Original Article

Journal of Iranian Medical Council, Volume 7, Issue no. 1
http://dx.doi.org/10.18502/jimc.v7i1.14199

The COVID-19 Infection in Heart Transplant Recipients: A Cohort Study

Farah Naghashzadeh[1], Zargham Hossein Ahmadi[1], Arezoo Mohamadifar[2], Seyed Alireza Naji[3], Mohammad Sadegh Keshmiri[1], Sina Aghdasi[1], Maryam Hajimoradi[1], Mahsa Riahi[1], Alireza Jahangirifard[1], Leila Saliminejad[1], Shadi Shafaghi[1], Babak Sharif-Kashani[4] and Sima Noorali[1]*

1. Lung Transplantation Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Chronic Respiratory Disease Research Center, Masih Daneshvari Hospital, ShahidBeheshti University of Medical Sciences, Tehran, Iran
3. Virology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Tobacco Prevention and Control Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*** Corresponding author**

Sima Noorali, MD
Lung Transplantation Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Tel: +98 21 2712 2522
Fax: +98 21 2610 9484
Email: simanoorali@yahoo.com

Received: Nov 29 2022
Accepted: Jun 14 2023

Citation to this article:
Naghashzadeh F, Ahmadi ZH, Mohamadifar A, Naji SAR, Keshmiri MS, Aghdasi S, et al. The COVID-19 Infection in Heart Transplant Recipients: A Cohort Study. *J Iran Med Counc.* 2024;7(1):40-4.

Abstract

Background: Infectious diseases are major complications after solid organ transplantation. Heart transplant patients have a high mortality rate after Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection. Coronavirus disease 2019 (COVID-19) vaccines have shown efficacy in generating specific immune response. This study aims to describe the COVID-19 infection before and after vaccination in heart transplant recipients.

Methods: This was a single-center cohort study including 95 heart transplant recipients with laboratory radiological confirmed COVID-19.

Results: COVID-19 infection was present before vaccination in 33 (35.78%) patients. The most frequent COVID-19 clinical presentations before vaccination were cough in 21 (63.63%) and myalgia in 19 (57.57%) patients; 12 (36.36%) were hospitalized; 17 (51.51%) cases had oxygen depletion and required supplemental oxygen; none of them needed invasive ventilation. Of the entire 33 COVID-19 patients, two patients (6.06%) re-experienced the disease about two months after complete vaccination and both of them were recovered. 63 heart transplant patients had not experienced COVID-19 before vaccination, of which 59 patients received vaccination. After two months, 23 vaccinated patients were infected with COVID-19 again, and 2 of the 3 patients who were not vaccinated were also infected. Five patients passed away in the whole study.

Conclusion: Heart transplant patients infected with SARS-CoV-2 are at greater risk of severe infection and death compared with immunocompetent individuals. Thus, COVID-19 vaccination for all HT recipients is of paramount importance.

Keywords: Communicable Diseases, COVID-19, SARS-CoV-2, Transplant Recipients, Vaccination

Introduction

The pandemic of COVID-19 disease has led to the deaths of hundreds of thousands of people worldwide (1,2). Elderly people and those with chronic medical conditions and compromised immune systems such as transplant recipients are at higher risk for unfavorable outcomes (3). Organ transplant recipients as a vulnerable population are a high-risk group against infections due to chronic immunosuppression, especially COVID-19 with a mortality rate of 20 to 35.7% before vaccination programs (3,4).

In Heart Transplant (HT) patients in comparison to the general population, the hospitalization is about five times higher and there is a significant difference in mortality rate and prognosis (5). A systematic review and meta-analysis showed 2.54% infection, 82.9% hospitalization, and 27.6% mortality rate in HT recipients which means the mortality proportion of 0.92% (5).

As the COVID-19 vaccination programs were launched globally, remarkable improvements were noticed in disease prognosis so that in overall estimation measured in the general population during 6 months of all vaccine platforms full doses, there was about 80% to 100% protection against death or severe infections and 65% to 90% against the infection itself (6) dysregulation of the immune system may play a crucial role in the progression of the disease. In this study, the lymphocyte subsets were evaluated in patients with different severities of COVID-19.Materials and Methods: In this prospective study, the frequencies of peripheral lymphocyte subsets (CD3+, CD4+, and CD8+ T cells; CD19+ and CD20+ B cells; CD16+/CD56+ NK cells, and CD4+/CD25+/FOXP3+ regulatory T cells.

