

## Review Article

# Laboratory biosafety measures in receiving, preparation and processing of pathology specimens in suspected and positive coronavirus infection

Anuradha Sekaran\*, Niharika R. Yandapally, Veena P. Vanere

Department of Pathology, AIG Hospitals, Hyderabad, Telangana, India

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### \*Correspondence:

Dr. Anuradha Sekaran,

E-mail: [dr.sanuradha@aighospitals.com](mailto:dr.sanuradha@aighospitals.com)

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### ABSTRACT

COVID-19, caused by SARS-CoV-2 virus which is declared as a pandemic by the WHO on March 2020 has made a huge difference in the practice and daily activities of the laboratory services. There are high chances of receiving potentially infectious samples to the laboratory for various tests. Authors propose a few biosafety measures in the preparation and processing of various pathology specimens received to the lab during this pandemic time in correlation with guidelines given by WHO. These safety measures aim at protecting and safe guarding the laboratory staff, trainees, and pathologists by minimizing the exposure to COVID-19.

**Keywords:** COVID-19, Laboratory guidelines, Laboratory tests, Pathology specimens, Safety precautions

## INTRODUCTION

COVID-19, within a span of few months of its appearance in China, was declared a pandemic (March 11, 2020). WHO, announced on February 11, 2020, that the disease is caused by a novel Coronavirus and termed it as COVID-19 (coronavirus disease 2019).

This new virus appears to be very contagious and is rapidly spreading globally and has adverse effects on the world health care system. This disease started in India on January 30<sup>th</sup> 2020 and currently around 27,890 cases with 1,079 deaths as of 27<sup>th</sup> April.

Keeping in view of preventive strategies, health care associations have recommended to reduce non-essential hospital visits, reduce general out-patient procedures and elective surgeries.

Basic goal of this article is to follow all possible safety precautions to prevent infection to the laboratory staff.

## *Patho-physiology*

Coronavirus is an enveloped, positive single-strand RNA virus belonging to the Orthocoronavirinae subfamily, with the characteristic crown-like spikes on their surfaces and belong to the genus beta-coronavirus.<sup>1</sup>

Spike surface glycoprotein of the virus binds to the host receptor binding domains of the angiotensin converting enzyme 2 (ACE2), which is present on type II alveolar cells. SARS-CoV-2 attaches to a target cell, the virion releases RNA into the cell, initiating replication of the virus which further disseminates to infect more cells.

SARS-CoV-2 produces several virulence factors that promote shedding of new virions from host cells and inhibit immunological response.

However the exact course of disease and therapeutics are not clear and hence this pandemic has led to panic among the health care workers and general public.

## REVIEW OF LITERATURE

According to World health organization, Centers for disease control and prevention there were recommendations for sample collection and transportation of samples in order to prevent breakage or spill over to minimise exposure to potential infectious samples.

They also proposed instructions regarding the procedure for processing of various specimens and that all lab workers should wear personnel protective equipment, keep work area dry and use 1% sodium hypochlorite as a disinfectant for all lab purposes.

Various risk assessment templates were provided by WHO and can be used in hospitals to evaluate the likelihood of risk and prioritize the laboratory activity into very low, low, medium, high, very high risk categories and establish a periodic review to assess the changes in the laboratory procedures, changes in the disease progression/process and upgrade lab policies according to the findings from the audit, day to day lab incidents and feedback from lab staff.

Some studies also proposed to have minimal working conditions with specific changes in routine lab settings and also precautions for reporting by pathologists

## DISCUSSION

Laboratory biosafety measures for handling and processing specimens related to coronavirus.

All specimens collected for laboratory investigations must be considered potentially infectious. It is advisable for all pathologists and technical staff to adopt few measures to minimize risk of infection

### *Pre-analytical*

#### *General safety guidelines for staff*

- Ensure that health-care workers who collect specimens use appropriate personal protective equipment (PPE) i.e. eye protection, a medical mask, a long-sleeved gown, and gloves. If the specimen is collected with an aerosol-generating procedure, personnel should wear a particulate respirator at least as protective as a NIOSH certified N95, an EU standard FFP2, or the equivalent.<sup>2</sup>
- Do not eat food or drink, or keep personal items such as coats and bags in the laboratory. Frequent hand washing must be encouraged.<sup>3</sup>
- Better to keep all doors opened instead of opening and touching frequently and sanitize if necessary.
- Thoroughly washing hands under running water and soap, after handling of any biological material, before leaving the laboratory. Alternatively, an alcohol based hand sanitizer containing at least 62%

alcohol can be used, if soap and water are not available.

