Summer Training Report

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Early Detection and Diagnosis of COVID-19: Issues in Indian Response

INTRODUCTION

- Coronavirus ailment 2019 (COVID-19) is a kind of extreme intense pneumonia brought about by the novel coronavirus contamination, authoritatively named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
- For average , it takes 5-6 days for someone to show signs to get infected with the virus, but it can take up to 14 days. Specific therapeutic drugs and vaccines against COVID-19 are currently under development; therefore, early detection and immediate isolation of COVID-19 positive cases is recommended.
- To prevent exponential growth in the number of cases and to contain this pandemic, there is need for more testing in all countries, including India.
- To tackle this demand, Indian government has allowed two different methods for testing of COVID-19, namely the real-time reverse transcription polymerase chain reaction (RT- PCR), and the rapid antigen detection test.

- Indian Council of Medical Research (ICMR) has set certain guidelines for diagnosing COVID-19. The RT-PCR test should only be conducted by a laboratory with a National Accreditation Board for Testing and Calibration Laboratories (NABL) accreditation. RT-PCR, and rapid antigen detection tests are recommended by Indian government.
- Those who test negative in the rapid antigen test should then be RT-PCR screened to rule out infection. WHO has issued COVID-19 testing guidelines that describe all the required safety measures while performing laboratory tests.
- Biological specimens such as nasopharyngeal swabs, sputum, other lower respiratory tract secretions, blood, and faeces can detect COVID-19.
- Currently, upper respiratory tract nasopharyngeal swab is the preferred method for collecting sample for COVID-19 detection

OBJECTIVE

The objective of this literature review was to explore the current understanding of various diagnostic approaches to detect COVID-19 and the most effective and useful method.

METHOD

- MEDLINE, PUBMED, and Mesh databases were searched and publications on COVID-19 laboratory testing were reviewed. This study presents the current status of best practices for detecting COVID-19 as well as future perspective on diagnostic approaches

FINDINGS

RAPID TESTING OF COVID-19

- In response to the growing COVID-19 pandemic and the shortage of laboratory-based molecular testing capacities and reagents, several diagnostic assay manufacturers have developed and started to sell quick and easy-to-use equipment or devices to facilitate testing outside the laboratory setting.
- Such basic test kits are based on either the detection in respiratory samples of SARS-CoV-2 viral proteins (e.g. sputum, throat swab) or the detection in blood or serum of human antibodies produced in response to SARS-CoV-2 infections.

RAPID DIAGNOSIS OF COVID-19

1) Rapid diagnostic tests (RDT) kit based on antigen detection

- RDT may detect the presence of SARS-CoV-2 viral proteins (antigens) expressed in an individual. If enough concentration of the target antigen is present in the sample, binding to specific antibodies attached to a paper strip contained in a plastic enclosure and generating a visually detectable signal, typically within 30 minutes.
- The identified antigen(s) are expressed only when the virus actively replicates; thus, these tests are ideally suited to diagnose acute or early COVID-19 infection.
- Based on the experience with antigen based RDTs for other similar respiratory diseases, it is expected that the sensitivity of these tests varies from 34% to 80%.

2) Rapid diagnostic tests based on antibody detection

- This test detects the presence of antibodies in the blood of a person who is suspected of having SARS-CoV-2.
- Antibodies take several days to weeks to become detectable after an infection. Response strength depends on several factors, including age, nutritional status, disease severity, and certain drugs or infections that suppress the immune system.
- Antibody detection tests targeting COVID-19 can also cross-react with other pathogens, including other human coronaviruses, and give false- positive results.
- Rapid antibody tests can be used for disease surveillance, help measure the extent of infection in a community, and predict the attack rate within a population.
- Based on the current data, WHO is not recommending the use of antibodies to detect rapid patient care diagnostic tests.

DIAGNOSTIC APPROACHES FOR COVID-19 IN INDIA

Enzyme-linked immunosorbent assay (ELISA)

- The ELISA test is of two types depending on the antibody tested (immunoglobulin G [IgG] or immunoglobulin M [IgM]).
- IgG antibodies develop later in the infection stage whereas IgM antibodies are detectable early in the infection stage.

Real time-Polymerase chain reaction

- The worldwide test used for individual diagnosis and treatment of COVID-19 is RT-PCR.
- It was previously used to diagnose Ebola and Zika.
- The procedure includes taking swabs from nasal or oral tracts, extracting the viral RNA in a printer-like unit, and amplifying it for SARS-CoV-2 detection.
- In addition to nasal or oral swabs, the RT-PCR sample may be collected using the bronchoalveolar lavage (BAL) method, in which a bronchoscope is passed to obtain fluid from the lungs or sputum.
- Sputum or BAL has a higher viral load than nasal or oral swabs, which allows viral identification more likely.

TrueNat

- This is a private test, which works on the same principle as RT-PCR, but with a smaller kit and faster outcomes.
- Commonly used for checking for tuberculosis and HIV.
- If a sample tests negative, it must be treated as negative; if it tests positively, a second test, called confirmatory assay of the RdRp gene, must be carried out.
- The TrueNat computer is compact and lightweight, runs mainly on batteries and delivers results within 60 minutes. This involves taking swabs at the nasal or oral levels.

THE TESTS, THEIR RUNTIME AND THEIR COST

	RT-PCR	Rapid Antibody	ELISA	TrueNat
Use	To diagnose	For surveillance, to detect exposed population	For surveillance, to detect exposed population	To diagnose
Time taken to test	3 hours	30 minutes	60 min	60 min
Cost	Earlier capped at at ₹4,500, now no price cap	₹600	Not fixed	₹1,000-1,500

ICMR RECOMMENDS ANTIGEN-BASED TESTING KIT FOR FASTER DIAGNOSIS

- The ICMR has suggested the use of COVID-19's first antigen-based test kits to allow for faster diagnosis at lower levels and without laboratory sample analysis.
- It is able to detect the presence of SARS CoV-2 in the sample collected via nasal swab.
- Maximum duration for interpreting a positive or negative test through the antigen-based kit is 30 minutes.
- The kit's assessment showed that it has a very high specificity or the capacity to identify true negatives ranging from 99.3% to 100%.
- While no confirmatory tests are required for samples testing positive, ICMR recommends that those that test negative should be screened for RT-PCR to rule out infection.

CONCLUSION

- RT-PCR is currently the frontline gold standard tool for COVID-19 diagnosis. The RT-PCR procedure takes at least 2–5 hours including the time taken to transport the sample.

DISCUSSION

- Effective diagnosis of COVID-19 is important for treating and preventing diseases. Chest CT imaging could be a more accurate, realistic, and rapid method of diagnosing and assessing COVID-19 compared with RT-PCR.
- Several external factors can affect RT-PCR test results, including sampling operations, specimen source (upper or lower respiratory tract), timing of sampling (different time of development of disease), and detection performance of the kit.
- The newly launched antigen detection kit is highly sensitive (99.3%–100%), and its cost is approximately ten times less than RT-PCR.