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Original Article

Evaluating IgG Levels, Vaccination Effects, and COVID-19 Infection Severity in Renal Transplant Recipients

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Abstract

Several studies have reported that different factors play an important role in the production of IgG after COVID-19 vaccination. This study aimed at studying COVID-19 infection rates and severity in renal transplant recipients and vaccine responsiveness. In this cross-sectional study, IgG levels was measured in renal transplant recipients using automated benchtop immunoanalyzer Vidas at the Duhok Center for Kidney Disease and Transplantation. In this study group, only 30 individuals experienced the SARS-CoV-2 infection, with only three cases being severe. The most frequently reported symptoms of SARS-CoV-2 virus infection were fatigue (18/30) 60%, high temperature (17/30) 56%, headache (12/30) 40%, and poor endurance (11/30) 36.6%. The IgG titers were significantly different between the vaccinated 33.067 ± 2.5 versus unvaccinated individuals 23.916 ± 3.31with p value = 0.025. On the other hand, demographic characteristics of the cohort including: comorbidities, hemodialysis, different age groups, gender, infection/no-infection differences had no statistically significant impact on the IgG titers. In conclusion, vaccination significantly increased the levels of protective IgG level in kidney transplant recipients. It is crucial to focus on increasing the acceptance of vaccination among kidney transplant recipients to prevent infections from other COVID-19 variants or pathogen outbreaks.

Keywords: Renal transplant, COVID-19, Vaccination, Immunosuppression

INTRODUCTION

According to the World Health Organization (WHO), since the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak since December 2019, 6.59 million of people around the world have died from the virus itself or due to its complications. Among high-risk members mainly recipients of solid organ transplants (SOT), the infection can cause a wide range of severe symptoms, necessitating intensive care and leading to a 25% higher mortality rate compared to other population groups [1]. Vaccines were developed in 2021 to protect the population from the virus, reducing hospitalizations and fatalities [2,3]. Immunosuppression regimens nonspecifically inhibits B and T cells, leading to inadequate antibody production or a negative response to vaccines [4,5]. The production of neutralizing immunoglobulin G (IgG) has been identified as the primary protection for transplant recipients[6,7]. Several studies have demonstrated the significance of creating antibodies that neutralize the spike protein of SARS-CoV-2, thereby preventing the virus from replicating and preventing the virus from entering cells [8]. It was previously shown that 30%-40% of solid organ recipients, with triple immune suppression, had a negative serological response after three to four doses of COVID-19 vaccine [9,10]. Therefore, it is crucial to give these patients extra attention as they receive the third dose and booster shots that will protect them from potentially fatal viral infections [11].To gauge the gravity of the same issue in this setting, this study has been conducted to gain insight on the state of kidney transplant recipients at the Duhok Kidney Disease and Transplantation

Centre to evaluate the immune response to COVID-19 vaccines.

MATERIALS and METHODS

The Basic Demographic Data Collection

A questionnaire was used to collect basic demographic data that included, age. gender, hemodialysis, renal failure causes (hypertension, diabetes, ischemic heart disease, inherited, others), comorbidities (hypertension, diabetes, ischemic heart disease, others), number of vaccinations, type of vaccine, number of COVID infections, severity of the infection, immune suppressants used (mycophenolate, tacrolimus, prednisolone, others), other medications, and symptoms experienced during/after four weeks of infection of 100 KTRs were collected at Duhok Kidney Transplant and disease center between October 2022 to December 2022.

IgG Level Determination and Analysis Methods

The IgG titers were measured using Vidas [12]; with considering IgG levels above 1.2 positive and below that level measured as negative based on the manufacturer's instructions. The data analyses were performed with the unpaired-t test and the one-way ANOVA in GraphPad Prism 9.0 with considering the mean standard error between different categories; and we used Microsoft Excel to organize and visualize the results.

Ethical Approval

Written consent was obtained from all participants. The consent and the study protocol were approved by the Ethics committee in the College of Medicine, University of Zakho.

