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Clinical characteristics and outcomes of patients with severe COVID-19 and cirrhosis or liver transplant in a Brazilian quaternary center

Tulio L **CORREA**, Mariana Sandoval Terra Campos **GUELLI** and Ricardo Tavares de **CARVALHO***

* Faculdade de Medicina, Universidade de São Paulo, Hospital das Clínicas, Equipe de Cuidados Paliativos, São Paulo, SP, Brasil.

HIGHLIGHTS

- Specific associations between liver cirrhosis and liver transplant with poorer outcomes in COVID-19 are still not clear.
- We aimed to evaluate the clinical characteristics and outcomes of patients with COVID-19 and cirrhosis or liver transplant.
- Patients with liver cirrhosis had more endotracheal intubation and a higher risk of death than liver transplant recipients.
- Patients with higher MELD- Na scores had increased death rates and lower survival probability and survival time.

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Corresponding author: Tulio Loyola Correa.
E-mail: tulio.correa@ufpel.edu.br

ABSTRACT – Background – Specific associations between liver cirrhosis and liver transplant with poorer outcomes in COVID-19 are still not completely clear. **Objective –** We aimed to evaluate the clinical characteristics and outcomes of patients with severe COVID-19 and cirrhosis or liver transplant in Sao Paulo, Brazil. **Methods –** A retrospective observational study was conducted in a quaternary hospital. Patients with COVID-19 and liver cirrhosis or liver transplant were selected. The clinical and demographic characteristics, as well as the outcomes, were assessed using electronic records. **Results –** A total of 46 patients with COVID-19 and liver condition were included in the study. Patients with liver cirrhosis had significantly more endotracheal intubation and a higher relative risk of death than liver transplant recipients. Patients with higher MELD-Na scores had increased death rates and lower survival probability and survival time. **Conclusion –** Patients with liver cirrhosis, especially those with higher MELD-Na scores, had poorer outcomes in COVID-19. Liver transplant recipients do not seem to be linked to poorer COVID-19 outcomes.

Keywords – COVID-19; pandemics; liver cirrhosis; liver transplantation; outcome research.

INTRODUCTION

On March 11, 2020, three months after the discovery of the new coronavirus (SARS-CoV-2) in Wuhan (China), the World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) a pandemic[1,2]. Brazil had its first case reported in February 2020. In April 2023, facing a national scenario with more than 37 million confirmed cases and 700,000 deaths, the country is still largely affected by the disease[3]. Considering its high transmissibility and the increase in hospital admissions, health systems face the risk of being overloaded, without sufficient resources to care for everyone who needs them, especially in low- and middle-income countries[4].

Most patients with COVID-19 are asymptomatic or present with mild symptoms, such as fever, malaise, dry cough, sore throat, and changes in taste and/or smell[5]. However, COVID-19 can also involve the lower respiratory tract and progress to acute respiratory distress syndrome (ARDS) in about 20% of the patients[6]. Therefore, among hospitalized patients, about 40% require intensive care unit (ICU) admission and 23% need invasive mechanical ventilation[7]. The severe presentation of COVID-19 is highest among older patients with comorbidities and can be life-threatening[8]. Patients with chronic diseases such as malignancies, cardiopathy, and neuropathy, as well as immunosuppression and comorbidities are at greater risk of severe symptoms and mortality related to COVID-19[9].

The systemic effects of COVID-19 can range to the liver, causing liver damage and transaminases elevation[10]. The entry of SARS-CoV-2 inside the hepatocytes is mediated by angiotensin-converting enzyme (ACE-2) receptors present on liver cells[9]. The possible mechanisms of liver injury in COVID-19 include immune-mediated damage, direct cytotoxicity, drug-induced liver injury, reactivation of pre-existing liver disease, mitochondrial dysfunction, and hypoxic/ischemic hepatitis[10]. However, the association between liver conditions, especially cirrhosis and liver transplant, and poor outcomes in COVID-19 is still not completely clear[11].

Therefore, this study aimed to evaluate the clinical characteristics and outcomes of patients with severe COVID-19 and cirrhosis or liver transplant in a quaternary hospital in Sao Paulo, Brazil.

METHODS

A retrospective observational study was conducted at *Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo* (HCFMUSP) following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[12]. The HCFMUSP is a major quaternary hospital center composed of many health institutes. The Central Institute of HCFMUSP received COVID-19 patients from the other health institutes during the viral pandemic. The population of this study was composed of hospitalized adult patients (≥18 years) diagnosed with severe COVID-19 by reverse transcription polymerase chain reaction (RT-PCR) from March 2020 to November 2020.

The clinical and demographic characteristics, as well as the outcomes, were assessed using electronic records. Chronic diseases and comorbidities were searched by the International Classification of Diseases (ICD-11) codes using medical records[13]. To evaluate mortality after hospital discharge, the patients and their families were reached out in October 2022 by the phone numbers provided at hospital admission.

PALI-COVID groups

A palliative care protocol (PALI-COVID) was created by the HCFMUSP palliative care team to assist patients during the COVID-19 pandemic[14]. The PALI-COVID protocol was proven to be effective in identifying patients who had a higher risk of death and needed palliative care (PC) support[15].

