

A comparative study of conjunctivitis in COVID-19 patients between the first and second wave of COVID-19 at a tertiary care center



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Submission: 02-05-2022

Revision: 25-07-2022

Publication: 01-09-2022

ABSTRACT

Background: SARS CoV-2 has become a household name since early 2019 and till very recently has shown many mutations, some of which were predictable in behavior whereas some have been quite bizarre. With all these surreal mutants of the virus, the basic signs and symptoms of the infection also were diversified. A few studies compared the conjunctivitis features of the first and second wave of coronavirus disease 2019 (COVID-19) outbreak.

Aims and Objectives: The purpose of this study was to compare the evidence of conjunctivitis between the first and second wave of COVID-19 patients. **Materials and Methods:** In this retrospective and observational research, clinical and laboratory characteristics of the patients with COVID-19 admitted to a tertiary care hospital in Western Maharashtra. We evaluated the patients including detailed history taken from the medical records and ocular evaluation was carried out by a trained ophthalmologist who was posted in the COVID-19 ward at that time. The patient's symptoms were compared with the severity of COVID-19 disease classified as mild, moderate, and based on oxygen support given to the patient. **Results:** A total of 150 patients were evaluated in this study, of which 50 patients were from the first wave and 100 were from second wave of COVID-19. Among the total patients, about (80%) of patients with mild severity of COVID-19 disease were from in first wave v/s (61%) patients with mild severity of disease were from the second wave. Furthermore, it was observed that disease severity with moderate patients from the first wave was around (20%) v/s (39%) in the second wave. Among the total patients' data, 66% of patients infected with conjunctivitis were in the first wave of COVID-19 and approximately 56% of patients infected with conjunctivitis were found in the second wave, respectively. About 18% of patients from the first wave and 39% of patients from the second wave with moderate severity required oxygen support. The fluorescein staining, as well as congestion, showed no significant difference in the number of patients between both waves. **Conclusion:** The present study concludes that both the waves only reported dryness and no clinical signs of conjunctivitis. The present study concludes that increased oxygenation support may act as one of the contributing factor for increased dryness and thereby may lead to various ocular infections.

Key words: Coronavirus disease 2019; Conjunctivitis; Disease severity; Congestion; Type of discharge; Fluorescein staining and oxygen support

INTRODUCTION

SARS CoV-2 which had become a household name since early 2019 till very recently had shown many mutations, some of which were with predictable behavior, some were quite bizarre. With all these surreal mutants of the

virus, the basic signs and symptoms of the infection also were diversified; ranging from the very commoner cough, cold, fatigue, and pneumonia to atypical ones including gastrointestinal, neurological, and keratoconjunctivitis. Moreover, it was reported that the incidence of these atypical symptoms especially keratoconjunctivitis was more with

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v13i9.44793

E-ISSN: 2091-0576

P-ISSN: 2467-9100

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asymptomatic cases.¹ The buzz around keratoconjunctivitis is fueled also because of the dominance of SARS-CoV-2 binding angiotensin converting enzyme-2 receptors in the conjunctiva along with all other differentiated tissues. Hence, some researchers investigated the ocular signs and symptoms in patients with SARS CoV-1 and SARS CoV-2.² Various pieces of evidence have suggested that many patients with coronavirus disease 2019 (COVID-19) showed ocular abnormalities and manifestations most common of which was ocular congestion. Thus, the crux of all the published findings suggested that ocular symptoms commonly appeared in patients from mild-to-moderate or it may vary with disease severity.³ Furthermore, the vigorous oxygen supplementation and oxygen therapy administered to the patient showed detrimental effects on the ocular mucosa and conjunctiva. These secondary effects on the eye due to oxygen therapy are also not reported much in the literature.⁴

The purpose of this study was to find out the comparison between the first and second wave of COVID-19 patients in reference to conjunctivitis and other manifestations. The study thereby put forward the ocular implication of COVID-19 and the need for proper eye care along with other treatment protocols.

Aims and objectives

The aim and objective of this study was to compare first and second wave of COVID-19 patients in reference to conjunctivitis and other manifestations.

MATERIALS AND METHODS

Place and ethical approval of the research

This was a retrospective and observational type of study. The research was conducted in the COVID-19 isolation wards at a tertiary care center in Western Maharashtra. Information of patients was taken from hospital records, duration of this study was 2 months (May 2020–June 2020 for the first wave and from April 2021 to May 2021 for the second wave). Approval from the Institutional Ethics Committee had been obtained before the commencement of the study.

