

Outcomes of liver transplantation patients infected with COVID-19: pandemic hospital experience from Turkey

Taner Akyol¹, Tolga Düzenli^{2,3}

¹Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Samsun University, Samsun, Turkey

²Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Hitit University, Çorum, Turkey

³Department of Gastroenterology, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, University of Health Sciences, İstanbul, Turkey

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ABSTRACT

Aims: There are conflicting results for the course of the disease and mortality rates for liver transplantation patients infected with COVID-19. In this study, we aimed to present the outcomes of our liver transplant patients who were hospitalized and followed up in our tertiary hospital, which served as a pandemic hospital for COVID-19.

Methods: Patients hospitalized with the diagnosis of COVID-19 between March 1, 2020 and March 1, 2022 in Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital and Prof. Dr. Feriha Öz Pandemic Hospital were included. In this retrospective observational study, the clinical data of the patients, the need for intensive care hospitalization, and mortality rates were recorded by hospital computer system. The relationships were analyzed with SPSS v20.0.

Results: There were 25996 patients who were hospitalized with the diagnosis of COVID-19 and 28 of them were with the history of liver transplantation. Ages of the liver transplant patients ranged from 18 to 73, with a median age of 52. 82.1% of the patients were male and 17.9% were female. Intensive care unit hospitalization rate was 25% and mortality rate was 14.3%. The relationships according to the age groups revealed that all of the women were under the age of 50 ($p=0.008$) and the patients who deceased were male patients over the age of 50 ($p=0.044$).

Conclusion: Mortality rates and intensive care unit requirements of chronically immunosuppressed liver transplant patients with COVID-19 infection were similar with general population. Complete immunosuppression withdrawal should not be urged in this population.

Keywords: COVID-19, infection, liver, mortality, transplantation

INTRODUCTION

Coronaviruses (CoV) are single-stranded, enveloped RNA viruses of Coronaviridae family.¹ The spectrum of diseases caused by CoV in humans ranges from mild infections to severe infections.²⁻⁶ The effect of this virus, which started at the end of 2019 and caused a large number of mortality and morbidity, has decreased with the mutations and developments in the treatment and prevention in the period to date, but it still continues to exist.

Liver transplant patients are a group of patients who are followed and treated cautiously for COVID-19 due to their current conditions and immunosuppressive drugs.⁷ The incidence of COVID-19 in liver transplant patients is higher than in the general population.⁸ However, there are conflicting results regarding the course of the disease and mortality rates. Liver transplant patients, who were considered a very risky patient group at the beginning of the pandemic, were speculated to have similar risks to other patient groups in the following

period.⁸ Nevertheless, there is no definitive consensus in this context in the literature, and there is still a need for studies on real-life data and outcomes of liver transplant patients.

In this study, we aimed to present the outcomes of our liver transplant patients for the course of COVID-19 disease and mortality rates who were hospitalized and followed up in our tertiary hospital, which serves as a pandemic hospital for COVID-19.

METHODS

The study was carried out with the permission of University of Health Sciences Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (Date: 09.03.2022, Decision No: E-46059653-020). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Corresponding Author: Tolga Düzenli, tolgaduzenli@yahoo.com



Patients who were hospitalized with the diagnosis of COVID-19 in Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital and Prof. Dr. Feriha Öz Pandemic Hospital between March 1, 2020 and March 1, 2022 were included in the study.

COVID-19 infection has been diagnosed according to the COVID-19 infection guideline recommended by the World Health Organization and published by the "T.C. Ministry of Health General Directorate of Public Health" by the scientific committee. These patients were those with positive real-time fluorescence (RT-PCR) detection of 2019-nCoV nucleic acid, with positive serum 2019-nCoV-specific IgM antibodies, and with thorax CT COVID-19 pneumonia findings. It was not considered COVID-19 if two consecutive tests of 2019-nCoV nucleic acid (sampling time at least 24 hours apart) were negative or if the 2019-nCoV-specific IgM/IgG antibodies were still negative after 7 days. 2019-nCoV nucleic acid detection was tested in nasopharyngeal swabs, sputum, other lower respiratory tract secretions (sputum or airway extracts).

In this retrospective observational study, the clinical and radiological data of the patients, the need for intensive care unit (ICU) hospitalization, and mortality rates recorded in hospital computer systems has been examined.

Statistical Analysis

SPSS Statistics (Version 20.0. Armonk, NY: IBM Corp.) was used for the statistical analysis. A Chi-square test was used to determine the significance of the relationships between categorical variables. A p-value of ≤0.05 was considered statistically significant.

RESULTS

There were 28 patients with the history of liver transplantation among a total of 25996 patients who were hospitalized with the diagnosis of COVID-19 in Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital and Prof. Dr. Feriha Öz Pandemic Hospital between March 1, 2020 and March 1, 2022.

Ages of the study group ranged from 18 to 73, with a median age of 52. 82.1% of the patients were male and 17.9% were female. Demographic characteristics of the liver transplant patient group are presented in **Table 1**. Seven of the 258 patients were followed up in the intensive care unit, and four of them died.

When the relationships between the age groups of <50 and >50 were evaluated, it was found that all of the women hospitalized and followed up were under the age of 50 (p=0.008) and all of the patients who died were male patients over the age of 50 (p=0.044) (**Table 2**).