Patients were screened for PC needs using The Supportive and Palliative Care Indicators Tool (SPICT-BR) to identify patients with a terminal underlying medical condition[16]. A clinical prediction model was also used to identify patients with a high risk of death: COPD ≥ three decompensations in six months; heart failure ≥ three decompensations in six months or use of inotropic agents; metastatic cancer with Karnofsky Performance Status (KPS) Scale ≤40%; dementia with Clinical Dementia Rating of 3 and/or frequent infections/hospitalizations; stroke sequelae and degenerative syndromes with low functionality and/or frequent hospitalizations.

Using these two criteria, patients were classified into three groups: red group (RG), yellow group

(YG), and green group (GG). Patients in the RG did not meet the SPICT criteria for an underlying disease or the high risk of death criteria. Patients in the YG met the SPICT criteria but did not meet the high risk of death criteria. Patients in the GG met both the SPICT criteria and the high risk of death criteria, indicating PC referral.

MELD-Na Scores

The Model for End-Stage Liver Disease sodium (MELD-Na) score was calculated only for patients with cirrhosis, as the MELD score does not predict patient survival in living donor liver transplant recipients[17].

The MELD-Na score was calculated using the online calculator provided by the Organ Procurement and Transplantation Network (https://optn.transplant.hrsa.gov/resources/allocation-calculators/meld-calculator/). Levels of serum creatinine, bilirubin, international normalized ratio (INR), and serum sodium were measured at the time of hospital admission. If the patient had been dialyzed twice within a week before the serum creatinine test, the value for serum creatinine was considered 4.0 mg/dL[18]. MELD-Na scores were categorized into three groups: group one was for patients with scores from 1–10, group two had scores from 11–20, and group three from 21–40.

Statistical analyzes

Data were projected to an Excel 16.0 spreadsheet by two researchers. Later, the spreadsheet was reviewed by one other researcher in search of inconsistencies. Statistical analyses involving qualitative variables were performed using Fisher's exact test. To estimate the relative risk (RR), the Poisson regression model with robust variance was used[19]. To relate survival time with the variables of interest, the Cox proportional hazards model was proposed. The statistical analyses were performed using SAS 9.4 statistical software, and $P \leq 0.05$ was considered statistically significant. The presented graphs were elaborated using the R programming language for statistical computing and graphics.

Ethical approval

All methods were conducted under the ethical standards of the Declaration of Helsinki. The project was approved by the Research Ethics Committee of the *Hospital das Clinicas*, Faculty of Medicine, University of São Paulo (CEP/HCFMUSP) under number 31385420.6.0000.0068.

RESULTS

A total of 3309 patients were included in the study, of which 28 (0.85%) had liver cirrhosis, and 18 (0.54%) were liver transplant recipients (LTRs). TABLE 1 presents the demographic and clinical characteristics of the patients. The median age was 61 years old; most patients were males (55.7%) and were admitted to an ICU (46.4%). Patients with liver conditions (cirrhosis or liver transplant) had significantly less hypertension (P=0.04) and dyslipidemia (P=0.02). They also met SPICT criteria in a higher proportion and were less assigned to the RG. However, they had similar mortality rates to patients without known liver conditions.

TABLE 2 compares the clinical and demographic characteristics and outcomes of patients with liver cirrhosis to those of LTRs. While 16 (57.1%) patients with cirrhosis died, only 2 (11.1%) LTRs died. Patients with liver cirrhosis had significantly more endotracheal intubation (P<0.01) and a higher relative risk of death than LTRs.

TABLE 3 compares the clinical characteristics and outcomes of patients with liver cirrhosis based on the MELD-Na scores. Patients with higher MELD-Na scores had increased death rates (P<0.01). They also met SPICT criteria and were intubated and assigned to the GG in higher degrees.

TABLE 4 analyzes in-hospital survival based on the clinical characteristics of the patients. The MELD-Na score was a predictor of lower survival probability and survival time (FIGURE 1). GG patients also died faster and had lower survival probabilities in 7 and 14 days than patients in the RG (FIGURE 1).

Of the 28 patients with liver conditions discharged from the hospital, we had contact with 20, of which three had died. For the patients with liver conditions, the post-discharge mean (95%CI) survival time was 17.95 (16.02–19.88) days. The survival probability was 0.95 (0.85–1.00) in 7 days and 0.9 (0.77–1.00) in 14 days.

TABLE 1. Clinical and demographic characteristics of the patients admitted to the HCFMUSP with COVID-19 stratified by the presence of liver conditions.