RESULTS

Descriptive analysis of the study group

In our study, 100 KTR were recruited, among the KTRs 65 were males, and the average age was 42.6 ± 13.36. Among the 100 KTRs, 46 had no comorbidities, while 41/54 (75%) had hypertension, 18/54 33% had diabetes, and ischemic heart disease (ISH) was 12/54 (22%), The primary cause of renal failure in 51/100 (51%) of KTRs was unknown, whereas the cause of renal failure was hypertension in 12/100 (12%), genetic causes in 10/100 (10%) and diabetes in 6/100 (6%) patients. In terms of immune suppression treatment along with other medications that the KTRs were receiving, 82/100 (82%) of the patients were on triple immunotherapy of mycophenolate, tacrolimus, and prednisolone, and 73/100 (73%) patients were on other medications that needed to regulate their comorbidities. The incidence of COVID infection occurred in 30/100 (30%) cases; 19/30 (63%) of the males and 11/30 36% were females. Further, the majority of people who reported experiencing the infection had fatigue (18/30) 60%, a high temperature 17/30 (56%), a headache 12/30 (40%), or low endurance 11/30 (36%), and other symptoms were experienced less frequently. Further, the severity of the infected KTRs was mainly mild 18/30 (60%), with a few moderate cases 9/30 (30%), and only three severe cases, of which two of these patients were not vaccinated, and one had a negative response to vaccination with negative IgG.

Table 1. A demographic data of the KTRs in this study

Feature	Males	Females	Total
Number	65	35	100
Median age	45	42	-
Vaccinated	39	22	61
Infection before	17	5	22
Vaccination	2	6	8
Infection after vaccination			
Two dose or more	36	20	56
COVID infection	19	11	30
Mild	11	7	18
Moderate	7	2	9
Severe	1	2	3
Times of infection			
One	18	6	24
two	1	5	6
Hemodialysis	47	26	73
Renal failure	30	19	49
Comorbidities	18	36	54

The IgG titers analysis of the KTRs

In our study, we showed that there was significant increase in IgG levels in KTRs who received the vaccine regardless of its type in comparison to those KTRs who did not receive any vaccinations, with 33.067 ± 2.5 and 23.916 ± 3.31

p < 0.05 (Table 2). There was no significant difference between the infected and non-infected KTRS, with 24.046 ±3.33 and 31.835 ±2.5, respectively. There were no significant differences between the males and females' IgG levels or between different age groups at p > 0.05 (Table 2). Furthermore, hemodialysis had no significant effect on the IgG levels of KTRs compared between patients that were undergoing hemodialysis 28.62±2.31 versus those were not 31.55±3.91 with p value 0.5205. Finally, there were no significant difference between the individuals who had comorbidities such as hypertension, diabetes, or ischemic heart diseases, and those without comorbidities with p value being 0.324. Additionally, in terms of vaccination, only 61 of the KTRs were vaccinated, with Pfizer accounting for 53/61 (86%), AstraZeneca for 8/61 (8%), and Sinopharm for only 1/61 (1.6%).

Table 2. The statistical difference between the IgG levels between different features of the patients

Feature	Level of antibody		P value
	(Yes)	(No)	
Vaccinated (mean±MES)	33.067 ±2.5	23.916±3.31	0.025
Infected (mean±MSE)	24.046 ±3.33	31.835 ±2.5	0.08
Comorbidities (mean±MSE)	31.36±2.69	27.32±2.95	0.324
Hemodialysis (mean±MSE)	28.62±2.31	31.55±3.91	0.5205
Gender (mean ± MSE)	(M) 31.68±2.56	(F) 25.43±3.31	0.1434
20-35	30.76±4.01		
36-50	30.92±2.96		0.2717
>50	23.36±3.83		

Comorbidities include: hypertension, diabetes, ischemic heart disease, and others.