Table 1. Demographic characteristics of the liver transplant patient group

Liver transplant COVID 19 patients	Total (n)	Total %
Gender		
Female	5	17.9
Male	23	82.1
Age		
<50 Years	13	46.4
>50 Years	15	53.6
Year of referral		
2020	15	53.6
2021	9	32.3
2022	4	14.1
Graft dysfunction		
No	28	100
Yes	0	0
Intensive care unit hospitalization		
No	21	75
Yes	7	25
Mortality		
No	24	85.7
Yes	4	14.3

Table 2. Relationships between the liver transplant patient group according to age groups

Liver transplant COVID 19 patients	Age<50 years	Age>50 years	P
Gender			
Female	5	0	0.008*
Male	8	15	
Year of referral			
2020	7	8	0.380
2021	3	6	
2022	3	1	
Smoking			
Missing	6	8	0.569
No	6	5	
Yes	1	2	
Body mass index			
Missing	7	10	0.892
<30 kg/m ²	3	3	
>30 kg/m ²	3	2	
Immunosuppressive drugs			
Prednisone or prednisolone	4	10	0.067
Tacrolimus	11	13	0.846
Mycophenolate mofetil	7	7	0.925
Time between LT and COVID-19, years			
Median	4	7	0.493
Intensive care unit hospitalization			
No	11	10	0.274
Yes	2	5	
Mortality			
No	13	11	0.044*
Yes	0	4	

*p<0.05 was considered statistically significant.

DISCUSSION

Liver transplant patients need lifelong immunosuppression therapy and are therefore at risk for both community and opportunistic infections throughout their lives.⁷ Although COVID-19 is mainly characterized by respiratory symptoms, systemic involvement can also occur. However, there is limited information about the course of COVID-19 disease in liver transplant patients.⁹ In our study, we evaluated the patients who needed hospitalization among COVID-19 positive patients with liver transplant who referred to our hospital, which is the reference pandemic hospital of the region and found 14.3% mortality and 25% ICU rates.

In a study conducted in 142 liver transplant patients followed in a transplantation center from Turkey, the authors reported that the incidence of COVID-19 was higher in liver transplant patients than in the general population. However, mortality rates were low. The authors stated that liver transplantation can be continued by following the general precautions during the pandemic period.⁸

In a study of 846 liver transplant patients infected with COVID-19 from Turkey, despite the use of immunosuppressive drugs, the requirement for intensive care and the length of stay in the intensive care unit was found to be low.¹⁰ In the epidemiological study of Canbaz et al.¹¹ in which all solid organ transplant patients were recruited, the mortality rate in organ transplant patients diagnosed with COVID-19 was found to be 7.38%. In a meta-analysis by Kulkarni et al.¹² involving 18 studies with a total of 1522 COVID-19 infected liver transplant recipients, there was no difference in mortality between liver transplant and non-liver transplant recipients up to 1 year post-transplant period.¹² In the perioperative period, the clinical course was not more severe in those who had COVID-19 in the pre-/post-operative period.¹³ Data for morbidity and mortality were also similar in pediatric patients.^{14,15}

In the study of another experienced center in Turkey with 250-300 transplants per year, it was shown that COVID-19 vaccination reduced the risk of mortality by 100 fold.¹⁶ In the study of Moon et al.¹³ it was shown that vaccinations contributed positively to the course of the disease and reduced the need for intensive care and also reduced mortality. In our study, it is noteworthy that the number of hospitalized patients decreased over the years, although it was not statistically significant. We consider that a possible reason for the higher mortality and morbidity in unvaccinated patients in the early stages of COVID-19 is the lack of vaccination.^{16,17} In addition to that, increased experience of healthcare providers about COVID-19, treatment alternatives and different disease

courses in mutated variants might also be other reasons. It is also noteworthy that in our study, death times of the deceased patients were in the first year of the pandemic, in 2020. After this first year group of patients who were not vaccinated, in 2021 and 2022, mortality did not occur and also hospital/ICU hospitalizations decreased.

In a prospective cohort study of 111 patients with liver transplant who were hospitalized for COVID-19 in Spain, the mortality rate was found to be 18%, and this rate was lower than the matched general population.¹⁸ Although it was pointed out in this study that the incidence of COVID-19 was higher in liver transplant patients than in the general population, it is not possible to compare this result, because in our study, only COVID-19 positive patients who needed hospitalization were included. Another remarkable result of our study was that all of the patients who died were in the elderly group. This brings to mind the increasing comorbidities with age. In this context, as Bhoori et al.¹⁹ and Webb et al.²⁰ stated in their studies with liver transplant patients, mortality may increase with the effect of other comorbidities as age progresses. In a study of 16 patients from Turkey, the authors stated that the course of COVID-19 in liver recipients without any underlying disease other than transplantation is similar to that of the healthy population.²¹

Since we did not have detailed information about the comorbidities and drugs used by the patients in our study, it would be inconvenient to make a definite comment on this issue. However, it can be speculated that the fact that only the elderly-not the young-had died in the current study, supports this outcome.

Another important issue in this patient group is the status of immunosuppressive drugs. It is unclear whether immunosuppression is an advantage or a disadvantage in these patients. Some studies offer recommendations for reducing immunosuppression in liver transplant patients.²² However, the short-term results in patients receiving immunosuppression were the same as in the general population, suggesting that immunosuppression might have a protective effect in these patients.²³ Because of these different views, transplant centers need to monitor their own patients and manage their patients according to these results. In our study, current immunosuppressive treatments were continued in all patients without dose reduction or discontinuation. And mortality rates and ICU requirements were similar with general population.

Our study had some limitations. The main one was the low number of patients. Another limitation was that the comorbidity information that could affect mortality rates could not be obtained due to the retrospective design of the study.

CONCLUSION

Mortality rates and ICU requirements of chronically immunosuppressed liver transplant patients with COVID-19 infection were similar with general population. Complete immunosuppression withdrawal should not be urged in this population.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of University of Health Sciences Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (Date: 09.03.2022, Decision No: E-46059653-020).

Informed consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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