

CASE REPORT

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# Coronavirus disease 2019 outcomes in heart transplant recipients: a single-center case series

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## Abstract

**Background:** With the rapidly expanding pandemic of severe acute respiratory syndrome coronavirus-2, a chronic immunosuppressed state in solid organ transplant recipients is a concern. We reported coronavirus disease 2019 in heart transplant recipients and described the patients' course from diagnosis to either hospital admission or improvement in symptoms.

**Case presentation:** This study retrospectively identified 13 white (Iranian) heart transplant patients with coronavirus disease 2019 between December 2019 and October 2020. The mean age of patients was 43.7 years (19–65 years); seven (70%) were men. Laboratory and treatment data were collected for those admitted or managed as outpatients. Outcomes were also recorded for all patients. This report demonstrates a range of symptoms, clinical severity, and disease course in heart transplant recipients with coronavirus disease 2019, including ten hospitalized patients and three patients, managed entirely in the outpatient setting. One patient passed away, and none of them experienced an episode of clinically overt rejection.

**Conclusions:** We would like to emphasize the importance of being alert in these patients to consider testing in a broad range of clinical presentations and gathering more data for better management.

**Keywords:** COVID-19, Heart transplantation, Solid-organ transplantation, Immunosuppression

## Introduction

The recently novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), emerged in China in December 2019 and caused a highly contagious disease called coronavirus disease 2019 (COVID-19) [1]. In less than 3 months, it spread throughout the globe and was declared a global pandemic by the World Health Organization on 11 March 2020 [2]. To date, COVID-19 has affected over 9 million people worldwide. The clinical manifestations of COVID-19 range from minimally symptomatic individuals to severe courses with the

requirement of invasive mechanical ventilation and multiorgan failure [3, 4].

Risk factors for morbidity and mortality include older age, cardiovascular disease, diabetes, chronic respiratory disease, hypertension, obesity, and cancer. A particular concern also exists regarding the vulnerability of pharmacologically immunosuppressed patients before or during this pandemic [3, 5]. Thus, solid organ transplant (SOT) recipients, including heart transplant (HTx) recipients, are considered to be vulnerable to COVID-19 infection because of immunosuppression and the presence of comorbidities. Epidemiologic and clinical characteristics of HTx recipients during the SARS-CoV-2 pandemic are largely unknown [6].

The following report describes 13 cases of HTx recipients with laboratory-confirmed SARS-CoV-2 and reviews

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the clinical presentations, treatment strategies, and short-term outcomes.

## Case presentation

### Patient population

In this single-center case series of 135 recipients of HTx, 25 confirmed COVID-19 recipients from December 2019 to October 2020 were presented, but information of only 13 patients was available. Demographic data including age, sex, and medical history were collected for each patient. Clinical presentations and laboratory data, therapeutic management, and outcomes were collected and analyzed for those admitted to our hospital or managed as outpatients. Nasopharyngeal swab RT-PCR testing was done in all of the patients with first mild symptoms and also in patients who were in touch with definite COVID-19 patients.

### Statistical analyses

All quantitative variables are expressed as means.

## Results

### Demographic data

In this case series, we presented 13 patients with laboratory-confirmed SARS-CoV-2. The mean age of patients was 43.7 years (19–65 years); seven (70%) were men. Previous history of diabetes mellitus was most frequently reported (three patients, 37.5%). Three patients (25%) had hypertension, and two patients had chronic kidney disease (Table 1).

### Clinical presentation and laboratory findings

The mean time between the transplantation and COVID-19 diagnosis was 6.4 years (1–12 years). Clinical presentations included fever (6, 50%), dyspnea or cough (7, 53.8%), myalgia or malaise (5, 38.4%), and gastrointestinal symptoms (3, 23%); and two (15.3%) patients were asymptomatic. Ten patients (76.9%) were admitted, three (23%) were managed as outpatients, and two (15.3%) of the inpatients required admission to the intensive care unit (ICU) (Table 1).

Notably, mean white blood cell count was about 4500/ $\mu\text{L}$  (1500–8000/ $\mu\text{L}$ ), with a mean absolute lymphocyte count of 1000/ $\mu\text{L}$  (300–3200/ $\mu\text{L}$ ). High-sensitivity C-reactive protein and erythrocyte sedimentation rate were greater than normal in all admitted patients. One patient had severe creatinine elevation termed acute on chronic kidney failure. All patients had a normal echocardiogram during hospitalization.

### Treatment and outcome

The therapeutic management involved an immunosuppressive regimen and supportive care in 13 patients.

