Does the severity of SARS-CoV-2 infection higher in liver transplant recipients?: A single-center experience.

Dilara Turan Gökçe[1], Derya Arı[1], Adalet Aypak[2], Osman Aydın[1], Sabite Kaçar[1], Erdal Bostanci[1], and Meral Akdoğan[1]

[1]Ankara City Hospital
[2]University of Health Sciences

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Abstract

Background: Liver transplant (LT) recipients with COVID-19 have been reported as a high-risk population for severe disease through the COVID-19 pandemic. Studies have shown that liver transplantation did not significantly increase the risk of death and severe disease in patients with SARS-CoV-2 infection. Methods: From September 2020- March 2021, we collected data and serum anti-SARS-CoV-2 IgM +IgG results for 91 liver transplant recipients. Study enrolment was performed when patients presented for scheduled routine follow-up. All participants with serum anti-SARS-CoV-2 IgM+IgG completed a questionnaire querying information including clinical symptoms in the last six months. We further collected 91 patients with anti-SARS-CoV-2 IgM + IgG results. Seven patients had a known history of symptomatic COVID-19 during the previous six months. Of the 84 participants included in the study, 21 (25 %) had positive anti-SARS-Cov-2 IgM + IgG results. In addition, we applied the COVID-19 PCR test to all 21 patients, and all of them were negative. Overall, only seven patients declared flu-like upper respiratory tract infection symptoms or diarrhea in detailed inquiry. Conclusion: We documented past SARS-CoV-2 infection in 25 % of our outpatient LT recipients, and the majority were asymptomatic. There was no significant relationship between symptoms and seropositivity for SARS-COV-2.

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Key Words: Liver transplant recipients, SARS-CoV-2 infection, serum anti-SARS-CoV-2 IgM+IgG

What's Known

Immunosuppressed patients are regarded as a high-risk cohort of COVID- 19

It is estimated that COVID-19 will be more symptomatic and severe in LT recipients due to immunosuppression treatments

What's New

Liver transplant recipients can asymptomatic of COVID- 19

Introduction

Coronavirus disease 2019 (COVID-19), caused by a novel coronavirus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is the most common global disease. The high-risk groups of this disease, which has been declared a pandemic by the world health organization (WHO) today, are still not fully determined. Immunosuppressed patients are regarded as a high-risk cohort. In this view, previous experience with similar viruses, such as SARS-CoV and MERS-CoV, suggests that solid organ transplantation (SOT) recipients would be prone to have increased morbidity and mortality. Early published studies in liver transplantation (LT) and SOT recipients with COVİD-19 reported a rate of up to %20 [1], exceeding the rate of the general population [2].

Initial symptoms of patients with COVİD-19 are various, and the percentage of mild illness symptoms seen is about 80% [3]. Patients with SARS-Cov-2 may be completely asymptomatic or progress with severe disease. Comorbidities and advanced age are the most important risk factors among LT recipients and the general population [1]. It is estimated that COVID-19 will be more symptomatic and severe in LT recipients due to immunosuppression treatments. Our study aims to determine the frequency of asymptomatic or mild disease in the LT recipients.

Methods:

For the study, patients who came for routine control between September 2020 and March 2021 in Ankara City Hospital Liver Transplant outpatient clinic were screened. All patients were older than 18 years of age and had undergone LT in the past. The ethics committee approved the study of Ankara Bilkent City Hospital (Approval number: E2-21-280). The study was conducted in accordance with good clinical practice principles and the Declaration of Helsinki.

Study enrolment was performed when patients presented for scheduled routine follow-up. Among all patients, patients whose serum COVID-19 IgM + IgG antibody was tested were recorded. Sars-Cov-2 polymerase chain reaction (PCR) test was performed with a nasopharyngeal-oropharyngeal swab in each patient with a positive antibody test within the first three days the results. All participants completed a questionnaire querying information including common clinical symptoms (fever, cough, diarrhea, myalgia, nausea, and vomiting) in the last six months. Additionally, we questioned all participants for a history of contact with a covid-19 positive patient or hospitalization.

