

Pre-Operative SARS CoV-2 Rapid Antigen Test and Reverse Transcription Polymerase Chain Reaction: A conundrum in surgical decision making

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Purpose: Since the eye is in close proximity to the oro-nasal cavity, transmission of SARS CoV-2 is higher during ophthalmic surgical procedures, it is vital to ensure the safety of the healthcare team by pre-operative Rapid Antigen Test (RAT) and real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) for SARS CoV-2 viral RNA of all patients planned for elective or emergency surgery. Hence, understanding the profile of pre-operative RAT and real-time RT-PCR among patients planned for various ophthalmic procedures, will help us make better decisions for future guidelines, for optimal planning of ophthalmic elective or emergency surgeries, keeping in mind the current scenario. **Methods:** This is a prospective descriptive study conducted on patients planned for elective or emergency ophthalmic surgeries, who had no COVID-19-related symptoms pre-operatively and were subjected to preoperative RAT and real-time RT-PCR of nasopharyngeal and throat swabs for SARS CoV-2 viral RNA. Data was compiled and statistically analysed. **Results:** 204 patients underwent pre-operative RAT and RT-PCR testing; of which, 85 were females and 119 were males. Mean age of the study population was 51.44 ± 16.501 years. Among the 204, 2 tested positive for SARS CoV-2 with Rapid Antigen testing as well as RT-PCR and 10 patients tested positive via RT-PCR after a negative RAT result of the same sample. **Conclusion:** Pre-operative testing for COVID-19 disease is indispensable as there is a high chance of transmission from patient to healthcare workers. RAT has the advantage of quick results and may play a role in case of emergency procedures. However, it is prudent to perform the more sensitive real-time RT-PCR before any elective, non-emergency procedures or surgeries to avoid any undue risk to the healthcare team.

Key words: Pre-operative, rapid antigen testing, real-time reverse transcriptase polymerase chain reaction, SARS CoV-2

During this global pandemic of a novel coronavirus, elective procedures and surgeries have taken a backseat. Yet, we need to adapt to this new normal of enhanced protection and safety protocols against SARS CoV-2 transmission as we step towards providing essential health services. As surgical procedures involve prolonged proximity to the patient's respiratory droplets and body fluids, they put the operating team at an occupational risk of acquiring nosocomial SARS CoV-2 infection.^[1]

Moreover, since the eye is in close proximity to the oro-nasal cavity, transmission of air-borne respiratory viruses such as SARS CoV-2 is higher during ophthalmic surgical procedures. Though the duration of ophthalmic surgeries are short, it is enough for successful transmission considering the proximity of the surgeon to the patient's face while operating.^[2] Moreover, SARS CoV-2 virus has been isolated from the tears of asymptomatic patients,^[3] hence it is vital to ensure the safety of the healthcare team by pre-operative Rapid Antigen Testing (RAT) and real-time Reverse Transcriptase Polymerase

Chain Reaction (real-time RT-PCR) for SARS CoV-2 viral RNA of all patients planned for elective or emergency surgery. However, sensitivity and specificity of these two tests vary.^[4,5] Hence, understanding the profile of pre-operative RAT and real-time RT-PCR in patients planned for various ophthalmic procedures, will help us make better decisions for future guidelines, for optimal planning of ophthalmic elective or emergency surgeries, keeping in mind the current scenario.

Methods

This is a prospective descriptive study conducted on patients planned for elective or emergency ophthalmic surgeries at a tertiary eye care centre in South India from September to November 2020.

Following the approval and clearance from the institutional ethics committee, the participants were enrolled for the study after applying the inclusion and exclusion criteria. Patients

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being planned for elective or emergency ophthalmic surgeries who had no COVID-19-related symptoms pre-operatively and were to undergo preoperative RAT and real-time RT-PCR for SARS CoV-2 viral RNA were included in the study after obtaining written informed consent. Participants were excluded when valid consent was not obtained or if patients were symptomatic prior to the pre-operative testing.

Demographic data such as name, age, gender as well as co-morbidities and symptomatology, if any, were recorded. As a part of pre-operative workup, all participants underwent nasopharyngeal and throat swabs irrespective of the type of ophthalmic surgery or anaesthesia planned for. Necessary infection prevention and control precautions were followed to minimize the risk of spread of infection from one to another.^[6] Their samples were placed into the viral transport medium: Hi media (HiMedia Laboratories Pvt. Ltd, Nashik, India. Catalog No: 0000431084). Samples were transported maintaining the cold chain to the specified lab facility.

In the laboratory, samples were subjected to both RAT and real-time RT PCR testing.