Inclusion and exclusion criteria's

The targeted patients were new patients getting admitted, who had not been started on any medication in the COVID ward and had confirmed SARS-CoV-2 infection, tested through RT-PCR test. Patients with pre-existing ocular inflammatory diseases, pre-existing lid deformities such as trichiasis, entropion, and ectropion, were excluded from the study. Patients with severe conditions of COVID-19 were also excluded from the study, as

patients were not considered fit for the case examination of the study.

Sample size

Fifty patients, fulfilling the targeted case study criteria, were selected from the first wave of COVID-19; whereas, 100 patients were studied from the second wave of COVID-19 spread.

Study methodology

A proper detailed history was taken from the medical records and an ocular examination was carried out by a trained ophthalmologist who was posted in the COVID-19 ward at that time.

The patient was examined on a torch light and magnifying loupe to see for any ocular manifestations such as redness, congestion, chemosis, and photophobia. A bedside vision assessment was done for all the admitted patients at that time. All the patients were examined by the ophthalmologist posted in the COVID ward at that time.

The patient's symptoms were compared with the severity of COVID-19 disease, that is, mild, moderate, and on the oxygen support given to the patient.

We examined the patients based on congestion, type of discharge, and fluorescein staining. A fluorescein test is performed using orange dye (fluorescein) and blue light to detect foreign bodies in the eye. This test can also detect damage to the cornea and conjunctiva. The cornea is the outer surface of the eye. Fluorescein staining of the cornea is performed by first placing a drop of sterile saline on a sterile fluorescein strip. The fluorescein is then placed in the inferior cul de sac of the eye by pulling down on the lower lid and gently touching the bulbar conjunctiva with the fluorescein strip. The patient blinks to distribute the dye and the cobalt blue light is used to determine if there are any corneal epithelial defects.

Statistical analysis

Data were collected using a preformed data collection form and case record form. Data entry was done in Microsoft Excel and analysis using Statistical Package for the Social Sciences software.

The categorical variable was expressed in terms of frequency and percentage and continuous variables in terms of mean and standard deviation.

Association between two categorical variables was analyzed using Chi-square test and two continuous variables Student's t-test was used with $P < 0.05$ were considered as statistically significant value at 95% confidence interval.

RESULTS

We collected the data of 150 patients with SARS-COV-2 infection, confirmed by RT-PCR, who were admitted to the D.Y. Patil Medical College, Hospital and Research Centre, Pimpri- Chinchwad, Pune.

A total of 50 patients were selected from the first wave of COVID-19. Whereas, a total of 100 patients were studied from the second wave of COVID-19. The patients were observed based on the severity of disease from mild-to-moderate. Among the total patients, about (80%) of patients with mild severity of COVID-19 disease were from in first wave v/s (61%) patients with mild severity of disease were from the second wave. Furthermore, it was observed that disease severity with moderate patients from the first wave was around (20%) v/s (39%) in the second wave.

Figure 1 shows that symptoms of conjunctivitis are found higher particularly in males when compared in both the first and second wave of COVID-19. Among the total patients' data, 66% of patients infected with conjunctivitis were in the first wave of COVID-19 and approximately 56% of patients infected with conjunctivitis were found in the second wave, respectively.

Congestion in first and second wave of COVID-19

The above graph (Figure 2a) represents ocular congestion in COVID-19. Only one patient out of 50 with mild severity reported congestion in the eye whereas, two patients having moderate severity showed the said symptom. Data from the second wave revealed that three patients out of 100 with mild severity and three patients with moderate severity of disease showed congestion from the second wave of COVID-19.

Besides, the above findings (Figure 2b) on congestion, it was observed that about 18% of patients from the first wave and 39% of patients from the second wave with moderate severity required oxygen support.