DISCUSSION

An important takeaway from the COVID-19 pandemic is the need to prioritize saving the lives of those most at risk. The worldwide deadly impact of the COVID-19 pandemic is beyond dispute. Higher rates of morbidity and mortality have been observed in the KTRs population because of factors such as immunosuppression treatment, advanced age, hemodialysis, and co-morbidities before developing the vaccine [13,14]. In terms of COVID-19 severity of the symptoms, fatigue, high temperature, headache, and poor endurance were the most common signs of infection among the patients studied; only the three severe cases had +10 of the symptoms.

In terms of serological differences, the impact of studied categories such as hemodialysis, infection, age, gender, comorbidities did not have statistically differences on the KTRs (Table 2). Despite the fact that several studies have demonstrated that both hemodialysis and comorbidities negatively impact patients' humoral responses [15]. This might be attributed to the genetic makeup of the patients or the small sample size recruited in this study. Besides, vaccination resulted in a significantly higher antibody titer for the vast majority of the study population with the exception of one patient who had a negative response to two doses of vaccination and developed a severe case of COVID-19 infection. Other studies reported the importance of vaccination on rejuvenating the immune system against the SARS-CoV-2, and have called for four or more vaccinations [16,17]. Since KTRs have a poor humoral response to the second and third doses of vaccine, numerous studies have stressed on the importance of implementing a vaccination system and booster injection to protect them [9,10,16,18]. Locally there were no specific legislations that regulate vaccination programs among solid organ transplants a part from research studies that included guidelines on preventative procedures [19]. This study population had a 39% non-vaccination rate, and only 2% of patients received all three doses of the vaccine. Considering that 82%

(82/100) of KTRs were on a triple immunosuppression that included mycophenolate, previously a study [10], suggests stopping mycophenolate immunosuppression at least by the time of vaccination. In addition, the low acceptance of vaccination in this study provides evidence in favor of employing new strategies for vaccination. Moreover, results from smaller regional study have also indicated that vaccination is not widely accepted [20]. To protect the vulnerable groups, it is necessary to implement a comprehensive vaccination plan, including public education and awareness strategies.

CONCLUSION

KTRs at the Duhok Center of Renal Transplantation and Diseases suffered mild or asymptomatic cases of COVID-19 infections. This needs further studies to explore the factors that may play a role in the severity of the disease. The data from this study clearly back previous study on the importance of vaccination preventing severe infection and death. KTRs here at the Duhok Center of Renal Transplantation and Diseases suffered mild or asymptomatic cases of COVID-19 infections compared to moderate or severe cases, which indicate successful management and medical care here at the center.

Conflict of Interest

The authors declare they have no conflicting interests.

