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Development of donor specific antibodies after SARS-CoV-2 vaccination: What do we know so far?

Ahmed Daoud, Karim Soliman, Maria Aurora Posadas Salas, Sakshi Vaishnav, Genta Uehara, Ahmed Abdelkader, Tibor Fulop, Michael J Casey

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Abstract

Vaccination against Coronavirus disease-19 (COVID-19) was pivotal to limit spread, morbidity and mortality. Our aim is to find out whether vaccines against COVID-19 lead to an immunological response stimulating the production of de novo donor specific antibodies (DSAs) or increase in mean fluorescence intensity (MFI) of pre-existing DSAs in kidney transplant recipients (KTRs). This study involved a detailed literature search through December 2nd, 2023 using PubMed as the primary database. The search strategy incorporated a combination of relevant Medical Subject Headings terms and keywords: "COVID-19", "SARS-CoV-2 Vaccination", "Kidney, Renal Transplant", and "Donor specific antibodies". The results from related studies were collated and analyzed. A total of 6 studies were identified, encompassing 460 KTRs vaccinated against COVID-19. Immunological responses were detected in 8 KTRs of which 5 had increased MFIs, 1 had de novo DSA, and 2 were categorized as either having de novo DSA or increased MFI. There were 48 KTRs with pre-existing DSAs prior to vaccination, but one study (Massa *et al*) did not report whether pre-existing DSAs were associated with post vaccination outcomes. Of the remaining 5 studies, 35 KTRs with pre-existing DSAs were identified of which 7 KTRs (20%) developed de novo DSAs or increased MFIs. Overall, no immunological response was detected in 452 (98.3%) KTRs. Our study affirms prior reports that COVID-19 vaccination is safe for KTRs, especially if there are no pre-existing DSAs. However, if KTRs have pre-existing

DSAs, then an increased immunological risk may be present. These findings need to be taken cautiously as they are based on a limited number of patients so further studies are still needed for confirmation.

Key Words: COVID-19; SARS-CoV-2 vaccination; Kidney; Renal transplant; Donor specific antibodies

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Core Tip: Our aim was to find out whether vaccines against Coronavirus disease 2019 (COVID-19) lead to an immunological response stimulating the production of de novo donor specific antibodies (DSAs) or increase in mean fluorescence intensity of pre-existing DSAs in kidney transplant recipients. We did a detailed literature search through December 2, 2023 using PubMed as the primary database. We used the following keywords: COVID-19, severe acute respiratory syndrome-coronavirus-2 vaccination, Kidney, Renal transplant, and DSAs. The results from related studies were collated and analyzed.

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INTRODUCTION

Vaccination against Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) was pivotal to limit spread, morbidity and mortality of Coronavirus disease-19 (COVID-19), ensuring a high rate of protective antibody formation in the general population[1,2]. Solid organ transplant recipients (SOTRs) are maintained on lifelong immunosuppression to reduce the risk of cellular and antibody mediated rejections. Unfortunately, immunosuppression therapy may also lead to increased COVID-19 mortality among SOTRs[3,4]. Since the introduction of the vaccination programs against SARS-CoV-2, vaccinating immunocompromised patients, including SOTRs has been considered as a priority[5].

The presence of anti-human leukocytic antigen (anti-HLA) donor specific antibodies (DSAs) is associated with antibody mediated rejection[6,7]. Do vaccines against SARS-CoV-2 accentuate an immunological response stimulating the production of anti-HLA DSA in kidney transplant recipients (KTRs)?

To answer this question, we conducted a detailed literature review, using PubMed as the primary database, with the search being completed by December 2nd, 2023. The search strategy incorporated a combination of relevant Medical Subject Headings terms and keywords: "COVID-19", "SARS-CoV-2 Vaccine", "Kidney, Renal Transplant" and "Donor Specific Antibodies". The results from related studies were collated and analyzed.

We screened 15 manuscripts, and excluded the following

Six unrelated articles that were mainly discussing safety, efficacy and response to COVID vaccines in KTRs.

One article described DSA formation, but was confounded by KTRs being hospitalized with an active COVID-19 infection[8].

This left us with 2 case reports and 7 studies. Abu-Khader *et al*[9] reported a case of 42-year-old who developed de novo DSAs and de novo anti-HLA non-DSAs after first dose of mRNA based COVID vaccine. Kim *et al*[10] reported a successful ABO-incompatible living donor kidney transplant in a patient who developed class I DSAs after COVID-19 vaccination.

There were 6 studies evaluating the development of DSAs after COVID vaccination, encompassing 460 KTRs vaccinated against COVID-19. Immunological responses were detected in 8 KTRs of which 5 had increased mean fluorescence intensity (MFI), 1 had de novo DSA, and 2 were categorized as either having de novo DSA or increased MFI [11-15]. There were 48 KTRs with pre-existing DSAs prior to vaccination, but one study (Massa *et al*[16]) did not report whether pre-existing DSAs were associated with post vaccination outcomes. Of the remaining 5 studies, 35 KTRs with pre-existing DSAs were identified of which 7 KTRs (20%) developed de novo DSAs or increased MFIs (Table 1). Overall, no immunological response was detected in 452 (98.3%) KTRs.

The findings of these studies are summarized in Table 1.

CONCLUSION

In conclusion, our study affirms prior reports that COVID-19 vaccination is safe for KTRs, especially if there are no pre-existing DSAs. However, if KTRs have pre-existing DSAs, then an increased immunological risk may be present. These findings need to be taken cautiously as they are based on a limited number of patients so further studies are still needed for confirmation.

Table 1 Immunological outcomes after coronavirus disease 2019 vaccination

Ref.	Number of patients vaccinated	Number of patients with pre-existing DSAs before vaccination	Type of vaccine	Number of patients who developed de novo DSAs	Number of patients with pre-existing DSAs who developed new DSAs or increased MFI post-vaccine
McCune <i>et al</i> [11]	100	5	Moderna 64 Pfizer 36	0	2 (Unreported whether new DSA or increased MFI)
Kueht <i>et al</i> [12]	96	16	Moderna Pfizer J and J	0	5 (All had increased MFIs)
Al Jurdi <i>et al</i> [13]	58	5	Moderna Pfizer	0	0
Russo <i>et al</i> [14]	82	1	Pfizer	0	0
Nishida <i>et al</i> [15]	63	8	mRNA vaccine (Moderna and/or Pfizer)	0	0
Massa <i>et al</i> [16]	61	13	Pfizer	1	Not reported
Total	460	48		1	7

DSAs: Donor specific antibodies; MFI: Mean fluorescence intensity.

FOOTNOTES

Author contributions: Daoud A designed and performed the research; Soliman K, Posadas Salas MA, Vaishnav S, Uehara G, Abdelkader A, Fulop T, and Casey MJ wrote the manuscript. All authors have read and approved the final manuscript.

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