PRESS RELEASE

ASN Contact: Christine Feheley
(202) 640-4638 | cfeheley@asn-online.org

STUDY PROVIDES INSIGHTS INTO HOW THE IMMUNE SYSTEM OF KIDNEY TRANSPLANT RECIPIENTS RESPONDS TO COVID-19

COVID-19 impairs their adaptive immunity even when their immunosuppressive medications are reduced.

Highlights

- Kidney transplant recipients experience immune-insufficiency during acute COVID-19.
- The finding may provide an explanation for the low rates of acute rejection observed in transplant recipients with COVID-19, even when their antirejection immunosuppressive medications are reduced to promote protective anti-COVID-19 immunity.

Washington, DC (August 30, 2022) — Kidney transplant recipients (KTRs) have experienced severe symptoms and poor outcomes with COVID-19. Because the long-term antirejection immunosuppressive drugs that KTRs take could inhibit the development of protective anti-COVID-19 immunity, most hospitals have reduced the drugs' doses in KTRs with COVID-19. Surprisingly, reported rates of acute rejection have been low despite reduced immunosuppression in these patients. A new study in *JASN* provides a potential explanation.

To study KTRs' immune responses in the face of COVID-19, a team lead by Madhav C. Menon, MBBS, MD (Yale University School of Medicine and Icahn School of Medicine at Mount Sinai) analyzed the blood of 64 KTRs with COVID-19, including 31 acute cases (< 4 weeks from diagnosis) and 33 post-acute cases (>4 weeks). Patients were enrolled form Mount Sinai and Montefiore hospital (Albert Einstein College of Medicine)—two hospitals at the forefront of the pandemic in its early months.

In the blood of acute cases, certain genes were over-expressed and others were under-expressed with higher COVID-19 severity. Analyses revealed increased expression of genes involved in innate immune pathways, but decreased expression of genes involved in the activation of adaptive immune pathways.

Comparison with post-acute cases showed "normalization" of these pathways after >4 weeks, suggesting recovery of adaptive immune system activation.

The findings of immune-insufficiency during acute COVID-19 provide an explanation for the low rates of acute rejection in KTRs despite reduced immunosuppression.

“We found that KTRs with COVID-19 showed signatures of immune-insufficiency in their peripheral blood that was even worse with severe illness—for instance among patients in the intensive care unit. We also noted that there were signals of recovery in the post-acute cases pointing to a temporary phenomenon during acute illness,” said Dr. Menon. “As this pandemic continues to affect KTRs, our collaborative findings will provide insights to the transplant community to manage anti-rejection medicines during acute COVID-19.”

Additional co-authors include Zeguo Sun, Zhongyang Zhang, Khadija Banu, Yorg Al Azzi, Anand Reghuvaran, Samuel Fredericks, Marina Planoutene, Susan Hartzell, Yesl Kim, John Pell, Gregory Tietjen, William Asch, Sanjay Kulkarni, Richard Formica, Meenakshi Rana, Jonathan S. Maltzman, Weijia Zhang, Enver Akalin, Peter S. Heeger, and Paolo Cravedi.

Disclosures: JSM has received honoraria from One Lambda, Inc/Thermo Fisher, is a member of the Qihan Biotech scientific advisory board, and has a family member who is employed by and has an equity interest in Genentech/Roche.

The article, titled “Blood transcriptomes of SARS-CoV-2 infected kidney transplant recipients associated with immune insufficiency proportionate to severity,” will appear online at http://jasn.asnjournals.org/ on August 30, 2022; doi: 10.1681/ASN.2022010125.

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