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Raju Vaishya, MS, MCh
Arpita Malani, MBBS, MBA
Leena Mendiratta, MBBS, MD
Hena Butta, MBBS, MD
 Indraprastha Apollo Hospitals
 New Delhi, India

Anupam Sibal, MD
 Apollo Hospital Group
 Indraprastha Apollo Hospitals
 New Delhi, India

Sujeet Kumar Singh, MBBS, DCH, MD
 National Centre for Disease Control
 New Delhi, India

Hari Prasad K, MBBS, MD
 Apollo Hospitals Enterprises Ltd
 Hyderabad, India

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ORCID

Raju Vaishya:  <https://orcid.org/0000-0002-9577-9533>

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HLA Antibody Rates Are
 Not Increased in a
 Regional Group of Male
 COVID-19 Convalescent
 Plasma Donors



To The Editor: Coronavirus disease 2019 (COVID-19) convalescent

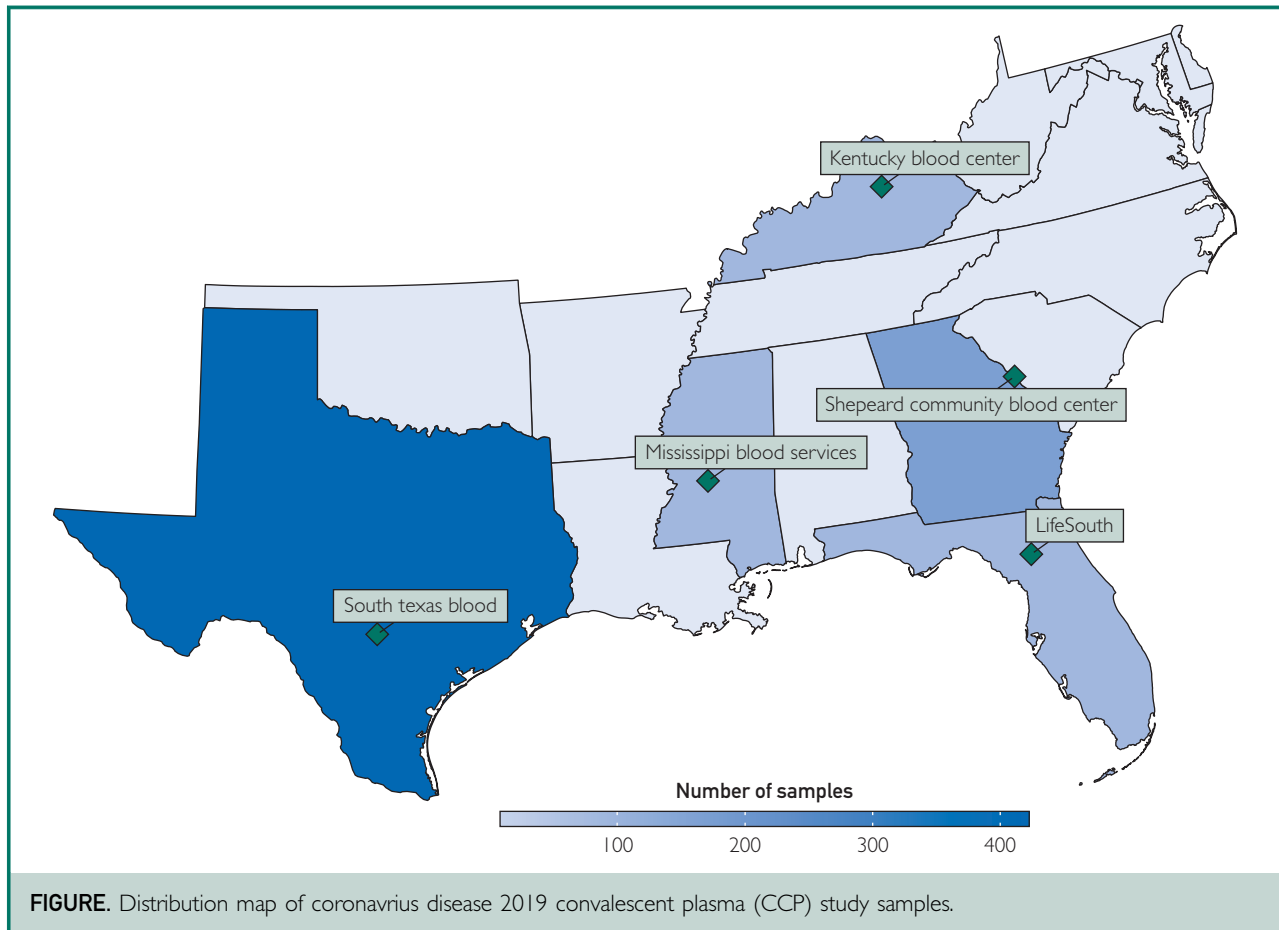
plasma (CCP) remains a widely used therapeutic option for patients hospitalized for COVID-19 as further variant strains continue to arise. We recently reported significantly elevated positivity rates ($P < .0001$) for HLA antibodies (HLA-Abs), a risk factor for transfusion-associated acute lung injury, in 5 of 69 local male CCP donors (7.2 %).^{1,2} As noted in a subsequent reply letter though, CCP has repeatedly exhibited a safety profile similar to standard plasma.^{3,4} Because HLA-Ab screening is not routinely performed on male donors, it remains unclear whether male CCP donors truly have an elevated HLA-Ab screening positivity rate and pose a potential increased transfusion-associated acute lung injury risk to CCP recipients. In collaboration with several blood donation organizations, we assessed the prevalence of positive HLA-Ab screening results in male CCP donors across the southeastern United States.

