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Mini Review Article

Covid-19 in Heart Transplant Recipients of Rajaie Heart Center, a Mini Review

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Abstract:

Introduction: *Heart transplant patients because of immunosuppressive treatment has increased susceptibility to COVID-19. We evaluated the clinical course of heart transplant patients with COVID-19.*

Methods and Results: *We enrolled twenty-two COVID-19 cases of adult heart transplantation from February 2020 to September 2021. The most common symptoms in patients were fever. The death occurred in 3 (13.6 %).*

Conclusion: *we didn't see any different clinical course of covid infection in heart transplant patients and common people, although heart transplantation mortality may increase in the acute rejection phase concomitant with COVID-19, immunosuppressive dose reduction may not be necessary for all heart transplant patients with COVID-19. Sirolimus immune suppressant may have antiviral effects in these patients.*

Introduction

After identifying several cases of unknown pneumonia caused by a Coronavirus variant, on December 2019, in Wuhan, China, concerns were raised among public health professionals about the spread of a new disease in the world. The SARS-COV-2(COVID-19) pandemic has deeply impacted the health care systems.

Patients receiving solid organ transplantation require lifelong immunosuppression, thus more susceptible to COVID-19 and COVID-19 pandemic has posed unprecedented health challenges1.

Heart transplant recipients have many comorbidities such as diabetes mellitus (DM), hypertension (HTN), chronic kidney disease (CKD), obesity, coronary heart disease, coronary allograft vasculopathy (CAV), and chronic lung diseases, making them prone to severe diseases2. While managing immunosuppressive medication in individuals with severe COVID-19 is uncertain, the relationship between COVID-19 and heart transplant rejection needs attention. Therefore, we evaluated the clinical outcomes of heart transplantation in patients with confirmed COVID-193.

As there are many unknown things about solid organ transplantation managing a critical heart transplant patient with COVID-19 is a great deal of these patient.

Method and Result

Rajaei cardiovascular center is a high volume heart transplant center We enrolled 22adult heart transplanted patient with coivd- 19 infection From February 2020 to September 2021 .SARS-CoV-2 PCR was negative in five individuals, a chest computed tomography (CT) scan suggested COVID-19. We had 2 heart transplant patients with 2 episodes of COVID-19 infection, one of them had second episode 2 weeks after vaccination.

31.8% of patients were hypertensive, 45.4% were obese ,22.7% had chronic kidney disease and 45.4% had diabetes mellitus.

Variables	**Mean ± SD**
Age (years)	34.95 ± 8.97
BMI (kg/m2)	26.23 ± 5.2
Years after transplant	3.09 ± 1.57
Hypertension	7 (31.8%)
Chronic kidney disease	5 (22.7%)
Obesity (BMI > 25)	10 (45.4%)
Diabetes Mellitus	10 (45.4%)
Mycophenolate mofetil use	22 (100%)
Tacrolimus use	16 (72.7%)
Cyclosporine use	5 (22.7%)
Sirolimus use	5 (22.7%)
D-dimer (µg/mL)	1.10 ± 1.5
Troponin (ng/dL)	0.67 ± 1.35
Pro-BNP (pg/mL)	342.5 ± 608.62
CRP (mg/dL)	32.22 ± 44.37
WBC (cell/mm3)	7449.47 ± 6211.51
Hemoglobin (g/dL)	12.52 ± 2.73
Platelet (103/mm3)	175.94 ± 56.83

Blood urea nitrogen (mg/dL)	17.84 ± 8.54
Creatinine (mg/dL)	1.23 ± 0.49

Table 1. On-admission characteristics, risk factors, and laboratory data

Variables	**Number of patients, n (%)**
Hospitalized patients	19 (86.36%)
Fever	16 (72.7%)
Myalgia and bone pain	15 (68.2%)
Cough	7 (31.8%)
Dyspnea	7 (31.8%)
Abdominal pain	5 (22.7%)
Positive troponin	5 (22.7%)
Positive Pro-BNP (Pro-BNP > 125ng/dl)	6 (27.3%)
Moderate to severe right ventricular dysfunction	6 (27.3%)
Pericardial effusion	2 (9%)
Change in immunosuppression therapy	16 (72.7%)
Steroid treatment for COVID-19	18 (81.8%)
Remdesivir use	13 (59%)
GCSF due to leukopenia	4 (18.2%)
Rejection during COVID-19 infection	Rejection during COVID-19 infection
Intubation and ICU admission	2 (9%)
Death	3 (13.6%)

Table2. Patients' outcomes and adverse events.

