

Application of Biosafety Principles in Laboratory Analysis of Clinical Samples from Patients with COVID-19

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Abstract

COVID-19 poses a great challenge to clinical and diagnostic services around the world. The need of biosafety practices can never be emphasised more than under current circumstances. The four pillars of biosafety namely, leadership, standard operating procedures, personal protective equipment (PPE) and engineering controls must be employed for effective and safe practices in the clinical setting in general and laboratory settings in particular. Risk assessment must be carried out before meeting up the diagnostic challenge for COVID-19 and essential biorisk management measures are required to be taken. In our resource-poor settings, we need to adapt safe but cost-effective and improvised solutions to ensure safe handling of clinical samples from COVID-19 patients in the laboratories. The correct use of PPE and their suitable alternatives are available for selection and use. Disinfection of the lab areas and safe disposal of the clinical samples from such patients is also of paramount importance.

Keywords: COVID-19, SARS-CoV-2, Biosafety, Personal protective equipment.

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Introduction

With the spread of coronavirus disease (COVID-19) and it acquiring the status of a pandemic, the medical world in general and diagnostics in particular, came under enormous pressure of meeting the demands of early and accurate diagnosis of a large number of suspected cases. Since the disease possesses exceptionally high potential of spread,¹ the safe laboratory handling of specimens became a real challenge for the laboratories all around the globe. Although World Health Organization² and Centre for Disease Control and Prevention, USA³ have issued detailed guidelines for the safe lab handling of clinical specimen of COVID-19 patients, the main emphasis of this review is to highlight the weak areas of safe laboratory practices and to recommend possible cost-effective solutions for diagnostic laboratories.

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Four Primary Controls of Biosafety

Biosafety is the practical application of the knowledge, techniques and equipment to mitigate the risk involved in handling the biological specimen.⁴ These practical applications rest on the four primary controls i.e.

- ◆ Leadership
- ◆ Standard Operating Procedures (SOP)
- ◆ Personal Protective Equipment (PPE)
- ◆ Engineering controls

Every clinical lab should formulate a strategy of safe handling of COVID-19 clinical samples by considering these primary controls.

The Leadership has to see the bigger picture of multifocal tasks. From specimen collection until the disposal of leftover specimens, every step has to be measured against the potential risks. Mitigation of every risk and addressing the protection of laboratory staff is the key concern. Comprehensive knowledge of biosafety is essential but at the same time, the cost of achieving these desired outcomes should be within the economical range of the laboratory or institute. Any lapse can bring catastrophic results. Meticulously done biorisk assessment remains the responsibility of the leadership. The pathologist/ laboratory director/ principal investigator/ laboratory manager are considered the leaders and the laboratory technologists and other staff are the workforce. The workforce expectations are directly proportional to their confidence in leadership and are reciprocated under all circumstances.

The SOP is merely a document if it is formulated on a desk and pasted on a wall. Unless the leadership is aware of the practical problems of the workforce, no SOP can prove to be helpful and is likely to be overruled by the person working on the bench. It would be a worthless debate about who is to blame once the damage is done. The consequences will be borne by all. While formulating an SOP for the laboratory, input from the workforce is essential and unless its practical application is ensured, its placement should be deferred.

The PPE needs to be arranged rationally as per the workload and actual needs of the workforce. Providing

less than anticipated demand will instil fear and distrust among the workforce. The selection of wrong PPE or incorrect use will have its detrimental effects.

The engineering controls i.e. the laboratory structure, air conditioning, airflow and movement of individuals can have an impact on the overall atmosphere. In many laboratories, airflow across the laboratory is usually compromised for the sake of effective air conditioning. Since procedures like vortex, grinding, blending or centrifugation etc. regularly result in aerosols,² therefore, addressing airflow direction is of paramount significance in preventing the spread.¹

Biorisk Assessment in COVID-19 Clinical Samples

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the biological agent of COVID-19, can be classified as a clinical containment level 3 organism⁵ and is spread through droplets.¹ Nevertheless, the aerosol spread potential cannot be ruled out.⁶ Considering the available evidence, laboratory personnel are at the risk of acquiring infection through the procedures that produce aerosols and droplets.²

Risk assessment should be done while preparing for the safe handling of COVID-19 clinical samples. With financial restraints, risk tolerance has to be given due importance i.e. making space for acceptable risk with known benefits allowing smooth work proceedings.⁷

WHO provides a risk assessment template² for the clinical laboratories. We found it to be a very useful tool but if it is considered complicated to comprehend and implement in a laboratory, then considering the basic framework of risk assessment,⁷ clinical laboratories can formulate their own risk assessment tool for the said purpose.

