

Vaccination in CKD and Kidney Transplant Recipients

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Infectious diseases are the second commonest cause of death in patients suffering from advanced chronic kidney disease (CKD)¹. Patients with CKD are vulnerable to vaccine-preventable infections (Hepatitis B & C, Herpes, H1N1, and community/hospital-acquired pneumonia's) because of impaired immunity, immunosuppressive treatment and dialysis^{2,3}. The recent COVID-19 infection has added to the woes of an already susceptible CKD and transplant population with higher morbidity and mortality in this group compared to the infection in the general population. It is without any argument that the pace at which vaccine/s has been developed to protect us from the ravaging pandemic of COVID-19 has been exemplary and will go a long way to decrease the morbidity and mortality, overall and specifically in the CKD and kidney transplant patients⁴.

Though vaccination leads to reduced infection rates with a reduction in morbidity and mortality, there is a reduction in vaccine effectiveness across the stages of CKD due to multiple abnormalities in innate and adaptive immunity, leading to inadequate immune response¹. In addition, there are safety concerns for transplant recipients, especially with live attenuated vaccines. Therefore, it is recommended that vaccinations should be given in the early stages of CKD and preferably before kidney transplants⁵.

COVID Vaccine in Dialysis patients

Dialysis patients are at an increased risk of adverse outcomes secondary to COVID-19 because of age, comorbidities such as diabetes, hypertension, and the need for multiple hospital contacts for dialysis. The mortality rate

reported in dialysis patients is 32.76%.

Given their high risk of infection and severe disease, patients receiving dialysis have been prioritized for SARS-CoV-2 vaccination. The dosage schedule recommended is the same as for the general population (2 doses 4/6/8 weeks apart, depending on the type of vaccine administered (Table 1). Systemic adverse events, including musculoskeletal pain, fever, diarrhea, fatigue, and reactions at the injection site, occur more frequently in patients on hemodialysis who receive an mRNA vaccine than those who receive a vector-based vaccine⁶.

There is clear evidence that vaccinated dialysis patients have less frequent and less severe subsequent SARS-CoV-2 infection. Individuals who had received even one dose of the vaccine had a 33% reduced risk of being infected with the virus 46% lower mortality risk. Two doses work much better than one, both in the frequency and the intensity of the serologic response. Therefore, FDA has cleared for a booster dose of COVID-19 vaccine in dialysis patients^{7,8}.

COVID-19 Vaccine in Kidney Transplant Recipients (KTRs)

Mortality rates in COVID-19-positive KTR appear to be higher than those in non-immunosuppressed patients, and increased mortality is noted among those requiring intensive care and those on ventilator support⁸. All transplant recipients are eligible for vaccination unless contraindicated (e.g., hypersensitivity to the vaccine or its

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components)(Table1).

Although the immunogenicity and efficacy of COVID-19 vaccines are uncertain in KTRs, the potential for benefit from vaccination likely outweighs this uncertainty⁹. The administration of a third dose of the mRNA vaccine to transplant recipients has improved the immune response without causing any short-term, serious adverse events. Therefore, it is approved by the FDA⁹. A modification in immunosuppressive agents at the time of vaccination to enhance the immunogenic response of vaccines is still a debatable issue, and recommendations in this regard may come soon.

Practical considerations regarding COVID-19 vaccination in KTRs include the following⁹.

- When possible, administer the vaccine in the pre-transplant setting.
- In post-transplant patients, wait at least 1-3 months after the transplant to provide vaccine (3 months in cases after T cell depleting agents (ATG) or specific B cell-depletion agents (rituximab).have been given.
- If transplant occurs between the first and second doses, provide the second dose at >1 month after transplant in case of no induction therapy with T cell depleting agents and three months later if the patient has received induction with a T cell or specific B cell depleting agent.
- If a patient has had COVID before, wait until symptom recovery before giving COVID vaccine.

Hepatitis B

Hepatitis B virus (HBV) is transmitted through percutaneous or mucosal exposure to infectious blood or body fluids. Persons with chronic HBV infections are at increased risk of cirrhosis and liver cancer. Patients on hemodialysis are especially at risk of contracting HBV infections because of blood transfusion and contamination of dialysis equipment. HBV infection become chronic in 30-60% dialysis patients compared to 10% non-uremic patients¹⁰.

HBV vaccination is advised in the early stages of progressive CKD. In the late stage of CKD-V, there is a lower seroconversion rate, leading to a less intense and less durable HBV-antibody response¹¹.

Current recommendations for adults on dialysis are to use 40 mg of recombinant hepatitis vaccine at 0, 1, 2 and 6

months (Table 1). The HBV-antibody titer should be measured at 1-2 months after the final dose; if the titer is <10 m IU/ml, the entire dosing series should be repeated, and antibody response tested after 1 to 4 months. A booster dose should be administered annually if the anti-HB level falls to <10 m IU/ml. In non-responders, strategies for increasing the response include intradermal administration, administration of levamisole or granulocyte-macrophage colony-stimulating factor^{10,11}.

Influenza vaccine

Influenza vaccination in CKD and transplant patients generates an adequate response and significantly reduces infection-related hospitalization and mortality. Therefore, routine yearly vaccination is recommended to all persons above six months by the Centre for Disease Control and Prevention (CDC).

