

## Musings

# COVID-19: Experience of a tertiary reference laboratory on the cusp of accurately testing 5500 samples and planning scalability

### INTRODUCTION

The world shifted gears in response to a virus that took flight in fancy aircrafts and before anyone could prepare, landed on near and far shores. Every industry responded by either contributing or staying in. Lean in was the clear directive for health-care, and because every patient management needs a diagnosis, we had to muster up all the resources and step up to screening to isolate and treat. Thus, began this journey, and now after testing 5500 fellow Indians, we can pause, reflect, and change gears for the next phase of the pandemic.

As more and more information is becoming available for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease 2019 (COVID-19), there is continuous monitoring and revision of recommendations as well as strategies. The decision to test for COVID-19 is based on the clinical findings and epidemiological factors, along with an assessment for the likelihood of infection. The case definitions are continuously being revised and updated to accommodate new information along with the changing epidemiology and risk factors, as per the containment strategies and available infrastructure.

As this has been a learning process, we would like to share our experience.

### TESTING METHOD

The RNA-based real-time reverse transcription-polymerase chain reaction (RT-PCR) is the diagnostic test of choice for all the suspected cases, including the asymptomatic ones. Further confirmation may be done via sequencing-based assays. Triaging helps to optimize the utilization of limited resources in an efficient manner. We started the testing process by upgrading the existing facilities. Infrastructure, kit/equipment performance, and staff competency were all assessed to ensure the preparedness of Metropolis Healthcare Ltd., for COVID-19 testing.

Indian Council of Medical Research (ICMR) directives included a laboratory with experience in RNA-based RT-PCR assays

as well as those with national or international accreditation (ISO/IEC 15189:2012) in diagnostics of respiratory infections, especially H1N1.<sup>[1]</sup> Our laboratory was assessed by the National Accreditation Board for Testing and Calibration Laboratories (NABL) assessors for preparedness, testing capabilities, and compliance. Upon successful assessment, a laboratory registration number was generated by the ICMR, which is mandatory to appear on all the reports. Close attention was paid to the national guidelines as well as recommendations of the Center of Disease Control and Prevention (CDC), World Health Organization (WHO), and other international organizations.<sup>[2,3]</sup>

### INFRASTRUCTURE

Infectious molecular laboratories are designed to ensure a unidirectional workflow. Ours is a biosafety level-3 laboratory, with negative pressure and a Class II biosafety cabinet to handle infectious specimens along with positive, negative as well as extraction and reagent controls. We also perform periodic tests to look for carryover contamination.

### PERSONNEL

Qualified and experienced staff were selected and trained and their competency was assessed. Training was provided for appropriate specimen collection, storage, packaging, and transport of samples. A task force was initially developed to assess and expand the testing capabilities. Adherence to infection prevention and control guidelines, such as proper use of personal protective equipment (PPE), hand hygiene, respiratory hygiene, handling, processing, and disposal of biological material in a manner compliant to special biomedical waste handling guidelines issued by the central and state pollution control boards, was ensured.<sup>[4]</sup> Close attention was given to the safety of the health-care workers, and the availability of PPE was ensured.

### TEST PROCEDURE

#### Assessment of testing

Thought leaders were brought in to impart their knowledge and experience in developing a scientific approach to testing and

validation. The SARS-CoV-2 was detected by an RT-PCR assay. The nasopharyngeal sample was collected and transported in viral transport medium (VTM). The RNA was extracted on the automated QIASymphony SP (Qiagen) platform using DSP Virus/Pathogen Kit from Qiagen. The RT-PCR assay was performed using RealStar® SARS-CoV-2 RT-PCR Kit (Altona Diagnostics GmbH, Germany) and PathoDetect COVID-19 assay (Mylab Discovery Solutions, India). The RealStar® SARS-CoV-2 RT-PCR is a single-tube assay comprising primer/probes for the amplification of the Envelop (E) gene that detects betacoronavirus (B-βCoV) and the Spike (S) gene that is specific for SARS-CoV-2. The PathoDetect COVID-19 assay is a 3-tube assay that detects the E gene along with the SARS-CoV-2-specific RNA-dependent RNA polymerase (RdRp) gene. Various kits were assessed; however, because of the accuracy and reproducibility, the Altona and Mylab kits were chosen.

### TEST METHOD VERIFICATION

A thorough assay verification was carried out prior to patient testing to ensure accurate reporting. The following test parameters were verified:

#### Accuracy

Accuracy of the assay was estimated with a set 20 samples (10 positive and 10 negative) that were tested on both the real-time PCR kits as well as at the Kasturba hospital, a government-approved referral center for COVID-19 testing. All the 20 samples gave expected results by both the kits indicating 100% concordance of data.