Characteristics	Liver condition		Total	*P* value
	No	Yes		
	(n=3263)	(n=46)	(n=3309)	
Gender				0.19
Female	1451 (44.5)	16 (34.8)	1467 (44.3)	
Male	1812 (55.5)	30 (65.2)	1842 (55.7)	
Median age [IQR]	61 [48–71]	61 [48–66]	61 [48–71]	
Age (years old)				
<20	47 (1.4)	2 (4.3)	49 (1.5)	
20–59	1463 (44.8)	18 (39.1)	1481 (44.8)	
60–79	1423 (43.6)	26 (56.5)	1449 (43.8)	
80–89	281 (8.6)	0 (0)	281 (8.5)	
≥90	49 (1.5)	0 (0)	49 (1.5)	
Elderly (≥60) (yes)	1753 (53.7)	26 (56.5)	1779 (53.8)	0.71
Admission				0.13
Wards	845 (25.9)	16 (34.8)	861 (26.0)	
Emergency	895 (27.4)	15 (32.6)	910 (27.5)	
ICU	1521 (46.6)	15 (32.6)	1536 (46.4)	
PC unit (yes)	129 (4.0)	0 (0)	129 (3.9)	0.17
Comorbidities (yes)				
Hypertension	1592 (48.8)	15 (32.6)	1607 (48.6)	**0.04**
Diabetes mellitus	1029 (31.5)	13 (28.3)	1042 (31.5)	0.75
Dyslipidemia	640 (19.6)	3 (6.5)	643 (19.4)	**0.02**
Admitted from				
Home	392 (12.0)	7 (15.2)	399 (12.1)	
Secondary care	936 (28.7)	7 (15.2)	943 (28.5)	
PC clinic	22 (0.7)	3 (6.5)	25 (0.8)	
InCor	269 (8.2)	9 (19.6)	278 (8.4)	
ICESP	295 (9.0)	1 (2.2)	296 (8.9)	
Other HCFMUSP institutes	69 (2.1)	4 (8.7)	73 (2.2)	
Other tertiary center	730 (22.4)	9 (19.6)	739 (22.3)	
Field hospitals	496 (15.2)	4 (8.7)	500 (15.1)	
Missing	54 (1.7)	2 (4.3)	56 (1.7)	
SPICT criteria (yes)	857 (26.3)	19 (41.3)	876 (26.5)	**0.02**
Risk of death (yes)	317 (9.7)	6 (13.0)	323 (9.8)	0.45
PALI-COVID group	(n=2815)	(n=38)	(n=2853)	**0.03**
Red	1987 (70.6)	20 (52.6)	2007 (70.3)	
Yellow	571 (20.3)	14 (36.8)	585 (20.5)	
Green	257 (9.1)	4 (10.5)	261 (9.1)	
Assisted by the PC team (yes)	278 (8.5)	1 (2.2)	279 (8.4)	0.12
Death (Yes)	1106 (33.9)	18 (39.1)	1124 (34.0)	0.44
Relative risk of death (95%CI)	1	1.15 (0.8–1.66)		0.44

IQR: interquartile range; PC: palliative care; InCor: Heart Institute of the HCFMUSP; ICESP: Institute of Cancer of Sao Paulo; CI: confidence interval.

TABLE 2. Clinical and demographic characteristics of the COVID-19 patients admitted to the HCFMUSP with liver conditions stratified by liver transplant and cirrhosis.

Characteristics	Liver transplant (n=18)	Cirrhosis (n=28)	Total (n=46)	*P* value
Gender				0.23
Female	4 (22.2)	11 (39.3)	15 (32.6)	
Male	14 (77.8)	17 (60.7)	31 (67.4)	
Median age [IQR]	61 [43–66]	61 [49–65]	61 [48–66]	
Admission				0.07
Wards	10 (55.6)	6 (21.4)	16 (34.8)	
Emergency	4 (22.2)	11 (39.3)	15 (32.6)	
ICU	4 (22.2)	11 (39.3)	15 (32.6)	
Comorbidities (yes)				
Hypertension	6 (33.3)	9 (32.1)	15 (32.6)	0.99
Diabetes mellitus	5 (27.8)	8 (28.6)	13 (28.3)	0.99
Dyslipidemia	2 (11.1)	1 (3.57)	3 (6.52)	0.55
SPICT criteria (yes)	6 (33.3)	13 (46.4)	19 (41.3)	0.38
Risk of death (yes)	2 (11.1)	4 (14.3)	6 (13)	0.76
PALI-COVID group (n=38)				0.99
Red	8 (57.1)	12 (50.0)	20 (52.6)	
Yellow	5 (35.7)	9 (37.5)	14 (36.8)	
Green	1 (7.14)	3 (12.5)	4 (10.5)	
Endotracheal intubation (yes)	3 (16.7)	17 (60.7)	20 (43.5)	**<0.01**
Death (yes)	2 (11.1)	16 (57.1)	18 (39.1)	**<0.01**
Relative risk of death (95%CI)	1	5.14 (1.34–19.75)		**0.02**

IQR: interquartile range; SPICT: Supportive and Palliative Care Indicators Tool; PALI-COVID: palliative care in COVID-19 protocol; CI: confidence interval.

TABLE 3. Clinical and demographic characteristics of the COVID-19 patients admitted to the HCFMUSP with liver cirrhosis stratified by MELD-Na score groups.