The present study shows the examinations which are consistent with a mild follicular conjunctivitis. The parameters included on which conjunctivitis was assessed were oxygen support given, the severity of disease, fluorescein staining, and clinical signs of congestion. Positive response were shown by 8% of patients for fluorescein staining in the first wave whereas only 14% of patients from the second wave showed a positive response for the same, indicating dryness in eyes (Table 1). The oxygen support given to the number of patients (18%) was in the first wave whereas, 39% of oxygen support was given in the second wave of COVID-19. On the other hand,

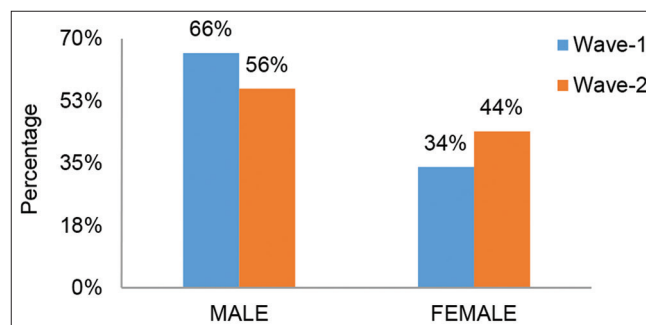


Figure 1: Percentage of distribution of male and female during the first and second waves

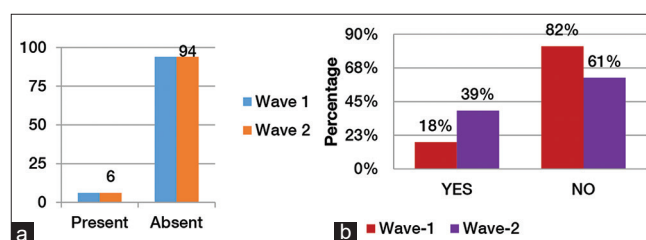


Figure 2: The comparative (a) analysis of congestion and (b) oxygen support in the first and second waves

the fluorescein staining, as well as congestion, showed no significant difference in the number of patients between both waves. Along with the above signs and symptoms, the patients infected with SARS-CoV-2 had other symptoms those of including acute conjunctivitis. The clinical symptoms of acute conjunctivitis were accessed on type of discharge, that is, mucoid and mucopurulent. Discharge that is clear or white and frothy is referred to as mucoid denoting normal features of the eyes. Whereas, the type of discharge that is slightly thicker, cloudy, or opaque is referred to as mucopurulent, indicating infection and inflammation. Mucopurulent discharge from the eyes caught in the eyelashes is the hallmark sign of bacterial conjunctivitis.

Interpretation of Chi-square and t-test

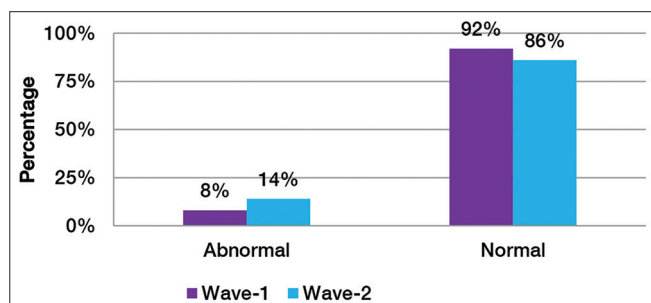
The statistical analysis puts forward the difference in the severity of the disease and conjunctival manifestations between the first and the second wave, Chi-square test highlighted that there is no difference in conjunctival manifestations in the first and the second wave.

Furthermore, the Student's t-test concludes that the age difference between the first and second wave (47.98 vs. 53.17; $P=0.0308$) is statistically significant.

Figure 3 represents that the percentage of fluorescein stain was found higher in the second wave of COVID-19. Results shows that were 8% in the first wave whereas 14% of fluorescein staining was found in the second wave which represents dryness in the eyes.

Table 1: Clinical characteristics of the patients between first and second wave

Feature	First wave (n=50) or %	Second wave (n=100) or %	P-value
Fluorescein staining +ve reports for patients	8 (8)	7 (14)	0.2482
Oxygen support	9 (18)	39 (39)	0.0093
Moderate severity of disease	10 (20)	39 (39)	0.0193
Ocular congestion	3 (6)	6 (6)	1

