Laboratory practice in the face of Covid-19

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Abstract

In December 2019, the COVID-19 outbreak began in Wuhan and quickly spread over the world. Hospitals have had to make drastic changes to normal workflows and practices to handle the current pandemic. Laboratories face unique challenges in the management of the investigation of COVID-19. Not only must we consider the safe collection and delivery of samples, but we must also observe the latest guidelines in testing for the virus. We have introduced several new measures in our laboratory to accommodate the collection and testing of samples for COVID-19 from both within the hospital and external screening sites. These changes encompass the pre-analytical (sample collection, packaging, and delivery), analytical (evaluation, handling and preparation of samples) and post-analytical (result reporting within the hospital and to external bodies) aspects of both routine (biochemistry, haematology, transfusion and urine, stool and body fluid testing) and COVID-19 testing, to ensure the safe and efficient testing of any patient samples. In addition, more practical matters, such as laboratory staffing and continuing staff education, have also been changed to ensure the safety and well-being of laboratory staff. With the implementation of new rules and regulations, we seek to safeguard the health of all healthcare workers while streamlining the workflow for the large amount of testing required during this period. As the pandemic continues, new tests (e.g. COVID-19 serology and IL6 testing for prognosis or monitoring) are being requested, requiring even more changes and assay evaluation before implementation. All laboratories must be ready to adapt to these new challenges during the COVID-19 pandemic.

Keywords

COVID-19, laboratory management, SARS-CoV-2

Introduction

In December 2019, the COVID-19 outbreak began in Wuhan and quickly spread over the entire globe. COVID-19 has a propensity to affect older male patients, with some studies showing a median age of 41 years. Meta-analyses have also shown that existing comorbidities, including hypertension, respiratory system disease and cardiovascular disease, also serve as risk factors for more severe infection. The mortality predictions of the pandemic are profoundly serious, with some estimating a one-year mortality as high as 4.46%. Several articles from Singapore have added to the COVID-19 literature, for example, highlighting its asymptomatic or pre-symptomatic transmission, local epidemiologic features and clinical course.

Changi General Hospital (Singapore) is a 1000-bed acute care general hospital accredited by the Joint Commission International and our laboratory is also accredited by the College of American Pathologists (CAP). We serve an average of 500–600 emergency patients and 1000–1500 outpatient attendances daily. During this pandemic period, our hospital had to make drastic changes to accommodate the COVID-19 emergency. Several outpatient clinics had to downsize operations and postpone non-urgent appointments, with doctors offering remote consulting for patients instead. Elective surgeries that were not urgent were postponed, and in the wards patients who were stable and recovering had to be discharged to community facilities to make additional space. Some general wards were converted into COVID-19 isolation wards. In the emergency department, sections had to be cordoned off as holding areas for suspected COVID-19 cases. Early on, even routine physiotherapy and occupational therapy services had to be suspended. The hospital also introduced several phone applications to help trace daily temperature, check-in and knock-off times and movements of staff, which are easy to use without the need for a computer.

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Testing for COVID-19 is an essential cornerstone in our battle against the virus. The Centers for Disease Control and Prevention (CDC) recommends that any hospitalized patients, healthcare facility workers, workers in communal living settings, first responders and residents in long-term care facilities or other communal living settings with symptoms have a high priority for COVID-19 testing. The CDC continues to recommend that only viral (nucleic acid or antigen) testing should be used to diagnose acute infection, which is also echoed by a statement by the Royal College of Pathologists of Australia. In addition to identifying priority cases, the evaluation of COVID-19 tests supports other functions in the hospital and community, such as the decision for discharge of confirmed COVID-19 patients, the screening of asymptomatic contacts in the community, and the investigation of unknown respiratory syndromes in this time period.

**Laboratory operations**

Laboratories face unique challenges in the management of the investigation of COVID-19. Not only must we consider the safe collection and delivery of samples, but we must also observe the latest guidelines in testing for the virus. For example, in the Mayo Clinic, working arrangements had to be modified in both their laboratories, and some in-house tests had to be redirected to reference laboratories to prioritize COVID-19 testing. Inspections by CAP in the USA and internationally have been delayed or suspended until further notice. Proficiency samples for CAP also faced some delays. Our laboratory had to make several changes to our regular practice to accommodate the current exceptional circumstances. During this pandemic, in addition to processing samples from our own hospital, we also received samples from external screening centres in affected areas of the community that were set up to screen high risk populations. We describe our laboratory’s experience in changes we had to implement during this COVID-19 period.