For RAT, STANDARD™ Q COVID-19 Ag test kits were used. For specimen extraction, swabs were inserted into individual buffer tubes and stirred while squeezing the buffer tubes, swabs were removed while squeezing the sides of the tube to extract liquid from the swab and nozzle cap was applied tightly. In case of specimens in VTM, using a micropipette, 350 microlitre of specimen was extracted from the VTM and mixed with the extraction buffer and nozzle cap was applied tightly. For analysis, 3 drops of the extracted specimen were applied to the specimen well of the test device and the results read in 15-30 minutes. A coloured line appears in the top section of the result window to show that test is working properly called the control line. A coloured band appearing the lower section of the result window is the test line of SARS CoV-2 antigen. Presence of any line no matter how faint, the result was considered positive.

For real-time RT-PCR of SARS CoV-2 viral RNA samples were extracted using the magnetic bead extraction method (Thermo scientific viral isolation kit—5XMagMAX, Thermo Fischer scientific Baltics UAB, Vilnius, Lithuania) in Biomek 4000 platform as per the manufacturer's instructions. In eight strip PCR tubes, 22.5 µL of the mixed reaction solution or master mix (SARS CoV-2 Detection kit; Fortitude 2.0) was loaded. To this, 2.5 µL of the extracted nucleic acid was added to each well, covered and the PCR was performed using the CFX96 real time PCR (Bio Rad). After the completion of the PCR run, the amplification curves were judged to decide if the results were negative or positive. A cut off cycle threshold (Ct) value of 40 was considered as positive as per the manufacturer's instructions. Test results were obtained.

Patients requiring emergency surgeries were taken up for the procedure on the basis of the RAT reports, RT-PCR reports were obtained subsequent to the procedure and patients planned for elective procedure were taken up only after RT-PCR reports. Optimal IPC measures as per the guidelines of Ministry of Health and Family Welfare, Republic of India^[6] were followed including adequate PPE for the entire surgical and anaesthesia team.

Test results were obtained. Data was compiled and entered into Microsoft excel sheet and analysed using software SPSS version 20.0. Data was analysed using descriptive statistics (frequencies, mean, standard deviation and percentages).

Results

A total of 204 patients underwent pre-operative RAT and RT-PCR testing; of which, 85 were females and 119 were males. Mean age of the study population was 51.44 years (standard deviation = 16.501 years). Of the 204, 25 were planned for emergency ophthalmic procedures, 148 for cataract extraction, 17 for cornea and refractive surgery, 14 for oculoplasty. 2 pediatric cases were planned under general anaesthesia and rest were either local or topical anaesthesia. Of the 204, 2 patients tested positive for SARS CoV-2 with RAT as well as RT-PCR and 10 patients tested positive via RT-PCR after a negative RAT result of the same sample.

Discussion

In an effort to contain the spread of COVID-19 and conserve health and human resources, policy makers and health administrators laid down some strict protocols and brought in some drastic changes of curbing all routine outpatient visits, elective diagnostic and surgical procedures.^[7] As restrictions were relaxed there was resumption of routine health services. Yet, there has been some reluctance in presuming elective procedures due to the risk of nosocomial transmission of infection.

Elective procedures are those that are not deemed emergency, yet are essential for the health outcomes of the patient. Complete shutdown of the essential elective services has impacted many dimensions, primarily affecting health outcomes adversely due to delay in diagnostic procedure as well therapeutic elective surgeries. Such delays can be detrimental in case of life-threatening conditions like malignancy as delay in diagnosis or intervention can prove fatal.

Maringe *et al.*,^[8] estimated that substantial increase in the number of avoidable cancer deaths in England are to be expected as a result of diagnostic delays due to the COVID-19 pandemic in the UK. Alongside these deleterious impacts on patient health, impending surgical backlog has strained hospital resources. As we move towards catering to the moral obligation of essential patient care alongside this pandemic, we need to be cautious while we care, as healthcare workers are at an unprecedented risk of acquiring nosocomial COVID-19 infection compared to the general population.^[1] Ophthalmic surgical procedures put the ophthalmologist at an added risk due to the proximity of the surgeon's and the patient's face while operating. Studies have shown that large respiratory droplets arising from a cough or sneeze can be propelled for up to 6 m by exhaled air,^[2] well within the proximity between the patient and ophthalmologist while operating with or without the aid of a microscope. Moreover, many studies have shown that SARS CoV-2 can be isolated from tears and conjunctival secretions/scrapings even among patients who are asymptomatic systemically with or without ophthalmic manifestations.^[3,9]

Hence, it is of utmost importance to make sure that a patient is not actively infected when a surgical procedure is planned for the sake of the safety of the healthcare team. Elective procedures also give us the opportunity to plan well ahead of time and patients can be tested for SARS CoV-2 infection pre-operatively as a part of mandatory pre-op evaluation.

