MARCH 2021

CONSENSUS STATEMENT

COVID-19 VACCINATION

FOR CHRONIC KIDNEY DISEASE PATIENTS

CHAPTER OF RENAL PHYSICIANS
COLLEGE OF PHYSICIANS, SINGAPORE

ACADEMY OF MEDICINE
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BACKGROUND

Persons suffering from Chronic Kidney Disease (CKD) have a higher rate of complications and death from COVID-19 infection. The Ministry of Health, Singapore (MOH) Expert Committee on COVID-19 Vaccination has published recommendations for its use as well as contraindications and precautions for certain groups. The Chapter of Renal Physicians COVID-19 Workgroup has the following guidance to provide better clarity for different sub-groups within the CKD population.

GUIDING ETHICAL PRINCIPLES

A. Patients with CKD stage 1-5 (non-dialysis)

- Although there are no COVID-19 vaccination studies specifically directed at CKD patients, it is the understanding of the wider medical community that the vaccine is effective for most, including patients with CKD. There is also consensus across the medical community that it can be safely administered to all patients (including those with CKD) with the exceptions of those conditions listed by the MOH Expert Committee on COVID-19 Vaccination.
- We strongly advise that all CKD stage 1-5 patients be vaccinated against COVID-19; unless contraindicated.

B. Patients with CKD stage 5-Dialysis

- Similar to CKD stage 1-5, patients on dialysis should also receive COVID-19 vaccination unless contraindicated. Priority and urgency should be given to those who receive maintenance hemodialysis treatment in a shared facility as these patients cannot totally isolate themselves from other patients.
- Depending on the type of vaccine made available locally, some dialysis centers can facilitate the adoption of this vaccination exercise by availing it at the dialysis center itself. The protocol for storage, dilution, administration and period of mandatory observation must be followed in accordance to the FACT SHEET (Full Prescribing Information) for Healthcare Providers issued by the manufacturer.

C. Patients with Glomerulonephritis receiving Immunosuppression (Refer to Appendix A for discussion)

- It is generally safe to have the COVID-19 vaccine alongside immunosuppression, but the patient may not mount such a good immune response and thus should continue to follow all current MOH guidance to avoid exposure to protect against COVID-19 infection.
- In cases where the immunosuppression can be safely delayed as part of a shared decision-making between patient and the managing nephrologist, immunosuppression should be given after completion of the vaccination.
- In patients who are already on immunosuppression or where further immunosuppression is necessary, vaccination should not be delayed.

- Special considerations for patients about to receive rituximab, as part of shared decision making between patient and the managing nephrologist, include considerations for whether it would be preferable to complete the full course of COVID-19 vaccine dosing (if rituximab can be safely delayed), or to seek alternative immunosuppression if available.

D. Kidney Transplant Recipients, Candidates and Donors (Refer to Appendix B for discussion)

- Kidney transplant recipients and candidates are at a higher risk of complications from COVID-19 infection.
- However, there is no data currently available on the safety, efficacy and immunogenicity of the COVID-19 vaccine in kidney transplant recipients. Response to vaccination in organ transplant recipients is variable and generally lower than in the general population. In addition, the risk of de novo HLA antibody generation and consequent possibility of antibody-mediated rejection or immune-mediated disease in the allograft should be counselled in patients at higher risk for these complications.
- The decision to proceed with COVID-19 vaccination in kidney transplant recipients should depend on the individual's risk of exposure to COVID-19, degree of immunosuppression, presence of additional high-risk comorbidities, and the underlying immunological risk. The balance of risk and benefit should be discussed with the patient's managing nephrologist in order for the patient to make an informed decision.

Post-transplant

- We advise vaccination in kidney transplant patients who are stable on maintenance immunosuppression, at least 3 months post-transplantation.
- We advise delaying vaccination after treatment of acute rejection, as for example at least 3 months after IV methylprednisolone and 6 months after lymphocyte depleting agents e.g. Thymoglobulin, Rituximab or Alemtuzumab.
- We advise caution in kidney transplant recipients with a history of antibody-mediated rejection or in the presence of donor-specific antibodies; the decision for vaccination to be discussed with the managing nephrologist.
- We strongly advise vaccination in kidney transplant recipients working in front-line occupations e.g., healthcare workers, border control and ports of entry personnel etc.

Pre-transplant

- We strongly advise vaccination prior to transplantation for kidney transplant candidates, with the vaccination course ideally to be completed at least 2 weeks before transplantation.

Donors and household contacts

- We strongly advise vaccination of donors and household contacts of kidney transplant recipients, unless otherwise contraindicated.

APPENDICES

Appendix A

Rationale for section C: ***Patients with Glomerulonephritis receiving Immunosuppression***

General

Patients on immunosuppression may be at increased risk of developing severe COVID-19 infection, and, hence, all patients with no contraindications are encouraged to be vaccinated against SARS-CoV-2.