We evaluated the performance of COVID-19 serology testing on chemiluminescent immunoassay (CLIA) per manufacture's protocol (ADVIA Centaur®) SARS-CoV-2 Total (COV2T) (Siemens Healthcare Diagnostics Inc., NY, USA) (Siemens Test). These serological tests use the SARS-CoV-2 Spike protein (S protein) as a viral labeling protein to detect anti-SARS-CoV-2 antibodies. Test results were interpreted as positive if the signal value of the Siemens Test (index) [?]1.0 of total antibodies. All serum Anti-SARS-CoV-2 Total results of all patients were collected before the vaccination for COVİD-19.

The statistical analyses were performed with IBM SPSS Statistics for Windows, Version 26.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as median and range. Categorical variables were summarized as count and percentage. Between-group comparisons were performed using the Mann-Whitney U test for continuous variables and a chi-squared test (or Fisher's exact test where appropriate) for

categorical variables. P values are given as indicated using the x^2 test or a non-parametric t-test. A p-value <0.05 was considered to indicate statistical significance.

Results:

We conducted a retrospective study of 91 LT recipients at an LT center in Ankara City Hospital, with sample collection taking place between September 2020- March 2021. Serum anti-SARS-CoV-2 IgM + IgG results were positive in 32 of 91 patients. Seven (21.8%) of 32 patients included in the study were not included in the analysis because they had a known history of OCVID-19. Three of seven (42.8 %) had self-limited disease, and none required hospitalization or supplemental oxygen treatment for COVİD-19. On the other hand, three of seven (42.8%) needed hospitalization, and one of seven (14.4 %) was already in the hospital when he was diagnosed with COVID-19. Twenty-one patients (21/28, 75%) had no history of SARS-COV-2 infection and specific symptoms. We tested all patients with positive serum antibodies for a naso-oropharyngeal swab PCR test and, the results were negative.

The remaining 84 patients were included in the study (median age 52.1 years [IQR 21-68]; 60 (76.2%) men, 14 (23.8 %) women). Hypertension was the most common comorbid disease (15/84, 17.8 %), followed by type 2 diabetes (10/84, 11.9 %) (Table-1). All participants were contacted and retrospectively surveyed for clinical symptoms of COVID-19 in the prior six months (Table-2). There were no significant differences between patients' symptoms with positive test results (serum Ig G+IgM) and negative test results. While 7 of 28 patients with positive serum antibody test were previously symptomatic patients who were diagnosed, seven patients developed at least one nonspecific symptom, but there was no diagnosis of COVID-19. Fourteen (50%) of a total of 28 patients were followed up completely asymptomatic. All seropositive patients for SARS-Cov-2 were compared with seronegative patients in terms of symptoms. There was no relationship between the findings of the participants' system inquiries and COVID-19 seropositivity (Table-3).

Characteristics of seronegative and seropositive participants were examined. While the mean age of the seropositive participants was 51.5 ± 9.8 years, the mean age of the seronegative group was 52.3 ± 11.5 years (p: 0.378). There was no significant difference between the two groups in terms of gender, body mass index (BMI), aspartate aminotransferase (AST), alanine aminotransferase (ALT) (Table-2).

Covid antibody positivity was observed in four (36.3%) of 11 people with a history of risky contact with people diagnosed with COVID 19. Serum SARS-COV-2 IgM + IgG antibody positivity was detected in six (30%) of 20 patients with a history of hospitalization. There was no significant difference between hospitalization and serum antibody positivity (p:0.554).

Discussion

In our study, patients who applied to our liver transplant outpatient clinic were evaluated in terms of serum SARS-COV-2 Ig M + IgG level and history of COVID-19 disease. The Serum antibody positivity rate was 30.7% in liver transplant patients participating in our study. The seroprevalence values for the region in which we conducted the current study are unknown. However, seropositivity was found to be 12.3% (115/932) in a seroprevalence study conducted on healthcare professionals in Turkey. The seropositivity among previously undiagnosed healthcare workers was calculated as 2.7% [4].

Limited data are available for asymptomatic or subclinical infections in the transmission of the SARS-CoV-2 virus [5]. In our study, the rate of participants with an asymptomatic history of covid-19 was 7.6% (7/91). Seventy-five percent of all antibody-positive patients were not diagnosed with COVID-19, and their inquiries had no specific symptoms of COVID-19. When all participants were evaluated, 23% (21/91) subclinical or asymptomatic seropositivity was detected.

