

COVID-19 positivity rate in corneal tissue donors – A cause for concern!

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Purpose: To determine the postmortem positivity for COVID-19 among voluntary eye donors who had been certified to have died of non-COVID-19 causes. **Methods:** All donors who donated their corneas (from March 2021 onward) were assessed for COVID-19 positivity tested by nasopharyngeal swab reverse transcription-polymerase chain reaction (RT-PCR) test. Relevant screening history was taken prior to collection. Strict precautions were taken during the retrieval as per the guidelines issued by the National Program for Control of Blindness and Visual Impairment and the Eye Bank Association of India, and the tissues were handled as per standard operating protocol. **Results:** 85 eye calls were attended during this period, of which 56 were home-based and 29 were from a hospital setting. Samples from 12 of the former group of donors were found to be positive for COVID-19 (14%). **Conclusion:** This study highlights the possibility of postmortem RT-PCR positivity in voluntary corneal tissue donors without a prior history of symptoms, signs, or diagnosis of illness suggestive of COVID-19. It is recommended that postmortem testing of donors should be done by RT-PCR for retrievals made during the pandemic.

Key words: COVID-19, donor corneas, eye banking, risk, standard operating protocol

COVID-19, caused by SARS-CoV-2, a novel member of the SARS family of coronaviruses, is a rapidly transmissible, highly infectious disease with high rates of morbidity and mortality.^[1] In India, like in many other affected countries, the healthcare system has been overwhelmed by the large number of patients affected by COVID-19.^[2] The actual risk of transmission of SARS-CoV-2 virus postmortem is currently not known,^[3] but the presence of the virus in tears and the possible transmission through the conjunctiva has been reported.^[4,5] As ocular surface handling is inevitable during the retrieval of donor tissue, the eye banking staff have a potential risk of being exposed to and contracting the infection if not adequately protected. The Eye Banking Association of India (EBAI) along with the All India Ophthalmological Society released a consensus statement and updated protocols for eye banking during the COVID-19 pandemic in the year 2020. Revised donor selection criteria, eye collection procedure, and eye preservation protocols were elaborated.^[6] An advisory was issued that retrieval from voluntary donors at their homes be put on temporary hold during the peak of the pandemic. As the pandemic seemed to abate in India and as the incidence of new infections reduced, home cornea retrieval procedures were gradually restarted with all COVID-19-related precautions.^[7]

With the second wave of the pandemic, there has been a steady increase in the number of infections in India again.^[8] While there are no statistics as yet on increased death rates at home during this pandemic, there is uncertainty about the

cause of demise. Given the limited awareness of the infection, the stigma and fear of being infected, affordability for testing and hospitalization, access to healthcare, and asymptomatic disease, it is plausible that some of the deaths at home could be secondary to COVID-19. This study aims at assessing the frequency of voluntary donors, who were certified to have died of natural causes, testing positive for COVID-19 by RT-PCR postmortem.

Methods

Data of voluntary donors who presumably died of non-COVID-19 conditions during March and April 2021 was analyzed. Eyes/corneas were retrieved from an eye bank associated with a tertiary eye care institute. The study was approved by the institutional ethics committee and was conducted in accordance with the tenets of the Declaration of Helsinki. Eyes were retrieved from donors who were screened as per the eye bank's protocols in addition to screening for COVID-19 as elaborated below [Fig. 1]:

Preretrieval risk assessment

The following historical data are taken from the relatives of the donor on the phone to assess the risk of COVID-19 infection. Positive history of any of these is considered an exclusion for tissue retrieval.^[6]

