



OCULAR MANIFESTATIONS IN COVID-19 PATIENTS IN NORTHERN INDIAN POPULATION- AN ARCHETYPE

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ABSTRACT **AIM:** Aim of our study was to depict prevalence of ocular symptoms in COVID-19 patients in Indian population along with their complete clinical characteristics.

METHODS: Our study included 471 patients of COVID-19 admitted in a dedicated COVID care hospital. All patients were asked to fill a questionnaire giving information about their symptoms and clinical profile.

RESULTS: Out of 471 patients, 38 (8%) patients showed one or other ocular symptoms. Most common ocular symptom seen was redness in the eyes (55.26%) followed by itching (39.47%). Amongst patients with ocular symptoms, 60.53% patients gave history of frequent hand - eye contact as compared to 7.16% in patients without ocular symptoms. 13.5% of the patients without any eye protection had ocular symptoms in comparison to 6% of patients using some type of eye protection. Pre-existing or chronic ocular ailments were seen in 14% of the patients. In 18 patients, ocular manifestations appeared prior to any systemic symptom. Fever was seen as the most common systemic symptom seen in 217 (46%) patients followed by cough (38%). Most common systemic comorbidities seen in patients with ocular symptoms was diabetes mellitus (10.53%) and hypertension (10.53%).

CONCLUSION: COVID-19 virus affecting various systems of the body is well reported but there is drought of literature in respect of complete clinical profiling of patients with ocular involvement especially in Indian population. Furthermore our study imposes the importance of eye protection and hand-eye hygiene, hence enforces the recommendations on the usage of all protective measures by ophthalmologist during ocular examination.

KEYWORDS : SARS-CoV-2, COVID-19, Hand eye hygiene and ocular symptoms

INTRODUCTION -

SARS-CoV-2 (COVID -19), the novel coronavirus that started from Wuhan in Hubei province has been declared as a global public health emergency by WHO on 30 th Jan 2020⁽¹⁾. This highly contagious novel virus affects various systems of the body eventually progressing to acute respiratory stress and death⁽²⁾. Association of SARS-CoV virus with ocular involvement is quite well documented in literature along with evidence of its presence in tears⁽³⁾. Since chromosome of SARS-CoV-2 virus is 82% similar to SARS-CoV⁽⁴⁾ and it shares the similar receptor binding motif for ACE-2⁽⁵⁾, there are high chances that this virus can be transmitted through ocular surface or secretions like the earlier⁽⁶⁾. Studies have shown varied spectrum of ocular manifestations by corona virus in animals extending from mild conjunctivitis to vision threatening retinitis and optic neuritis⁽⁶⁾. Although few studies have shown ocular manifestations of this novel virus in humans but still the published literature is deficit. Former studies had shown a eclectic range for prevalence of ocular symptoms varying from 0.8% to 31.6%⁽⁷⁻⁹⁾.

There is dearth of literature in respect of ocular presentation of COVID-19 virus in Indian population that differs in ethnicity, socio-cultural and geopolitical parameters from the study population of earlier studies. Also, there are limited studies that encompasses comprehensive profiling of patients with ocular symptoms in term of associated comorbidities, eye protection and hand eye hygiene.

This study intends at portraying the prevalence of ocular symptoms in COVID -19 patients in North Indian population along with ample clinical profiling. This study also emphasis on protective role of eye gears and hand eye sanitation.

METHOD

This study was conducted at dedicated COVID care hospital in north India. All patients were diagnosed by RT-PCR using nasopharyngeal swab. The hospital received COVID patients of all severity ranging from being asymptomatic to patients on assisted ventilations from various cities in north India. All admitted patients in the duration of 2 month (August and September) were included in this study. Inclusion criteria:- Confirmed cases of COVID -19, admitted in the COVID care hospital. Exclusion criteria :- Ventilated COVID-19 patients and patients who refused questionnaire or consent. The study adhered to the tenets of the Declaration of Helsinki and was approved by institutional review board. After applying exclusion parameter 471 patients were included in the study. Written consent, complete demographic, clinical and epidemiological data of all patients were obtained from electronic data record of the hospital. All patients were asked to fill a questionnaire on their smart phones, any inquiry regarding same was rectified by ophthalmologist over telephone. All patients who had ocular complaints were seen by ophthalmologist in torch light only. Slit lamp examination and detailed ophthalmic examination were not done in view of safety against infection spread.