- Any item that is worn regularly in work area should be cleaned and decontaminated
- Refraining from using non-essential electronic devices (e.g mobile telephones, tablets, laptops, flash drives, memory sticks, and cameras) within the work space area. Shoe covers should be worn in high risk areas.<sup>3</sup>
- Surface disinfection: The virus can remain viable on surfaces (especially plastic and stainless steel surfaces) for up to 72hours, it is recommended to decontaminate all work surfaces atleast twice daily. Metallic surfaces like door and cupboard handles, security keys and locks etc should be disinfected frequently.
- Microscopes should also be wiped with alcohol. Slides may also be a source of contamination so wipe with alcohol before reporting.<sup>3</sup>
- Microscopy: During microscopy keep at one meter distance from residents and other colleagues. Preferably use remote operated or telepathology method of reporting<sup>3</sup>
- Staff can be divided into 2-3teams to minimize the exposure rates.
- Patients should be asked to wear mask before samples are collected from them
- All staff need training regarding proper donning and doffing of PPE
- All equipment (e.g tourniquet, chairs) should be sanitized frequently.
- Access to the laboratory should be minimized
- All lab staff should report any symptoms like fever, fatigue, cough, respiratory symptoms to the designated infection control officer of the hospital.
- Ensure that all personnel who transport specimens are trained in safe handling practices and spill decontamination procedures.<sup>2</sup>
- Sanitation workers must use separate cleaning equipment and use disposable gloves while at work
- Sink ,floor and soap dispensers should be cleaned daily with detergent, water and then air dried
- Taps and fitting should be cleaned with warm water and soap water frequently.

### *Analytical*

#### *Specimen collection and transportation*

- Any procedure with the potential to come up with aerosols or droplets (e.g. vortexing) should be performed in a certified Class II Biological Safety Cabinet (BSC)<sup>2</sup>
- Propogative work like culture of viruses and its isolation should be done at containment laboratory with inward direction of flow i.e BSL-3<sup>2</sup>
- Non propogative diagnostic laboratory work like nucleic acid sequencing must be done at a facility

by using procedures that are equivalent to biosafety level-2<sup>2</sup>

- Deliver all specimens by hand whenever possible. Don't use pneumatic-tube systems to transport specimens.<sup>2</sup>
- All samples transported between labs should be placed in a secondary container to minimize the potential for breakage or a spillage.
- Samples like nasopharyngeal and oropharyngeal swabs and aspirates, broncho-alveolar lavages, sputum, stool, urine, tissue from biopsy or autopsy should be sent in sterile containers at 2-8°C
- Serum, whole blood can be collected in serum separator and collection tubes at 2-8°C
- Inform the laboratory person as soon as sample is being labelled and transported
- Transport the samples in a vaccine/ice box type container.

#### *Various samples in the lab<sup>5</sup>*

- *Virology tests:* Routine testing for influenza and other respiratory viruses can be stopped and should be done only if SARS-CoV-2 is negative with symptoms
- *Swab specimens:* Wound and genital swabs has low clinical value hence can be rejected.
- *Sputum specimens:* sputum for SARS-CoV RTPCR can be done and non-purulent samples for routine cultures can be stopped.
- *Reduce and refine drug resistant organism testing:* It is appropriate to restrict screening of methicillin resistant staphalococcus aureus to high risk areas like ICU. Carbapenem-resistant enterobacteria and vancomycin-resistant enterococcus screening can be deferred in low risk areas
- *Routine mycology testing may be stopped.*
- *H pylori antigen and antibody testing:* can be avoided in most cases.
- *Reduce blood screening tests:* In the current scenario there is reduced outpatient testing volume with most patients having online consultations, so investigations with low value, particularly if not automated can be deferred (e.g vitamin D if done by tandem mass spectroscopy). Serum electrophoresis is labour intensive and can be reduced by not doing electrophoresis on all immunoglobulin requests.
- *Cancer and cancer screening programmes:* Symptomatic cases to be prioritised as usual.
- *Routine infertility:* testing of semen postponed for atleast 3-6months in the first visit but post vasectomy testing should continue.
- *Turn around time:* Certain specialist tests and batch tests which could,with minimal risk can be moved to less frequent testing .e.g thrombophilic disorders testing. Complex tests can be consolidated to one central lab minimizing pressure on work force.

