COVID-19 INFECTIONS – DIAGNOSTIC CHALLENGES

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Since late 2019, a pandemic of coronavirus disease 2019 (COVID-19) has emerged as a global crisis. The causative agent is a beta coronavirus, SARS-CoV-2, that can cause a range of respiratory features and can even progress to respiratory failure and death in high risk individuals. On follow-up of the patients, the virus has been found to cause symptoms even external to the respiratory tract, and can lead to inflammatory complications in several organs, resulting in an increased range of associated clinical features. Early and accurate diagnosis is the need of the hour for prevention and pandemic control. The non-specificity and variety of clinical manifestations, from asymptomatic cases to severe illness, emphasizes the need for diagnostic tests which have good sensitivity as well as specificity [1].

Molecular tests based on real-time reverse transcription PCR (rRT-PCR), currently are gold standard for both screening as well as diagnosis of COVID-19 during early phase. These assays verify the course of infection, as well as estimate the extent of viremia. RT-PCR is highly specific; however, it shows a variable sensitivity to detect COVID-19 infection. Many studies have reported high rate of false-negative results of RT-PCR testing for SARS-CoV-2 detection. Fang Y *et al* has reported chest CT having greater sensitivity than RT-PCR (98% vs 71%, respectively) [2]. Li *et al* has also reported a high rate of false negative results for RT-PCR testing in 610 clinically diagnosed hospitalized cases, and found that several RT-PCR tests performed from same patients at different times during the course of management showed variable results [3]. This highlights the importance of CT scan chest for screening of COVID-19 in patients having suggestive clinical and epidemiologic features, especially when RT-PCR test results are negative. Lan *et al* reported 4 recovered cases of COVID-19 whose RT-PCR had turned negative, that after 5-13 days turned out to be RT-PCR positive again (these individuals were still asymptomatic and had no change on chest CT scan compared to previous findings, the patients had no history of contact or exposure again)[4]. Yuan *et al* reported 25 out of 172 patients discharged from hospital (14.5%), who came back with newly positive RT-PCR test results for SARS-CoV-2. Before being discharged the first time, all these patients had improvement on chest CT scan and had 2 consecutive negative results of PCR testing done at 24-hour interval [5].

Moreover, the sampling for RT-PCR tests has also been a matter of discussion since the beginning of this pandemic. The current guidelines suggest nasopharyngeal swab specimen testing by RT-PCR for diagnosis of COVID-19, however, saliva specimens are also considered to be an alternative diagnostic sample. Wyllie *et al* have highlighted the issue of variation in nasopharyngeal sampling that might be a reason of false negative RT-PCR results, and have compared sensitivity of saliva and nasopharyngeal swab specimens for detecting SARS-CoV-2, supporting the potential of saliva specimens in SARS-CoV-2 diagnosis [6].

Serological immunoassays are being used at present for estimation of seroconversion in seroprevalence surveys in those suspected of present or past SARS-CoV-2 infection by IgG and IgM testing [7]. Serological testing can play a supportive role with RT-PCR testing in COVID-19 diagnosis, about 10 days or more after symptoms begin. These tests can also be useful in assessing past infections as well as defining humoral responses of individuals or patient cohorts receiving certain forms of treatment.

Rapid antigen detection tests are being developed for detection of active infection; however, limited number of these tests is available at present. Compared to RT-PCR, antigen detection tests are less sensitive, and because of increased chance of false-negative results, antigen detection is considered to be an adjunct to RT-PCR testing [8].

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