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ORIGINAL ARTICLE

Liver Injury and Severe Covid 19 Associated without Prior Liver Disease

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ABSTRACT

Objective: The aim of current study is to determine the association in liver injury in patients without preexisting liver disease by severe pandemic disease coronavirus.

Study Design: Observational study

Place and duration: THQ Hospital Kamalia. April 2020-March 2021

Methods: There were one hundred and three patients had corona virus illness were presented in this study. After obtaining informed written permission, the demographics of enrolled patients, including age, sex, and BMI, were recorded. Comorbidities signs and symptoms of disease were also recorded. Severity of disease and its adverse outcomes on liver were assessed in regular follow up. SPSS 21.0 was used to analyze complete data.

Results: The mean of the patients was 52.4 ±12.37 years and had mean BMI 27.2±8.51 kg/m^2. Majority of the patients 63 (61.2%) were males and remaining 40 (38.8%) were females. There were 55 (53.4%) patients had hypertension and 32 (31.1%) cases had diabetes. Most common symptoms were fever, cough dyspnea among all cases. This study found a strong association between severe COVID-19 and an increased AST > 2ULN, GGT > 2ULN, lower albumin (p = 0.020), higher SIRS (p = 0.045), higher procalcitonin, higher ferritin, lower pO2 (p = 0.044), and an elevated SOFA (p = 0.002), which is indicative of an inflammation response. A greater rate of COVID-19-related mortality was found to be associated with elevated levels of direct bilirubin, low albumin, tachypnea, and leukocytosis, according to the study's findings.

Conclusion: We found that individuals with COVID-19 have indications of liver damage, which we believe is due to an inflammatory response that corresponds with the severity of COVID-19.

Keywords: Liver Injury, Covid 19, Comorbidities, Liver Enzymes

INTRODUCTION

There are a number of viruses known as coronaviruses, which tend to infect the upper respiratory tract and cause mild to severe sickness, ranging from the common cold to pneumonia in severe instances. Covid-19 patients reported recurrent gastrointestinal complaints in the late stages of illness progression [2]. These symptoms were linked to an increase in disease severity.

Study results indicated that more than half of individuals infected with the SARS virus had increased liver enzymes [3]. Non-hepatic causes may be responsible for the significant prevalence of aberrant aminotransferase levels in individuals with severe COVID-19 [4]. One of the hallmarks of severe/critical COVID-19 was found to be elevated alanine aminotransferase (ALT) activity [5]. There is a possibility that abnormal liver tests are linked to either the infection or the medication. An acute viral insult or the incubation of a portion of the infection-associated complicated systemic inflammatory response syndrome (SIRS) may result from the hepatic damage discovered in the early stages of the viral illness [6]. Several blood tests may be used to determine the health of the liver. Serum aminotransferases, bilirubin, alkaline phosphatase, albumin, and prothrombin time are some of the most frequently performed tests in clinical practise. These tests are commonly referred to as "liver function tests," although this phrase is deceptive since most of them do not truly represent how well the liver is working, and aberrant results may be caused by disorders that are not connected to the liver. Additionally, these tests may be normal in individuals with advanced liver disease; in COVID, we mentioned that liver enzymes are abnormal and we explored it in the "Discussion" section.

It is possible that Covid-19's acute damage might extend to other organ systems. If you're in your 30s or 40s, you're more likely to suffer from diabetes, hypertension and obesity, as well as cardiovascular disease and chronic liver disease (CLD). No one knows how common liver disease is, although it was responsible for 4.6% of all deaths [8]. MAFLD (metabolism-related liver disease), alcohol-related liver disease, and viral hepatitis are all examples of liver disorders that affect the global health burden. In the event of a COVID-19 pandemic, persons with chronic lung disease are more prone to get SARS-CoV-2. As a result, many cirrhotic patients are regularly exposed to the SARS-CoV-2 virus. Patients with CLD already exhibit lymphocytopenia, leukopenia, thrombocytopenia, and elevated fibrinogen degradation products as a consequence of bone marrow suppression and cirrhosis-associated immune dysfunction syndrome (CAIDS) [10-13].

Toxicology studies reveal that even the healthiest people might suffer from acute liver injury. Currently, the impact of SARS-Cov-2 on pre-existing CLD, compensated and decompensated cirrhosis is unknown. An rise in liver enzymes, whether or not accompanied by jaundice, may be temporary and disappear on its own if the liver is in good working order at the time. However, it is not known whether SARS-Cov-2 infections may worsen pre-existing decompensated liver disease or create acute on chronic liver failure (ACLF) in a cirrhotic organ, even though they may cause significant and prolonged liver damage in persons with CLD.

