

MEASURING ANTI-SPIKE IgG ANTIBODY RESPONSE TO SARS-COV-2 VACCINATION IN PATIENTS RECEIVING HEMODIALYSIS AT A TERTIARY CARE HOSPITAL OF LAHORE.

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Abstract

Background and Objectives: The current state of the evidence is equivocal for IgG antibody response to COVID-19 vaccination in dialysis patients. Here, we assess the antibody concentration in dialysis patients who have received a complete series of vaccines with or without a history of prior COVID infection irrespective of the vaccine administered.

Methods: In this cross-sectional study, we obtained serum samples from 101 Hemodialysis patients and compared the antibody level among those patients who had received a two-dosage vaccine regimen within the last six months versus those who had completed the same regimen more than six months ago. Participation in the study was completely voluntary by HD patients who gave informed consent and results were noted in a designed proforma.

Results: Our study found that nearly three-quarters of patients (72.2%) received 2 dosages of Sinopharm or Sinovac vaccine, and ninety-seven percent of participants were considered seropositive (COVID Ab titers > 7.1 BAU/ml). The average SARS-COV-2 spike antibody levels were 1892.4 BAU/mL, while the median levels were 971 BAU/mL. Mean and median antibody titers were 1895.8 and 792 BAU/mL in the group who had received the vaccine within the last six months as compared to 1981.1 and 1033 BAU/mL respectively in the group who had received the vaccine later than six months, with p-value 0.84 indicating no significant difference. Additionally, there were no statistically significant variations in IgG antibodies observed when examining subgroups based on diabetes, hypertension, coronary artery disease (CAD), or gender. However, it was found that older patients (aged >55 years) exhibited significantly higher anti-spike antibody titers compared to younger patients (2417.8 BAU/mL vs. 1377.3 BAU/mL, P value 0.008).

Conclusion: The result of this study provides important evidence, which can lead to vaccine efficacy, especially in older populations. Future studies should address whether booster vaccination may play a role in providing an effective and long-lasting protection among vulnerable patients undergoing hemodialysis care.

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Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) raised significant health worries worldwide, with especially bad outcomes for hemodialysis (HD) patients globally, with a death rate much

greater than that of the common populace.¹ A sizeable population of HD patients is immunocompromised, along with numerous health conditions, for example, elevated blood pressure, coronary artery disease, and diabetes mellitus, making them further vulnerable to SARS-CoV-2 infection and other various illnesses.²⁻³ Therefore, patients undergoing hemodialysis require special attention in this regard.

Observational data from various studies on hepatitis B and influenza vaccination indicate evidence of diminished and shortened immune response to immu-

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nization in individuals undergoing dialysis.^{4,8} This raises a concerning possibility that patients on dialysis may also experience reduced efficacy of the SARS-CoV-2 vaccine. The introduction of new vaccines targeting SARS-CoV-2 in the beginning of 2021 facilitated worldwide distribution, resulting in a substantial decrease in the likelihood of death among the general population.⁹ Nevertheless, individuals with chronic kidney disease and undergoing hemodialysis were not included in these cohorts.

Many studies have been done in the Western world on the immune response to COVID-19 Vaccines in hemodialysis recipients. They have shown that dialysis patients have low antibody titers 2 weeks after a complete vaccine series as compared to healthy individuals. Moreover, this antibody response deteriorates more rapidly over weeks to months in dialysis patients, and at 6 months post-vaccination, a significant majority of dialysis patients have undetectable COVID-19 antibodies.¹⁰⁻¹³ This has led to the recommendation of a booster vaccine dose 6 months after a complete vaccine series in many countries now.¹⁴⁻¹⁷ The majority of these studies have been done on patients who received mRNA-based vaccines- Pfizer BioNTech, J&J, and Moderna.¹⁸⁻²¹ Although Data on antibody response to conventional inactivated virus vaccines (Sinopharm and Sinovac) is limited not only in the general population in Pakistan but especially in dialysis patients.²² Recent studies conducted in Pakistan showed a comparable immune response after SARS-COV-2 deactivated virus vaccination in hemodialysis patients. Interestingly, diabetic patients undergoing hemodialysis (HD) exhibited a lower response rate, while individuals with a history of previous SARS-CoV-2 infection demonstrated a more favorable response.

In this study, we have sought to assess the medium and long-term antibody response in dialysis recipients who have obtained a complete series of vaccines with or without a history of prior COVID infection irrespective of the vaccine administered.

