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Prevalence of liver involvement in COVID-19 patients; a multicenter study

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Abstract

Liver consequences of a SARS-CoV-2 infection are now considered to be part of it. The present study was a descriptive epidemiological multicenter study conducted on 242 patients with COVID-19. All examined patients were examined for clinical symptoms, underlying diseases and outcomes, laboratory findings such as LFT and troponin were reviewed in all patients, and finally, all patient information was recorded.209 patients were male. In the present study, underlying diseases such as HTN, DM, and cardiac disease were found to have a significant association with the outcomes and outcomes of patients with COVID-19 infection. Mortality rate in patients with above-mentioned underlying diseases was significantly higher than in other patients ($P \leq 0.05$). BUN, Cr, CPK and LDH had a significant association with the prognosis and outcomes of patients with COVID-19. However, there was no significant association between liver function markers and patients' prognosis ($P>0.05$).The results of the present study showed that liver function markers had no impact on preventing the sequelae and mortality of COVID-19 patients. However, inflammatory and tissue damage markers such as LDH, CPK and renal function markers were significantly associated with the mortality rate in patients with COVID-19 infection admitted to intensive care units.

Keywords:COVID-19, outbreak, liver involvement, SARS-CoV-2

Introduction

The family of coronaviruses presents a significant global health threat, capable of causing respiratory and multi-system diseases in a large number of individuals. The causative agent of the coronavirus disease (COVID-19), known as SARS-CoV-2, is a novel coronavirus that was identified in 2019 (1-4). There are four main subgroups of coronaviruses: alpha, beta, gamma, and delta, with SARS-CoV-2 falling under the beta subtype. This virus shares similarities with other zoonotic viruses such as SARS-CoV-1 and MERS-CoV (5-7). COVID-19, caused by SARS-CoV-2, has become a major public health crisis worldwide. Coronaviruses are enveloped single-stranded RNA viruses that can infect humans, as well as other mammals and birds, leading to respiratory or enteric illnesses. Severe cases of COVID-19 can result in multi-organ failure and lead to respiratory, intestinal, liver, and nervous system complications, often with a high mortality rate (8-13).

Computed tomography (CT) shows the characteristic opacity of the lung vitreous even in asymptomatic patients. Because ACE2 is highly expressed on the apical side of lung epithelial cells in the alveolar space, it is likely that the virus can penetrate and destroy them, consistent with the fact that primary lung damage often occurs in the distal airway (14, 15). Epithelial cells, alveolar macrophages, and dendritic cells (DCs) are the three major components of respiratory innate immunity (16). DCs lie beneath the epithelial cell layer. Macrophages are located on the apical side of the epithelium. DCs and macrophages act as cells of the innate immune system to fight viruses until adaptive immunity occurs. Increasing evidence suggests that immune patterns are closely related to disease progression in patients infected with the virus. This report shows that rapid decline in peripheral T cell subsets is a unique feature in patients with SARS during acute infection (17-20). Six types of coronaviruses cause illness in humans. Four viruses 229E, OC43, NL63 and HKU1 are common and usually cause cold symptoms in immunocompromised people (21, 22). The acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in the city of Wuhan, Hubei Province in central China and was responsible for the coronavirus disease 2019 (COVID-19) in December 2019. 20 million patients with COVID-19 have been diagnosed and infected with more than 700,000 deaths (23, 24).

At this time, there is no single treatment that is fully successful in treating SARS-CoV-2 infection. However, commonly used drugs include antiviral agents, anti-inflammatory agents, low molecular weight heparins, plasma, and hyperimmuneimmunoglobulins. Antiviral agents may help prevent disease progression in the early stages of infection, while a combination of immunomodulatory and antiviral drugs seems to improve clinical outcomes for patients with severe cases of COVID-19.

Materials and Methods:

The present study was a descriptive epidemiological study conducted in 2020 on patients with COVID-19 infection in Zabol, Iran. The study population included all patients hospitalized in the ICU of Amir Al MomeninZabol Hospital and Shariati and Rajaei Karaj Hospitals and admitted to the ICU of the above-mentioned hospitals with a clinical and

laboratory diagnosis of COVID-19. Inclusion criteria included infection with COVID-19 by PCR test and hospitalization in the intensive care unit. Patients with a history of various liver diseases or incomplete medical records were excluded from the study. The present study was approved by the Ethics Committee of the Faculty of Medicine, Zabul Medical University after obtaining the required code of ethics.

Statistical issues

All examined patients were examined for clinical symptoms, underlying diseases and outcomes, laboratory findings such as LFT and troponin were reviewed in all patients, and finally, all patient information was recorded. After collecting the data, the data is displayed in the form of frequency. Percent; The mean and standard deviation were analyzed using SPSS 22 software. Chi-square tests and Fisher exact tests were used to determine the relationship. A significance level of 0.05 was considered.

Results

According to Table 1, there was a significant relationship between HTN and DM, cardiac illness, and patient outcome; as a result, 24.8% of the patients who passed away had underlying HTN disease (p=0.000). Furthermore, 10.45% of patients who passed away had cardiac disease (p=0.002), and 18.95% of patients with diabetes eventually died (p=0.031). Furthermore, there was no positive troponin in any of the patients who eventually recovered from COVID-19, indicating a significant relationship between positive troponin and the mortality rate of these patients (p=0.008). Nevertheless, there was no statistically significant relationship found between the study patients' outcomes with COVID-19 infection and the incidence of cancer (p=0.123). The average liver enzymes (AST and ALT) in the patients who recovered and eventually passed away are shown quantitatively in Table 2 as 77.53±82.54, 67.66±71.69, and 118.94±75.14, 145.55±93.54, respectively. ESR levels were significantly higher in the patients who ultimately passed away than in the recovered patients, and this difference was statistically significant (p=0.001). The average CRP enzyme in patients who eventually died and recovered was 119.80±76.32 and 111.14±72.87, respectively (P=0.326). LDH levels were significantly higher in the patients who ultimately passed away than in the recovered patients, and this difference was statistically significant (p=0.007). In patients who eventually passed away and recovered, the average CPK enzyme was 311.38±297.90 and 338.26±254.92, respectively.