Immunocompromised patients will benefit from vaccination but are less protected in comparison with the immunocompetent population (7). Recent studies demonstrated 80% of effectiveness among single organ transplant recipients with two doses of mRNA vaccines (7).

This study was aimed at describing the incidence of COVID-19 infection before and after vaccination in heart transplant recipients.

Materials and Methods

Study design and participants

This was a single center cohort study including 95 HTx recipients with laboratory or radiologically confirmed COVID-19 who were hospitalized at Masih Daneshvari Hospital, a tertiary center, from December 2019 to December 2021. Demographic and clinical data were collected and analyzed for each patient from the patients' medical records or call interview, including age, sex, and medical history, clinical presentations, laboratory data, therapeutic management, and outcomes before and after COVID-19 vaccines. The vaccination protocol consisted of the administration of two doses one month apart. This study was approved by the Iran National Committee for Ethics in Biomedical Research (Ethic code: IR.SBMU.NRITLD.REC.1400.090) and followed the ethical guidelines of the Declaration of Helsinki.

Statistical analysis

Quantitative data are presented as mean ± SD, and qualitative data were evaluated as percentages. The data was analyzed using SPSS software version 22.

Results

Patients' characteristics

In this descriptive cohort study, 95 HTx recipients, at a mean time after transplant of 6 years (range, 5 months to 15 years), were enrolled. The mean ±SD age of the patients was 46.5514± years73. patients (76.84%) were male. 41 (43.15%) patients had underlying diseases with the most frequency of diabetes mellitus (68.29%) and hypertension (41.46%) (Table 1).

Before vaccination

COVID-19 infection before vaccination was present in 33 (35.78%) patients. The most frequent COVID-19 clinical presentations before vaccination were cough in 21 (63.63%) and myalgia in 19 (57.57%) patients; 12 (36.36%) were hospitalized; 17 (51.51%) cases had oxygen depletion and required supplemental oxygen; none of them needed invasive ventilation. 20 (60.60%) patients showed ground-glass opacification with occasional consolidation in the periphery in their chest CT scans as the predominant imaging pattern; 70% of them were bilateral (Figure 1).

Vaccination

96.8% of all enrolled patients were fully vaccinated with two doses, which included all of the COVID-19 affected patients and 59 of 62 patients in negative

COVID-19 group. The vaccines injected were Sinopharm BIBP (94.9%), ChAdOx1 (1.7%), and COVIran Barekat (3.4%). No serious adverse event was reported after any vaccine platform.

After vaccination

Of the entire 33 COVID-19 patients, two patients (6.06%) re-experienced the disease about two months after complete vaccination. Finally, both of them were recovered. The most immunosuppressive regimen was tacrolimus and mycophenolate in 63 (66.31%) and 71 (74.73%) patients, respectively. The medication regimen in 20 patients was not changed, but in 45 patients was reduced temporarily. The results indicated that two male patients experienced transplant rejection, which had positive COVID-19 PCR test and also at least one symptom; but they were not hypoxemic and hospitalized and had recovered after few days.

Serological assessment

Assessment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) neutralizing antibody, anti-spike IgG, and SARS-CoV-2 RBD IgG was performed in 18 patients at a mean time of 1.5 months after vaccination. The mean ± SD level of them was 14.14±7.70, 22.06±3.74 and 16.73±2.78, and the level of antibodies <2.5, 8, and 5 was considered as a negative response to vaccination, respectively.

Mortality

The total mortality rate in Iran was 1.93% (6,8) dysregulation of the immune system may play a crucial role in the progression of the disease. In this study, the lymphocyte subsets were evaluated in patients with different severities of COVID-19. Materials and Methods: In this prospective study, the frequencies of peripheral lymphocyte subsets (CD3+, CD4+, and CD8+ T cells; CD19+ and CD20+ B cells; CD16+/CD56+ NK cells, and CD4+/CD25+/FOXP3+ regulatory T cells and in our study, five patients (5.26%) passed away; two people were injected with two doses of vaccine and the others were unvaccinated.

Discussion

This study described the COVID-19 infection before and after vaccination in heart transplant recipients. Of the total 33 COVID-19 patients, disease recurred in only two patients (6.06%) about two months after complete vaccination and both recovered; and the seroconversion occurred in those assessed.