The two widely used testing methods for SARS CoV-2 are RAT and real-time RT-PCR for viral RNA.

Rapid antigen detection tests are rapid qualitative tests for the determination of presence of SARS-CoV-2 antigen.

RAD tests detect viral antigen by the immobilized coated SARS-CoV-2 antibody on the device and can be interpreted without any specialized instrument and available within 30 min.^[4] RAD tests can deliver results within a short time and is easier to perform as well as less expensive. WHO recommends at minimum, antigen-rapid detection tests to have at least $\geq 80\%$ sensitivity and $\geq 97-100\%$ for their implementation. In our study, STANDARD™ Q COVID-19 Ag Test kits were used with a sensitivity of 96.52% (95% confidence interval: 91.33-99.04%) and specificity of 99.68% (95% confidence interval: 98.22-99.99%) as established by prospective, multi-institute, randomised single blinded study.

In our study, among the 12 patients with RT-PCR confirmed infection, only 2 tested positive with the initial STANDARD™ Q COVID-19 Ag RAD test of the same specimen sample.

Mak *et al.*,^[4] in their comparative analysis of RAD and RT-PCR indicated that RAD test was capable of detecting SARS CoV-2 virus in various specimens with different sensitivities, yet it was less sensitive than RT-PCR. Studies have shown that real-time RT-PCR can detect < 10 transcript copies, therefore has greater relative sensitivity compared to cell culture isolation and conventional RT-PCR and augments detection of the low viral titres in respiratory secretions during early infection.^[5] In our study, 10 of the 12 confirmed infected patients tested negative with RAD and were detected only after real-time RT-PCR of the same sample specimen, indicating that though RT-PCR is time consuming and more expensive, yet is more sensitive and proves to be a mandatory pre-operative testing strategy for SARS CoV-2 before taking up patients for elective surgeries.

Hirotsu *et al.*,^[10] in their comparative analysis showed that in specimens with >100 viral copies and between 10 and 100 copies, the antigen test showed 100% and 85% concordance with RT-PCR, respectively and concordance declined with lower viral loads. Therefore, in case of an emergency, risk stratification needs to be done, considering the time taken to obtain RT-PCR results, hence RAT maybe done as a preliminary 'point of care' test to rule out cases with high viral loads. Among the 12 positive cases, elective procedures were deferred in case of 10 patients in view of active SARS CoV-2 infection. However, 2 were planned for emergency procedures, namely primary lid tear repair and primary repair for globe rupture under local anaesthesia, therefore in view of the emergency nature of the procedure, both these patients were operated by the ophthalmic surgical team under due risk, while having donned adequate PPE and following optimum IPC protocols as per the guidelines of the Ministry of Health and Family Welfare, Republic of India.^[6] Primary lid tear repair was performed in the emergency surgery operating room (OR) of the dedicated COVID-19 hospital within the premises of the our ophthalmic hospital campus, whereas the primary repair for globe rupture was taken up in the non-COVID-19 ophthalmic emergency OR within our ophthalmic hospital, as the procedure required the aid of an operating microscope and fine ophthalmic instruments. The OR was later fumigated as per IPC protocols. Entire operating team of both these cases, self-quarantined themselves for a week and resumed work after a negative SARS CoV-2 real-time RT-PCR test.

Hence, all emergency procedures done on the basis of RAT results, when RT-PCR is awaited need to be undertaken under strict IPC protocols and with adequate PPE protection. As most

ophthalmic surgeries are elective procedures, that are essential for positive health outcomes and are not deemed emergency, they should be taken up only after a negative RT-PCR report, without risking the health of the surgical team.

Conclusion

Pre-operative testing for COVID-19 disease is indispensable as there is a high chance of transmission from patient to health care workers. RAT has the advantage of quick results and may play a role in case of emergency procedures, when it might not be practical to wait for RT-PCR results. However, it is prudent to perform the more sensitive real-time RT-PCR before any elective, non-emergency procedures or surgeries to avoid any undue risk to the healthcare team. Furthermore, it is advisable for the surgical and anaesthesia team to use adequate PPE and strictly follow IPC protocols irrespective of the patient's infection status in order to reduce their occupational risk of acquiring nosocomial COVID-19 infection.

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Conflicts of interest

There are no conflicts of interest.

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