STATISTICAL ANALYSIS

The statistical analysis was performed on SPSS statistical software version 25;0. Chi-square test/ Fischer's exact were used to find the association between ocular manifestations with various variables. P-value less than 0.05 was considered statistically significant.

RESULTS

A total of 471 patients were included in our study. All patients were diagnosed using RT-PCR. Out of 471, 256 (54.4%) patients were in age group 18 to 44 years followed by 45 to 64 years (27.4%), ≥ 65 years (15.5%) and <18 years (2.7%). 349 (74%) patients were males and 122 (26%) patients were females. In terms of occupations, 224 (47.6%)

patients were employee, 81 (17.2%) patients were self-employed and 166 (35.2%) patients had other occupations. History of contact with any known COVID-19 patients within last 14 days was given by 176 (37.4%) patients. Smoking history was given by 27% of the patients (Table 1).

Table 2, represents all ocular characteristics of the patients including symptoms, their duration, history of eye protection and pre-existing ocular comorbidities. Amongst study population, 38 (8%) patients had ocular symptoms and 92% patients were without any ocular symptoms. Amid patients with ocular symptoms, 20 (52.63%) patients were in age group 18 to 44 years, followed by 16 (42.11%) patients in age group 45 to 64 years. 24 patients were male and 14 patients were female in patients with ocular symptoms. In patients with ocular symptoms 57.89 % patients denied any definitive history of contact with confirmed COVID-19 patients within last 14 days, while 42.11% patients gave history of contact. In our study out of 38 patients, 21 (55.26%) patients had redness of the eyes, followed by itching (in 15 patients (39.47%)). Other symptoms seen were watering (18.42%) and eye pain (15.79%). Mean duration of these symptoms was 3 to 7 days in 22 (57.89%) patients followed by < 3 days in 14 (36.84%) patients. Amongst patients with ocular symptoms, 15 and without ocular symptom, history of frequent hand eye contact was given by 23 (60.53%) and 31 (7.16%) patients respectively followed by often hand eye contact in 11 (28.95%) and 69 (15.94%) patients and seldom hand eye contact in 04 (10.53%) and 333 (76.91%) patients respectively. In our study population only 17 patients had some pre-existing ophthalmic comorbidities. Amongst these 17 patients, 10 patients had refractive error followed by 03 patients of allergic conjunctivitis.

Table 3, represents systemic involvement with 371 (68.2%) patients with one or more systemic symptoms. Most common systemic symptom recorded in our study in patient with or without ocular symptoms was fever (44.74% and 46.19% respectively) followed by cough (34.21% and 38.34% respectively), sore throat (15.79% and 11.78% respectively) and shortness of breath (10.53% and 15.70% respectively). Amongst patients with ocular symptoms, 04 (10.53%) patients had diabetes mellitus and 04 (10.53%) patients had hypertension. In patients without ocular symptoms, 84 (19.4%) patients diabetes mellitus (19.4%) and 87 (18.71%) patients had hypertension. Other comorbidities reported were respiratory and cardiovascular diseases with 13 (3%) patients and 10 (2.3%) patients respectively.

DISCUSSION

Presently entire world is dealing with the pandemic of COVID -19 and a whole scientific research is betrothed in knowing the manifestation and management of this fatal virus. This study is to understand the ophthalmic perspective of this virus with more emphasis on salient features to differentiate between patients with and without ocular involvement. This cross-sectional study included 471 COVID -19 patients admitted in a dedicated COVID care hospital. All patients were diagnosed by RT- PCR using nasopharyngeal swab. Their age group varied from 7 years to 80 years with median age of 40 years age. Mean age reported in a study by Wu et. al⁽⁷⁾ was 65.8 years. Majority of patients (55%) were from age group 15 to 44 years and similar demography was seen by Chen et al⁽¹⁰⁾. In our study, 349 (74%) patients were males and 122 (26%) patients were females. This higher prevalence amongst males is in accordance with former studies^(10,11). More than half of the patients (60.53 %) with ocular symptoms were employee, followed by being self-employed (28.95%)⁽¹⁰⁾. In our study 37.4 % patients gave history of contact with COVID 19 patients, which was in accordance with earlier studies⁽¹²⁾.