Cost-Effective but Safe Strategies for Dealing COVID-19 Clinical Samples

Clinical laboratories perform a variety of tests on clinical samples. During this pandemic, coordination with the clinical team is essential. The clinical team must inform the laboratory staff before sending specimens from a patient suspected of COVID-19. The clinical team must also be informed and trained about obtaining minimum samples from suspected patients to reduce the risk to ward staff drawing the samples, potential loss of viability of virus during transportation and risk to laboratory technologists.

WHO emphasises on adapting 'core requirements'² for conventional clinical laboratories for dealing with clinical samples from COVID-19. Handling of all such samples by trained laboratory technologists with demonstrated capability can never be stressed more.

We recommend that laboratories using open systems for biochemical and haematological analysis involving manual pipetting etc. should refrain from dealing with clinical samples from COVID-19 patients. Resource-poor labs still using open systems would likely be unable to cater for the recommended biosafety requirements for COVID-19 clinical samples. Hospitals should either equip their laboratories with closed-system analysers or make arrangements to get the analysis done from better-equipped laboratories.

Most clinical analyses require specimen centrifugation, mixing on rotator plates and manual handling of specimens containing infective agents. All such procedures for COVID-19 patients' specimens should be performed in Biosafety Cabinet (BSC) Class II type A2 or an equivalent European standard type (CEN 12469).^{2,3} WHO supports Class I BSC as a better alternative due to simpler design and effectively addressing worker protection where sample protection is not the top priority. We suggest that if a laboratory decides to procure BSC, it should be BSC II-A for offering a wider spectrum of protection, wider customers and insignificant cost difference from Class I BSC. We have noticed a few laboratories mistakenly procuring and using laminar flow cabinets for handling biological samples. Laminar flow cabinet may appear similar to a BSC but does not serve the same purpose. Rather these are more dangerous as they expose the laboratory staff directly to the airflow carrying potential biohazard laden aerosols.

In case if BSC is not available and centrifugation has to be carried out, centrifuges with safety cups and sealed rotors provide a high degree of protection for lab technologists from aerosols and droplets. If such protected centrifuges are not available, fully capped tubes should be put in a well-balanced centrifuge placed in well-ventilated/open area. The centrifuge must not be opened after at least two to three minutes of completion of the operation to allow aerosols inside the container to settle. No effort to be made to manually stop the centrifuge or open in haste. Laboratory technologists must wear appropriate PPE throughout the processing of such samples.

Basic PPE for attending COVID-19 patients or dealing with clinical samples from such patients includes N-95 (US nomenclature)/FFP-2 (European nomenclature) masks, goggles or face shields, long-sleeved water-resistant gown and gloves.¹

Most surgical masks do not qualify as respiratory protective equipment.⁷ N-95 offers better protection if used properly and fitted well. N-95 although limits the transmission of viruses, it does not completely block it. At the same time it does not mean that transmission of virus will result in transmission of infection.⁸ Wearing N-95 is the

most effective way among the available options. People with beards are not protected from aerosols even if they are wearing N-95 masks.⁹ For such people working in high containment areas, the alternative is power air purifying respirator (PAPR) which is an extremely expensive equipment. Shaving the beard for the sake of the safety of the worker seems to be only a workable solution. As for N-95, it does not have a cost-effective and equally efficient replacement. We have experienced that the face shield is very effective in preventing direct splash or soiling. If so, and N-95 is fitting well and the filter is not causing breathing resistance, N-95 can be reused for many days.¹⁰

We have experienced that face shields (visors) offer better ergonomics as compared to safety goggles. The use of goggles with masks often results in the accumulation of mist around the goggles in a short time, hindering the view. Cost-effective face shields can be obtained from the open market or improvised solutions can be devised (Figure-1 and 2). Face shields and goggles can be reused after appropriate disinfection.

