Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Brief communication

COVID-19 vaccine does not alter panel reactive antibody or flow cytometric cross match in kidney transplant candidates

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To the editor

Vaccines are generally considered sensitizing events in the kidney transplant population [1]. COVID-19 Vaccine response rates as assessed by serology in the end-stage kidney disease (ESKD) population are reported to be statistically lower (96%) as compared to healthy normal controls (100%) [2]. However, this response rate is far superior to the post-transplant vaccine response of 54% after the second dose of SARS-CoV-2 mRNA vaccine [3].

Virtual cross matching, instead of a physical cross match, is frequently utilized as a strategy to reduce post-kidney transplant cold ischemia time [4]. However, it is unknown if SARS-CoV-2 mRNA vaccination prior to transplant leads to antibody mediated immune response against human leukocyte antigens (HLA) antigens, in turn affecting the panel reactive antibody (PRA) of the recipient and the flow cross match (FCXM) reactivity at kidney transplant.

Between January 2021 and July 2021, we assessed changes in PRA and FCXM in 17 adult transplant candidates at the top of our center waiting list. Their serum was evaluated for PRA changes utilizing both the Immucor Luminex intermediate level and single antigen assays. A total of 14/17 (82%) candidates had completed both vaccine doses prior to last PRA check while the remaining 3/17 (18%) received a kidney transplant after their first dose of the vaccine. Overall, at a median follow-up of 86 (Range: 20–188) days post vaccination, the Class I PRA remained unchanged pre- and post-vaccine at a median value of 0% (Range: 0–24%) ($p = 0.5$). Similarly, the Class II PRA remained unchanged from a pre-vaccine median value of 0% (Range: 0–97%) to the post-vaccine median of 0% (Range: 0–97%) ($p = 1.0$). Prior to vaccination, one patient had a Class I PRA of >20% with an immunodominant HLA specific antibody (iDSA) of 23,000 Mean Fluorescent Intensity (MFI), which remained unchanged 98 days after the second vaccine. Six (of 17, 29%) patients had a Class II PRA of >20% with a median iDSA of 1000 MFI (Range: 700–14,000). At a median follow-up of 98 days after the second vaccine these remained unchanged with a median iDSA of 1000 MFI (Range: 500–15,000).

A total of 14/17 (82%) candidates underwent successful kidney transplantation. 11 (of 14; 79%) had received both mRNA vaccines by the time of their transplant. Twelve (of 14, 86%) recipients had a negative virtual (and later physical) FCXM at the time of transplant, with testing performed on serum drawn on the day of transplant prior to initiation of immunosuppression. Only one of these recipients with negative physical FCXM had marginal class II DSA < 1000 MFI. Two recipients had a positive B-Cell FCXM of 103 and 122 median channel shifts with no identifiable pre-formed HLA-DSA, however one of these recipients had a history of rituximab exposure prior to kidney transplant that may explain the positive crossmatch [5]. At a median follow-up of 58 days (range: 14–93) post-transplant, none developed acute rejection, two highly sensitized recipient developed low grade (<5000 MFI) de-novo DSA. Three (of 14, 21%) recipients had pre-formed DSA prior to transplant and these remained unchanged during the follow-up period post-transplant.

Based on this limited series, we report that the SARS-CoV-2 mRNA vaccine may not be a significant source of allosensitization. The limitations of our study lie in the fact that this a small cohort of mostly non-sensitized kidney transplant candidates. More data especially on sensitized candidates is needed to further ascertain the immunogenicity of the SARS-CoV-2 mRNA vaccine. Herein, we report that even with an imminent transplant, centers should continue to encourage vaccination among kidney transplant candidates to take advantage of the favorable vaccine response rates prior to immunosuppression initiation.

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Abbreviations: Coronavirus Disease 2019, (COVID-19); End-Stage Kidney Disease, (ESKD); Severe acute respiratory syndrome coronavirus-2, (SARSCoV-2); Cold Ischemia Time, (CIT); Human Leukocyte Antigens, (HLA); Panel Reactive Antibody, (PRA); Flow Cross Match, (FCXM); Immunodominant Donor Specific Antibody, (iDSA); Mean Fluorescent Intensity, (MFI).

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All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication.

Specific contributions

Dhiren Kumar: research design, writing of paper, performance of research, data analysis.

Pamela Kimball: writing of paper, performance of research, data analysis data analysis.

Gaurav Gupta: research design, writing of paper, performance of research, data analysis.

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Ethics statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study meets criteria for exemption from approval from an ethics board.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

References

[1] S. Brakemeier, B. Schweiger, N. Lachmann, et al., Immune response to an adjuvanted influenza A H1N1 vaccine (Pandemrix(®)) in renal transplant recipients, Nephrol. Dial. Transplant. 27 (1) (Jan 2012) 423–428, https://doi.org/10.1093/ndt/gfr278.

[2] A. Grupper, N. Sharon, T. Finn, et al., Humoral response to the Pfizer BNT162b2 vaccine in patients undergoing maintenance hemodialysis, Clin. J. Am. Soc. Nephrol. (Apr 2021), https://doi.org/10.2215/CJN.03500321.

[3] B.J. Boyarsky, W.A. Werbel, R.K. Avery, et al., Antibody response to 2-Dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients, JAMA (May 2021), https://doi.org/10.1001/jama.2021.7489.

[4] V.S. Rohan, N. Pilch, O. Moussa, et al., Virtual crossmatching in kidney transplantation: the wait is over, J. Am. Coll. Surg. 230 (4) (2020) 373–379, https://doi.org/10.1016/j.jamcollsurg.2019.12.031.

[5] P. Gatault, G. Philippe, I. Jollet, et al., Very low residual concentrations of rituximab long after infusion still induce positive B-cell complement-dependent cytotoxicity-crossmatch, Hum. Immunol. 74 (12) (Dec 2013) 1616–1618, https://doi.org/10.1016/j.humimm.2013.08.278.