In previous studies, acute and past SARS-COV-2 infections were documented in 3.7% of LT recipients. In the same study, the asymptomatic seropositivity rate was evaluated as 62.5% (5/8) [6]. The rate of asymptomatic COVID-19 in liver transplant recipients has been determined by 6% in the Spain series and 14% in a multinational study (n = 151) [7, 8].

In our study, 66% of patients with seropositive (14/21) were utterly asymptomatic; at least one symptom was observed in seven participants. However, there was no significant difference between the symptoms of both groups.

There was no difference between serum AST and ALT levels in patients with seropositive and seronegative. But we do not know serum AST and ALT values in possible disease processes. Studies have been shown to be a relationship between severe disease and elevated liver enzymes in patients with COVID-19. In infected individuals with SARS-COV-2, increased serum liver enzyme levels had seen approximately 15% [9]. In our clinical data, serum AST or ALT levels were found to be two times or higher in 23% of patients diagnosed with symptomatic covid (n=4/17). Increased liver enzymes are usually reversible. As expected, seropositivity is not associated with alone increased liver enzymes.

Asymptomatic or subclinical COVID-19 participants with seropositivity include the history of risky contact with people diagnosed COVID-19 in 19% and the history of hospitalization in 28%. In contrast to the expected, the higher rate of seropositivity was not associated with contact with risky people or hospitalization.

Our limitation of the study is that patients are evaluated in a wide period of 6 months to determine seroprevalence as serum antibody tests are observed during routine follow-up.

In conclusion, studies related to the course of the disease in liver transplant recipients are increasing gradually. However, the frequency of asymptomatic or subclinical disease is not precise yet. Although the number of patients in our study was low, the seropositivity rate (30.7%) and the rate of asymptomatic (75%) among all the participants were higher than expected. We need large-scale seroprevalence studies to reach more reliable data.

References

1. Becchetti C, Zambelli MF, Pasulo L, et al. COVID-19 in an international European liver transplant recipient cohort. Gut [Internet]. 2020 Oct 1;69(10):1832 LP – 1840. Available from: http://gut.bmj.com/content/69/10/1832.abstract

2. Fishman JA, Grossi PA. Novel Coronavirus-19 (COVID-19) in the immunocompromised transplant recipient: #Flatteningthecurve. Vol. 20, American journal of transplantation: official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2020. p. 1765–7.

3. Oran DP, Topol EJ. Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review. Ann Intern Med. 2020 Sep;173[5]:362–7.

4. Alkurt G, Murt A, Aydın Z, et al. Seroprevalence of coronavirus disease 2019 (COVID-19) among health care workers from three pandemic hospitals of Turkey medRxiv (2020)

5. Weitz JS, Beckett SJ, Coenen AR, et al. Modeling shield immunity to reduce COVID-19 epidemic spread. Nat Med. 2020 Jun;26[6]:849–54.

6. Rauber C, Tiwari-Heckler S, Pfeiffenberger J, et al. SARS-CoV-2 Seroprevalence and Clinical Features of COVID-19 in a German Liver Transplant Recipient Cohort: A Prospective Serosurvey Study. Transplant Proc [Internet]. 2020; Available from: https://www.sciencedirect.com/science/article/pii/S0041134520329043

7. Colmenero J, Rodríguez-Perálvarez M, Salcedo M, et al. Epidemiological pattern, incidence, and outcomes of COVID-19 in liver transplant patients. J Hepatol. 2021 Jan;74[1]:148–55.

8. Webb GJ, Marjot T, Cook JA, et al. Outcomes following SARS-CoV-2 infection in liver transplant recipients: an international registry study. lancet Gastroenterol Hepatol. 2020 Nov;5(11):1008–16.

9. Sultan S, Altayar O, Siddique SM, et al. AGA Institute Rapid Review of the Gastrointestinal and Liver Manifestations of COVID-19, Meta-Analysis of International Data, and Recommendations for the Consultative Management of Patients with COVID-19. Gastroenterology. 2020 Jul;159[1]:320-334.e27.

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