SARS-CoV-2 Variants and their Clinical Implications

ELEFTHERIOS MYLONAKIS, MD, PhD

The COVID-19 pandemic continues to impact every aspect of our daily lives and stress our health resources and the SARS-CoV-2 variants have contributed to this unpredictable dynamic. This aspect of the pandemic was underappreciated during its early stages, but with millions of infections around the world and each infected individual having billions of copies of the virus, it was only a matter of time for clinically important variants to emerge.

At the beginning of the pandemic, variants of SARS-CoV-2 containing the D614G aspartic acid-to-glycine substitution at amino acid position 614 of the spike (S) protein rapidly became dominant, mostly due to increased receptor-binding avidity to the angiotensin-converting enzyme 2 (ACE2) receptor. Then, the B.1.1.7 (Alpha) and P.1 (Gamma) moved from the UK and Brazil, respectively, and necessitated national and global monitoring and naming systems, such as the one coordinated by the World Health Organization (WHO).[2]

Importantly, these variants of concern (VOCs) are associated with changes in transmissibility and make a difference in the dynamic of the pandemic and move epidemiologic and modeling targets, including of the so-called "herd immunity." Moreover, preliminary data suggest that even some of the monoclonal antibodies may be less effective for treating cases of COVID-19 caused by certain variants.[3] It is remarkable how small changes in the virus can have such profound clinical ramifications. For example, the B.1.1.7 (Alpha) variant carries a mutation in the S protein (N501Y) that, along with numerous other B.1.1.7 lineage-defining mutations, alter the conformation of the receptor-binding domain. This relatively small change was enough to make this the predominant variant around the globe.

In this issue, Kantor et al. present the important landscape of the SARS-CoV-2 variants in RI. They report that these variants represent the major lineages noted among the 3,963 SARS-CoV-2 RI sequences detailed in their paper.[1] As they show, a number of variants of interest (VOI) and all four VOCs (the term that describes VOIs with demonstrated ability to alter the epidemiologic and/or clinical aspects of COVID-19) have been detected in our state and they are: B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta).[1]

Also, the report by Kantor et al. hints at the next "elephant in the room." The report notes 9 cases associated with B.1.617.2 (Delta) between 4/2021 and 5/25/2021. We have been following the unthinkable loss of life and human suffering in India and around the world that B.1.617.2 (Delta) has been causing. This variant had an exponential increase over the past several weeks and currently is associated with the vast majority of cases in the US. Preliminary reports detail that this variant causes clinical disease up to 2 days earlier, can result in viral loads in the respiratory tract that are 1,000-fold higher, and cause more reinfections or even evade, in some degree, vaccine-induced immune responses. Even the clinical symptomatology, with more patients presenting with pharyngitis and upper respiratory symptoms, seems to be different. Indeed, in the few weeks that have passed between the submission of the Kantor et al. paper and the writing of this editorial, the Delta variants in RI have increased, and at the time of this writing amount to 42 and have become the majority of sequenced SARS-CoV-2 isolates in RI (https://ri-department-of-health-covid-19-variant-data-rihealth.hub.arcgis.com/).

Looking at this rapidly evolving dynamic, one question comes to mind: When will the virus reach peak fitness? Coronaviruses, as other RNA viruses, acquire mutations quickly during viral replication in the host cytoplasm. With vaccinations in some countries not expected to start in earnest for over a year from now, with immune-suppressed individuals who have marginal response to the vaccine and long periods of viral shedding, and with the potential for declining immunity that could necessitate boosters and next- generation vaccines, it is reasonable to assume that changes in the virus will continue to challenge us.

However, the emergence of variants should not compromise our determination, but reinvigorate our unwavering adherence to disease-control measures, masking, and vaccination.[4] Science will continue to provide us with tools to fight the virus. The RI-centric genomic surveillance program described by Kantor et al. monitors the prevalence of SARS-CoV-2 variants in our state and provides invaluable information in order to prepare our health systems, advise our patients, and optimize the deployment of resources. The health partnership between the Kantor Laboratory at the Providence-Boston Center for AIDS Research and The Miriam Hospital, the RI State Health Laboratory (RISHL), and their collaborators[1] provides essential and clinically relevant information for the more equitable distribution of vaccines and other resources, as well as for updating best practices in real time. As the pandemic will continue to seek and exploit our weaknesses, it is the realization that we need to come together that will guide us out of the pandemic quicker and with the least possible human loss and despair.

References

1. Kantor R, Novitsky V, Carpenter-Azevedo K, Howison M, Manne A, Darpolor JK, Bobenchik A, Tripathi A, Huard RC, King E. SARS-CoV-2 Variants in Rhode Island. R I Med J (2013). 2021 Sep 1;104(7):16-20.PMID: 34279520
2. Tracking SARS-CoV-2 variants. Available at https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/(accessed7/27/21)
3. Hoffmann M, Arora P, Groß R, Seidel A, Hörnich BF, Hahn AS, Krüger N, Graichen L, Hofmann-Winkler H, Kempf A, Winkler MS, Schulz S, Jäck HM, Jahrsdörfer B, Schrezenmeier H, Müller M, Kleger A, Münch J, Pöhlmann S. SARS-CoV-2 variants B.1.351 and P.1 escape from neutralizing antibodies. Cell. 2021 Apr 29;184(9):2384-2393.e12. doi: 10.1016/j.cell.2021.03.036. Epub 2021 Mar 20.PMID: 33794143
4. Abdool Karim SS, de Oliveira T. New SARS-CoV-2 Variants - Clinical, Public Health, and Vaccine Implications. N Engl J Med. 2021 May 13;384(19):1866-1868. doi: 10.1056/NEJMc2100362. Epub 2021 Mar 24. PMID: 33761203

Author

Eleftherios Mylonakis, MD, PhD, Charles C.J. Carpenter Professor of Infectious Disease; Chief, Infectious Diseases Division, The Miriam and Rhode Island Hospitals; Professor of Medicine and Professor of Molecular Microbiology, Warren Alpert Medical School of Brown University, Providence, RI.

Correspondence

Eleftherios Mylonakis, MD, PhD
Rhode Island Hospital
593 Eddy Street, POB, 3rd Floor
401-444-7856
Fax 401-444-8179
emylonakis@lifespan.org