State of the Globe: Navigating the Impact of SARS-CoV-2 Mutations on COVID-19 Testing

The SARS-CoV-2 virus has been a persistent challenger from 2019 causing the ongoing COVID-19 pandemic. The occurrence of numerous mutations over the passage of time leads to the emergence of new variants. These variants have posed significant challenges to our efforts to control the spread of the disease. One particular area where their impact has been felt is in COVID-19 testing. In this editorial, we would try to explore the consequences of SARS-CoV-2 mutations on COVID-19 testing and discuss the strategies to address these challenges.

As viruses replicate, they naturally accumulate mutations in their genetic material. The SARS-CoV-2 virus is no exception, and it has undergone several significant mutations. Some of the most well-known variants include the Alpha, Beta, Gamma, and Delta variants, each with its unique set of mutations.[1] These variants have shown increased transmissibility, altered disease severity, and, in some cases, reduced susceptibility to certain therapeutics.

SARS-CoV-2 mutations have introduced new challenges to COVID-19 testing efforts worldwide. Diagnostic tests, such as polymerase chain reaction (PCR) and antigen tests, rely on detecting specific genetic sequences or viral proteins associated with the virus.[2] Mutations in these regions can potentially affect the accuracy and sensitivity of these tests. First, some mutations can lead to false-negative or false-positive results. A false-negative result could occur if the mutation alters the primer binding sites in the PCR test, leading to decreased sensitivity and missed detection. Conversely, false-positive results might arise if the mutation leads to cross-reactivity with non-SARS-CoV-2 viruses or other respiratory pathogens. Second, the increased transmissibility of certain variants can result in higher viral loads in infected individuals. This heightened viral load can impact the timing of test positivity, leading to earlier detection or shorter incubation periods. It necessitates careful consideration of the optimal testing window for accurate diagnosis.

To combat the challenges posed by SARS-CoV-2 mutations, several strategies need to be implemented:[3]

1. Genetic surveillance: Increased genomic surveillance is crucial for tracking the emergence and spread of new variants. This involves sequencing the viral genomes from positive samples to identify mutations and their potential impact on testing and public health measures
2. Test optimization: Continuous evaluation and adjustment of testing protocols are necessary to ensure their effectiveness against new variants. This includes the regular assessment of primer and probe sequences used in PCR tests, as well as the development of new tests targeting different regions of the virus
3. Diversification of testing approaches: Employing multiple testing methods, such as combining PCR and antigen tests can enhance accuracy and compensate for limitations posed by specific mutations. Serological testing can also provide valuable information about past infections and immune responses
4. Vaccine monitoring: Ongoing surveillance of vaccine efficacy against emerging variants is crucial. Monitoring breakthrough infections among vaccinated individuals can help identify the need for booster doses or modifications to existing vaccines.

The Food and Drug Administration (FDA) provides the following recommendations to developers regarding the impact of viral mutation on the performance of diagnostic tests:[4]

1. Developers are advised to design their tests in a manner that minimizes the influence of viral mutations on test performance
2. Regular monitoring for viral mutations that might affect test performance
3. Test limitations should be clearly communicated in the test's labelling.

The tests designed to target and detect specific known variants are likely to become outdated rapidly due to the ongoing mutation of the virus. Given this situation, the FDA believes that whole genome sequencing tests may be the most suitable option for genotyping claims. These tests have the capability to detect both known and emerging mutations and variants. Developers of "sequencing tests" who seek Emergency Use Authorization with a genotyping claim are advised to initiate early discussions with the FDA.

By following these recommendations, developers can contribute to the development of effective diagnostic tests that account for viral mutations and provide accurate results for patient care.

The impact of SARS-CoV-2 mutations on COVID-19 testing highlights the need for continuous adaptation and vigilance in our testing strategies. As the virus evolves, so must our diagnostic approaches. Collaboration between researchers, public health agencies, and healthcare providers is paramount to stay ahead of the virus and effectively respond to the challenges it presents. By embracing innovative solutions and maintaining a robust surveillance system, we can ensure accurate testing and better control of the COVID-19 pandemic.

Rohit Kumar Varshney

Department of Emergency Medicine, Teerthanker Mahaveer Medical College and Research College, TMU, Moradabad, Uttar Pradesh, India

Address for correspondence: Dr. Rohit Kumar Varshney, Department of Emergency Medicine, Teerthanker Mahaveer Medical College and Research College, TMU, Moradabad, Uttar Pradesh, India.
E-mail: rohitmaxy@gmail.com

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