



Evaluation of the Correlation Between the Severeness of Lung Involvement and Fatty Liver Disease in Covid-19

Covid-19'da Akciğer Tutulumu Şiddeti İle Yağlı Karaciğer Hastalığı Arasındaki İlişkilerin Değerlendirilmesi

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Abstract

Aim: The aim of the study is to investigate whether there is a correlation between the severity of pneumonia and fatty liver disease in COVID-19.

Material and Method: In this study chest computed tomography (CT) images of 168 patients who were confirmed to be COVID-19 positive according to nasopharyngeal swab specimens were evaluated. The severity of pneumonia and the presence of hepatic steatosis were evaluated on CT images.

Results: The patients were aged between 26 and 89, and the mean age was 63.6 ± 12.4 years. 101 (60.1%) of the patients were male. Hepatic steatosis was observed in 51 (30.4%) patients. No significant difference between the severity of pneumonia and hepatic steatosis on CT ($p = 0.715$) was found. No significant difference was found in the presence of hepatic steatosis in patients who died because of COVID-19 compared to patients who recovered ($p = 0.938$).

Conclusion: This study revealed that there is no relationship between the severity of COVID-19 pneumonia and hepatic steatosis.

Keywords: COVID-19, chest CT, hepatic steatosis, lung

Öz

Amaç: Çalışmanın amacı, COVID-19'da pnömoni şiddeti ile yağlı karaciğer hastalığı arasında korelasyon olup olmadığını araştırmaktır.

Materyal ve Metot: Bu çalışmada nazofarengeal sürüntü örneklerine göre COVID-19 pozitif olduğu doğrulanan 168 hastanın göğüs bilgisayarlı tomografi (BT) görüntüleri değerlendirildi. BT görüntülerinde pnömoninin şiddeti ve hepatik steatoz varlığı değerlendirildi.

Bulgular: Hastaların yaşları 26 ile 89 arasında olup, yaş ortalaması 63.6 ± 12.4 yıl idi. Hastaların 101'i (%60.1) erkekti. 51 (%30.4) hastada hepatik steatoz gözlemlendi. BT'de pnömoni şiddeti ile hepatik steatoz arasında anlamlı fark saptanmadı ($p = 0.715$). COVID-19 nedeniyle ölen hastalarda hepatik steatoz varlığında iyileşen hastalara göre anlamlı fark saptanmadı ($p = 0.938$).

Sonuç: Bu çalışma, COVID-19 pnömonisinin şiddeti ile hepatik steatoz arasında bir ilişki olmadığını ortaya koymuştur.

Anahtar Kelimeler: COVID-19, göğüs BT, hepatik steatoz, akciğer

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INTRODUCTION

Corona virus disease 2019 (COVID-19), an acute respiratory disease, was first detected in Wuhan, China in December 2019 and then spread throughout China and the world (1). COVID-19 has a wide clinical spectrum from asymptomatic cases to cases resulting in acute severe respiratory failure requiring intensive care (2).

In a study conducted in China, it is found that the average age is 47, the disease is more common in men, and 23.7% of patients have at least one concomitant chronic disease (such as hypertension, diabetes, chronic obstructive pulmonary disease (3). The median incubation period of COVID-19 is 5 to 6 days, symptoms may occur within 2-14 days after contact, and infectiousness may begin 1-2 days before symptoms (4).

Although different COVID-19 symptoms may also be observed: fever, coughing, gastrointestinal diseases, headache, conjunctival hyperemia, nasal congestion, sore throat, increased secretion, sputum, malaise, hemoptysis, nausea vomiting, diarrhea, stomach pain, myalgia, rash, decreasing taste and smelling are among those reported. (3). The correlation between non-alcoholic fatty liver disease (NAFLD) and COVID-19 has been investigated in the limited availability of studies (5). In the post-mortem liver biopsy studies in patients who died from COVID-19, microvesicular steatosis accompanied by over activation of T cells is shown (6).

How liver abnormalities can affect virus infection is still unknown. The genetics, lifestyle, and underlying comorbidities of the person infected with the virus may also be critical in understanding the follow-up process of patients with liver damage. The present study aims to retrospectively evaluate the chest computed tomography (CT) of PCR (+) COVID-19 patients to investigate whether there is a correlation between the severity of pneumonia and fatty liver disease.

MATERIAL METHOD

CT images of 168 patients, who were randomly selected from inpatients with SARS-CoV-2 positive nasopharyngeal sampling, non-contrast thoracic tomography, and with no chronic liver disease hospitalized in Malatya Training Research Hospital in September, October, and November 2020, were evaluated by two radiologists.

The CT scans of the patients were performed using a 16-slice multidetector CT (Philips Medical System, MX). The tube voltage was 110 kV. Two radiologists retrospectively evaluated the CT images through picture archiving and communication systems (PACS). Radiologists were unaware of the clinical findings and prognoses of the patients.