- *Interlab electronic communication:* To avoid repeated data entry connecting labs allowing end to end transmission of results to patient records is a priority which also improves the quality, reduce turn around time and free staff from manual entry of requests and results.

These guidelines allow us to reduce pressure on workforce and have minimal impact on patient care.

#### ***Handling of pathology specimens***

##### *In haematology*

- Haematology technicians processing fresh samples must wear appropriate PPE.
- Do not send blood/serum samples rolled up in the forms
- Processing of samples like loading and unloading of sealed centrifuge cups should be done by trained personnel.
- A leak proof vacutainer should be used.
- Pipetting by mouth must be strictly avoided
- All technical procedures should be performed in a way that minimizes the formation of aerosols and droplets .The use of hypodermic needles and syringes should be limited.
- Caps of all vacutainers should be opened with the help of gauge soaked in 1% hypochlorite solution and in a *direction away from face* and preferably in biosafety cabinets.
- Cauterization of used needles should be avoided as it can generate aerosols and should be discarded in sharp-resistant waste containers
- There is variation in the guidelines for review of blood films across the country.Hence labs with high rate of film reviews should consider implementing more rigid protocols
- Smears can be avoided in samples with normal blood counts and without any flagging on fully automated high end hematology analysers
- For cases where smear preparation is done it is preferable to fix the smears in methanol for 1-2mins
- Bone marrow aspirations and biopsy procedures can be done with taking all precautions.

##### *In clinical pathology<sup>5</sup>*

- *Urine samples:* Regular clear urine samples need not go through regular testing procedures. Report may be signed as Clear urine, possibility of infection is minimal or empirical treatment can be given according to the symptoms. Pre-operative specimens which are clear may be signed off with a comment Urine clear .Use standard prophylaxis.
- *Fecal specimens:* Routine culture of non-bloody stool samples may be stopped. Fecal microscopy can be minimized and done only in samples with

travel history, or requested by a consultant gastroenterologist. FIT testing for occult blood for colorectal cancer in symptomatic and screening of patients should continue.

#### *In cytology*<sup>6</sup>

- Cytology samples like fluids (ascitic, pleural, pericardial, BAL fluid, synovial fluids) must be tightly-capped, sealed in a bio-hazard zip-lock bag kept inside a leak-proof cryo box or in a triple packaging system and sent to lab with appropriate forms and clinical details.
- During FNA procedure material from the syringe and needle hub has a risk of aerosol generation, hence hub may be broken and put in 10% formalin for cell block preparations to minimize aerosol exposure.
- Avoid shaking and blowing air for drying of the smears, air drying should be undertaken in class II biosafety cabinets.
- Rapid onsite evaluation (ROSE) procedure done routinely in hospitals set ups for EUS-guided FNA (Endoscopic ultra-sonography) and EBUS-guided FNA (Endoscopic trans-bronchial ultra-sonography) can be avoided and if absolutely necessary should be done with wearing a PPE.
- Tele-ROSE pathology is preferred in the present situation

#### *In histopathology*

- All pathology covid19 suspicious /confirmed specimens must be labelled clearly.
- The Coronavirus gets fixed in 24hrs with formaldehyde and 48hrs in glutaraldehyde.
- All specimens transferred into formalin –filled properly sealed containers with adequate amount of formalin to cover the tissue in the container, must be further placed in a secondary container to minimize the risk of breakage or a spill.
- All these containers should be put in a large plastic box with biohazard label.

#### *In molecular and genomic testing*<sup>5</sup>

- Continue testing for all clinically appropriate tests to inform diagnosis, therapy choice and patient management and even for all prenatal diagnosis, rapid exome sequencing, new born screening programme.
- Residual disease monitoring, chimeric testing for stem cell transplant monitoring and test for myeloproliferative neoplasms can be partially stopped.
- All other rare disease testing can only be done if there is lab resource available and above that required to support SARS-CoV-2 testing.