#### Precision

A set of 3 positive and 3 negative samples were tested in three consecutive runs, and the reproducibility of the results was observed indicating good precision of both the assays.

#### Inter-instrument comparison

A set of 10 samples were run on Qiagen's Rotor Gene Q (RGQ) and Applied Biosystems 7500 Fast platforms; the results were 100% concordant.

#### Competence assessment

The same set of samples was assayed by two different technologists to assess staff competency. Besides, the testing personnel had to undergo extensive theoretical training, followed by examination through the online learning management module of Metropolis.

Based on the validations above, a solid testing approach was developed. A report format was created on the basis of the national and international guidelines. The workflow for sample collection included home visits and sample collection

from the hospitals. The technicians were trained in sample collection, keeping in mind the high number of false-negative tests with nasopharyngeal swabs attributed to faulty sample collection. A separate entrance for technicians was designed with frequent sanitization. Patients were discouraged from coming to the laboratory, and an email address was taken to share the reports with the patient.

#### Sample of choice

Currently, only the upper respiratory tract specimens, including the nasal secretions collected using nasopharyngeal and oropharyngeal swabs, are permitted to be tested as per the ICMR guidelines; however, other specimens may be considered depending on the evolution of the pandemic and the changing test strategies and recommendation by the ICMR and WHO. Co-testing is permitted and carried out based on the doctor's prescription to look for influenza-like illnesses, such as H1N1, and other respiratory infections.

#### Sample requisition form

It is mandatory to have a doctor's prescription as well as the complete demographics, including the exact current address and phone number for contact tracing, so that the patient can be categorized as per the levels and risk of exposure. The sample requisition form is constantly updated by the ICMR to include all clinical, medical, and epidemiological information.

#### Result reporting

The results generated are reported and notified as per the national guidelines provided by the ICMR. An online portal for uploading the results and a system for real-time data notification are in place. These tasks are carried out by the authorized signatories, supported by dedicated and trained data entry operators. Apart from the ICMR, the epidemiology cell is notified in real time about the positive and negative cases tested for isolation/quarantine. The state authorities such as directorate health services/IDSP are also similarly notified on a real-time basis. All the positive samples are submitted to the National Institute of Virology, which is a WHO-approved national reference laboratory for COVID-19 testing. This laboratory serves as a repository for all the positive samples. A constant communication channel has been developed between the customers and the laboratory. In addition, close communication with the ICMR has been important in this process to ensure quality and accuracy.

### DISCUSSION

Introduction of a new test in an accredited laboratory assuring superior quality standards would ideally require detailed planning, accreditations, and approvals over a period of time. However, in a global crisis like COVID-19, where the

companies are manufacturing and marketing kits widely to help to understand the pathobiology of this novel disease while government and state health regulatory bodies are defining and re-defining the guidelines of the patient and test selection, developing a laboratory test with the highest quality standards is difficult. Yet, the laboratory must deliver and innovate in parallel.

This challenge is not only limited to testing methods but also impacts various other aspects of testing. The CDC has updated over time the guidelines for:

- Sample to be collected: The recommendations were initially nasopharyngeal and oropharyngeal swabs. Now, they are allowing self-collected nasal swabs (due to the demand and supply imbalance of PPE)
- Transport medium – Initially VTM was the only transport medium allowed; now, the use of saline in situations where VTM is not available is permissible
- PPE – Initially, only the disposable N95 masks were allowed; this has evolved to allowing a “5-day” method and various disinfection methods.

Under the trying and turbulent circumstances, what a laboratory can do is to identify and uphold the critical-to-quality aspects by implementing the following:

1. Method verification
2. Strict internal quality control
3. Interlaboratory comparison
4. Training and competence assessment of personnel
5. Automation and alignment of pre- and post-analytical processes to analytical processes
6. Quality assurance.

### Expansion of testing

To meet the national demand for COVID-19 testing, we are planning to scale up the testing by setting up testing units in other NABL-certified laboratories of Metropolis across the nation as well as by increasing the number of operational hours within the unit while ensuring personnel comfort and safety. Further expansion and scalability is being assessed in the form of mobile units for samples to preserve PPEs.

Another expansion would be in the test menu with the inclusion of serological testing. A screening tool needs to be looked at to see which patients can go back to work.

### Lessons learnt

A close channel of communication is essential during this pandemic with physicians and patients to ensure that they know the status of the sample and the result, thus decreasing their anxiety. It is essential to work closely with the government, paying close attention to guidelines being

effected or revised to provide the most appropriate service at this time. Resources are also needed to share the data generated in real time with the governing bodies so that they know which way to act. These are unusual times which call for unusual measures. Metropolis is proud to provide its services and share our experiences as we scale up our operations.

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### Conflicts of interest

There are no conflicts of interest.

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