Liver density was measured as Hounsfield unit (HU), excluding vessels and bile ducts as much as possible from the right lobe of the liver to an area of 150 mm² (Fig. 1). If the density of the liver was at least 10 HU lower than the density of the spleen or if the liver density was below

40 HU, it was accepted as hepatic steatosis. CT images were also evaluated for the severity of pneumonia. The lung involvement area was evaluated as stated in the articles of Pan et al (7). Subsequently, the patients were divided into four groups according to the severity of pneumonia as 1-25%, 26-49%, 50-75%, and > 75%.

Intensive care unit (ICU) treatment and mortality evaluated as an indicator of poor prognosis. It was thought that the patients treated in the ICU had a worse prognosis than the patients who did not receive intensive care treatment, and the patients who died compared to the patients who recovered. Whether the patients had comorbid diseases was checked at the information system of the hospital.

Ethical approval was obtained from the Malatya Turgut Özal University Clinical Research Ethics Committee (Approval No. 2021/37).

Strengths and Limitation

In view of the strengths of our meta-analyse, we followed a strict technique and did not change from the pre-study protocol, except for the addition of mortality in our research. First of all, We excluded patients with additional diseases such as a malignant mass in the liver, hydatid cyst, patients with a malignant mass in the lung and those receiving chemotherapy due to other malignant tumoral diseases, and we did not include these patient groups in our study. Secondly, studies in the literature are still limited on this subject. Finally, the studies were retrospective and were conducted in a limited number of patients.

Statistical analysis

IBM SPSS Statistics for Windows 22.0 was used to perform the analysis of the data, and P-values were calculated using the chi-square test and analysis of variants (ANOVA). P < 0.05 value was considered significant.

RESULT

The patients are aged between 26 and 89, and the mean age was found to be 63.6 ± 12.4 years. 101 (60.1%) of the patients were male. 116 (69%) patients were treated in the inpatient treatment unit and 52 (31%) patients in the intensive care unit. 122 (72.6%) patients recovered and were discharged. 108 (64.3%) patients had an accompanying comorbid disease such as diabetes mellitus, hypertension, heart failure. Hepatic steatosis was observed in 51 (30.4%) patients.

The patients were divided into 4 groups according to the severity of pneumonia. The mean age of the groups was similar, and no significant difference was found between the groups in terms of mean age (p = 0.170). Additionally, no difference was found between the groups in terms of comorbid diseases (p = 0.987).

Although the incidence of hepatic steatosis increased in accordance with the percentage of involvement in the groups categorized after their severity of pneumonia, no significant difference was found between the groups in terms of hepatic steatosis (p = 0.715). The frequency of

steatosis according to the lung involvement rate groups is present in Table 1.

The incidence of hepatic steatosis increased with age, and this was statistically significant ($p < 0.001$). There was no significant difference between men and women in terms of hepatic steatosis between those with and without comorbid diseases. The values of p respectively: $p = 0.821$, $p = 0.438$.

Although the rate of hepatic steatosis was slightly higher in patients treated in the ICU compared to those not treated in the ICU, it was not statistically significant ($p = 0.938$). The rate of hepatic steatosis was slightly higher in patients who died due to COVID-19 compared to patients who recovered however it was not statistically significant ($p = 0.697$) (Table 2).

Table 1. Hepatic steatosis incidence rates in groups according to the severity of pneumonia

Lung involvement	HS present n(%)	HS absent n(%)	Total n(%)	P value
1 - 25%	17(25.8)	49(74.2)	66(100)	0.715
26-49%	13(31.0)	29(69.0)	42(100)	
50-75%	10(33.3)	20(66.7)	30(100)	
>75%	11(36.7)	19(63.3)	30(100)	
Total	51(30.4)	117(69.6)	168(100)	

Lung involvement: Percentage of lung involvement according to the severity of pneumonia; HS: Hepatic steatosis; n: number of patients

Table 2. The incidence of hepatic steatosis according to the prognostic characteristics of the patients.

	HS present n(%)	HS absent n(%)	Total n(%)	P value
ICU hospitalization	16(30.8)	36(69.2)	52(100)	0.938
Non-ICU hospitalization	35(30.2)	81(69.8)	116(100)	
Death	15(32.6)	31(67.4)	46(100)	0.697
Recovering	36(29.5)	86(70.5)	122(100)	

