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ORIGINAL ARTICLE

SARS-COV-2 Antibody Response after a Third Dose of Covid-19 Vaccine in Patients Receiving Maintenance Hemodialysis

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ABSTRACT

Background: Patients undergoing hemodialysis are at a higher risk of contracting COVID-19 infection, a virus linked to elevated mortality rates globally. By monitoring antibody levels, it is possible to evaluate the immunogenicity and potential benefits of an additional vaccine dose to guide vaccination strategies and support recommendations for a third dose to maximize protection against COVID-19 in immunocompromised dialysis patients.

Objective: To evaluate the effect of the SARS-CoV-2 antibody response following a 3rd dose of the COVID-19 vaccine in patients undergoing maintenance hemodialysis.

Methodology: This cross-sectional study was conducted in the Department of Nephrology at Shaikh Zayed Hospital, Lahore from 20th February 2023 to 20th August 2023. Sixty adult patients (both male and female) undergoing maintenance hemodialysis (HD), who had previously received two doses of a COVID-19 vaccine, were enrolled in the study. The humoral immune response following the second dose was assessed using the Roche Elecsys® Anti-SARS-CoV-2 S assay, which quantifies total immunoglobulin (IgG and IgM) levels directed against the spike protein (S1) of the virus. Following informed consent, a third vaccine dose was administered. The antibody response was reassessed three weeks after the third dose.

Results: The mean age was 44.3±4.39 years. Majority were males 83.3%, while females accounted for 16.7%. Following the third vaccine dose, an effective antibody response was observed in 88.3% of patients, compared to 76.7% after the second dose.

Conclusion: Administration of a 3rd dose of the COVID-19 vaccine significantly enhanced humoral immune response in patients receiving maintenance hemodialysis, demonstrating improved efficacy compared to the standard two-dose regimen in patients on maintenance hemodialysis.

Keywords: SARS-CoV-2, COVID-19 vaccine, Hemodialysis, Humoral response, Vaccine efficacy

INTRODUCTION

Patients undergoing maintenance hemodialysis (HD) are particularly vulnerable to COVID-19 infection due to their immunocompromised state and associated comorbidities.[1] Since the declaration of COVID-19 as a global health emergency in December 2019,[2] the disease has led to over seven hundred seventy million confirmed cases and more than 6.9 million deaths worldwide, according to the WHO. In Pakistan, SARS-CoV-2 infection rates among HD patients range from 2–28%, with a significantly higher mortality rate (14-51%) compared to the general population.[3]

COVID-19 can present with a wide spectrum of symptoms, from asymptomatic cases to severe respiratory illness,[4,5] especially in individuals over 60 years or those with underlying conditions such as diabetes, hypertension, cardiovascular disease, or cancer.[6,7] Hemodialysis patients in low-income countries face additional challenges, including limited access to healthcare facilities and insufficient implementation of infection control measures.

Vaccination remains the most effective strategy to prevent severe COVID-19 outcomes. However, HD patients often exhibit a reduced and short-lived immune response due to chronic inflammation and accumulation of uremic toxins. Like with the hepatitis B vaccine, they may require additional doses for effective immunization.[8] Among the various COVID-19 vaccines developed, Sinovac, a whole inactivated virus vaccine, has been widely used and demonstrates approximately 90% efficacy in the general population. Recent studies have shown a high rate of seroconversion in vaccinated HD patients.[9,10] In light of this, health authorities such as the French National Authority for Health recommend administering a 3rd vaccine dose to dialysis patients to enhance and prolong immune protection.[11]

PATIENTS AND METHODS

This cross-sectional research was carried out in the Department of Nephrology, Shaikh Zayed Hospital, Lahore. Sixty adult patients (aged 20–50 years) undergoing maintenance hemodialysis who had previously received two doses of the vaccine, were enrolled using a non-probability consecutive sampling technique. Their baseline antibody response after two doses SARS-CoV-2 vaccines was measured and third dose was administered after taking the informed Consent. Antibody response was again measured after three weeks of 3rd dose of Vaccine. Side effects after 2nd dose and 3rd dose were also documented. Patients with a prior renal transplant, those not on dialysis, immunocompromised individuals (including those with malignancy, chronic liver disease, or diabetes), and those who declined participation were excluded. Demographic and clinical data including age, sex, dialysis frequency, and duration of chronic kidney disease were obtained through patient interviews and medical records. The humoral immune response was evaluated using the Roche Elecsys® Anti-SARS-CoV-2 S assay, which quantitatively measures total immunoglobulin (IgG and IgM) levels directed against the receptor-binding domain (RBD) of the spike (S1) protein of the virus. Antibody titers were expressed in Arbitrary Units per milliliter (AU/mL). Based on predefined thresholds, patients were categorized as non-responders (< 0.8 AU/mL), weak responders (0.8-50 AU/mL), or responders (>50 AU/mL), reflecting increasing levels of vaccine-induced humoral immunity. Data were analyzed using SPSS version 2.2. Categorical variables were expressed as frequencies and percentages, and continuous variables as medians. Stratified analyses were performed for age, gender, CKD duration, and dialysis frequency, with statistical significance determined using the chi-square test ($p < 0.05$).