Characteristics	MELD-Na score group			Total	*P* value
	1	2	3		
	(n=8)	(n=8)	(n=12)	(n=28)	
Gender					0.53
Female	3 (37.5)	2 (25)	6 (50)	11 (39.3)	
Male	5 (62.5)	6 (75)	6 (50)	17 (60.7)	
Median age [IQR]	61 [55–66]	61 [42–60]	61 [56–66]	61 [49–65]	
Admission					0.74
Wards	2 (25)	1 (12.5)	3 (25)	6 (21.4)	
Emergency	4 (50)	4 (50)	3 (25)	11 (39.3)	
ICU	2 (25)	3 (37.5)	6 (50)	11 (39.3)	
Comorbidities (Yes)					
Hypertension	3 (37.5)	3 (37.5)	3 (25)	9 (32.1)	0.78
Diabetes mellitus	3 (37.5)	2 (25)	3 (25)	8 (28.6)	0.88
Dyslipidemia	1 (12.5)	0 (0)	0 (0)	1 (3.57)	0.57
SPICT criteria (Yes)	0 (0)	5 (62.5)	8 (66.7)	13 (46.4)	**<0.01**
Risk of death (Yes)	0 (0)	1 (12.5)	3 (25)	4 (14.3)	0.29
PALI-COVID group (n=24)					**0.03**
Red	6 (100)	3 (42.9)	3 (27.3)	12 (50)	
Yellow	0 (0)	4 (57.1)	5 (45.5)	9 (37.5)	
Green	0 (0)	0 (0)	3 (27.3)	3 (12.5)	
Endotracheal intubation (yes)	1 (12.5)	6 (75)	10 (83.3)	17 (60.7)	**<0.01**
Death (yes)	0 (0)	6 (75)	10 (83.3)	16 (57.1)	**<0.01**

IQR: interquartile range; SPICT: Supportive and Palliative Care Indicators Tool; PALI-COVID: palliative care in COVID-19 protocol.

TABLE 4. In-hospital survival analyses based on the clinical characteristics of the COVID-19 patients admitted to the HCFMUSP.

Characteristics	Total	Deaths	Survival time in days (95%CI)		Survival probability (95%CI)				*P* value*	HR (95%CI)	*P* value
			mean	median	7 days	14 days	30 days	60 days			
Liver condition											
No	3263	1106	45.1 (42.1–48)	29 (27–32)	0.9 (0.89–0.91)	0.75 (0.73–0.77)	0.48 (0.45–0.51)	0.29 (0.25–0.33)	0.11	1.46 (0.91–2.37)	0.12
Yes	46	18	22.5 (16.8–28.1)	17 (16–31)	0.83 (0.7–0.95)	0.75 (0.6–0.9)	0.34 (0.11–0.57)	0.13 (0.0–0.33)			
Type of liver condition											
Transplantation	18	2	NA	NA	NA	NA	NA	NA			
Cirrhosis	28	16	21.2 (14.9–27.5)	17 (9–31)	0.75 (0.58–0.92)	0.65 (0.45–0.85)	0.33 (0.1–0.56)	0.12 (0.0–0.33)	0.3	2.17 (0.47–9.96)	0.32
MELD-Na score group											
1	8	0	NA	NA	NA	NA	NA	NA			
2	8	6	25.7 (12.7–38.7)	31 (2-NA)	0.71 (0.38–1.00)	0.71 (0.38–1.00)	0.57 (0.21–0.94)	0.21 (0–0.56)	**<0.01**	NA	NA
3	12	10	12.4 (7.9–16.9)	11 (6–17)	0.64 (0.35–0.92)	0.42 (0.12–0.73)	NA	NA			
PALI-COVID group											
Red	20	5	31.5 (22.3–40.7)	41 (16–41)	0.89 (0.75–1.03)	0.82 (0.63–1.01)	0.68 (0.39–0.97)	NA		1	
Yellow	14	8	17.9 (11.9–24)	17 (11–31)	0.85 (0.66–1.04)	0.76 (0.51–1)	0.25 (0.0–0.55)	0.13 (0.0–0.36)	0.1	2.08 (0.68–6.41) 3.94 (1.03–15)	0.2 **0.04**
Green	4	4	13.8 (4.6–22.9)	11.5 (6–26)	0.5 (0.01–0.99)	0.5 (0.01–0.99)	NA	NA			

CI: confidence interval; HR: hazard ratio; NA: not applicable. * Logrank test.