HS: Hepatic steatosis; n: number of patients; ICU: Intensive care unit

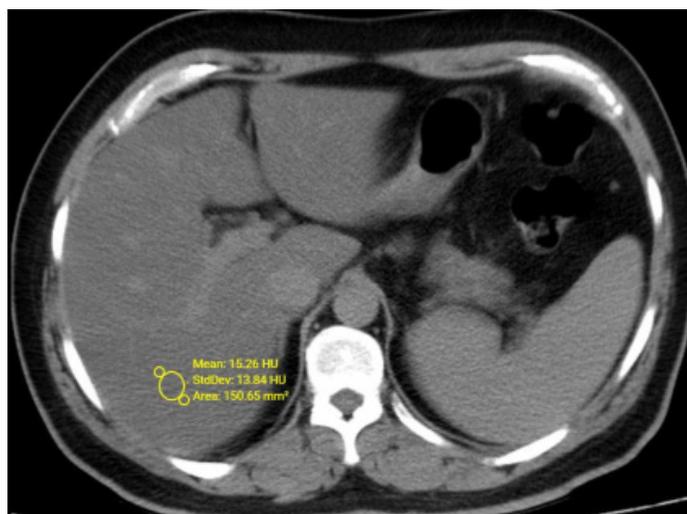


Figure 1. Axial CT image showing measurement of hepatic steatosis in the liver.

DISCUSSION

The pathogenesis of gastrointestinal symptoms and liver injury due to COVID-19 is still investigated. The glycoprotein spikes (S protein) on the outer surface of SARS-CoV-2 bind to the ACE2 (Angiotensin-Converting Enzyme 2) receptor of the host cells, therefore allowing the virus to enter the cell (8). Although ACE2 is not expressed in Kupffer cells, hepatocytes, and the endothelium of liver sinusoids, it has been shown in studies conducted in a culture medium that ACE2 expression is produced in hepatocytes by hypoxia. This situation is thought to indicate the damage to the liver in hypoxia condition occurring in COVID-19 (9). In our study, hepatic steatosis was observed in only 30.8% of the patients treated in the intensive care unit and 30.2% of the inpatients. These results suggest that hepatic steatosis has no effect on disease severity in COVID-19.

Hepatic steatosis is a deposition of fat in hepatocytes. Although the most common cause of hepatic steatosis is

non-alcoholic fatty liver disease, many other causes such as alcoholism, chronic viral hepatitis, drug toxicity, storage diseases, obesity, autoimmune-hereditary diseases, and malnutrition may lead to fatty liver (10).

It has been reported in studies that COVID-19 infection is more common in individuals with chronic diseases, and it has a more severe course. In a study published in Wuhan in January 2020, it was found that about half of the patients have at least one chronic disease (11). Comorbidities such as hypertension, diabetes, asthma, chronic obstructive pulmonary disease and cardiovascular diseases are also more common among severe COVID-19 patients (12). In this study, similar to other studies, the rate of comorbid diseases was high, and it was found to be 64.3%.

It is thought that a proinflammatory response to viral infection may increase in obesity due to weak immune system activity. In a study, it has been asserted that in the case of hepatic steatosis in the liver, it increases inflammation and may cause liver damage (13). However, in our study, there was no statistically significant difference in the rate of hepatic steatosis among the patients who were treated in the intensive care unit and the service and died. We think that it would not be valid to associate the issue that hepatic steatosis causes an increase in inflammation and worsen the patient's condition only with hepatic steatosis.

In a liver autopsy study in the literature, steatosis was observed in 8 of 14 patients, and it is thought that the observed fatty liver disease may be associated with metabolic diseases, and it has been suggested that there is not enough evidence to support the correlation between COVID-19 infection and the development of fatty liver disease (14). In a study, it was found that liver enzymes were abnormally high in COVID-19 patients. It has been reported that the reason for this may be due to systemic inflammation caused by the virus (15). In a study on how COVID-19 disease can affect the liver in patients with and without liver disease, it has been shown that pre-existing liver disease has little effect on getting COVID-19 infection (16). As stated in the previous studies, the fact that hepatic steatosis in COVID-19 disease was not found to be a significant difference in deceased intensive care and deceased service patients in our study, suggests that it should not be seen as a risk factor alone.

It was found that the presence of fatty liver disease in hospitalized patients who were COVID-19 positive, was not associated with adverse outcomes, and there was no difference in mortality classified by age, and fatty liver was observed in significantly young patients at admission (17). On the contrary, in our study, we found that the incidence of hepatic steatosis increases as age increase. It is thought that this is due to genetic and cultural differences. In our study, no significant difference was found between the groups in terms of hepatic steatosis. It would not be accurate to say that hepatic steatosis increases the severity of pneumonia. For this reason, we think that the presence of hepatic steatosis alone cannot

constitute a risk factor in terms of the course of the disease.

CONCLUSION

It would not be accurate to claim the hepatic steatosis the only risk factor in COVID-19 disease and that it worsens the course of the disease. We think that knowing all the comorbid factors that worsen the course of the disease will provide better control over the disease and the treatment should be administered accordingly.

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Conflict of Interest: The authors declare that they have no competing interest.

Ethical approval: Ethical approval was obtained from the Malatya Turgut Özal University Clinical Research Ethics Committee (Approval No. 2021/37).

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