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Role of diagnostics in combating COVID-19

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As the knowledge and experience with COVID-19 advance, the laboratory's approach and role are also evolving

The Coronavirus 2019 (COVID-19) first emerged in December 2019 and the disease has rapidly evolved into a pandemic that. As soon as the causative pathogen, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified and its genome sequence determined, a laboratory diagnosis based on nucleic acid amplification technologies was quickly established and has played essential roles in the confirmation of a clinical diagnosis.

Diagnostic strategies that can precisely detect the disease and stratify patients for types of care are urgently needed for increasing the cure rate and preventing exacerbation of the disease with limited healthcare resources. Serological testing for antibodies against SARS-CoV-2 is becoming available for complementary diagnosis, identification of convalescent plasma, and epidemiologic studies.

Additional laboratory biochemical tests, C-reactive protein, interleukin-6, lactate dehydrogenase, Procalcitonin, neutrophil-to-lymphocyte ratio, D-dimer, cardiac troponin, renal biomarkers, lymphocytes and platelet count, are also critical in combating COVID-19. Nevertheless, with overwhelming numbers of patients and potentially large numbers of asymptomatic cases, clinical laboratories encounter enormous challenges in diagnostic approaches that can rapidly and accurately identify infected persons.

Laboratory diagnosis of COVID-19

The Gold standard for detection SARS-CoV-2 is PCR. PCR is a highly sensitive technology for detecting pathogen-specific nucleic acid in samples by monitoring the amplification of the nucleic acid molecules in PCR with sequence-specific primers and probes. The relative stability of the SARS-CoV-2 viral genome makes design of PCR primers and probes easier for laboratory diagnosis. These tests are designed for those actively infected and shedding virus. Their analytic sensitivity and specificity are considered excellent, with limitations related to mismatches between the DNA primers and small alterations in the SARS-CoV-2 RNA genome.

By using antigen tests, the presence of the virus can be confirmed within minutes to hours. The viral antigen is detectable at

the first sign of COVID-19. However, it will only show if the patient has a current infection. It cannot indicate recovery from the virus. The results of antigen tests are usually accurate, but negative results need to be confirmed with RT-qPCR assays, especially when an individual is showing COVID-19 symptoms. Compared to molecular analysis, this test has more probability of missing an active infection.

Serological tests of SARS-CoV-2-specific antibodies are becoming available since the COVID-19 outbreak with technologies varying from lateral flow immunoassays and enzyme-linked immunosorbent assays (ELISAs) to chemiluminescent immunoassays. Previous studies of dynamic changes of the serum antibodies specific for SARS-CoV in SARS patients show that antibodies were not detected within the first 7?days of illness. However, both IgG and IgM increased dramatically on day 15. Whereas IgM reached a peak rapidly and was undetectable after 11?weeks, IgG reached a peak on day 60 and remained high until day 180.

Laboratory markers to Differentiate Mild and Severe Infection

Several laboratory parameters may facilitate the assessment of COVID-19 severity, discriminating mild from severe COVID-19 disease. While the clinical status, in particular peripheral oxygen saturation (SpO2) levels, and concurrent comorbidities of COVID-19 patients largely determine the need for their admittance to ICUs, several laboratory parameters may facilitate the assessment of disease severity in the clinical setting, routine laboratory biochemical tests including complete blood counts, liver function, renal function, cardiac function, electrolytes, blood gas, coagulation, and inflammation should be provided to support the diagnosis and patient management, in particular, for those patients in critical conditions. Clinicians should consider low lymphocyte count as well as the serum levels of CRP, D-dimers, ferritin, cardiac troponin and IL-6, which may be used in risk stratification to predict severe and fatal COVID-19 in hospitalized patients. It is more likely that the course of the disease will be unfavorable if some or all these parameters are altered. interleukins (IL) (IL-2, IL-6, IL-7, IL-10) were significantly associated with disease severity and particularly observed among cases admitted to ICUs. IL-1 and IL-8 were not associated with severity. Apparently, the serum levels of some interleukins have the potential to discriminate between mild and severe disease and possibly may be used as prognostic markers.

Among hematological parameters, lymphopenia is clearly associated with disease severity; patients who have died from COVID-19 have had significantly lower lymphocyte counts than survivors. In fact, repletion of lymphocytes may be an important factor for recovery. Patients with severe COVID-19 appear to have more frequent signs of liver dysfunction than those with milder disease. An increase in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin levels has been observed among many ICU patients. Infection of liver cells with SARS-CoV-2 cannot be excluded as 2–10% of patients with COVID-19 have diarrhoea and viral RNA has been detected in both stool and blood samples, which implies the possibility of hepatic virus presence. It is also likely that any immune-mediated inflammation, in particular cytokine storm, but also pneumonia-associated hypoxia, may lead to liver damage in critically ill COVID-19 patients. C-reactive protein (CRP) levels are increased in COVID-19 patients and it has been shown that survivors had median CRP values of approximately 40?mg/L, while non-survivors had median values of 125?mg/L, indicating a strong correlation with disease severity and prognosis. Other predictors of poor outcome include the serum levels of ferritin and lactate dehydrogenase (LDH). Elevated ferritin levels due to secondary haemophagocytic lymphohistiocytosis (sHLH) and cytokine storm syndrome have been reported in severe COVID-19 patients.

Correlations of abnormal coagulation parameters with poor prognosis have been observed. Coagulopathy and overt disseminated intravascular coagulation appear to be associated with high mortality rates. Among the coagulation parameters, D-dimer elevation > 1 ug/L was the strongest independent predictor of mortality.

As the knowledge and experience with COVID-19 advance, the laboratory’s approach and role are also evolving. Nevertheless, combating a pandemic requires global collaboration at all levels, including healthcare professionals, scientists, policy makers, patients with the disease, family members, and communities. In combating COVID-19, all human beings are in the same boat.

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