**Table 1** Patient characteristics, symptoms, treatment, and outcomes

Demographics	No.
Total, no.	13
Age, mean (years)	44.3
Male	9
Time, post-transplant, mean (years)	6.4
Hypertension	3
Diabetes mellitus	3
Chronic kidney disease <sup>a</sup>	2
Maintenance immunosuppression	
Total, no.	13
Tacrolimus	10
Cyclosporine	3
Mycophenolate mofetil	6
Mycophenolate sodium	7
Methylprednisolone	5
No. of immunosuppressive medications	
3	13
Symptoms	
Total, no.	11
Asymptomatic	2
Fever	6
Myalgia or malaise	5
Shortness of breath or cough	7
Gastrointestinal symptoms	3
Treatment	
Total inpatients and outpatients, no.	13
Remdesivir	9
Tocilizumab	1
Interferon beta	1
Intravenous immunoglobulin	2
Dexamethasone	7
Reduction in immunosuppression medications	8
Mycophenolate mofetil held	9
Supplemental oxygen	6
Outcome	
Total, no.	13
Overall survival	12
Overall mortality	1
Hospitalized	10
In-hospital mortality	1
ICU admission	2
Discharged	12
Managed as outpatient	3
Clinically overt rejection	0

<sup>a</sup> Defined by a glomerular filtration rate less than 30

Supplemental oxygen was required in six of the hospitalized patients. Routine immunosuppressive regimens in HTx recipients included calcineurin inhibitors

(cyclosporine, tacrolimus), mycophenolate, and corticosteroid. Three patients received cyclosporine, tacrolimus was administered in ten, mycophenolate mofetil in six, mycophenolate sodium in seven, and methylprednisolone in five cases. During infection with COVID-19, mycophenolate was discontinued in nine admitted patients for at least 1 week, and the dosage of calcineurin inhibitors was reduced to a lower limit of suitable blood level for transplant age in eight cases. All of the patients received azithromycin, nine admitted patients with pulmonary involvement received remdesivir 200 mg stat on the first day, and then 100 mg daily for four consecutive days. Tocilizumab was administered in one patient and interferon beta in another one. Two patients underwent intravenous immunoglobulin therapy, seven patients with mild pulmonary involvement received intravenous dexamethasone instead of oral prednisolone, and five patients with moderate-to-severe pulmonary involvement received pulse therapy with methylprednisolone.

Twelve patients survived, but one of the ICU admitted patients underwent hemodialysis and finally died from respiratory and kidney failure. None of the survived patients experienced an episode of clinically overt rejection (Table 1).

## Discussion

The COVID-19 pandemic has presented the medical community with unique challenges and severely impacts large parts of the world. Further development of this disease cannot be predicted, and especially knowledge regarding outcomes of at-risk patients such as transplant recipients is still evolving [7]. The immunosuppressants used to prevent and treat rejection in transplant recipients leave patients susceptible to infectious complications, of which pulmonary infections are the leading cause of morbidity and mortality [8].

The first case of COVID-19 in HTx was a 51-year-old man with a severe presentation from China [9]. Available reports of COVID-19 in SOT recipients from China, Italy, France, Germany, the USA, and Spain highlight variable presentations and outcomes, despite immunosuppression [4, 10–21]. There are no published reports of COVID-19 in the heart transplant recipient population in Iran. This study reviews clinical parameters and outcomes of 13 cases of HTx recipients with laboratory-confirmed SARS-CoV-2 followed by our transplant center in Tehran, Iran. These cases presented with a range of severity of clinical presentations and course of hospitalization, including ten patients requiring admission and three managed as outpatients. Despite risk factors for severe disease, including older age, immunosuppression, and other comorbidities, most of the

patients had mild symptoms, but one (7.6%) of them died from respiratory and kidney failure. In a study conducted in Spain with 18 SOT [kidney (44.4%), liver (33.3%), and heart (22.2%)] recipients diagnosed with COVID-19, the case fatality rate was 27.8% [22]. Based on another cohort from the USA, with 90 patients, the mortality rate was 18% [23].

The general approach followed in the published reports was to decrease or hold the immunosuppressant [7]. In this series, we held mycophenolate mofetil in six patients, and this was due to concern for the worsening of COVID-19 disease. Despite all require maintenance immunosuppression that predisposes recipients to greater infectious risk, immunosuppression has also been theorized to be protective against cytokine storm [24]. It should be noted as a limitation that this case series presents a small number of patients, which limits the ability to evaluate the efficacy of the treatment strategy. It will certainly be beneficial to collaborate with other high-volume centers to gather more data on the disease and gain better insight into the clinical course and optimal management of this disease in these immunocompromised patients.

## Conclusion

We presented our experience of HTx recipients who acquired the SARS-CoV-2 virus at a tertiary care transplant center. This study reflected the diagnosis and management of COVID-19 in immunocompromised patients. We would like to emphasize the importance of being alert in these patients to consider testing in a broad range of clinical presentations—even in asymptomatic patients that have been in contact with definite cases—and gathering more data for better management.

## Abbreviations

COVID-19: Coronavirus disease 2019; HTx: Heart transplant recipients; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2; SOT: Solid organ transplantation.

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Not applicable

## Authors' contributions

FN participated in the research design; SS participated in the research design, performance of the research, and writing of the paper; BS-K participated in the research design; PT participated in the research design; LS participated in the performance of the research; SN participated in the writing of the paper. All authors read and approved the final manuscript.

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## Availability of data and materials

The data are available in Table 1.

## Declarations

### Ethics approval and consent to participate

This study followed the principles of the Declaration of Helsinki and was approved by the medical ethics committee. All of the patients signed informed consent according to the medical ethics committee.

### Consent for publication

Written informed consent was obtained from the patients for publication of this case series and any accompanying images. A copy of the written consents is available for review by the Editor-in-Chief of this journal.

### Competing interests

The authors declare no conflicts of interest.

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