One observational study conducted by Peters *et al* showed that COVID-19 vaccination is associated with fewer symptoms, hospitalizations, and deaths. The mortality rate in this cohort among unvaccinated patients with HT was 9% and much higher than that observed among vaccinated recipients (4%) and the general population (9). In parallel, in our study, the rate of COVID-19 infection after vaccination was very lower.

In general, the serological response to vaccines in the solid organ transplant population is poor. Furthermore, knowledge is limited, due to the absence of well-defined clinical trials in this population (10). In a systematic review conducted by Eckerle *et al*, it was reported that response varies with vaccine type, age and organ transplanted and in some vaccines, the antibody titer decreases quickly (11). For COVID-19 vaccines, as with any other vaccine in the transplant population, it is important to know

Table 1. Demographic characteristics of heart transplant patients

		Percent	Frequency
Age	< 20	3.50	3
	21-30	10.60	9
	31-40	16.50	14
	41-50	28.20	24
	51-60	24.70	21
	> 61	16.50	14
Sex	Male	76.84	73
	Female	23.16	22
Underlying Diseases	Yes	43.15	41
Hypertension	No	58.54	24
	Yes	41.46	17
Diabetes Mellitus	No	31.71	13
	Yes	68.29	28
Chronic Kidney Disease	No	82.50	33
	Yes	17.50	7
Liver Disease	No	95.00	38
	Yes	5.00	2

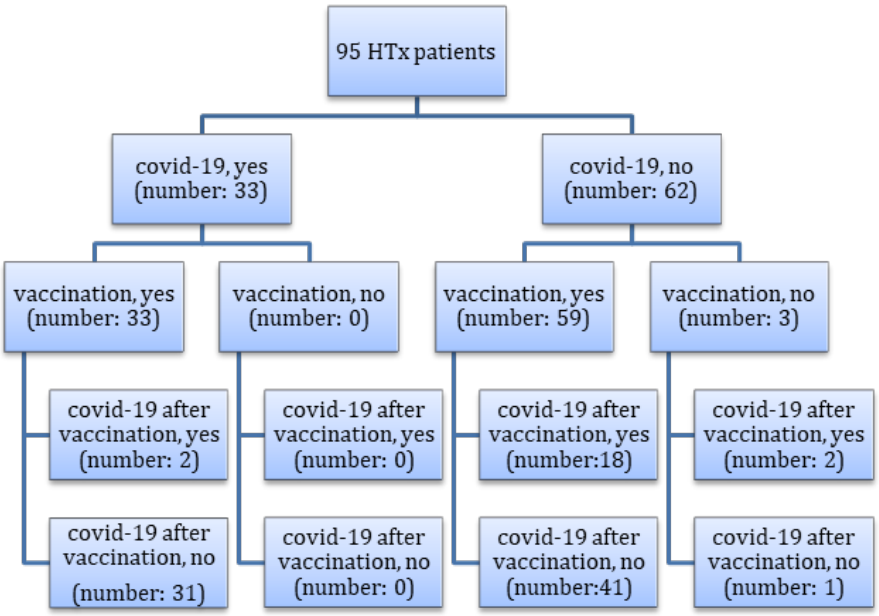

Figure 1. Vaccination status.

the efficacy in preventing the disease as well as its safety in terms of adverse reactions to the vaccine or risk of rejection (10). Based on some studies despite a third or fourth COVID-19 vaccine dose, rate of seroconversion remains usually lower in solid organ transplant recipients than in the community (12-15). For instance, Peled *et al* found a positive antibody response in 67% of the HT recipient 18 days after a third dose of BNT162b2 vaccine (14). In contrast, in another study conducted by Caillard *et al*, there was a very high seroconversion rate in their cohort of HT vaccinated with BNT162b2 more than 3 years after transplantation (13).

A study with 436 solid organ recipients evaluated the immune response to the first dose of mRNA vaccines and found anti-Spike IgG antibodies in only 17% of the participants after a median follow-up of 20 days (16). In our study, there was seropositivity in all HT patients who were assessed; also, no serious adverse event was reported after vaccination.

In a case series study conducted by Ballout JA *et al*, management of immunosuppressive medications was similar in all the patients. Mycophenolate was held in all the patients, since lymphopenia is associated with worse outcome in COVID-19 patients and all of them had lymphopenia on admission labs, calcineurin inhibitors were also continued, unless trough levels were supratherapeutic (17). In our study, the most immunosuppressive regimen was tacrolimus and mycophenolate. The medication regimen in twenty patients was not changed, but in 45 patients was reduced temporary.