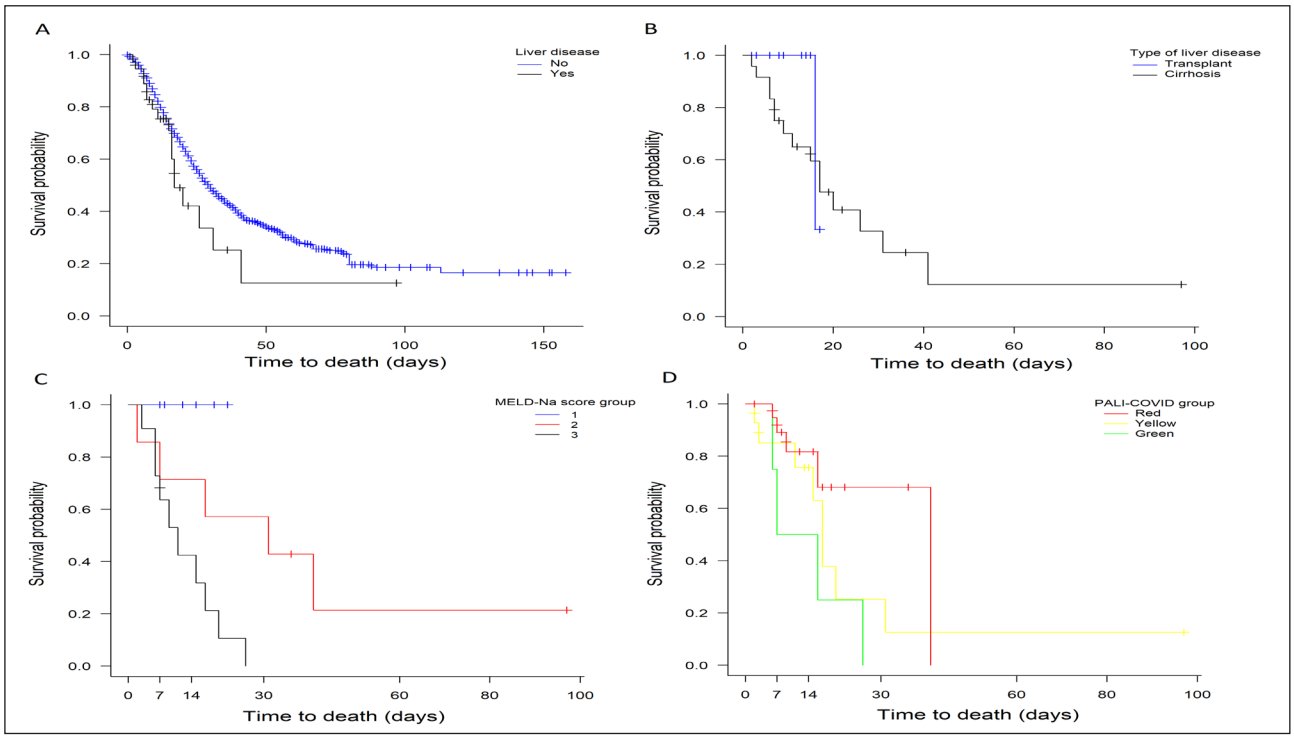

FIGURE 1. A) Survival probability of the patients admitted to the HCFMUSP with COVID-19 stratified by the presence of liver condition. B) Survival probability of the patients with liver conditions stratified by the presence of liver transplant or cirrhosis. C) Survival probability of the patients with liver cirrhosis stratified by the MELD-Na score groups. D) Survival probability of the patients with liver conditions stratified by the PALI-COVID groups.

DISCUSSION

In our study, patients with liver conditions had significantly less hypertension and dyslipidemia. This can be explained by the arterial vasodilatation and hyperdynamic circulatory state in patients with cirrhosis. The portosystemic shunting leads to redistribution of the blood volume with an increase in circulating vasodilators such as nitric oxide, arachidonic acid metabolites, and calcitonin gene-related peptides[20]. However, LTRs can still have increased blood pressure with suppressed circadian blood pressure variability[21]. In addition, cellular and plasma lipid homeostasis is impaired in a cirrhotic liver. The decrease in lipoprotein synthesis and degradation of lipoprotein complex can lower the levels of plasma cholesterol and lipoproteins in patients with cirrhosis[22].

Patients with liver conditions did not have a significantly higher number of deaths compared to patients without liver conditions. This can be explained by the other prevalent morbidities carried by the patients without liver conditions to a higher degree in our study, such as hypertension and dyslipidemia. There were also other comorbidities not considered in this study that may have played a role in the worse outcomes of patients without liver conditions. In previous analyses by our research group on the same population, patients with cardiovascular diseases, cancer, and/or dementia also had very high death rates[23-25].

The post-discharge survival probability for patients with liver conditions in our study was similar to that of the general population with COVID-19, in which 10.3% dies after recovery, being 5.4% within the first 14 days after hospital discharge[26].

However, patients with cirrhosis had significantly more endotracheal intubations and a higher risk of death compared to LTRs. The in-hospital survival probability for patients with cirrhosis in our study was nearly the same found by Elhence et al, in which there was a 75% survival probability in 7 days and 65% in 14 days[27]. These findings reinforce the idea that patients with cirrhosis are prone to poorer outcomes in COVID-19. A recent meta-analysis based on confounding cofactors-controlled data indicated that cirrhosis was an independent predictor for COVID-19 mortality (pooled effect = 1.64, 95%CI 1.37–1.96)[28].

In addition, patients with higher MELD-Na scores also had higher mortality rates in our study. This finding is in agreement with the results of previously published studies, in which the MELD score was found to be an independent predictor of ICU admission, endotracheal intubation, and in-hospital mortality[27,29,30]. The Child-Turcotte-Pugh (CTP) class also seems to be positively correlated with an increase in COVID-19 mortality[27,29].