It is generally safe to have the COVID-19 vaccine alongside immunosuppression, but the patient may not mount such a good immune response, as immunosuppression may blunt the immune response against the vaccine. It is therefore important that patients should continue to follow all current MOH guidance to avoid exposure to protect against COVID-19 infection. Routine antibody testing is not currently recommended to assess for immunity to COVID-19 following COVID-19 vaccination.

There is no evidence to suggest that taking the vaccine will result in an inflammatory response (flare) for a person with glomerulonephritis or other autoimmune disease and hence, there is no contraindication for patients with active glomerulonephritis to receive the vaccine; this should be a shared decision to be made between the patient and the managing nephrologist, individualized to the patient's condition.

It may be appropriate to delay elective administration of systemic corticosteroids and/or rituximab, as part of maintenance therapy to facilitate vaccination. However, this should be a shared decision making between the patient and managing nephrologist, individualized to the patient's condition.

Patients about to receive immunosuppression

In cases where immunosuppression can be safely delayed, as part of a shared decision-making conversation between patient and clinician, it should be given after completion of the vaccination. Considerations for vaccination prior to commencing immunosuppression therapy (ideally at least two weeks after the second dose of vaccination) should be given, when their immune system is better able to mount a response. Where possible, it would also be preferable for the 2-dose schedule to be completed prior to commencing immunosuppression. This would entail offering the second dose at the recommended minimum for that vaccine (three or four weeks from the first dose) to provide maximum benefit that may not be received if the second dose was given during the period of immunosuppression.

Patients already on immunosuppression

In patients who are already on immunosuppression or where further immunosuppression should not be delayed, vaccination should not be delayed unless there are specific contraindications.

Patients receiving immunosuppression that may cause marrow suppression with low red/white blood cell count and thrombocytopenia should preferably be vaccinated when blood cell counts have recovered with platelet count of >50×109/L.

Patients on induction doses of corticosteroid therapy can be vaccinated although the immune response may not be robust. It would be preferable to avoid delaying vaccination if corticosteroids have been given or about to be given unless treatment for underlying disease can be safely delayed. Corticosteroid as rescue therapy for immune mediated disease flares may be given during the course of vaccination to avoid potential morbidity due to disease flare.

It may be appropriate to delay elective administration of systemic corticosteroids and/or rituximab, as part of maintenance therapy; this should be a shared decision making between the patient and managing nephrologist, individualized to the patient's condition.

Rituximab

Special consideration is given for patients about to receive or is receiving rituximab, as rituximab has a direct effect on the humoral response post-vaccination and that the effect of rituximab often lasts 24 weeks or more.

There may be a sub-optimal response to COVID-19 vaccines, especially for people within six months of the last dose of rituximab, or those who must have maintenance treatment due to their underlying clinical condition. Where clinically appropriate, and as part of a shared decision making between patient and managing nephrologist, suitable alternatives should be considered, balancing the risks and benefits of not using rituximab.

Appendix B

Rationale for section D: ***Kidney transplant recipients, Candidates and Donors***

General

COVID-19 is a very serious infection in kidney transplant recipients with various transplant programs around the world reporting high rates of mortality (10-50%), hospitalization (70-100%), acute kidney injury (30-76%) and admission to intensive care unit (10-61%). Therefore, the risks of complications are high in kidney transplant recipients. Furthermore, COVID-19 in kidney transplant recipients is aggravated by the presence of other comorbidities such as hypertension, diabetes mellitus, cardiovascular disease, chronic lung disease and obesity. Mortality has also been reported to be high at 32% in kidney transplant patients on the waiting list for a deceased donor kidney transplant.

Immune response

As a result, kidney transplant recipients and kidney transplant candidates on the waiting list should be considered a vulnerable patient population at high risk of COVID-19 complications. COVID-19 vaccination may mitigate the risks.

The immune response to vaccination in kidney transplant recipients is known to be poorer than that of the general population. Therefore, the COVID-19 vaccine response may be expected to be poorer in kidney transplant recipients and patients should therefore be advised that they must still adhere to mask wearing and social distancing precautions. It is therefore also ideal that vaccination should be completed prior to proceeding with transplantation and subsequent immunosuppression, as far as practicable.

De novo anti-HLA antibody generation has been reported in the vaccine literature on kidney transplant recipients. However, the frequency of de novo anti-HLA antibody generation following vaccination is low, amount of antibody measured by mean fluorescent intensity is not high, and the presence of these de novo anti-HLA antibodies does not seem to be associated with an excessive increased risk of antibody mediated rejection in most studies (as they are often not donor-specific). Hence, COVID-19 vaccination can be given to patients who have undergone high immunological risk kidney transplants provided they have been counselled on the risk of de novo anti-HLA antibody generation and are closely monitored for graft dysfunction. This may be particularly important for those in frontline occupations where COVID-19 exposure risk is very high.

Donors and household contacts

Donors, caregivers and household contacts should also be counselled to be vaccinated when the vaccines are made available to them and if they meet eligibility criteria for COVID-19 vaccination. This is to avoid household transmission of COVID-19 which is well documented in both the general and transplant population.

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