**Pre-analytical considerations**

Staff safety during specimen collection is of paramount importance, and our microbiology department (with advice from the infectious diseases department) has implemented new guidelines for personal protective equipment (PPE) usage for staff collecting samples from suspected COVID-19 cases. Following World Health Organization guidelines on safety procedures during specimen collection, all staff participating in sample collection are given the appropriate training for specimen collection, storage, packaging and transport. During sample collection, staff must wear a full set of PPE, which includes a hair net, face shield, N95 respirator mask, protective gown and gloves. All staff collecting specimens were given specific training in the proper donning, usage and removal of PPE. Singapore hospitals have previous experiences with SARS/H1N1 viral outbreaks; as a result every member of staff has been fitted for the correct size of N95 respirator mask, and all size requirements have been recorded. Our hospital knows how many N95 masks of a particular size are required for an outbreak beforehand.

Specimens collected for COVID-19 testing include upper respiratory tract swabs (nasopharyngeal (NP) swabs and oropharyngeal (OP) swabs (nylon flocked swab in a modified liquid Amies viral transport medium)) and lower respiratory tract specimens (e.g. sputum or bronchial washings) in sterile containers. Even for other types of samples for routine testing in patients who are positive for or suspected to have COVID-19 (blood, urine and stool samples), similar precautions are required and samples are collected using appropriate collection devices.

Extra precautions need to be taken in the packaging of samples from suspected or positive cases. Once the samples are collected, OP or NP swabs are first placed in a primary container with viral transport medium and sealed with a screw cap. The container is made of plastic that has a low risk of breakage. Sample labels are attached to the container with the patient’s name, identification number, an identification number barcode, date of birth and sex. These sample labels can also be generated at external sites. Orders for COVID-19 testing within the hospital are entered into an electronic ordering system, whereas orders for COVID-19 testing from external sites are accompanied with a specific order form for the test. Samples are then placed in double biohazard zipper bags (urgent samples are placed in red biohazard zipper bags). For the samples from external sites, a triple packaging system was implemented, with samples placed in shock-proof cooler boxes with internal cooling packs to keep the temperature at 2–8 °Celsius before being sent to our laboratory via couriers within 6–12 hours. All cooler containers were labelled as biohazard containers and reserved only for the transport of OP or NP swabs from external sites.

Within our hospital, our normal practice is for samples to be delivered to the laboratory via pneumatic tube. However, existing guidelines and those from the Ministry of Health do not recommend the use of pneumatic tubes to transport OP or NP samples from suspected or positive cases. Therefore, specific arrangements had to be made for the transport of these samples within the hospital. Porters were assigned for the physical transport of samples from the wards and emergency department from patients positive for or suspected to have COVID-19. Porters needed to wear gloves and surgical masks while transporting the specimens, and samples had to follow a triple packing protocol with the primary container; secondary bags and a tertiary shock-proof cooler box. This protocol has also been practised in other institutions in Singapore.

**Analytical processes**

When samples for COVID-19 testing arrive at the laboratory, they are processed within 4 hours of receipt. Our hospital employs our own laboratory-developed proprietary polymerase chain reaction (PCR) identification method to test samples for COVID-19. Only trained staff may handle these samples. When testing or handling samples in the laboratory, the staff must comply with full PPE protocols. In addition, specimens are processed in a class two biosafety cabinet (BSC) in a dedicated room attached to our laboratory. These safety measures are like the protocols that were developed earlier to handle samples for SARS and MERS-CoV testing.
The service for testing samples for COVID-19 is available from morning (8 a.m.) to night (10 p.m.) every day, and the microbiology staff involved in testing were divided into two groups, working alternate 12-hour shifts to reduce mingling. To accommodate the increasing number of samples for COVID-19 testing, two additional laboratories had to be set up in our adjoining research facility.

To appreciate what other lab practices are impacted by COVID-19, we provide a rundown of our usual processes. Different samples arrive at the laboratory for various tests, including biochemistry (general chemistry and immunoassays), haematology (blood cell counting and coagulation), transfusion, urinalysis (dipsticks and microscopy), stools (blood and microscopy) and body fluids (chemistry and cell counts). All staff working in the laboratory use standard PPE (surgical masks, gloves and laboratory coats). All staff not working in histopathology or microbiology are cross-trained in all the different sections. For general chemistry and some immunoassays (troponin, procalcitonin and B-type natriuretic peptide), we have a total lab automation system (Roche Cobas 8000) incorporating sample sorter, centrifuges, decapper and aliquoter. Other immunoassays (thyroid, HIV, hepatitis and tumour markers) are run on the Abbott Architect. Samples for testing on the Architect only are centrifuged separately at that workstation. Haematology blood cell counting on a Sysmex 9000 requires no centrifugation and the analyser has cap-piercing capability to aspirate the sample for analysis. The coagulation analyser also has cap-piercing capability after centrifuged samples are loaded. For transfusion, ethylenediaminetetraacetic acid (EDTA) tubes are centrifuged, carefully uncapped and then loaded onto an Ortho analyser for antibody identification and blood grouping. In urinalysis, plain vacutainer tubes are carefully uncapped prior to loading on a Coba 6500 urine analyser for dipstick chemical analysis and digital microscopy. Stool samples are processed in a biosafety cabinet for slide generation and sample loading for haemoglobin testing. Body fluid cell counting is done on a Sysmex, while chemical analysis (protein, glucose, uric acid and lactate dehydrogenase) is done on a Cobas 8000. Figure 1 shows the sample workflow.

