EDITORIAL

COVID -19: A Diagnostic Approach

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COVID-19 is a novel coronavirus, which has spread from Wuhan, China, and has been declared a pandemic by the World Health Organization (WHO).[1] It belongs to corona viridae family, beta corona virus which is a single stranded RNA virus causing illnesses ranging from common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). COVID-19 is caused by SARS-CoV-2. Coronaviruses are zoonotic, meaning they are transmitted between animals and people. Seven types of corona viruses are circulating in animals that have not yet infected humans but it appears that COVID-19 has crossed species from bats to snakes and pangolins then to humans, initially via the live animal 'wet markets' of Wuhan, China.[2,3,4]

COVID-19 molecular testing is a nucleic acid amplification test, such as real-time, reverse-transcription, polymerase chain reaction (PCR) test, with confirmation by nucleic acid sequencing. The PCR technique is based on DNA amplification of the viral genome. Since COVID-19 is a RNA virus so, it must be converted to DNA, before its replication. If there is no viral RNA, the test will be negative. However,one or more negative test results do not rule out the possibility of COVID-19 virus infection. Several factors can lead to a negative result in an infected individual, including poor quality of the specimens, inadequate patient materials, collection at late or very early stages of infection, improper handling or shipment, or technical reasons inherent in the test, e.g., virus mutation or PCR inhibition. Virus whole-genome sequencing can also help in molecular epidemiological study. Virus isolation is not recommended as a routine diagnostic procedure.[5,6] Specimen handling for molecular testing requires bio-safety level 2 facilities or standard equivalent.

Serological blood tests detect antibodies produced by the immune system in response to a SARS-CoV-2 infection. Presently, there are two potential serological tests for COVID-19. One determines viral proteins (likely a Western blot), while the other is an enzyme-linked immunoassay (ELISA) that detects the patient's antibodies against the virus. ELISA tests are based on the detection of immunoglobulin IgG and IgM antibodies. IgM test positivity indicates that the infection exists (demonstrating prolonged virus replication in infected patients), and high levels of IgM during the acute phase of infection can last more than 1 month. IgG test positivity indicates that the individual had a previous infection and/or the immune response has begun. The response of IgG later than IgM. Serological tests are not useful in detecting recently infected asymptomatic patients because it can take several days for antibodies to multiply and reach a detectable

level in the blood.[6,7] Therefore, this rapid diagnostic test (RDT) is used only for screening purpose not for diagnosis.

Radiological chest X-Ray and CT scan are one of the diagnostic methods for COVID-19. Chest X-ray findings are airspace opacities, ground glasopacities, and distribution is often bilateral, peripheral and lower zone. CT scan of the chest shows multiple bilateral lobular and subsegmental areas with ground-glass opacity or consolidation, crazy-paving pattern, air bronchograms, or a reverse halo/ perilobular pattern.[8,9]

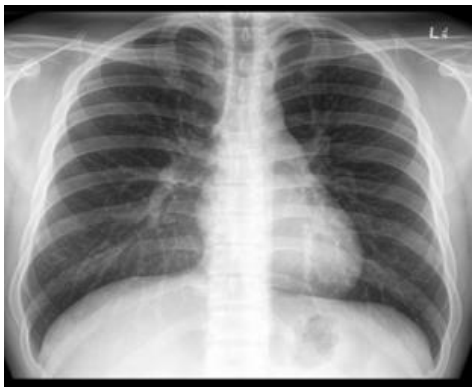

Fig. 1: Normal Lung

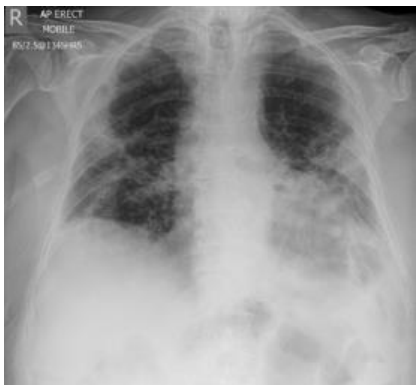

Fig. 2: Lungs of COVID-19 patient

Table: 1 Current Diagnosis method available for COVID-19

Method available	Working principle	Advantage	Time required	Disadvantage
Next generation sequencing (NGS)	Whole genome sequencing	● Highly sensitive and specific. ● Provide all related information. ● Can identify novel strain.	1–2 day	● High expertise needed . ● Equipment dependency and high cost. ● Highly sophisticated lab required.
RT-PCR	Specific primer-probe based detection	● Fast results. ● Higher sensitivity. ● Needs small amount of DNA. ● Can be performed in a single step.	3–4 h	● Higher costs due to the use of expensive consumables. ● Expensive lab equipment. ● Detection is also complex and time consuming.

LAMP	More than two sets of specific primers pair based detection	● Highly repeatable and accurate. ● Single working temperature.	1 h	● Too sensitive, highly prone to false positives due to carry-over or cross contamination.
Serological traditional	Antigen/ Antibodies IgG/IgM	● Sensitive and specific.	4–6 h	● Testing come positive after 3-4 days of infection.
Rapid serological IgG/IgM	Antigen/ Antibodies	● POCT	15–30 min	● Testing come positive after 3-4 days of infection.
CT scan	Chest images	● Enhance sensitivity of detection if findings combined with RT-PCR results.	1 h	● Indistinguishability from other viral pneumonia and the hysteresis of abnormal CT.

Table: 2 Below are the group of biochemical tests performed for the diagnosis, follow-up and treatment of COVID-19

Test	Diagnostic criteria
Complete blood count	● Leukopenia, lymphopenia, and leukocytosis. ● Neutrophilia, thrombocytopenia, and decreased hemoglobin levels. ● Lymphopenia and thrombocytopenia have been associated with increased risk of severe disease and are clinical indicators for monitoring disease progression.
Coagulation tests	● Elevated D-dimer: D-dimer level >1 microgram/L is associated with a poor prognosis, including high sequential organ failure assessment scores. ● Elevated prolonged prothrombin time. ● Elevated fibrinogen level (acute phase reactant).
Liver function test	● Elevated transaminases. ● Decreased albumin level (prognostic factor). ● Serum lactate dehydrogenase level might be elevated in patients with severe illness. ● Elevated serum lactate dehydrogenase level might be indicated by lysis of blood erythrocytes (hemolysis).

Renal impairment test	● Elevated creatinine level.
Serum procalcitonin	● May be elevated in patients with a secondary bacterial infection.
Serum C-reactive protein	● May be elevated in patients with a secondary bacterial infection. ● A prognostic factor.
Serum creatine kinase	● May be elevated in patients with muscle or myocardium injury.
Serum troponin level	● May be elevated in patients with myocardium injury.
Serum ferritin	● May be elevated. ● Indicates acute inflammation response.
Arterial blood gases (ABG)	● May show low partial oxygen pressure. ● May show low oxygen saturation (SpO<90%). ● ABG is ordered for patients with respiratory distress and cyanosis.

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