Vaccination should be given at the onset of the influenza season but can be given throughout. Single 0.5 ml of inactivated vaccine is recommended for patients with CKD and transplant recipients (Table 1). The quadrivalent vaccine can be given along with the pneumococcal vaccine, or a high dose trivalent vaccine can be given for patients > 65 years^{12,13}.

Pneumococcal Vaccine

Streptococcus pneumonia is the most common cause of community-acquired pneumonia in patients with CKD and renal transplant recipients. In addition, children with nephrotic syndrome and the elderly on dialysis are also at increased risk of pneumococcal infection.

Pneumococcal vaccine is recommended for all adults 19 to 64 years with CKD. Therefore, 13-valent pneumococcal conjugate vaccine (PCV13) should be administered to all adults with CKD aged ≥ 19 years, followed by a dose of 23-valent polysaccharide vaccine (PPSV23) eight weeks later. The second dose of PPSV23 is recommended five years after the first dose (Table 2)^{14,15}.

Tetanus, Diphtheria and Pertussis

Infants, children and adolescents are usually vaccinated for these diseases. Booster doses are recommended in adults to maintain seroprotection. In persons aged 11 to 64 years, a single dose of active booster vaccination against tetanus, diphtheria and pertussis is recommended, followed by a dose of tetanus and diphtheria toxoid booster every ten

TABLE 1: Various Types of COVID -19 Vaccines and Dosage

Type	Name	Primary Series(Dose)	Booster
Whole virus (inactivated)	Covaxin (BBV152) Sinopharm BIBP (BBIBP-CorV) Sinopharm WIBP	0.5ml 2 doses 28 days apart 0.5ml 2 doses 28 days apart	Not as yet Approved for all 6 months after last dose
Protein Subunit			
Nucleic acid(RNA)	- Moderna (mRNA-1273) - Pfizer-Biontech (BNT162b2)	2 doses 0.5ml IM 4 weeks apart 2 doses 3 weeks apart (Moderately to severely immunocompromised aged 12 yrs and above should get an additional primary shot at least 28 days after 2 nd shot)	Approved for all 6 months after last dose Approved for all 6 months after last dose
Nucleic acid(DNA)	Zydus Cadila	Intra-dermal	Not as yet
Vector based (non replicating viral vector)	- Covishield (AZD1222) - Johnson & Johnson's Janssen (JNJ-78436735) - Sputnik (Gam-COVID-Vac) - Sputnik Light	0.5ml 2 doses 4 to 12 weeks apart 1 dose only(IM) 2 dose schedule 3 weeks apart Single dose	2 months after the initial dose Not as yet Not as yet

TABLE 2: Vaccination in CKD and Kidney Transplant Recipients

Vaccine	Type	Dosage	Booster
Hepatitis B	Recombinant	- 20 ug (4 doses) at 0,1,2,6 months in CKD stages 4 - 40 ug 4 doses at 0,1,2,6 months for CKD stage 5 and ESRD	Once anti HBS titer <10mU/ml
Influenza	Inactivated quadrivalent	0.5ml single dose before onset of the flu season	none
Pneumococcal	Polysaccharide PPSV23 PCV13	Adults 19-64years PCV13 followed by PPSV23 8 weeks later	1 time PPSV23 five years after 1st
DPT	Live attenuated	Most have received during childhood If not then 3 doses(0,1,6 months)	Every 10 years
MMR	Live attenuated	Administer if no evidence of immunity 2 doses 28 days apart	
VAR(varicella)	Live attenuated	Administer if no evidence of immunity 2 doses 4- 8 weeks apart if not previously received If previously received 1 dose only	Every year
Zoster	-Recombinant -Live	For adults >50 yrs -2 doses 2-6 months apart regardless of the past episodes of herpes -2 doses 2-6 months apart For adults >60 years administer either	none

years (Table 2)¹⁶.

Hepatitis-A

Vaccinations against Hepatitis A Virus (HAV) induce 99% seroconversion, and injection with HAV provides lifelong immunity. However, the safety and efficacy of the HAV vaccine have not been studied in patients with CKD¹⁷.

Live-attenuated Vaccines (LAVs)

MMR and varicella immunizations are recommended in children with CKD. These LAVs are contraindicated in transplant recipients. MMR and varicella serology should be checked in transplant candidates and vaccine administered if seronegative. One or two doses of MMR and varicella can be given before the transplant. Seroconversion should be checked and vaccine re-administered if seroconversion does not happen. Two vaccines can be administered on the same day, but if not done on the same day, the unadministered vaccine should be administered >28 days later. Two doses of recombinant zoster vaccine 2 to 6 months apart to adults aged 50 years or above, regardless of past episodes of herpes zoster or live zoster vaccine live are recommended^{18,19}.

Summary of Vaccine Recommendations in CKD & Kidney Transplant Recipients

- Patients with early-stage CKD can be safely vaccinated
- Patients with ESRD should receive appropriate vaccinations, including live attenuated vaccines (LAVs).
- Age-appropriate vaccination must be recommended in the pre-transplant period at least one month before transplant
- Transplant recipients can safely receive inactivated vaccines. Safety of LAVs like measles, mumps, and rubella (MMR) and varicella-zoster virus (VZV) has not been documented in transplant recipients
- Transplant candidates, their household members and health care workers should receive recommended vaccines before transplantation.

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