1. Donor tested positive for or diagnosed with COVID-19

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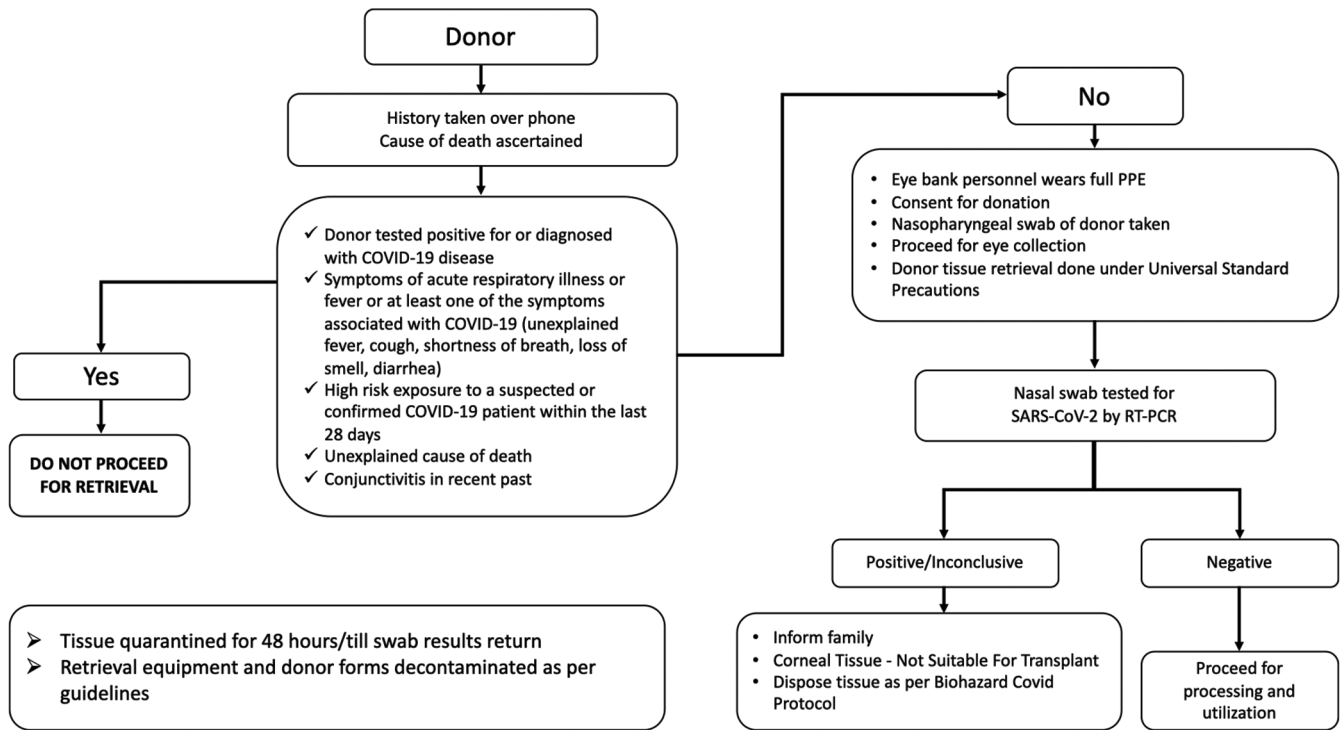


Figure 1: The suggested protocol for eye collection and measures to ensure the safety of eye banking personnel and optimal handling of tissue

1. disease in the past 28 days
2. Donor with history of fever, symptoms suggestive of a respiratory illness, or any symptoms suggestive of infection with SARS-CoV-2, such as fever, cough, breathing difficulty, loss of smell, and even diarrhea
3. Donor with direct high-risk exposure to a patient with suspected or confirmed COVID-19 within the last 28 days
4. Donor with an unexplained cause of death
5. Donor with a history of conjunctivitis or red eyes

If all the above history is negative, a doctor and eye bank personnel are sent for the eye collection.

Additional history taken prior to eye collection

1. Past history of cardiac disease/cardiac surgery/ cardiac-related procedure.
2. History of asthma and severity.
3. History of diabetes mellitus and hypertension.
4. History of high cholesterol or being on any medications for the same.
5. History of other chronic illnesses such as chronic kidney disease or liver disease.