Disposable gowns are the most preferred option for the workers' attire. Nevertheless, there may be an acute shortage of this useful commodity in demanding times like the current COVID-19 pandemic. Single-use plastic aprons can be used over the gown to add better protection. If linen gowns are used, these gowns must be doffed properly and autoclaved after every use before regular laundering and reuse.⁷

Donning of surgical gloves is relatively an easier issue but careless or hasty doffing after handling a biohazard can pose a threat of transmission of infection. "Beaking method" is a safe and effective way of doffing gloves and offers maximum protection to the user.¹¹

Histopathological samples whether fixed in formalin or otherwise inactivated tissues require BSC for handling and processing. Similarly microbiological sample processing continuously exposes the worker to aerosol generation. Other paraphernalia of use of PPE and adherence to well-crafted practical SOP is always essential.

Surface Disinfection of the laboratory work is usually a neglected aspect in day-to-day working. Among the many commercially available expensive surface disinfectants, we have chosen household bleach (approximate concentration 3-5%) as the cheapest and most easily available option. Different formulations available from various sources address the sodium hypochlorite concentration in percentages or parts per million (PPM). This may confuse or leave the calculations at the understanding of the individuals that can vary. We have found the most



Figure-1: In-house faceshield re-useable made from local resources (acrylic sheet plus foam and elastic). Approximate cost Rs 500.



Figure-2: In-house faceshield disposable made from local resources (transparency plus foam and elastic) Approximate cost Rs 50.

convenient option for surface disinfection is by 20 ml of household bleach dissolved in approximately 1000 ml of clean water (free from particles) to be sprayed over the

Table: Ten Commandments of biosafety.

1st Commandment	Leader of biosafety leads the way and takes the responsibility
2nd Commandment	Stick to the 'core requirements' of laboratory biosafety
3rd Commandment	You can only get into trouble when some SOP is violated.
4th Commandment	Do not work when you are HURT Hurry/ Upset/ Routine/ Tired
5th Commandment	You need to be FIT to be safe Focused/ Informed/ Trained
6th Commandment	Disinfect the laboratory before the start of work and at the end of work
7th Commandment	Be very careful about aerosol-generating procedures
8th Commandment	A 'near-miss' gives an equal lesson to learn at a lesser price than an accident
9th Commandment	Biosafety is everybody's responsibility
10th Commandment	Human behaviour is a bigger risk factor than the biological agent itself

SOP=Standard Operating Procedures.

workbench and allowed to stay for around 10 minutes.¹² The prepared solution should not be used beyond 24 hours and should be kept away from sunlight or heat.

Electro-medical equipment, electrical sockets and open connections should be spared of the spray of this corrosive liquid. Alcohol wipes can be used to disinfect the electrical equipment while disconnecting the power supply during disinfection. Walls and floors do not require disinfection and may be cleaned with ordinary soap and water solution. The frequency of disinfection/cleaning should be decided depending upon the use of the workplace. In case of spillage of biological material, the surface disinfectant described above will not be effective. Higher concentration of chlorine disinfectant (100 ml of household bleach in 1000 ml of clean water) will be required for such high-risk situations.¹²

Safe disposal of leftover specimen disposal has mostly been an overlooked aspect in our settings. The leftover specimens from COVID-19 patients pose biohazard threats like any other biological agent in a clinical specimen, no more no less.⁵ Therefore, all laboratories must ensure proper disposal of leftover specimens according to the local or international safety guidelines.

In the light of the above discussion, we recommend Ten Commandments of Biosafety (Table).

Conclusion

The application of principles of biosafety is of paramount significance in the handling of specimens from COVID-19

patients. In resource-poor settings like Pakistan, improvised solutions are present which can be adapted while still offering essential protection to our lab staff. The provision of safety equipment is not just enough but must be coupled with proper training of users. A risk assessment must be carried out at all levels and necessary steps should be taken to ensure quality diagnostic services to our dependent populace at these demanding times.

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