This can be linked to the systemic clinical deterioration seen in decompensated cirrhotic patients that can lead to severe COVID-19 symptoms. The liver is involved in the homeostasis of the systemic immune response. Therefore, patients with cirrhosis are predisposed to syndromic abnormalities of immune function, immunodeficiency, and systemic inflammation[31]. Also, patients with cirrhosis can develop malnutrition due to decreased energy and protein intake, inflammation, malabsorption, altered nutrient metabolism, and hypermetabolism[32]. Malnourished patients have decreased immune function and respiratory muscle strength, which can result in longer hospital stays with poor COVID-19 outcomes[33]. Hence, mortality from SARS-CoV-2 is largely determined by cirrhosis-associated comorbidities and extrahepatic organ failure[34].

Additionally, acute hepatic decompensation can still occur in up to half of the patients with cirrhosis and COVID-19, even without respiratory symptoms[29,35]. Multiple factors could contribute to this acute-on-chronic liver failure, including direct viral toxicity due to the hepatotropism of SARS-CoV-2 via ACE-2 receptor binding[36]. The cytokine storm in severe COVID-19 leads to the activation of the coagulation cascade, vascular microthrombi, and immune-mediated liver injury[37]. Many of the drugs used during hospitalization could also contribute to the occurrence of liver dysfunction in COVID-19[38].

LTRs had considerably low rates of endotracheal intubation (16.7%) and death (11.1%). This is similar to the findings of a meta-analysis on COVID-19 in solid organ transplant recipients, in which the pooled incidence of mortality was 11.8% (95%CI, 4.2%–19.3%) for LTRs[39]. A few studies indicate that adults with immunosuppression seem to have a favorable disease course[40]. Whereas broad immunosuppression in critically-ill patients might be harmful, some

degree of immunosuppression might be beneficial due to a milder COVID-19 presentation with a weaker immune response[41].

There was a considerable overall reduction in solid organ transplantation activity in many countries during the pandemic[42]. However, studies indicate that prior SARS-CoV-2 symptomatic infection does not affect early post-transplant survival[43], and the time since liver transplantation does not interfere with COVID-19 outcomes[44]. Therefore, while the waitlist mortality increases, the decision to postpone life-saving liver transplantations needs to be rational[45]. It is reasonable to individually balance the clinical benefits and risks of undergoing a liver transplant during the pandemic for each patient.

Strenghts and limitations

Exclusively, our study contained hospitalized patients in a quaternary referral center and therefore cannot be generalized to patients who either recovered or died without being referred to a high-complexity center. In this study, there was also a contextual limitation related to the use of the RT-PCR test, which can still produce a high proportion of false-negative results[46]. Thus, our study may have failed to include participants who tested negative for COVID-19, but were positive, which could have modified the results.

However, it is meaningful to report that this study proposes an unprecedented analysis of the clinical characteristics and outcomes of patients with COVID-19 and cirrhosis or liver transplant in Brazil. To our knowledge, this is the first study on the topic in the country. The strengths of this study also include the very specific sample and the low number of patients lost due to missing data. Therefore, it serves as a starting point for new studies assessing the clinical course of COVID-19 in patients with cirrhosis or liver transplant in Latin America.

Future studies could address other variables, such as clinical symptoms, medications administered, underlying diseases, laboratory results, etiology of cirrhosis, and time since transplant, which were not evaluated in our study.

CONCLUSION

Patients with liver cirrhosis had significantly more endotracheal intubation and a higher relative risk of death than LTRs. Among patients with cirrhosis, higher MELD-Na scores were associated with poorer outcomes. The PALI-COVID protocol properly discriminated the lower survival time and survival probability in this population.

However, more prospective studies with greater statistical power are still needed to better understand the clinical course of COVID-19 in patients with cirrhosis or liver transplant.

Authors' contribution

The authors confirm contribution to the article as follows: study conception and design by Correa TL, Carvalho RT; data analysis and interpretation of results by Correa TL, Carvalho RT, Guelli MSTC; draft article preparation by Correa TL, RT Carvalho, Guelli MSTC. All authors reviewed the results and approved the final version of the article.

Orcid

Tulio L Correa: 0000-0003-4524-6736.
Mariana ST Campos Guelli: 0000-0003-3954-9482.
Ricardo T de Carvalho: 0000-0003-0841-2985.

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RESUMO – Contexto – Associações específicas entre cirrose hepática ou transplante de fígado e piores desfechos na COVID-19 ainda não estão completamente claras. **Objetivo –** Nosso objetivo foi avaliar as características e desfechos clínicos de pacientes com COVID-19 grave e cirrose ou transplante de fígado em São Paulo, Brasil. **Métodos –** Foi realizado um estudo observacional retrospectivo em um hospital quaternário. Foram selecionados pacientes com COVID-19 e cirrose hepática ou transplante de fígado. As características clínicas e demográficas, bem como os desfechos, foram avaliados por meio de prontuários eletrônicos. **Resultados –** Um total de 46 pacientes com COVID-19 e problemas hepáticos foram incluídos no estudo. Pacientes com cirrose hepática tiveram significativamente mais intubação endotraqueal e maior risco relativo de morte do que pacientes transplantados. Pacientes com pontuações MELD-Na mais altas apresentaram taxas de mortalidade aumentadas e menor probabilidade e tempo de sobrevivência. **Conclusão –** Pacientes com cirrose hepática, especialmente aqueles com escores MELD-Na mais elevados, tiveram piores desfechos na COVID-19. Os pacientes com transplante hepáticos não parecem estar associados a piores desfechos da COVID-19.