Precautions during retrieval

1. The doctor and eye bank personnel wear personal protective equipment (PPE), including an N95 mask, cap, face shield, gloves, and gown during the entire eye collection procedure.
2. A nasopharyngeal swab of the deceased donor is collected by the trained doctor prior to the retrieval of donor tissue and transferred to a vial containing a universal viral transport medium for testing.
3. Peripheral blood is collected for testing for transmissible diseases as per standard eye banking guidelines.^[9]
4. Ocular tissue is examined for any signs of infection.

5. Ocular tissue is cleaned with povidone-iodine twice (to double the contact time) before the retrieval.
6. Retrieved corneal button is placed in storage media and transported to the lab in an icebox along with the nasal swab specimen for further testing.
7. Disposable parts of the PPE are removed before entering the eye bank and placed in a sealed bag for appropriate disposal. Nondisposable parts are cleaned with 70% isopropyl alcohol.

Post-retrieval procedure

1. The donor tissue is sealed, marked, and quarantined in a separate designated compartment of the refrigerator for 48 hours.
2. All the outer surfaces of the equipment used during the donor tissue retrieval are cleaned with isopropyl alcohol wipes or freshly prepared 1% sodium hypochlorite.
3. All the donor forms are exposed to ultra-violet light in a laminar hood for 30 minutes immediately after arrival at the eye bank.
4. The nasopharyngeal swab is tested for COVID-19 through RT-PCR.
5. The donor tissue is released for further assessment and utilization only after the nasopharyngeal swab tests negative for COVID-19 infection and the blood sample tests negative for transmissible infections as per the eye bank guidelines.
6. If the nasal swab sample tests positive for COVID-19:
 - a) The doctor and eye bank personnel who were involved in the recovery of the donor tissue are advised appropriate quarantine and tested for SARS-CoV-2, if need be, based on the local guidelines.^[10]
 - b) The donor ocular tissue is double bagged and sealed in a yellow biomedical waste disposal bag labeled as COVID-19 positive biomedical waste and sent for incineration as per the standard guidelines.^[11]
 - c) The immediate family members of the deceased are informed.

Table 1: Profile of donors who were found to be COVID-19 positive despite being certified as non-COVID-19 death

Age	Gender	Vaccination Status	Cause of death on Death Certificate	Past history of cardiac disease	Other comorbidities
67	M	None	Myocardial infarction	Yes	Type 2 diabetes mellitus, chronic kidney disease, hypertension
61	M	First dose	Myocardial infarction	No	Type 2 diabetes mellitus, hypertension, hypercholesterolemia
45	M	None	Myocardial infarction	Yes	Type 2 diabetes mellitus
58	M	First dose	Myocardial infarction	Past myocardial infarction	Type 2 diabetes mellitus, hypertension
49	M	None	Myocardial infarction	Angioplasty done 6 months back	Type 2 diabetes mellitus, hypertension, hypercholesterolemia
57	M	None	Myocardial infarction	None	Cerebrovascular accident 2 years back, Type 2 diabetes mellitus
72	F	None	Myocardial infarction	None	Type 2 diabetes mellitus, hypercholesterolemia
44	M	None	Myocardial infarction	None	None
58	M	First dose	Myocardial infarction	None	None
55	M	First dose	Myocardial infarction	None	None
82	M	None	Myocardial infarction	None	Type 2 diabetes mellitus
74	M	None	Myocardial infarction	None	None

The clinical data collected from the eye bank records for the analysis purpose were name, age, gender, recorded or presumed cause of death, associated ocular and systemic comorbidities, history of COVID-19 infection, and COVID-19 vaccination status of the donor [Table 1]. The outcome of the study is the percentage of donors whose nasal swab was COVID-19 positive (RT-PCR) during post-retrieval testing.