METHODS

The present cross-sectional, single-center study

took place at Jinnah Hospital Lahore (JHL) within the Department of Nephrology in April 2022, following authorization by the IRB. JHL is a specialty hospital renowned for its state-of-the-art renal care facility, comprising two dialysis units capable of accommodating 150 hemodialysis (HD) patients and conducting approximately 25,000 dialysis sessions each year. Virtually all chronic hemodialysis patients receive 4-hour dialysis treatments three times a week.

A total of 101 Hemodialysis patients were recruited through non-probability consecutive sampling. A study was carried out to compare the antibody levels in patients who had received a two-dosage vaccine regimen within the last six months with those who had completed the same regimen more than six months ago. It included both males and females, above >18 years of age. Participation in the study was completely voluntary by HD patients who gave informed consent.

The following criteria were used for exclusion: individuals who were under 18 years of age, who received booster vaccine dose against SARS-CoV-2, on peritoneal dialysis, with other serious medical and psychiatric problems like decompensated cirrhosis, congestive cardiac failure, recent stroke or acute coronary disease, Active cancer or on immunosuppressants, Alzheimer disease, schizophrenia. Furthermore, participants with a background of serious side effects & extreme hypersensitivity response to any element of the vaccine ingredients were excluded.

Basic demographic characteristics like name, age, and gender were noted. Blood samples were obtained from all participants and IgG antibodies to COVID-19 Spike Protein were measured. All the laboratory investigations were carried out at a local laboratory to minimize the risk of any discrepancy results. Patients were asked about co-morbid illnesses like hypertension, ischemic heart disease, Diabetes, etc. History of smoking, alcohol intake and substance abuse was also taken.

We obtained information regarding the vaccination of the participants. Vaccination of SARS-COV-2 was administered in accordance with the optimum quality of care, consisting of 2 dosages given 21 days apart. Information was obtained about the exact date

when the participants received 2nd dose of the vaccine. Blood was drawn in April 2022. Testing was performed by using Abbott Alinity CI. It utilizes a computerized, multistep process employing chemiluminescent micro-particle immunoassay (CMIA) technology for the quantitative recognition of IgG anti-S antibody to SARS-CoV-2 in human serum and plasma. A positive test result was considered as having an antibody titer equal to or greater than 7.1, as outlined by the maker's instructions.²³⁻²⁴ A result below 7.1 BAU/mL was considered negative for anti-SARS-CoV-2-S, while a result of 7.1 BAU/mL or higher was taken positive for anti-SARS-CoV-2-S.

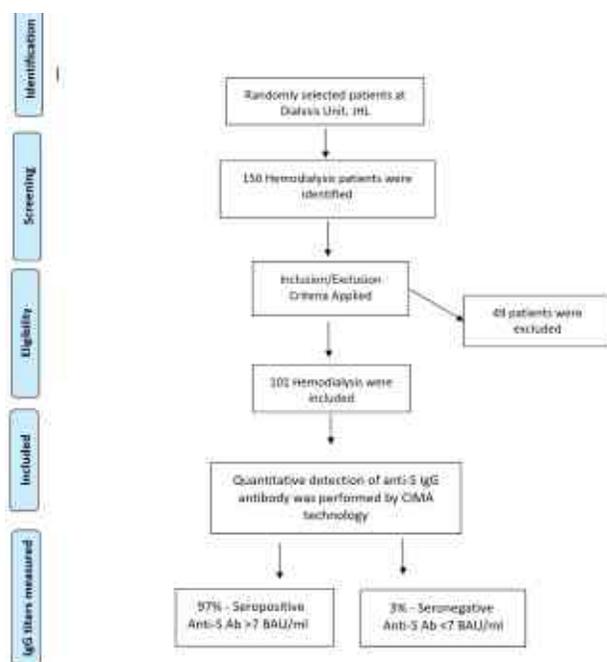


Figure 1: Flow Diagram of Evaluating Anti-S IgG Antibody response

SPSS v. 20 was utilized for entry and analysis of data. For quantitative variables such as age and IgG titers, means were calculated. Qualitative variables like gender and co-morbid conditions were analyzed by calculating frequencies and percentages. The data were analyzed separately for each time interval since the participants were fully vaccinated.

To compare proportions, the Chi-square test was applied for parametric data. Similarly, the Mann-Whitney test was done to compare the medians and

the T-test was utilized to compare the means. 95% CI reported for proportions and IQ range for medians. P values of <0.05 are considered significant.