**Changes to routine laboratory practice**

Any routine samples from suspected or positive COVID-19 cases are delivered in double bags by the pneumatic tube system. Except for respiratory samples, the CDC now allows transportation of all other laboratory samples to be delivered using the pneumatic tube systems. Routine processing of haematological and biochemical testing on blood, serum, urine and stool specimens gives minimal risk of aerosolization. The samples are thus processed and handled in a similar fashion to the general clinical specimens, although all staff are still advised to wear laboratory coats, eye protection, gloves and surgical masks. While uncapping samples is considered a low-risk procedure, we enforced a strict no-uncapping policy; for the Sysmex all testing is performed in the closed mode. Any uncapping that is required is performed in a biosafety cabinet (BSC) prior to loading onto the analysers. For haematology, all cell counting and white blood cell differentials will be issued as reported by the instrument without any smears being made. Similarly, urine cell morphology reported by the Coba6500 is reported as read by the instrument after online verification of images by the staff. Manual smear preparation is performed in the BSC and is avoided where possible, as this poses some risk for aerosol generation. A common practice in our hospital is to request for blood grouping and antibody screening (GXM) on admission for any patient who remotely needs transfusion. Our GXM analyser (Ortho Diagnostics) requires samples to be uncapped prior to loading on the analyser.
Postanalysis

Results of samples from within the hospital have always been relayed online to practising physicians through electronic medical records (EMRs), and COVID-19 testing results are similarly delivered for cases within the hospital. For samples from external sites, results are compiled into Excel spreadsheets and delivered to the physicians in charge of the external teams directly via email so that they can take action to alert the respective authorities. There were some challenges in reporting such a large number of results to external agencies, as the reporting was not within the normal framework of our hospital’s EMRs. Therefore, some staff had to be tasked to extract and convert results into a transferable format that could be sent to authorized agencies over secure channels. Despite the challenges that this presented, our staff were assisted by the involved agencies to facilitate the smooth and secure transfer of patient data.

Staff matters

One important change that we had to implement during the pandemic period was a change in how we assigned general laboratory staff not involved in COVID-19 PCR testing. We divided staff into two groups: Groups A and B. Each group consisted of day staff and four night staff who were fixed, with no interchange of day or night staff within each group. Groups A and B would then work on different days, with no group working more than 2 days in a row. For public holidays and weekends, where the workload is lighter, half of each group would take the day shift each day; for example, half of Group A would work on Saturday and the other half on Sunday. Any staff with any upper respiratory tract symptoms or fever must report to the emergency department immediately for evaluation. In addition, staffing had to consider that several members were withdrawn from normal duties to assist with COVID-19 sample collection at external sites. Within the laboratory, social distancing measures were enforced at workstations and pantry areas, as recommended by the International Federation of Clinical Chemistry and Laboratory Medicine.13

Education

Online resources are a great boon for our laboratory in this pandemic period. Because of the pandemic, all non-urgent staff meetings, continuing medical education teaching and laboratory or hospital symposia were postponed until further notice. Therefore, we have begun to utilize online platforms, such as Zoom, to hold essential meetings and teaching to continue the education of staff and discuss the existing measures taken during this period to see if there are any areas where we can improve our processes. Keeping abreast of the sudden influx of new literature about COVID-19 is very challenging. Our laboratory had to become acquainted with new websites, such as medRxIV, which makes available preprint, non-refereed manuscripts with the latest updates on COVID-19, including evaluations of COVID-19 assays. We also encouraged staff to visit educational websites, such as MedCram, which offers free, well-crafted updates on COVID-19 to further enrich their knowledge base.

Conclusion

During this COVID-19 pandemic, all sectors within our hospital have had to make changes to normal practice. With the implementation of new rules and regulations, we seek to safeguard the health of all healthcare workers while streamlining the workflow for the large amount of testing required during this period. As the pandemic continues, new tests (e.g. COVID-19 serology, IL6 testing for prognosis or monitoring) are being requested, requiring even more changes and assay evaluation before implementation. All members of staff have excelled themselves with their performance during this difficult period despite often short notices of new changes. We are profoundly grateful for all their cooperation with new and ever-changing practices during the pandemic.

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CS Lau, NA Kamaludin and TC Aw: All authors have contributed to the conception, writing and editing of this article.

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