Palavras-chave – COVID-19; pandemias; cirrose hepática; transplante de fígado; pesquisa de resultados.

REFERENCES

1. Hui DS, I Azhar E, Madani TA, Ntoumi F, Kock R, Dar O, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis. 2020;91:264-6.
2. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed. 2020;91:157-60.
3. Brazil Ministry of Health. Panel of coronavirus disease 2019 (COVID-19) cases in Brazil by the Ministry of Health. Available from: https://covid.saude.gov.br.
4. Socolovithc RL, Fumis RRL, Tomazini BM, Pastore L, Galas FRBG, de Azevedo LCP, et al. Epidemiology, outcomes, and the use of intensive care unit resources of critically ill patients diagnosed with COVID-19 in Sao Paulo, Brazil: A cohort study. PLoS One. 2020;15:e0243269.
5. Long B, Carius BM, Chavez S, Liang SY, Brady WJ, Koyfman A, et al. Clinical update on COVID-19 for the emergency clinician: Presentation and evaluation. Am J Emerg Med. 2022;54:46-57.
6. Parasher A. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. Postgrad Med J. 2021;97:312-20.
7. Ranzani OT, Bastos LSL, Gelli JGM, Marchesi JF, Baião F, Hamacher S, et al. Characterisation of the first 250,000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data. Lancet Respir Med. 2021;9:407-18.
8. Adab P, Haroon S, O'Hara ME, Jordan RE. Comorbidities and covid-19. BMJ. 2022;377:o1431.
9. Ejaz H, Alsrhani A, Zafar A, Javed H, Junaid K, Abdalla AE, et al. COVID-19 and comorbidities: Deleterious impact on infected patients. J Infect Public Health. 2020;13:1833-9.
10. Elnaggar M, Abomhya A, Elkhattib I, Dawoud N, Doshi R. COVID-19 and liver diseases, what we know so far. World J Clin Cases. 2022;10:3969-80.
11. Sharma A, Jaiswal P, Kerakhan Y, Saravanan L, Murtaza Z, Zergham A. Liver disease and outcomes among COVID-19 hospitalized patients - A systematic review and meta-analysis. Ann Hepatol. 2021;21:100273.
12. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke J, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg. 2014;12:1495-99.
13. World Health Organization. (2019). ICD-11: International classification of diseases (11th revision). Available from: https://icd.who.int
14. Carvalho RT, Crispim DH, Franck EM, Dei Santi DB, Anagusko SS, Fukuda MV, et al. Palliative care in the COVID-19 pandemic: Strategy of HCFMUSP. Clinics. 2022;77:100050.
15. Loyola Correa T, Salomão Simão ÁM, Barros Sobreira JV, Baeninger Anbar F, Yarshell F, Brandão AB, et al. Evaluation of a New Triage Protocol for Palliative Care for Patients with COVID-19 in Brazil. J Palliat Med. 2023;26: 253-6.
16. University of Edinburgh. Supportive and Palliative Care Indicators Tool: SPICT-Br (Brazilian version); 2016. Available from: https://www.spict.org.uk/the-spict/spictbr
17. Hayashi PH, Forman L, Steinberg T, Bak T, Wachs M, Kugelmas M, et al. Model for End-Stage Liver Disease score does not predict patient or graft survival in living donor liver transplant recipients. Liver Transpl. 2003;9:737-40.
18. Singal AK, Kamath PS. Model for End-stage Liver Disease. J Clin Exp Hepatol. 2013;3:50-60.
19. Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004;159:702-6.
20. Møller S, Bendtsen F. The pathophysiology of arterial vasodilatation and hyperdynamic circulation in cirrhosis. Liver Int. 2018;38:570-80.
21. Cífková R, Pit'ha J, Trunecka P, Lánská V, Jindra A, Plásková M, et al. Blood pressure, endothelial function and circulating endothelin concentrations in liver transplant recipients. J Hypertens. 2001;19:1359-67.
22. Privitera G, Spadaro L, Marchisello S, Fede G, Purrello F. Abnormalities of Lipoprotein Levels in Liver Cirrhosis: Clinical Relevance. Dig Dis Sci. 2018;63:16-26.
23. Correa T, Simao AMS, Sobreira JVB, Yarshell F, Anbar FB, De Carvalho RT. Palliative care for patients with cardiovascular disease and COVID-19 in a major referral hospital. Eur Heart J. 2022;43:ehab849.172.
24. Correa TL, Sobreira JVB, Simao AMS, Anbar FB, Yarshell F, de Carvalho RT. Abstract PO-122: Palliative care for 317 cancer patients with COVID-19 in a major public hospital in South America. Cancer Epidemiol Biomarkers Prev. 2022;31(Suppl 1):PO-122.
25. Correa T, Sobreira J, Simão Á, Yarshell F, Anbar F, Tavares De Carvalho R. Palliative care for patients with dementia and COVID-19: Analyses from a major referral hospital in South America. J Neurol Sci. 2021;429:119775.
26. Moestrup KS, Reekie J, Zucco AG, Jensen TØ, Jensen JS, Wiese L, et al. Readmissions, Postdischarge Mortality, and Sustained Recovery Among Patients Admitted to Hospital With Coronavirus Disease 2019 (COVID-19). Clin Infect Dis. 2023;76:e82-e89.
27. Elhence A, Vaishnav M, Biswas S, Anand A, Gunjan D, Kedia S, et al. Predictors of in-hospital Outcomes in Patients With Cirrhosis and Coronavirus Disease-2019. J Clin Exp Hepatol. 2022;12:876-86.
28. Wang Y, Hu M, Yang H. Cirrhosis is an independent predictor for COVID-19 mortality: A meta-analysis of confounding cofactors-controlled data. J Hepatol. 2023;78:e28-e31.
29. Marjot T, Moon AM, Cook JA, Abd-Elsalam S, Aloman C, Armstrong MJ, et al. Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: An international registry study. J Hepatol. 2021;74:567-77.
30. Kaya Y, Gülcü O, Aksakal E, Kalkan K, Aydın SŞ, Kaya A, et al. A significant predictor of in-hospital and long-term mortality and progression in COVID-19 patients: The end-stage liver disease (MELD) score model. J Med Virol. 2023;95:e28109.
31. Albillos A, Lario M, Álvarez-Mon M. Cirrhosis-associated immune dysfunction: distinctive features and clinical relevance. J Hepatol. 2014;61:1385-96.
32. Traub J, Reiss L, Aliwa B, Stadlbauer V. Malnutrition in Patients with Liver Cirrhosis. Nutrients. 2021;13:540.