RESULTS

In April 2022, a total of 101 dialysis patients participated in the research. Every participant had completed a two-dose series of SARS-COV-2 vaccines. The mean age of the participants was 50 years, and 28.7% (29/101) were females. Among the patients, 74.2% had elevated blood pressure, 38.6% had diabetes, and 19% possessed a background of HCV.

Around 72.2% of patients received 2 dosages of Sinopharm or Sinovac vaccine. SARS-COV-2 spike protein antibodies were measured in all participants, with a mean titer of 1892.4 BAU/mL & a median titer of 971 BAU/mL. Around 30% of the participants received their second SARS-COV-2 vaccine in under six months from the antibody titer assessment, while 70% received their 2nd dosage more than 6 months ago.

Among the entire sample, only 3 patients were seronegative. All patients who were given their second vaccine dosage within the past six months were positive. In the subgroup of patients who were given their 2nd vaccine dose 1, 65 out of 68 patients were positive. However, the slight variance was not statistically significant (p-value 0.55).

When dividing the sample in 2 different age groups (≤ 50 years and > 50 years), it was found that the elder patients had meaningfully higher anti-spike antibody levels when analyzed in comparison to patients of younger age (2417.8 BAU/mL vs. 1377.3 BAU/mL, P value 0.008).

A relative study was carried out to compare the antibody levels in patients who had received a two-dosage vaccine regimen within the last six months with those who had completed the same regimen more than six months ago. Among those who underwent the two-dose vaccine regimen within the last six months, the mean & median antibody titers were 1895.8 and 792 BAU/mL, respectively. For patients who completed the series more than 6 months ago, the mean and median antibody titers were 1981.1 and 1033 BAU/mL,

Table 1: Comparison of mean and median COVID anti-spike IgG levels

Variable	Variable categories	Frequency (n)	Mean IgG levels (BAU/mL)	Median IgG levels (BAU/mL)	SD	P value*
Duration after 2 nd vaccine dose	<6 months	29	1895.8	792.0	2119.8	0.849
	≥ 6 months	68	1981.1	1033.5	1961.4	
Age	≤50 years	51	1377.3	613.2	1765.6	0.008
	>50 years	50	2417.8	1696.5	2103.5	
BMI	<25	70	1773.8	895.4	1931.9	0.680
	≥25	31	2160.2	1311.0	2153.3	
Diabetes	Yes	39	1,768.2	534	1972.7	0.981
	No	62	1970.5	207	2005.5	
Hypertension	Yes	75	2011.2	1531	2050.8	0.472
	No	26	1549.8	1341	1776.1	
Gender	Male	72	1829.0	898.5	1995.5	0.428
	Female	29	2049.7	1521.0	2036.5	
Hepatitis C Hx	Yes	19	1303.4	792.0	1358.0	0.334
	No	82	2028.8	994.0	2102.7	

* P value was calculated with the T-test or Mann-Whitney U test where applicable.

respectively (P value 0.84). This indicates a significant difference in antibody concentrations between the two groups was not observed. Furthermore, no significant differences in antibody concentration amongst groups demarcated by diabetes, elevated blood pressure, ischemic heart disease, or gender were observed either.

DISCUSSION

This cross-sectional study was conducted to evaluate the variation over time in the anti-spike IgG levels secondary to the SARS-COV-2 vaccine in patients undergoing hemodialysis in Pakistan.

In this cross-sectional study, we examined the seropositivity of hemodialysis recipients who were already given at least 2 dosages of various vaccines (Sinopharm, Sinovac, Pfizer, and Moderna) at the time of recruitment in the study. Furthermore, we assessed the variations in the anti-spike IgG levels in two different groups. The first group had a vaccine 6 months ago and the second had a vaccine less than 6 months ago.

Many observational studies reported an equivocal response to mRNA SARS-COV-2 immunizations among HD patients. On the one hand, Longlune et al documented high immunogenicity after the mRNA vaccine in HD patients, while on the other hand, Simon et al noted a diminished response to the mRNA vaccine in dialysis recipients. A new systematic review found a

significantly high vaccine response rate of 87% among HD patients who received at least 2 dosages of mRNA vaccine and these findings corroborate with Longlune et al.²⁴

Although many studies have been published on mRNA vaccines' antibody response in HD patients, inactivated vaccines have received scant scholarly attention since the pandemic started.²⁵ In particular, there is a scarcity of data available on the efficacy of inactivated vaccines among the HD population in Pakistan and this research aims to fill this knowledge gap. Based on the information available to us, only one study in Pakistan analyzed the antibodies' response to the inactivated vaccine in dialysis patients.²⁰

We recruited 101 ESRD patients who met our inclusion criteria. The inclusion criteria were formulated after an extensive literature review to minimize the risk of selection bias. The study participants were routine dialysis patients in the Department of Nephrology, Jinnah Hospital Lahore (JHL). JHL is a tertiary care facility located in the heart of the city and serves over one million patients per year from all across the province of Punjab. It should be noted that JHL provides care for a diverse patient population in terms of their demographic characteristics, and they are good representatives of the entire province.