In reference to patients with ocular symptoms no statistically significant gender preposition was noticed, although 63.16 % of the them were males. Amongst patients with ocular symptoms, most common age group noticed was 18 to 44 years⁽¹²⁾. In our study prevalence of ocular manifestation was 8.06 % which was analogous to the finding reported by Chen et.al⁽¹⁰⁾. As per a latest study by Wu et al. ⁽⁷⁾ in Hubei province, prevalence of ophthalmic manifestations was 31.6%. Lower prevalence in our study may be because of exclusion of severe cases on ventilator. Another multicentre study involving 552 hospitals in China showed that only 0.8% patients out of 1,099 had ocular manifestation⁽⁸⁾ as conjunctival congestion. Most common ocular symptom noted in our study was redness of eye (55.26%) followed by itching (39.47%). In a recent study done by Chen et. al in China, most common ocular symptom noticed was dry eye followed

by conjunctival secretion. This variation may be attributed to the fact that many patients in that study had conjunctivitis and dry eye as pre existing disorder. Other ocular symptoms seen in our study were photophobia, ocular pain, defective vision etc, comparable to other studies done in China. The average duration of Ocular congestion/ ocular symptoms varied from one day to 10 days, with more than half of the patients (57.89%) belonging to 3-7 days group. Amongst 38 patients with ocular symptoms, 18 (47.37%) patients displayed ocular symptoms prior to any systemic symptom^(9,12). This advocates that apart from ophthalmologist, clinicians should also be more vigilant and also specifies the importance of stringent ocular examination in diagnosis as it may be the only intimation of this fatal virus. Major mode of transmission of COVID-19 is through aerosols and respiratory droplets, but ocular surface can also be a possible/potential threat^(13,14). Amongst patients with ocular symptoms, more than half of the patients (60.53%) gave history of frequent hand eye contact. Rubbing or touching of eyes has been confirmed as a risk factor for virus transmission by Artieda et.al⁽¹⁵⁾. Use of eye protection has been advocated since presence of SARS virus was noticed in tears⁽⁶⁾. Our study also clues about relation between COVID-19 eye disease and eye protection as 13.5% of the patients without any eye protection had ocular symptoms in comparison to 6% of patients using some kind of eye protection⁽¹⁶⁾. Further emphasis on the usage of all protective measures by ophthalmologist including googles and face shield as ophthalmic examination can inevitably result in physical contact with patient's eye. One or the other pre-existing/ chronic ocular illness were noticed in 09 (23.6%) patients with ocular symptoms and 49 (11.3%) patients without ocular symptoms⁽¹⁰⁾. No statistically significant association was seen between pre-existing ocular illness & occurrence of ocular symptoms in COVID-19 patients. Fever was the most common systemic symptom with 217 (46%) patients followed by cough (38%)^(12,17). Prior studies in China had also shown fever as the most common systemic symptom but with higher incidence as compared to our study^(18,19). Patients with cough and shortness of breath may progress to hypoxia and pneumonia⁽²⁰⁾ making it the most common serious systemic symptom. Non respiratory symptoms seen in our study were myalgia/fatigue, headache and gastrointestinal including vomiting, diarrhoea and haemoptysis^(21, 22, 23). Maximum patients in both groups were without any existing systemic comorbidities (69.2%). Most common pre-existing systemic comorbidities seen in patients with or without ocular symptoms were diabetes mellitus (10.53%,19.4%) and hypertension (10.53%, 18.71%) respectively^(18,19). No significant correlation between presence of ocular symptoms and pre-existing systemic comorbidities were seen in our study. Former studies had clearly stated that systemic comorbidities were important risk factor for patients to progress from mild to critical state⁽²⁴⁾ but no such correlation with ocular symptoms was noticed.