33. Vargas-Mendoza N, García-Machorro J, Angeles-Valencia M, Martínez-Archundia M, Madrigal-Santillán EO, Morales-González Á, et al. Liver disorders in COVID-19, nutritional approaches and the use of phytochemicals. World J Gastroenterol. 2021;27:5630-65.
34. Brozat JF, Hanses F, Haelberger M, Stecher M, Dreher M, Tometten L, et al. COVID-19 mortality in cirrhosis is determined by cirrhosis-associated comorbidities and extrahepatic organ failure: Results from the multinational LEOSS registry. United European Gastroenterol J. 2022;10:409-24.
35. Sarin SK, Choudhury A, Lau GK, Zheng MH, Ji D, Abd-Elsalam S, et al. Pre-existing liver disease is associated with poor outcome in patients with SARS CoV2 infection; The APCOLIS Study (APASL COVID-19 Liver Injury Spectrum Study). Hepatol Int. 2020;14:690-700.
36. Marjot T, Webb GJ, Barritt AS 4th, Moon AM, Stamataki Z, Wong VW, et al. COVID-19 and liver disease: mechanistic and clinical perspectives. Nat Rev Gastroenterol Hepatol. 2021;18:348-64.
37. Premkumar M, Kedarisetty CK. Cytokine Storm of COVID-19 and Its Impact on Patients with and without Chronic Liver Disease. J Clin Transl Hepatol. 2021;9:256-64.
38. Cai Q, Huang D, Yu H, Zhu Z, Xia Z, Su Y, et al. COVID-19: Abnormal liver function tests. J Hepatol. 2020;73:566-74.
39. Raja MA, Mendoza MA, Villavicencio A, Anjan S, Reynolds JM, Kittipibul V, et al. COVID-19 in solid organ transplant recipients: A systematic review and meta-analysis of current literature. Transplant Rev. 2021;35:100588.
40. Minotti C, Tirelli F, Barbieri E, Giaquinto C, Donà D. How is immunosuppressive status affecting children and adults in SARS-CoV-2 infection? A systematic review. J Infect. 2020;81:e61-6.
41. Ritchie AI, Singanayagam A. Immunosuppression for hyperinflammation in COVID-19: a double-edged sword? Lancet. 2020;395:1111.
42. Aubert O, Yoo D, Zielinski D, Cozzi E, Cardillo M, Dürr M, et al. COVID-19 pandemic and worldwide organ transplantation: a population-based study. Lancet Public Health. 2021;6:e709-19.
43. Belli LS, Duvoux C, Cortesi PA, Facchetti R, Iacob S, Perricone G, et al. COVID-19 in liver transplant candidates: pretransplant and post-transplant outcomes - an ELITA/ELTR multicentre cohort study. Gut. 2021;70:1914-24.
44. Jayant K, Reccia I, Virdis F, Pyda JS, Bachul PJ, di Sabato D, et al. COVID-19 in hospitalized liver transplant recipients: An early systematic review and meta-analysis. Clin Transplant. 2021;35:e14246.
45. Di Maira T, Berenguer M. COVID-19 and liver transplantation. Nat Rev Gastroenterol Hepatol. 2020;17:526-8.
46. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. Ann Intern Med. 2020;173:262-7.