EDITORIAL

RECENT UPDATES ON SARS-COV-2 TESTING, VARIANTS, AND VACCINES

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Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) which is the cause for coronavirus disease-2019 (COVID-19) emerged in 2019 in Wuhan city, China (1). Since its emergence, it has become the leading cause of morbidity and mortality worldwide. As of November 2021, 248 million cases and five million deaths have been reported worldwide. The United States of America, India, Brazil, the United Kingdom, and Russian are the top five countries in terms of the number of cases and mortalities. In Africa, about eight million cases and two million deaths were reported. In Ethiopia, about 365 thousand cases and six thousand deaths were reported (2).

SARS-CoV-2 is an enveloped, single-stranded positive-sense RNA virus that belongs to the family *Coronaviridae*. The family *Coronaviridae* is further classified into genera of αCoV, βCoV, γCoV and δCoV. Coronaviruses which can cause diseases in humans belong to the genera αCoV (OC43 and 229E) and βCoV (HKU1, NL63, SARS-CoV-1, MERS-CoV, and SARS-CoV-2). HKU1, NL63, OC43, and 229E cause mild respiratory and gastrointestinal diseases, whereas SARS-CoV-1, MERS-CoV, and SARS-CoV-2 are known to cause severe respiratory diseases (3, 4). The genome of SARS-CoV-2 is about 29 kb long and consists of fourteen open reading frames (ORFs). The first ORF comprises two-third of the genome and is located at the 5'-end. The ORF1 has ORF1a and ORF1b components which encode sixteen nonstructural proteins including RNA-dependent RNA polymerase. The remaining ORFs encode accessory and structural proteins. The major structural proteins of the virus are spike glycoprotein, nucleoprotein, envelope protein, and membrane glycoprotein (5).

Changes in the genetic material of SARS-CoV-2 occur over time. Most of the changes have little to no impact on their properties (6). However, some changes may affect its ability to spread, disease severity, the performance of vaccines, diagnostic tools, or other public health and social measures (7, 8). World Health Organization has classified SARS-CoV-2 variants into variants of concern (VOC) and variants of interest (VOI). The variants are designated as alpha, beta, gamma, delta, mu and lambda. For the VOCs, clear pieces of evidence are available indicating a significant impact on transmissibility, severity, and/or immunity that is likely to have an impact on the epidemiological situation. However, for VOI, evidence is available on genomic and epidemiologic properties which is still preliminary or is associated with major uncertainty (9). The delta variant is predominantly circulating worldwide and associated with increased transmissibility, disease severity and poor treatment outcome (8). New variant of concern named Omicron ´has been reported by WHO recently (10).

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The World Health Organization recommended preventive measures like physical distancing, quarantining, covering coughs and sneezes, and hand washing. The use of face masks has been recommended in public settings to minimize the risk of transmissions. Testing is a critical element to the overall prevention and control strategy for COVID-19 (11). The World Health Organization recommends that all individuals meeting the case definition for COVID-19 be tested for the presence of SARS-CoV-2 in respiratory specimens. Nucleic acid amplification test (NAAT) is considered as the gold standard for diagnosis of SARS-CoV-2 infection. Detection of viral antigen can be implemented as a complementary strategy (12).

Substantial numbers of COVID-19 vaccine candidates are under development and many of them are at different stages of the clinical trial (13). To date, two mRNA-based vaccines (Moderna's mRNA-1273 and BioNTech–Pfizer's BNT162b2), three adenovirus-based vaccines (Oxford–AstraZeneca's AZD122, Janssen's Ad26.COV2.3, and Serum Institute of India's Covishield), and three inactivated vaccines (Sinopharm's BBIBP-CorV, Sinovac's Coronavac and Baharat Biotech's Covaxin) have received approval for use by World Health Organization (14).
The emergence of new variants of SARS-CoV-2 has posed a huge challenge to the success and effectiveness of the available vaccines to halt the spread of the pandemic. Several studies have reported reduced effectiveness of the two mRNA-based vaccines (Pfizer BioNtech and Moderna) and AstraZeneca (AZD1222) against the delta variant of concern (15, 16). However, despite the reduced effectiveness against infection by new variants of concern, Pfizer BioNtech, Moderna, and Astra Zeneca have reduced the risk of death by more than 85% in UK, regardless of variants (17). Structural and functional analysis of the alpha, beta and gamma variants of concern revealed that mutations to the SARS-CoV-2 genome may result in diagnostic tests failures specially when it happens to the primer or probe binding sites of the target genes (18). For example, deletion of amino acids 69 and 70 within the spike (S) gene of SARS-CoV-2 B.1.1.7 (alpha variant) has resulted in S-gene target failure (SGTF) consequently false-negative test results (19).

The expedited development and approval of different diagnostic and vaccine platforms for emergency use by various regulatory bodies including the WHO has contributed a lot in reducing the spread of the disease. However, the emergence of new variants of concern with an increased transmissibility and virulence and reduced treatment outcome with convalescent sera and monoclonal antibodies is a critical challenge (20-22). Moreover, the emergence of new variants of concern has resulted in reduced effectiveness and performance of the available COVID-19 vaccines and diagnostic platforms respectively. Hence, a continues genomic surveillance and evidence-based modification of existing vaccine/diagnostic platforms would be of paramount significance to halting the spread of the pandemic.

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