Serological and Clinical Issues of COVID-19

Reza Nassiri

SARS-Cov-2 (COVID-19; WHO nomenclature), which originated from the city of Wuhan in China, has now spread to at least 175 countries and territories with unexpected societal and economic consequences. Infections with coronaviruses are not new to humans; they usually cause mild respiratory infections especially during winter months. However, to date, there are three recombinant coronaviruses that cause severe illness; SARS (2003, originated in China), MERS (2012, the disease emerged in Saudi Arabia), and 2019 SARS-Cov-2 known as COVID-19, it too, originated from China. Due to its rapid and wide global transmission, the WHO declared it as pandemic. Of note, the overall genomic sequence of SARS-Cov-2 differs from other known coronaviruses. Unlike its predecessors, SARS-Cov-2 genome facilitates viral binding to the host cells much more tightly compared to its common host cell receptor - a distinct feature of Spike proteins and the binding process is activated by certain cellular enzymes. It has been estimated about 10% of exposed individuals are asymptomatic carriers of the virus. SARS-Cov-2 replicates in the upper respiratory tract followed by a rapid extension of infection into the lower respiratory tract. While most infections are clinically mild especially in young adults, few cases particularly in elderly and those with comorbid conditions (e.g., primarily diabetes, hypertension, arrhythmias, cancer patients, immunocompromised individuals) present with severe form of infection which can be life-threatening, a condition known as acute respiratory distress syndrome (ARDS), a consequence of dysregulated immune response (cytokine storm syndrome).

There are numerous challenging issues surrounding SARS-Cov-2 serology including test quality, test accuracy, and serological interpretation of the rest results. Unlike RT-PCR, SARS-Cov-2 antibody tests may be better fit for public health monitoring. The spectrum of currently available antibody testing is variable which is a gap in clinical interpretation of serologic response. Thus, there is a substantial need to generate evidence for protective immunity. This also affects decisions regarding the need for PPE. Currently, there is no firm evidence that people who recovered from SARS-Cov-2 and have antibodies, are fully immune from a second infection. To confirm immune protection from SARS-Cov-2, it is fundamental to address two questions; what the level of convalescence antibody is, and, how long the antibody will last. Therefore, it seems ideal to monitor individuals with SARS-Cov-2 antibodies for several months compared to individuals without antibodies. This approach would elucidate if antibodies can provide an adequately long protection given the non-traditional patterns of SARS-Cov-2 serologic response which has been observed and reported in numerous countries. It is ironic SARS-Cov-2 is a different subtype of SARS. From the experience of SARS, those affected, continued having immune response for 5-6 years. Thus, in the context of SARS-Cov-2, more research is needed to design confirmatory tests to identify specific protein markers of a serologic and clinically valid antibody response.

On clinical grounds, the management of moderate to severe disease is challenging. Approximately 15-20% of patients develop moderate to severe disease that require hospitalization. About 5% of patients require admission to an Intensive Care Unit (ICU) with supportive therapies including intubation and ventilation. In addition to ARDS which is the most common complication in severe cases, sepsis and septic shock, multiple organ failure such as cardiac, renal, cerebral, neuronal, and GI are more common in at-risk individuals of older age as well as chronic co-morbid conditions. SARS-Cov-2 encompasses clinical syndromes beyond lungs with a complex pathophysiology. Therefore, a syndromic clinical management approach is warranted in the absence of a potent and directly acting antiviral agents. Recently, remdesivir, a nucleotide analog has been issued an emergency use authorization in the United Sates by the Food and Drug Administration (FDA). Remdesivir is the first antiviral agent which exhibited only modest effect in management of severe SARS-Cov-2 patients diminishing the time to recover from 15 to 11 days. Therefore, it may not be the silver bullet; however, it is the first step toward targeted antiviral therapy. Remdesivir in advanced stage of COVID-19 disease may not be as effective. Immune dysregulation and cytokine storm are critical issues of the advanced stage disease. Therefore, administration of hyper-inflammatory antagonists in combination with remdesivir is likely to produce better prognostic outcomes compared to remdesivir monotherapy. However, the drug must also be used in the early phase of COVID-19 as this phase is associated with much high viral load in order to suppress the viral life cycle as early as possible to prevent the likely progression to ARDS.

SARS-Cov-2 is associated with a wide range of clinical manifestations and its pathophysiology is complex. As we are learning more about the serologic and clinical features of this novel virus present in our community of human race, more studies are warranted to fully understand the syndromic features of this virus to effectively manage ARDS complications.

Name: Reza Nassiri

Afiliation: Departments of Pharmacology and Toxicology and Family and Community Medicine, Michigan State University, USA, Email: Reza.Nassiri@hc.msu.edu