compared with those who did not, the difference was found to be highly significant ( $p<0.05$ ). This means that patients with more of ocular symptoms during their stay in the hospital,

**Table 3:** Pre-existing ocular conditions

Known ocular disease	N	Percentage
Cataract	12	15.6
Diabetic retinopathy	12	15.6
Hypertensive retinopathy	7	9.1
Glaucoma	3	3.9
Refractive error	14	18.2

**Table 4:** Distribution of patients on the basis of their questionnaire scores

Score (out of 24)	N	Percentage
0 (No Symptoms)	8	10.4
1-8 (Mild)	28	36.4
9-16 (Moderate)	34	44.1
17-24 (Severe)	7	9.1

**Table 5:** Comparison of questionnaire scores among various parameters

Parameters	n (out of 77)	Mean Score (out of 24)	p Value
1. Age			
<50 years	34 (44.2%)	5.74	P= <0.001
>=50 years	43 (55.8%)	11.35	
2. Sex			
Male	51 (66.2%)	9.35	P= 0.302
Female	26 (33.8%)	7.92	
3. Category of covid disease			
Mild	27 (35.1%)	3.63	P= <0.001
Moderate	50 (64.9%)	11.70	
4. Systemic co-morbidities			
Present	50 (64.9%)	11.48	P= <0.001
None	27 (35.1%)	4.04	
5. Needed to consult an ophthalmologist			
Yes	27 (35.1%)	13.27	P= <0.001
No	50 (64.9%)	6.63	

**Table 6:** Post- COVID complications documented on basis of ophthalmologists' prescription after discharge from the isolation ward

Post covid complications	Frequency	Percent
HCQ related maculopathy	3	3.9
Progression of Cataract	8	10.4
Newly diagnosed diabetic retinopathy	10	13.0
Newly diagnosed hypertensive retinopathy	7	9.1
Progression of diabetic retinopathy	6	7.8
Progression of hypertensive retinopathy	3	3.9
Progression of glaucoma	2	2.6

which could be attributed to either their age, severity of COVID infection or co-morbidities, were more likely to develop post-COVID complications.

27 patients (35.1%) developed one or more ocular complications like progression of pre-existing ocular disease like cataract, glaucoma, diabetic and hypertensive retinopathy, newly diagnosed diabetic and hypertensive retinopathy and HCQ-related maculopathy. It is difficult to say whether the virus itself has aggravated these conditions or not, which warrants further study into this matter. A

logical explanation for the worsening of these conditions is the sedentary lifestyle of these patients during their stay in the isolation wards followed by periods of home quarantine and also the nationwide lockdown which prevented them from going for regular follow-up visits.

3 patients (3.9%) in the study developed HCQ-related maculopathy. All the three patients gave history of indiscriminate use of the drug following a popular notion that HCQ was not only useful in the treatment but also prophylaxis of COVID infection. All three patients also

received hydroxychloroquine while they were admitted in the corona ward.

It is difficult to say whether the virus itself aggravates the underlying condition or whether it is the patient-specific factors like their systemic co-morbidities and their immune response to the virus that can lead to these ocular manifestations. Further studies with bigger sample size, examination protocols, standardised data collection and analysis tools and follow-up routines may be required to confirm or refute the causal relationship of the novel coronavirus with the various reported ocular manifestations.

Limitations of our study include a small sample size. This is because of the elaborate PPE and precautions that need to be taken while attending patients with COVID-19 infection and also attributable to the fact that the patients in the isolation wards themselves are stressed and unamenable to such interviews which may not be directly related to their condition. There was a lack of ocular examination or any laboratory diagnosis measures. For this reason, our study could not determine the type of conjunctivitis or calculate the exact prevalence of conjunctivitis or post covid complications. What we have found may only be the tip of the iceberg. We chose to follow-up all patients telephonically to avoid losing patients to follow up because of the prevailing lockdown.

No serious ocular complications, as reported in other case reports from around the world,<sup>5–11</sup> were seen in our study. This study was conducted in the first COVID wave when complications like mucormycosis were much less rampant. The progression of pre-existing ocular disease, as seen in our study, is probably because of the delay in presentation to the hospital due to lockdown and fear of infection. A study conducted by Naresh et al. found that the OPD load in 2020 decreased to nearly 3.5% of its load during the corresponding time previous year.<sup>15</sup> The policy of social distancing to prevent the spread of the disease has also increased the chances of high-risk patients not receiving adequate treatment. This applies not only to COVID positive patients, but also the public in general.

The hustle with the COVID-19 pandemic is expected to continue for at least a few more years and the third wave is already upon us. The Spanish flu pandemic, caused by the H1N1 influenza A virus, lasted from 1918 through 1920, infecting about a third of the world's population at that time in four successive waves.<sup>16</sup> The Third bubonic plague pandemic began in 1955 and was considered active until 1960, killing about 10 million in India alone. In the absence of timely intervention, preventable and manageable ocular diseases will follow their natural course, resulting in progression to advanced stages unresponsive to treatment by the time this pandemic will end.<sup>17</sup> For example, the patients who reported progression of cataract could soon develop lens-induced glaucoma. We ought to make adequate arrangements for delivering safe, efficient and timely health-care to at least the high-risk patients while the pandemic

lasts.

## 6. Conclusion

Ocular discomfort has been variably described in its severity by different patients in the study. This can add to the anxiety, depression and frustration of patients admitted in the COVID isolation wards. Our study recommends addressal of these complaints which can improve the general and mental health of the patients. The ocular aspect of corona patients cannot be ignored, and we should look out for ophthalmic co-morbidities in these patients during and even after their infection.

COVID-19 related history and symptoms should be asked to every patient presenting to the ophthalmology clinic with conjunctivitis and ocular examination of such a patient should be exercised with extreme precautions.

Post-COVID complications seen in this study included an exaggeration of pre-existing disease in the eye and also treatment related complications like HCQ-related maculopathy. Thus, it is pertinent that every patient, at least those at higher risk of developing complications, undergo a detailed ophthalmic examination after they are discharged from the COVID ward.

The pandemic is here to stay. A significant number of people have not been able to get adequate treatment during the pandemic. Hospitals need to work on capacity building and look for alternatives, like telemedicine, to ensure timely eye care to all patients without compromising their safety.

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Nil.

## 8. Conflicts of Interest

There are no conflicts of interest.

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