#### ***Receiving and grossing room***

- Ensure complete personal protection is worn by technologist and resident. Most important is to wear face shield so that aerosols can be minimized. Always wear a disposable apron while grossing.
- Fix specimens for 24hrs with formaldehyde and 48hrs in glutaraldehyde
- All residents/ pathologist and histo-technologists doing grossing should clean all work surfaces with hypochlorite after every specimen.
- Don't use air drying of inks or any step that increases aerosols from specimens.
- The brushes used for inking are source of retained organisms so for inking use cotton wads or wisps and throw them.
- Slicing specimen after covering them with cotton will help reduce aerosols.
- Any electric bone saws used should have a vacuum that isolates aerosolized particles. If not then use band saws which generate less aerosols.

#### ***Frozen section in COVID 19***

- Reduce number of technologist performing frozen sections.
- Personnel should wear appropriate protective equipment (gloves, apron, eye protection and a surgical mask) at all times.
- Do not use free sprays to reduce aerosols for quick freezing.
- Cryostat cover should be adjusted in such a way to reduce aerosol exposure while cutting and the operator should wear a safety face shield.
- Decontaminate cryostats “frequently” with 70% alcohol preferably every day. Use of disposable plastic ware, which can be treated and discarded as dry waste, are highly recommended. Staining containers should be washed regularly.
- Instead of using a cutting board for grossing use disposable plastic sheets which are used in operation theatres.

#### ***General histopathology processing***

In a suspected COVID19 sample, automatic tissue processors should not be used because of the problems of disinfection. Manual processing with Jars and beakers (plastic) should be used. Remember complete formalin fixation will help us in killing the virus. Paraffin bath in processors produces sufficient heat to destroy the virus. So formalin fixed paraffin embedded tissues are considered safe.

#### ***Work area and equipment disinfection*<sup>6</sup>**

Irrespective of the containment level, work surfaces and equipment must be decontaminated after specimens have

been processed with sodium hypochlorite (1%) for a minimum contact time of 30mins

### **Management of sample spills<sup>6</sup>**

In the event of sample spillage decontamination of the surfaces should be done immediately using appropriate disinfectants (1% sodium hypochlorite solution)

#### *Post analytical*

- Do not store the blood samples after processing.
- Put all vacutainer and caps in sodium hypochlorite solution and then discard in double yellow bag labelled COVID
- After running the samples ,run 2 tubes of 1% hypochlorite before shutting down the analyser
- Slides and blocks can be stored as per guidelines

#### *Biomedical waste disposal*

- Infectious material to be disposed in a separate yellow bag labeled COVID as per individual hospital/institutional policies and as per guidelines and policies approved by central pollution control board of India.<sup>6</sup>
- The surface of bins, trolleys, containers used for storage of COVID waste should be disinfected properly with 1% sodium hypochlorite solution daily

#### *Autopsy<sup>7</sup>*

Health personnel performing the procedure should wear the PPE. Allow only one person to cut at a given time. Use a bio safety cabinet for handling and examining of smaller specimens and other containment equipment whenever required. Use caution when handling needles or other sharps and dispose of contaminated sharps in puncture proof labelled closable sharps containers.

#### *Precautions while reporting<sup>6</sup>*

- The concerned pathologist should wear a non-sterile gloves while handling the slides
- Microscopes should be regularly sanitized by 70% alcohol/hand sanitizer solution before reporting
- Independent reporting may be practised and in case 2 or more pathologists opinion may be required then multi-head station can be used keeping at least 1-meter distance
- Digital reporting may be implemented if possible
- All pathologists must wash hands at the end of reporting for >20s with hand sanitizer.

Thenceforth, by practicing good personal hygiene, maintaining social distancing, appropriate handling of blood samples and body fluids by wearing PPE and

proper fixation of pathological specimens for 24-48hrs with proper biomedical waste disposal can reduce the risk of COVID-19 to the laboratory personnel and alleviate their fear so that they can be able to serve the health care organisation in the best possible manner during this pandemic.

It is the good opportunity to implement and use digital technology like telepathology and artificial intelligence in reporting.

The safety of all doctors, technicians and other lab staff is of primary importance and the above suggested guidelines may be adopted to prevent lab outbreak of disease and help health care staff to provide services during the pandemic time.

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