There are some limitations to this study. This was a single-center analysis; also, there was poor patient's compliance for antibody evaluation due to the accessibility difficulties.

Conclusion

HT Patients infected with SARS-CoV-2 are at greater risk of severe infection and death compared with immunocompetent individuals. Therefore, COVID-19 vaccination for all HT recipients is of paramount importance.

References

1. Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. Crit Care 2020;24(1):1–4.

2. Hashemian S. Social media and the Iranian COVID-19 crisis. J Prev Diagnostic Treat Strateg Med 2023

Jan;2(1):1–2.

3. Klabunde M, Collado D, Bohon C. An interoceptive model of bulimia nervosa: A neurobiological systematic review. J Psychiatr Res 2017;94(3):36–46.

4. Naghashzadeh F, Shafaghi S, Sharif-Kashani B, Tabarsi P, Saliminejad L, Noorali S. Coronavirus disease 2019 outcomes in heart transplant recipients: a single-center case series. J Med Case Rep 2021;15(1):1–4.

5. Ahmed F, Abid M, Maniya T, Usman MS, Fudim M. Incidence and prognosis of COVID-19 amongst heart transplant recipients : a systematic review and meta-analysis. Eur J Prev Cardiol 2021;1–3.

6. Rezaei M, Marjani M, Tabarsi P, Moniri A, Pourabdollah M, Abtahian Z, et al. Evaluation of Lymphocyte subtypes in COVID-19 patients. Tannaffos 2022;21(3):293–301.

7. Embi PJ, Levy ME, Naleway AL, Patel P, Gaglani M, Natarajan K, et al. Effectiveness of 2-dose vaccination with mRNA COVID-19 vaccines against COVID-19–associated hospitalizations among immunocompromised adults—nine states, January–September 2021. MMWR Morb Mortal Wkly Rep 2021;70(44):1553–9.

8. https://www.worldometers.info/coronavirus/country/iran/.

9. Peters LL, Raymer DS, Pal JD, Ambardekar AV. Association of COVID-19 vaccination with risk of COVID-19 infection, hospitalization, and death in heart transplant recipients. JAMA Cardiol 2022 Jun;7(6):651–4.

10. Crespo-Leiro MG, Barge-Caballero E, Gustafsson F. Efficacy of the COVID-19 vaccine in heart transplant recipients: what we know and what we ignore. Eur J Heart Fail 2021 Sep;23(9):1560-2.

11. Eckerle I, Rosenberger KD, Zwahlen M, Junghanss T. Serologic vaccination response after solid organ transplantation: a systematic review. PLoS One 2013;8(2):e56974.

12. Tanner R, Starr N, Chan G, Dempsey E, Heffernan E, Newman E, et al. Humoral response to SARS-CoV-2 adenovirus vector vaccination (ChAdOx1 nCoV-19 [AZD1222]) in heart transplant recipients aged 18 to 70 years of age. J Heart lung Transplant 2022 Apr;41(4):492–500.

13. Caillard S, Thaunat O, Benotmane I, Masset C, Blancho G. Antibody response to a fourth messenger RNA COVID-19 vaccine dose in kidney transplant recipients: a case series. Ann Intern Med 2022 Mar;175(3):455–6.

14. Peled Y, Ram E, Lavee J, Segev A, Matezki S, Wieder-Finesod A, et al. Third dose of the BNT162b2 vaccine in heart transplant recipients: immunogenicity and clinical experience. J Heart lung Transplant 2022 Feb;41(2):148–57.

15. Marinaki S, Degiannis D, Roussos S, Xagas E, Tsoutsoura P, Adamopoulos S, et al. Head-to-head comparison of response rates to the two mRNA SARS-CoV-2 vaccines in a large cohort of solid organ transplant (SOT) recipients. Vaccines (Basel) 2022 Jan;10(2).

16. Boyarsky BJ, Werbel WA, Avery RK, Tobian AAR, Massie AB, Segev DL, et al. Immunogenicity of a single dose of SARS-CoV-2 messenger RNA vaccine in solid organ transplant recipients. JAMA 2021 May;325(17):1784–6.

17. Ballout JA, Ahmed T, Kolodziej AR. COVID-19 and heart transplant: a case series and review of the literature. Transplant Proc 2021 May;53(4):1219–23.