Our research found that ninety-seven percent of

participants were considered seropositive (COVID Ab titers > 7.1 BAU/ml). Interestingly, the proportion of seropositive individuals who received their vaccine more than 6 months ago was substantially higher than those who received the vaccine less than 6 months ago, the former constituted 68 % and the latter 29%.

Several Western studies reported the attenuated antibody response 6 months after receiving the 2nd dose of the vaccine.⁹⁻¹¹ On the contrary, our study found that vaccine-induced immunity did not wane over time, and therefore, anti-spike IgG Ab titers were not statistically different in either group that received the 2nd dose less than or more than 6 months ago, p-value = 0.849. Similarly, no significant differences were noted across other variables such as gender, hypertension, diabetes, the viral status of hepatitis C, and body mass index (BMI).

The majority of study participants received inactivated vaccines (Sinopharm or Sinovac) in this study compared to the Western studies that measured the IgG titers for mRNA or viral vector vaccines. The difference in the vaccine types studied could be one likely explanation as to why our study noticed steady levels of antibodies. These results point to the need for conducting experimental studies that compare the IgG antibody titers for various vaccine types including inactivated, mRNA, and viral-vector vaccines, and measure the IgG titers at 3, 6 & 9 months.

Our research revealed that HD recipients above 50 years of age developed significantly higher IgG antibody titers (median=1696.5) compared to those who were below 50 years (median=613.2), p-value = 0.008. It could be possible that the older study group (>50 years) had previously developed SARS-COV-2 infection and were already seropositive before being enrolled in the study. Nonetheless, our findings are contrary to Gustafson et al. who displayed a lower protective capacity due to vaccine-induced antibodies in older individuals. Previous research suggests that older individuals are more likely to suffer from severe COVID infections, therefore, they have elevated IgG titers. This finding corroborates with Soyta Bai R et²⁶ who also noticed persistently higher IgG levels among

the older age group (> 60 years), secondary to SARS-COV-2 infections. Several other research articles reported similar findings by explaining an association between high IgG titers and the severity of COVID infections among older individuals.²⁷⁻²⁸ Only minor side effects were reported by the study participants such as fatigue, headache, and pain at the injection site due to the SARS-COV-2 vaccines. These findings were supported by various other studies.

This research possesses several strengths and limitations. One of the main strengths of this research is the high response rate (96%) to various vaccine types in a large cohort of dialysis patients from a single center. Another strength is a detailed and thorough analysis of the participants' demographics and clinical comorbidities such as hypertension, and diabetes. It is important to note that these factors are proven to be linked with the compromised immune response¹²⁹¹. Lastly, given the diversity in patient demographics served at JHL, this study's findings can be effectively generalized to the rest of the Punjab province of Pakistan. Our study has two limitations. First, we were unable to measure the baseline IgG antibody levels before enrolling study participants due to the limited resources, and therefore, we could not differentiate the vaccine-induced or infection-vaccine-induced seropositivity. Second, we did not perform a control or healthy group analysis to compare the IgG levels in both healthy and HD patients.

CONCLUSIONS

Hemodialysis patients (HD) have experienced significant consequences due to SARS-COV-2, including an elevated susceptibility to infection, poorer patient outcomes, and greater death rates compared to the overall populace. While several studies have focused on measuring antibodies to multiple SARS-CoV-2 antigens, IgG antibody response to SARS-CoV-2 vaccination in hemodialysis patients has received scant scholarly attention. We fill this knowledge gap by examining the seropositivity of HD patients who received at least two doses of various vaccines (Sinopharm, Sinovac, Pfizer and Moderna), and assessed the variations in the anti-spike IgG levels in two different

groups, those who received vaccine 6 months ago vs those who received vaccine less than 6 months ago. The medium and long term antibody response, irrespective of their prior SARS-COV-2 status, was found to be excellent in maintenance hemodialysis patients of Lahore, Pakistan.

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