Table 1: Comparison of outcomes according to past medical history of the patients

Variable		Outcome		P value
		Recovery	Death	
DM	Yes	44(29.93%)	29(18.95%)	0.031
	No	103(70.06%)	124(81.04)	
HTN	Yes	72(48.97%)	37(24.18%)	<0.001
	No	75(51.02%)	116(75.81%)	
Cardiac Disease	Yes	35(23.80%)	16(10.45%)	0.002
	No	112(76.19)	137(89.54%)	
Cancer	Yes	0(0%)	4(0.026%)	0.123
	No	147(100%)	149(97.38%)	
Troponin	Yes	0(0%)	8(5.36%)	0.008
	No	131(100%)	141(94.63%)	

Table 2: Comparison of outcomes according to paraclinical results of the patients

Variable	Outcome		P value
	Recovery	Death	
AST	71.69±67.66	82.54±77.53	0.229
ALT	93.54±145.55	75.14±118.94	0.265
ESR	49.07±30.29	64.26±47.63	0.001
CRP	111.14±72.87	119.80±76.32	0.326
LDH	581.19±297.51	675.23±264.69	0.007
CPK	254.92±338.26	297.90±311.38	0.294
BUN	20.68±12.03	36.57±29.20	<0.001
Cr	1.26±0.34	1.72±1.34	<0.001

Discussion

Hepatic consequences of SARS-CoV-2 infection are now considered part of the complications of this disease, but the clinical effects of direct viral infection on liver cell types are not yet clear. Underlying medical conditions play an important role in the outcome, disease severity and high mortality rate of COVID-19 cases. Patients with high blood pressure, cardiovascular disease, and diabetes should be closely monitored and familiarized with health protocols (25). Because liver involvement plays an important role in patient outcomes (26), the aim of this study is to determine the frequency of liver involvement in patients with COVID-19 infection and its association with patient outcomes. In the present study, it was found that underlying diseases such as HTN, DM and cardiac diseases had a significant association with the outcomes and outcomes of patients with

COVID-19 infection, so the incidence of mortality was significantly higher in patients with the above-mentioned underlying diseases than in other patients. These findings were consistent with the results of the study by Mahamid et al., this study also found that underlying diseases such as HTN, obesity and metabolic syndrome had a significant association with the mortality rate of patients with COVID-19. 19 infections. Therefore, people with underlying medical conditions have been recommended to take more serious preventive measures (27). SARS-CoV-2 infection is often associated with varying degrees of liver function test abnormalities, especially transaminases, which are usually transient and mild (3).

As Sharma et al. showed, acute liver injury and liver dysfunction, particularly elevated AST and ALT levels, are not only common in COVID-19 but also associated with poor outcomes. Therefore, the cause of liver injury should be carefully monitored during this infection, as it may help with early triage, careful monitoring of the occurrence of liver injury, and careful use of medications (28). Despite all this, the results of the present study suggest that liver function tests did not influence the outcomes of patients admitted to the intensive care unit. Consistent with the results of the present study, Singh et al. showed by evaluating patients with COVID-19 hospitalized in the intensive care unit that the increased risk of infection with COVID-19, hospitalization in intensive care units and ultimately mortality is not related to liver function tests. However, many studies have shown that the most common liver function abnormality was hypoalbuminemia, followed by gamma-glutamyltransferase and aminotransferase disorders, and these abnormalities were more common in severe disease (29). As Tellez et al. showed the presence of MAFLD or NAFLD was associated with more severe COVID-19 disease. Metabolic disorders can also have a more negative impact on the course of COVID-19. Accordingly, healthcare providers should closely follow patients with liver disease and take preventive measures in these high-risk populations. Therefore, weight loss and regular physical activity should be a priority in Nonalcoholic fatty liver disease (NAFLD) patients (30). These findings were inconsistent with the results of the present study. The reasons for the difference are the sample size of the two studies and the use of effective drugs in treating patients' liver function. However, the results of the present study showed that renal function tests including BUN and Cr and tissue damage markers including CPK and LDH had a significant association with the prognosis and outcomes of patients with COVID-19 and were able to predict the mortality rate of patients up to one certain point. Cheng y et al. also found that the prevalence of kidney disease was high in patients with COVID-19 admitted to a hospital in Wuhan, China. Thus, kidney disease during admission and AKI during hospitalization were associated with an increased risk of in-hospital death (31). Taking into account that at the time this article was published, the world was experiencing the most significant medical epidemic in history (COVID-19), which had an impact on every bodily and psychological aspect of a person, including the kidneys, liver, lungs, and blood system, etc. due to the potential for drug interactions with COVID-19, it is advised to check before taking hepatotoxic medications (32-39).

Conclusion

The results of the present study showed that liver function markers had no impact on the prevention of the sequelae and mortality of COVID-19 patients. However, inflammatory markers and tissue damage such as LDH, CPK and renal function markers were significantly associated with mortality in COVID-19 patients admitted to intensive care units.

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