REFERENCES

1. Vishnevetsky A, Levy M. Rethinking high-risk groups in COVID-19. *Multiple Sclerosis and Related Disorders*. 2020;42:102139. doi:10.1016/j.msard.2020.102139
2. Andrews N, Tessier E, Stowe J, et al. Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines. *New England Journal of Medicine*. 2022;386(4):340-350. doi:10.1056/NEJMoa2115481
3. Liang LL, Kuo HS, Ho HJ, Wu CY. COVID-19 vaccinations are associated with reduced fatality rates: Evidence from cross-county quasi-experiments. *Journal of Global Health*. 2021;11. doi:10.7189/jogh.11.05019
4. Dahdal S, Saison C, Valette M, et al. Residual Activatability of Circulating Tfh17 Predicts Humoral Response to Thymodependent Antigens in Patients on Therapeutic Immunosuppression. *Front Immunol*. 2018;9:3178. doi:10.3389/fimmu.2018.03178
5. Duchini A, Goss JA, Karpen S, Pockros PJ. Vaccinations for adult solid-organ transplant recipients: current recommendations and protocols. *Clin Microbiol Rev*. 2003;16(3):357-364. doi:10.1128/CMR.16.3.357-364.2003
6. Modelli de Andrade LG, de Sandes-Freitas TV, Requião-Moura LR, et al. Development and validation of a simple web-based tool for early prediction of COVID-19-associated death in kidney transplant recipients. *American Journal of Transplantation*. 2022;22(2):610-625. doi:10.1111/ajt.16807
7. Requião-Moura LR, Sandes-Freitas TV de, Viana LA, et al. High mortality among kidney transplant recipients diagnosed with coronavirus disease 2019: Results from the Brazilian multicenter cohort study. *PLOS ONE*. 2021;16(7):e0254822. doi:10.1371/journal.pone.0254822
8. Saghazadeh A, Rezaei N. Towards treatment planning of COVID-19: Rationale and hypothesis for the use of multiple immunosuppressive agents: Anti-antibodies, immunoglobulins, and corticosteroids. *International Immunopharmacology*. 2020;84:106560. doi:10.1016/j.intimp.2020.106560
9. Benotmane I, Gautier G, Perrin P, et al. Antibody Response After a Third Dose of the mRNA-1273 SARS-CoV-2 Vaccine in Kidney Transplant Recipients With Minimal Serologic Response to 2 Doses. *JAMA*. 2021;326(11):1063. doi:10.1001/jama.2021.12339
10. Osmanodja B, Ronicke S, Budde K, et al. *Serological Response to Three, Four and Five Doses of SARS-CoV-2 Vaccine in Kidney Transplant Recipients*. Nephrology; 2022. doi:10.1101/2022.03.23.22270017
11. Altheaby A, Alloqmani D, AlShammari R, et al. Safety and Efficacy of the COVID-19 Vaccine in Kidney Transplant Recipients. *Cureus*. Published online May 5, 2022. doi:10.7759/cureus.24753
12. Renard N, Daniel S, Cayet N, et al. Performance Characteristics of the Vidas SARS-CoV-2 IgM and IgG Serological Assays. *Journal of Clinical Microbiology*. 2021;59(4).
13. Kates OS, Fisher CE, Rakita RM, Reyes JD, Limaye AP. Use of SARS-CoV-2-infected deceased organ donors: Should we always "just say no?" *Am J Transplant*. 2020;20(7):1787-1794. doi:10.1111/ajt.16000
14. Ravanan R, Callaghan CJ, Mumford L, et al. SARS-CoV-2 infection and early mortality of waitlisted and solid organ transplant recipients in England: A national cohort study. *Am J Transplant*. 2020;20(11):3008-3018. doi:10.1111/ajt.16247
15. Hussein NR, Naqid IA, Jamal SA, et al. A Study of Relationship between SARS-CoV-2 Antibodies Levels and Host Factors among General Population in Zakho City, Iraq. *J Contemp Med Sci| Vol*. 2022;8(4):250-253.
16. Alejo JL, Mitchell J, Chiang TPY, et al. Antibody Response to a Fourth Dose of a SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series. *Transplantation*. 2021;105(12):e280-e281. doi:10.1097/TP.0000000000003934
17. Caillard S, Chavarot N, Francois H, et al. Clinical Utility of Biochemical Markers for the Prediction of COVID-19−Related Mortality in Kidney Transplant Recipients. *Kidney International Reports*. 2021;6(10):2689-2693. doi:10.1016/j.ekir.2021.06.034
18. Charmetant X, Espi M, Barba T, et al. Predictive factors of a viral neutralizing humoral response after a third dose of COVID-19 mRNA vaccine. *American Journal of Transplantation*. 2022;22(5):1442-1450. doi:10.1111/ajt.16990

19. Hussein NR, Saleem ZSM, Rashad BH, et al. Home management scheme for patients with severe covid-19 in Duhok city, Kurdistan region of Iraq: a possible role for family physicians. *J Family Med Prim Care*. 2021;10(11):4260-4263. doi:10.4103/jfmpc.jfmpc_166_21

20. Abdulah DM. Prevalence and correlates of COVID-19 vaccine hesitancy in the general public in Iraqi Kurdistan: A cross-sectional study. *Journal of Medical Virology*. 2021;93(12):6722-6731. doi:10.1002/jmv.27255