As a follow-up to our initial findings, we noted any abnormalities in liver function tests (LFTs) in the patients hospitalized with COVID-19 and tracked each case's inflammatory markers, renal functions, coagulopathy, type of admission ward vs ICU, medication offered, and outcomes.

MATERIAL AND METHODS

This observational study was conducted at THQ Hospital Kamalia and comprised of 103 patients. Informed written consent was obtained before any data on patients' age, gender, or BMI was collected. Excluded from the trial were patients with a history of liver illness and those who had not signed a written permission form.

Patients having three months of COVID-19-PCR positive in their nasopharynx were eligible for inclusion. A patient's baseline labs, comorbidities, disease progression, and treatment all have to be considered when assessing how severe COVID-19 was associated to abnormal liver enzyme levels in a particular patient. There was a combination of the APACHE II score, the CLIF-SOFA score, and the number of organ failures used to grade the

disease's progression. Organ failures and the SOFA score were also taken into account.

Mean and standard deviation of continuous data were determined using the Mann-Whitney U test. Analyzing categorical data required the use of Fisher's exact test. In order to be considered statistically significant, a p-value of 0.05 or below has to be met.

A patient had acute liver damage if they had any of the following symptoms:

i. Having a total bilirubin of more than 3 mg/dl, i.e., jaundice

ii. Blood urea nitrogen (BUN), creatinine (CK), and creatinine phosphate (CP) levels are all over the usual range for these enzymes in the liver (2xULN),

iii. In the absence of a history of liver disease, an INR greater than 1.5 is considered normal.

RESULTS

The mean of the patients was 52.4 ±12.37 years and had mean BMI 27.2±8.51 kg/m^2. Majority of the patients 63 (61.2%) were males and remaining 40 (38.8%) were females. Most common symptoms were fever, cough and dyspnea among all cases.(table 1)

Table-1: Baseline detailed demographics of enrolled cases

Variables	Frequency	Percentage
Mean age (years)	52.4 ±12.37	
Mean BMI (kg/m^2)	27.2±8.51	
Gender		
Male	63	61.2
Female	40	38.8
Symptoms		
Fever	40	38.8
Cough	35	33.9
Dyspnea	28	27.2

There were 55 (53.4%) patients had hypertension and 32 (31.1%) cases had diabetes.(fig 1)

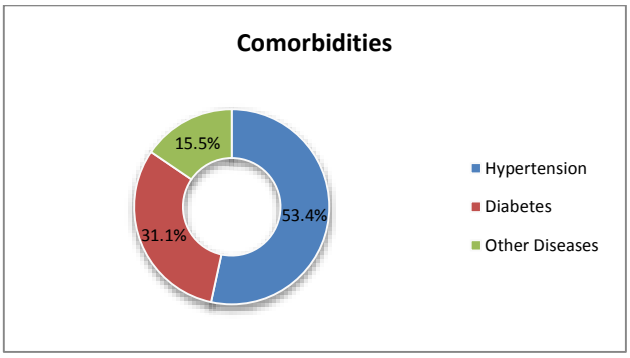

Figure 1: Comorbidities with enrolled cases

Table 2: LFTs exhibiting severe Covid 19

Variables	Moderate Patients	Severe Patients
LFTs		
INR	1.13±0.76	1.78 ± 2.31
Albumin (g/dl)	4.1±2.25	3.36±3.41
ALP (U/L)	85.14±17.17	95.19 ±51.66
GGT (IU/L)	102.11±102.5	149.61 ±163.42
AST (U/L)	92.6 ± 231.32	133.31 ± 200.41
ALT (U/L)	85.17 ± 202.18	104.15 ±162.41
Total bilirubin (mg/dl)	0.701± 1.34	1.87± 1.65
Albumin < 3.5 g/dl	5.67 ±1.62	3.45 ± 2.53
Elevated GGT ≥ 2xULN	48.7±59.31	521.7±452.41
Elevated AST ≥ 2xULN	45±51.61	661±531
Elevated ALT ≥ 2xULN	481± 61.31	565.4±365.76