Fever (16 (72.7%)) was the most common symptom in our patients. Three patients (13.6%) died in this research, one with severe gastrointestinal complications and suspicion of acute rejection. Another patient suspected of acute rejection and experiencing cough and dyspnea was treated with methylprednisolone. Three days after discharge, he was readmitted with COVID-19 to the ICU and ultimately expired. The last patient, with early COVID-19 after the transplant, had a severe clinical course with sepsis and multiple end-organ failures, which led to death. Risk factors in died and improved patients of COVID-19 infection was not different but in hospitalized and non-hospitalized patients we had higher frequency of diabetes and CKD in admitted patients.

Due to severe leukopenia, immunosuppressive discontinuation and mycophenolate mofetil dosage reduction was required in 2 (9%) and 7 (31.8%) patients, remdesivir had been used as coivd -19 treatment on 59% of patients and we used IVIG prescribed in 2 patients. Most patients were on treatment with tacrolimus and mycophenolate mofetil treatment and 3 patients were on sirolimus treatment, we didn't see severe clinical course of the disease in these patients.

Risk factors	**COVID-19 non-survivors (n = 3), n (%)**	**COVID-19 survivors (n = 19), n (%)**	***P* Value**
Diabetes mellitus	2 (66.7%)	9 (47.36%)	0.534
Hypertension	1 (33.3%)	6 (31.57%)	0.951
Obesity	1 (33.3%)	9 (47.36%)	0.650
Chronic kidney disease	1 (33.3%)	4 (21%)	0.222

Table3. Comparison of the risk factors in COVID-19 non-survivors and survivors.

Discussion

COVID-19 is more common in solid organ transplant recipients compared to the general population. This increased prevalence is probably due to increased susceptibility to infections due to their chronic use of immunosuppressant and patients risk factors4 .mortality rate has range of 10-30% in different studies (13.6% in our study compared to previous studies10%, 29.7%, 28.75%, and 22.7% in the studies by Fernando Luis Scolari et al , Bottio et al., Rivinius et al., and Singhvi et al., respectively4-7).The higher prevalence could be due to the higher prevalence of risk factors or older patients in the mentioned studies.

Carlos Diaz-Arocutipa5 systematic review analysis of Thirty-nine articles (22 case reports and 17 cohorts) involving 415 patients were included. the hospitalization rate was 77%. The most common symptoms were fever and cough like our study. Hydroxychloroquine , azithromycin , and lopinavir/ritonavir were the most commonly used drugs, but we didn't use them in our study , Forty-nine percent of patients discontinued the baseline regimen of antimetabolites ,In contrast, 59% and 73% continued the same regimen of calcineurin inhibitors and corticosteroids, respectively. Short-term mortality among cohorts limited to inpatients was 25%. Comparing mortality rate, it was lower in our center, this may be due to different immunosuppressive treatment and novel treatment of covid -19 infection.

According to WHO data of Iranian society the mortality rate of general population in covid 19 pandemic era was about 1.92%, in heart transplant patients it was more but it need comparing with highrisk patients of general population

In the present study, only 2 patients (9%) required immunosuppressive discontinuation due to sepsis and severe leukopenia, while 7 patients (31.8%) required mycophenolate mofetil dosage reduction due to leukopenia. Even though we did not reduce the dosage in other patients, we witnessed a reduced death rate. As a result, maintaining antimetabolite dosage in individuals without leukopenia seems reasonable. Discontinuation of these medicines solely due to COVID-19, without adverse effects or complications, is not recommended.

Sirolimus as an immune suppressant that has antiviral effects too, in our study patients with sirolimus added immune suppressive therapy had a better course of COVID-19 infection, it may be due to this effect but it needs more evaluation with higher population study.

Conclusion

In present study despite we had a high rate of COVID-19 in our transplant patients, we didn't see any different clinical course of covid infection in heart transplant patients versus common people, although heart transplantation mortality may increase in the acute rejection phase concomitant with COVID-19, immunosuppressive dose reduction may not be necessary for all heart transplant patients with COVID-19. Sirolimus immune suppressant may have antiviral effects in these patients and it needs further studies to see its effect on covid 19 infection coarse in heart transplant patients.

Ethical Approval

The RHC's ethics review committee approved this study with the ethics code IR.RHC.REC.1400.076. We adhered to the declaration of Helsinki in this investigation. All patient records were kept confidential.

Conflict of interest:

The authors declare no conflict of interest.

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