Title: Assessment of Immune Response to the Pfizer–BioNTech BNT162b2 Anti-SARS-CoV-2 Vaccine in Kidney Transplant Recipients

I**ntroduction**: Immunosuppressive therapy is crucial for kidney transplant recipients to prevent graft rejection. However, it also weakens the immune system, increasing susceptibility to SARS-CoV-2 infection and severe COVID-19. Mortality from COVID-19 in kidney transplant recipients is high, making vaccination a key strategy for protection. Understanding factors affecting vaccine response is essential.

Objective: To evaluate the immune response to the Pfizer–BioNTech BNT162b2 anti-SARS-CoV-2 vaccine in kidney transplant recipients.

Methods: The study involved 538 participants: a control group of 413 healthy individuals and a study group of 125 kidney transplant recipients on immunosuppressive therapy (tacrolimus+MMF, cyclosporine+MMF, or other drugs). All participants received two doses of the BNT162b2 vaccine. Data was collected via questionnaires on post-vaccination adverse reactions, COVID-19 incidence, symptoms, and severity. In the kidney transplant group, data was also collected on the primary cause of kidney disease, time since transplantation, and immunosuppressive therapy. Anti-SARS-CoV-2 post-vaccination antibody titers were measured enzymatically at 3, 6, and 9 months after the second vaccine dose. Titers ≥7.1 BAU/mL were considered seroconversion.

Results: COVID-19 incidence was similar in both groups (29.78% vs. 28.00%; control vs. study group). Kidney transplant recipients were more likely to be hospitalized for COVID-19 (7.20% vs. 0.73%; study vs. control group) and its complications (3.20% vs. 0.00%; study vs. control group). They also experienced more severe COVID-19 symptoms (dyspnea - $p=0.026$; respiratory failure - $p=0.002$). Vaccine Response: Kidney transplant recipients had a lower immune response to the vaccine (1st dose - $p<0.001$; 2nd dose - $p=0.025$). Antibody titers were higher in those with prior COVID-19 (in both control and study groups). Immunosuppressive Therapy: Immunosuppressive therapy reduced vaccine response in kidney transplant recipients, but different regimens (tacrolimus+MMF, cyclosporine+MMF, other drugs) did not affect response differently (1st dose - $p=0.958$, 2nd dose - $p=0.680$, 3rd dose - $p=0.330$).

Conclusions: 1/ Vaccine response to COMIRNATY (Pfizer–BioNTech) depends on age, COVID-19 history (regardless of timing or severity), time since vaccination, and immunosuppressive therapy. **2/** Healthy individuals and kidney transplant recipients differ in vaccine response, impacting COVID-19 severity. **3/** Booster shots are necessary to maintain immunity against SARS-CoV-2. **4/** Pausing immunosuppressive therapy adjustments to enhance vaccine response in post-COVID-19 kidney transplant recipients should be considered. **5/** Kidney transplant recipients on different immunosuppressive regimens should not be treated differently regarding COMIRNATY (Pfizer–BioNTech) vaccination strategies. **6/** Preventive programs for kidney transplant recipients, especially older adults without prior SARS-CoV-2 infection, those vaccinated long after transplantation, and those transplanted within 12 months, should be considered. This should include additional booster shots and education on SARS-CoV-2 infection prevention measures.