RESULTS

The mean age of 44.32 ± 4.39 years and majority of participants were males 83.3% while females comprised 16.7%. After receiving the 2nd dose of the COVID-19 vaccine, 76.7% of patients demonstrated an effective antibody response (>50 AU/ml). However, 7 (11.6%) were classified as non-responders (<0.8AU/ml), and another 7 (11.6%) were categorized as weak responders (0.8-50 AU/ml). After receiving a third (booster) dose, the overall efficacy increased, with 88.3% of patients mounting a detectable antibody response (Table 1). Notably, all seven patients

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who had shown a weak response after the second dose exhibited increased antibody levels following the third dose. Among the seven initial non-responders, four developed a weak antibody response after the booster 3rd dose, while three remained non-responders

Patients on hemodialysis for less than 36 months exhibited a higher response rate (95.3%) compared to those on dialysis for over 36 months (70.6%). However, this difference did not reach statistical significance (Table 2). In contrast, patients receiving thrice-weekly hemodialysis demonstrated a significantly better immunological response (95.6%) compared to those on twice-weekly dialysis (66.7%), with a statistically significant p-value of 0.003. No considerable difference was identified in side effects between the 2nd and 3rd doses of the vaccine (Table 3).

Table 1: Antibody response after 2nd and 3rd dose (n = 60)

Efficacy	Response Rate		P Value
	2nd Dose	3rd Dose	
Adequate	46 (76.7%)	53 (88.3%)	0.023
Week	7 (11.6%)	4 (6.6%)	
Non Responder	7 (11.6%)	3 (5.0%)	

Table 2: Effect of gender, age, duration and frequency of dialysis on adequate response to 3rd dose of vaccine

Variable	Yes	No	P value
Age (years)			
20–40 (n=10)	8 (80%)	2 (20%)	0.371
>40 (n=50)	45 (90%)	5 (10%)	
Gender			
Male (n=50)	44 (88%)	6 (12%)	0.841
Female (n=10)	9 (90%)	1 (10%)	
Duration of CKD (months)			
≤36 (n=43)	41 (95.3%)	2 (4.7%)	0.007
>36 (n=17)	12 (70.6%)	5 (29.4%)	
Dialysis Frequency			
Thrice/week (n=45)	43 (95.6%)	2 (4.4%)	0.003
Twice/week (n=15)	10(66.7%)	5 (33.3%)	

Table3: Side Effects Between the 2nd and 3rd Doses of the Vaccine

Side effects	2nd dose Vaccine	3rd dose Vaccine
Soreness at site	15 (25%)	18(30%)
Fatigue	21 (35%)	24(40%)
Headache	24(40%)	18(30%)
Muscular skeletal pain	22(37%)	21(35%)
Chills/Fever	27(45%)	30(50%)
Nausia vomiting	21 (35%)	24(40%)

DISCUSSION

In this study, the effectiveness of the 3rd COVID-19 vaccine dose in individuals undergoing maintenance hemodialysis (HD) was 88.3%, compared to 76.7% after two doses. The third dose boosted anti-S1 antibody levels, with comparable side effects and tolerance similar to the second dose. Notably**,** all patients who were initially classified as weak responders demonstrated a marked increase in antibody titers, with levels rising into the responder range following the third dose, indicating a robust booster effect in thesepatients.[12]

Among initial non-responders (23.3%), most had comorbidities and advanced age. After the third dose, 3 patients remained seronegative, while others showed a 2.4-fold increase in antibody levels, highlighting the impact of immune status on vaccine response. These findings align with existing literature indicating diminished humoral responses in patients with chronic diseases and those on HD.[13] Furthermore, recent research has shown that dialysis patients experience a rapid decline in antibody levels following recovery from COVID-19. In an effort to prolong vaccine-induced protection among high-risk populations, a more intensive vaccination regimen has been proposed.

Patients with shorter dialysis duration (≤36 months) had a higher response rate (95.3%) compared to those with longer dialysis duration (>36 months) (70.6%). Moreover, patients receiving thrice-weekly hemodialysis had a significantly better immunological response (95.6%) compared to those on twice-weekly hemodialysis (66.7%) (p=0.003). These findings indicate that dialysis timing and intensity are critical factors. The poorer uremic state in twice-weekly dialysis patients, coupled with chronic inflammation and malnutrition-inflammation complex in long-term hemodialysis patients, may compromise immune response.[14]

This study focused on humoral response, which was robust, but did not assess cellular immunity. Prior research suggests a potential disconnect between humoral and cellular responses in dialysis patients, raising uncertainty about the durability of immunity.[15] A recent study in hemodialysis patients found that while 95.4% of patients exhibited humoral responses, only 62% demonstrated cellular responses.[16] Furthermore, research indicates that antibody levels may decline within six months post-infection, although some patients retain T-cell responses, highlighting the complex nature of immune response in this population.[17]

Limitations of this study include its single-center design, small sample size, lack of a control group, and exclusive focus on humoral response. Prior asymptomatic infections and variability in dose intervals may also confound results. Nevertheless, this is the first study at our center to systematically evaluate the humoral response to a 3rd vaccine dose in HD patients.

CONCLUSION

A 3rd dose of the COVID-19 vaccine effectively boosted antibody levels in maintenance hemodialysis patients especially those with weak or no response after the second dose. Patients with shorter dialysis duration and those receiving thrice-weekly hemodialysis exhibited better immune responses. The third dose did not increase the frequency or severity of adverse events.While the immunogenic benefits are clear, further research is needed to determine the clinical effectiveness of a third booster dose in preventing SARS-CoV-2 infection and related complications in this population.

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