**Figure 3:** Fluorescein positive stain results in the first and second waves

DISCUSSION

Along with the many established spread routes for COVID-19, it has also been established that the spread of the viral infection can also occur through tears; hence, eye infections can also be one of the manifestations of COVID-19.⁵ Fluorescein dye in combination with cobalt blue light highlights any abnormalities or abrasions on the cornea and dryness of eyes due to trauma or damage. Studies have not reported many cases of conjunctivitis in the first wave, whereas there are many reports of conjunctivitis from the second wave in support of the theory.⁶ It was an observation that the first wave had more shortcomings than the second wave in utilizing safety measures, treatments, drugs, and awareness. However, according to our patient study reports, it has been seen that the second wave showed comparatively higher signs of ocular manifestations than the first wave as shown in Figure 3, 14% of positive fluorescein staining in the first wave as compared with the second wave. Some studies suggest, viral RNA was found in many patients who had conjunctivitis concluding that conjunctivitis is related to COVID-19.^{7,8} The mixed study reports the presence or absence of conjunctivitis in COVID-19 makes it a debatable sign; and also, there are no study reports that have compared conjunctivitis in the first and second wave of COVID-19.⁹

The present study was thereby aimed to study conjunctivitis as a manifestation of COVID-19 and to compare its occurrence in the first wave and second wave of the disease. According to the present retrospective and observational research study, there was only dryness as a symptom and no concrete evidence was noted in regards to conjunctivitis.

The present study evidenced that patients tested positive in both the waves reported symptoms of significant ocular dryness only; and no features of conjunctivitis. The second wave shows more dryness which could be because of oxygen support and showed severe-to-moderate dryness on the fluorescein eye stain test. If dryness is to be considered as one of the symptoms for conjunctivitis, it could also be due to increased oxygenation which plays as a contributing factor for conjunctivitis among the moderate-to-severely ill patients in COVID-19.⁸ A study was done in Dr Rajendra Prasad Centre for ophthalmic sciences, AIIMS, New Delhi, India which showed the presence of conjunctival congestion in nine patients of the 127 patients examined and had a prevalence of 6.29%¹⁰ A study done by Kumar et al., on the detection of viral RNA in conjunctiva of COVID-19 patients also showed the presence of viral RNA in the conjunctiva on RT-PCR but out of 45 patients only one tested positive.¹¹ The present study is in discordance with many studies that have reported conjunctivitis as a major manifestation of COVID-19. However, this is a single center study with a limited sample size and hence larger studies with the more widespread study of the population are warranted to accurately establish the link between COVID-19 and conjunctivitis.

Limitations of the study

1. The study was done over a longer period due to the pandemic the appropriate sample size was restricted.
2. It was a single – center study

CONCLUSION

The present study concludes that both the waves only reported dryness and no clinical signs of conjunctivitis whatsoever. As a fact, the second wave showed remarkable patients with eye infections, especially with moderate COVID-19 infection. The result of the study although did not conclude conjunctivitis as an exclusive manifestation of COVID-19 as further evaluation on slit lamp to ascertain the type of conjunctivitis could not be done. The present study understates that increased oxygenation support may act as one of the contributing factors for increased dryness and thereby may lead to various ocular infections. COVID-19 is a life-threatening disease; as a consequence, any abnormality or any infection caused through the same virus may also show severe outcomes. Hence, it is advisable not to ignore any signs and take due precautions for the same.

The lesson learnt from the first and second waves will help us to deal with the panic of the third wave of the pandemic situation across the world. With the evolving fear of the delta plus and Omicron variant which is spreading enormously throughout the world; the experiences from the first and second wave in diagnosis, prognosis and treatment of COVID-19 will help us to increase our preparedness for the forthcoming complications.

Ethical statement

There is no ethical permission required.

Consent for publication

All authors give permission for the publication.

Data availability

The data that support the findings of this study are available from the corresponding author, [N.D.], upon reasonable request.

ACKNOWLEDGMENTS

We gratefully acknowledge Neuron Institute of Applied Research Amravati for their generous help in editing and writing the article.

AUTHOR CONTRIBUTIONS

ND– Topic finalization, methodology, prepared first draft of manuscript, AA- Interpreted the result, KN- coordination, MP - prepared first draft of manuscript, SPP – Interpreted the result, VM - coordination.

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Authors Contribution:

ND, SPP, and VM- Concept and design of the study, prepared draft of manuscript, review the literature and manuscript preparation, and interpretation of results and analysis and AA, KN, and MP- Concept, coordination, statistical analysis and data interpretation, preparation of manuscript, and revision of the manuscript.

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Source of Funding: None, Conflicts of Interest: None.