Shivani Jain
L2
LSU Health Sciences Center, New Orleans, LA

Dr. Michael E. Hagensee, MD, PhD
LSUHSC, Professor of Medicine – Department of Medicine and Microbiology

"Utilizing Quantitative COVID-19 Serological Testing to Assess Pathophysiological Importance of Complement Activation in Disease Severity"

Background. COVID-19, the clinical syndrome caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), continues to cause high disease burden in the world. Not enough is known about immunological mechanisms driving COVID-19 disease severity in patients hospitalized in the ICU compared to those who test positive but do not develop severe disease. Extreme activation of the immune system has been linked to disease course complications in COVID-19. The complement system plays a key role in the innate immune response, and it has previously been suggested that it may be driving these disease complications. Immunoglobulin G (IgG) activates the classical complement pathway by binding of complement factor C1q to the Fc region of IgG. Of the 4 subclasses of IgG, IgG1 and IgG3 bind most strongly to C1q. Individuals with greater IgG1 and IgG3 seropositivity to SARS-CoV-2 surface spike protein receptor binding domain (RBD) may have increased activity in the classical complement pathway. Thus, it was hypothesized that complement activation partially drives the excessive immune response in those with severe disease sequelae after SARS-CoV-2 infection.

Methods. Serum samples from 75 IgG-seropositive individuals with a documented SARS-CoV-2 positive RNA test were compared to serum samples from 19 individuals hospitalized in the intensive care unit (ICU) due to severe COVID-19 complications. All subjects were tested for IgG1 and IgG3 seropositivity against the SARS-CoV-2 surface spike protein receptor binding domain (RBD) via enzyme-linked immunoassay (ELISA). The magnitude of seropositive responses was assessed with endpoint dilution titers against RBD. Subjects were also compared in terms of demographic variables collected at baseline. Data were analyzed using statistical methods of two-sample t-test, Fischer's exact test, and chi-squared test.

Results. ICU subjects had higher mean titer values of IgG1 antibodies compared to non-ICU subjects, but the difference was not statistically significant (p-value = 0.221). ICU subjects also had higher mean titer values of IgG3 antibodies compared to non-ICU subjects, and the difference was statistically significant (p-value = 0.046). The two study groups did not show statistically significant differences across demographic variables of sex, race, or age.

Conclusions. Small sample size for ICU subjects may be suppressing the true magnitude of difference in mean titer values that exists between study groups. Furthermore, while this study focuses on the classical complement pathway, research is being undertaken to explore how the lectin pathway and the alternative pathway of complement activation may each play a greater role in driving the extreme immune response that is strongly correlated with COVID-19 severity.