Results

A total of 85 tissue retrieval visits (170 eyes) were done from March 2021 onwards. The eye collections were home calls in 56 cases and hospital-based retrieval in 29. The mean age of the donors was 65.84 ± 17.08 years; 49 were males and 36 were females. Out of these, 12 donors' swabs tested positive for COVID-19 during the post-retrieval testing. Though the overall percentage positivity was 14%, the month-wise distribution showed a higher positivity for April (25%), directly reflecting the rising infection in the community. All the donors were certified to have died of myocardial infarction with no history of COVID-19 infection or any other relevant positive history suggestive of COVID-19 infection. One patient had undergone coronary angioplasty. Four of the deceased had received their first dose of vaccination against COVID-19 but none of them had completed the full schedule of vaccination. Sixteen out of 24 corneas were of A-grade quality and would have been suitable for optical keratoplasty and the remaining were of therapeutic grade, but all eyes were deemed not suitable for surgery once the RT-PCR was found to be positive. Table 1 lists the clinical details of the COVID-19-positive donors.

Discussion

Currently, RT-PCR is the gold standard for analyzing swabs collected from patients and is a widely accepted method for SARS-CoV-2 screening.^[12] Human clinical samples used so far for testing include blood, saliva, tears, urine, semen, stools, and exhaled breath.^[13] Tear collection is noninvasive, but due to the few microliters of sample that can be collected, obtaining reproducible results is challenging.^[14] The percentage of

patients with proven COVID-19 infections with the presence of SARS-CoV-2 virus in tears ranges from 0% to 55%.^[15-17] The variation between the results could be explained by the difference in time of testing since the contraction of infection, viral load on the ocular surface, severity of the disease, and the sampling and testing techniques. In addition to the detection of SARS-CoV-2 RNA in tear samples, viable virus has also been detected in tears by inoculating the positive samples in Vero E6 cells and observing cytopathic effect at 5 days post inoculum.^[18] This could imply the possible risk of virus transmission from the ocular surface and more so from subjects with conjunctivitis, thereby increasing the chances of ophthalmologists acquiring the novel coronavirus pneumonia. Direct exposure of clinicians and technicians to patients' ocular fluids can also occur during tissue retrieval postmortem.^[19,20]

There are currently no validated techniques for SARS-CoV-2 testing in post-mortem specimens, and the viability and infectivity of the virus post-mortem is unclear. A study reported the persistence of viral RNA in nasal swabs for several days after death and a significant correlation with histopathological evidence of COVID-19.^[21] Eye banking personnel are at particular risk due to their close and prolonged contact with the deceased during the recovery of donor tissue. Hence, as per our hospital eye banking protocol during COVID-19, we performed RT-PCR testing of postmortem nasal swabs of all deceased donors.

The significant percentage of positivity of donor swabs for the SARS-CoV 2 virus points to undiagnosed COVID-19 infections and corresponds to the sudden upsurge of cases in the community.^[22] All sudden deaths in our series occurred due to presumed acute coronary events. They may also be attributed to severe systemic inflammation due to SARS-CoV-2, which may cause myocardial injury. Furthermore, circulating cytokines and mediators can cause myocardial infarction due to thromboembolic mechanisms.^[23]

With the above evidence, there is a definite risk of exposure of eye bank personnel and secondary exposure of their family

members to COVID-19. Tests from the conjunctiva, anterior cornea, and posterior cornea of donors with COVID-19 infection at the time of death demonstrated the presence of both SARS-CoV2 viral RNA and its envelope and spike proteins in the epithelium of the cornea.^[24] Hence, a recipient of the tissue from such a donor also faces a theoretical risk of infection. Donated tissues treated with povidone-iodine did not possess the viral RNA in the anterior corneal tissue samples, suggesting a strong viricidal activity of this molecule.^[24] Whether the virus is viable and transmissible to the recipient through the transplanted tissue needs further research.^[25,26]

Conclusion

To conclude, our study shows the prevalence of asymptomatic COVID-19 infection among voluntary donors who presumably died of non-COVID-19 causes. Though there are no reports of transmission of SARS-CoV-2 virus from corneal transplant to the recipient, eye bank personnel are exposed to the risk of COVID-19 infection during the recovery of donor tissue. It is important to be aware of this risk and take appropriate safety measures during home-based retrieval of corneal tissue. Informing the family is also key to break the transmission chain and safe disposal of tissue from swab-positive donors are other important considerations.

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Conflicts of interest

There are no conflicts of interest.

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