Male CCP donors who donated from April 27 through August 24, 2020, at Kentucky Blood Center, Life-South Community Blood Centers, Mississippi Blood Services, Sheppard Community Blood Center, and South Texas Blood & Tissue Center with sufficient residual serum and de-identified demographic data available were eligible for this cross-sectional study. All CCP donors provided permission to use de-identified donor information and serum samples for research. Given the de-identified nature of this study, clinical information on COVID-19 infection and past pregnancy, transfusion, or transplantation history was not available. Each male CCP serum sample was identified using the associated CCP unit's ISBT 128 donation identification number. This study was approved by the local institutional review board.

All CCP serum samples were screened for HLA-Abs using the same LABScreen Mixed Class I and Class II assays (One Lambda) and performed by the same American Society for Histocompatibility & Immunogenetics-accredited tissue typing laboratory that offers blood donor HLA-Ab screening.¹ Positive screening cutoff ratios for these HLA-Ab screening assays (class I ratio, >30 ; class II ratio, >18) had been previously established by the laboratory using a +5SD mark in a population of male never-transfused blood donors following a published methodology.⁵

Five hundred twenty-six male CCP donors with sufficient residual serum and de-identified demographic information available were screened for HLA-Abs (Figure). The median donor age at the time of CCP collection was 48.8 years (range, 16.0-85.5 years). Only 2 of 526 male CCP donors screened positive for HLA-Abs (0.3%) within the expected less than 1% screening positivity rate. These 2 male CCP donors screened positive only for class I HLA-Abs (class I ratios, 33.74 and 60.91), were collected at different blood donation organizations, and were older at CCP donation (age, 68.8 and 73.3 years) than most male CCP donors. The positivity rate in this male CCP donor population significantly differed from the previously reported 7.2% HLA-Ab screening positivity rate (Fisher exact, $P = .001$).

This larger cross-sectional study does not support an association between increased HLA-Ab screening positivity rates and recent COVID-19 infection in male CCP donors. These discrepant findings between these 2 male CCP groups may be due to time differences since donor COVID-19 infection or regional differences in infecting COVID-19 strains or may indicate a false-positive study result in our initial report.



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Justin E. Juskewitch, MD, PhD
Jonathon W. Senefeld, PhD
Patrick W. Johnson, BS
John R. Mills, PhD

Michael J. Joyner, MD
Manish J. Gandhi, MD
Mayo Clinic
Rochester, MN

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ORCID

Justin E. Juskewitch: <https://orcid.org/0000-0002-7868-28522>; Jonathon W. Senefeld: <https://orcid.org/0000-0001-8116-35383>; Patrick

W. Johnson: <https://orcid.org/0000-0001-8365-13754>; John R. Mills: <https://orcid.org/0000-0003-1025-47605>; Michael J. Joyner: <https://orcid.org/0000-0002-7135-76436>; Manish J. Gandhi: <https://orcid.org/0000-0001-7210-1909>

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