CONCLUSION-

The pathogenicity of novel COVID-19 virus in respiratory system is well researched but its ocular implications are not well documented. Our study helps in understanding its ocular manifestations and enhances the difference in clinical spectrum of patients with and without ocular manifestations in Indian population. Our study imposes the importance of eye protection and emphasis on hand eye hygiene. This study emphasizes on more prospective and comprehensive studies in the field of ocular involvement by this lethal virus.

Limitation –

Sample size was small and serious patients on ventilators were not included. Since all findings were only declared by patients and no slit lamp examination or fundus examination was done, clinical reliability was limited.

REFERENCES

1. Organisation WH. Statement on the second meeting of the international health regulations (2005) emergency committee regarding the outbreak of novel coronavirus (2019-nCoV).
2. World Health Organization. Novel coronavirus (COVID-19) situation, 2020. Available: <https://experience.arcgis.com/experience/685d0ace521648f8a5beeeee1b9125cd>
3. Loon S– C, Teoh SCB, Oon LLE, et al. The severe acute respiratory syndrome coronavirus in tears. *Br J Ophthalmol*. 2004;88(7):861– 863.
4. Chan JF– W, Kok K– H, Zhu Z, et al. Genomic characterization of the 2019 novel human– pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect*. 2020;9(1):221– 236.
5. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. *J Virol*. 2020. epub ahead of print.
6. Seah I, Agrawal R, Can the Coronavirus Disease 2019 (COVID-19) Affect the Eyes? A Review of Coronaviruses and Ocular Implications in Humans and Animals. *Ocular*

- immunology and inflammation. 2020 Mar 16
7. Wu P, Duan F, Luo C, Liu Q, Qu X, Liang L & Wu K (2020): Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020.1291
 8. Guan W, Ni Z, Hu Y et al. (2020): Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 382:1708–1720.
 9. Xia J, Tong J, Liu M, Shen Y & Guo D (2020): Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. *J Med Virol* 92: 589–594.
 10. Chen L, Deng C, Chen X, et al. Ocular manifestations and clinical characteristics of 535 cases of COVID-19 in Wuhan, China: a cross-sectional study [published online ahead of print, 2020 May 18]. *Acta Ophthalmol*. 2020
 11. Sun K, Chen J, Viboud C. Early epidemiological analysis of the SARS-CoV-2 outbreak based on a crowdsourced data. medRxiv. 2020.
 12. Chen N, Zhou M, Dong X et al. (2020): Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 395: 507–513.1
 13. Belsler JA, Rota PA & Tumpey TM (2013): Ocular tropism of respiratory viruses. *Microbiol Mol Biol Rev* 77: 144–156.
 14. Stiles J (2014): Ocular manifestations of feline viral diseases. *Vet J* 201: 166–173.
 15. Artieda J, Montes M, Vicente D, Martinez C, Pineiro L & Mendiola J (2010): Outbreak of follicular conjunctivitis caused by adenovirus in a geriatric centre. *Enferm Infecc Microbiol Clin* 28: 690–693.
 16. Li JO, Lam DSC, Chen Y, Ting DSW. Novel Coronavirus disease 2019 (COVID-19): The importance of recognising possible early ocular manifestation and using protective eyewear. *Br J Ophthalmol*. 2020;104(3):297–298.
 17. Pengfei Sun, Xiaosheng Lu, Chao Xu, Wenjuan Sun, Bo Pan, Understanding of COVID-19 based on current evidence, Understanding of COVID-19 based on current evidence *Journal of medical virology* (2020)
 18. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, Akdis CA, Gao YD. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy* 2020 Feb 19
 19. Huang C, Wang Y, Li X et al. (2020): Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 395: 497–506
 20. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020 Feb 7.
 21. Song Y, Liu P, Shi XL, et al. SARS-CoV-2 induced diarrhoea as onset symptom in patient with COVID-19. *Gut* 2020;gutjnl-2020-320891.
 22. Pauline Vetter, Diem Lan Vu, Arnaud G L'Huillier, Manuel Schibler, Laurent Kaiser professor, Frederique Jacqueroz, Clinical features of covid-19, *BMJ* 2020;369:m1470
 24. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y, Pan S, Zou X, Yuan S, Shang Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centred, retrospective, observational study. *Lancet Respir Med* 2020 Feb 24