This study found a strong association between severe COVID-19 and an increased AST > 2ULN, GGT > 2ULN, lower albumin (p = 0.020), higher SIRS (p = 0.045), higher procalcitonin, higher ferritin, lower pO2 (p = 0.044), and an elevated SOFA (p = 0.002), which is indicative of an inflammation response. A greater rate of COVID-19-related mortality was found to be associated with elevated levels of direct bilirubin, low albumin, tachypnea, and leukocytosis, according to the study's findings.(table 2)

It was also determined that 62 individuals with an AST under 80 improved and 13 died as a result of the treatment. When AST levels exceeded 80, 15 patients recovered and returned home, whereas 14 died. (p = 0.021).(table 3)

Table-3: Prevalence of mortality among cases

Variables	AST <80	AST >80
Mortality		
Yes	13	16
No	62	12

There were also greater disease severity calculators in severe patients than in mild to moderate patients, such as the APACHE II Score 4.13± 1.53 vs 13.9±4.61 (p < 0.001)and the SOFA Score 2.1 ±0.19 vs 5.4± 4.31 (p < 0.001). Because their arterial oxygen levels were so low at arrival 87.43±8.51 vs 95.16 ±4.51 (p = 0.002) and their respiratory rates were so low, these patients had to be given oxygen by face mask, high-flow nasal cannula (HFNC), noninvasive ventilation (NIV), or a ventilator to keep them breathing normally.(table 4)

Table-4: Factors that contribute to death

Variables	Discharged	Died
APACHE II Score	4.13± 1.53	13.9±4.61
SOFA Score	2.1 ±0.19	5.4± 4.31
Mean Arterial oxygen levels	87.43±8.51	95.16 ±4.51

DISCUSSION

As a result of an immediate insult to the previously healthy liver, LFTs become deranged in patients with acute liver damage. There have been several reports of people suffering liver damage as a result of infection with COVID-19. [16] The exact cause of the liver damage is unknown, but several studies have shown that it may be caused by the production of angiotensin-converting enzyme II (ACE-II), which has been identified as the primary receptor for the entrance of COVID-19 into cell. These findings may indicate that COVID-19 has a direct and immediate impact on the hepatic system, which may be followed by further inflammation as the result of COVID-19 exposure. [17] ACE-II expression analysis vary across ethnicities, and this might be a contributing factor, although additional research is needed. Another theory argues that a cytokine storm, i.e., the production of several pro-inflammatory cytokines, such as IL-6, which causes both pulmonary and extrapulmonary damage, including liver damage, is responsible for the inflammatory response. [19] Hypoxia and hypotension are common in patients with severe illness, which might be a contributing factor to acute liver damage. [20] Finally, many critically sick patients are receiving a range of drugs and parenteral nourishment, both of which may add to the liver damage. Affected COVID-19-infected individuals are most often blamed for both direct and indirect hepatic impairment.

In current study 103 patients had coronavirus disease were included. The mean of the patients was 52.4 ±12.37 years and had mean BMI 27.2±8.51 kg/m^2. Majority of the patients 63 (61.2%) were males and remaining 40 (38.8%) were females. Most common symptoms were fever, cough and dyspnea among all cases. Results from this study were in line with those from earlier ones. [21,22] Since high blood pressure is a common comorbidity, medication history may have a role in increasing abnormal liver enzyme levels. Pre-admission, 27 percent of patients were taking diuretics, 25 percent were on ACE inhibitors, 31 percent were using beta-blockers, and the rest were taking statins (16.4 percent). Insufficient evidence exists to support the use of these

medications prior to admission to the hospital as a means of altering liver enzymes.[23]

Patients with severe instances of COVID-19 had greater abnormal values of liver enzymes than those with mild or moderate symptomsBoth enzymes indicate liver injury. Only a few patients exhibited elevated TB and ALP (mean TB = 0.95, mean ALP = 91.59), although they were mainly within normal ranges (mean TB = 0.95). Several studies have used these biomarkers with varied degrees of effectiveness, some revealing a significant spike in TB [24], while others found comparable results. [25] This is closer to the lower normal limit than Alb = 3.82, but not statistically significant. The SOFA and APACHE II scores were calculated to compare the severity of liver enzyme abnormalities. Compared to mild/moderate patients, SOFA and APACHE II scores were three times higher (mean SOFA = 4.33, mean APACHE II = 12.83). These calculations reveal a substantial spike in infective markers and LFTs, indicating a systemic effect of the COVID-19 virus. [24]

Biomarkers related with COVID-19 mortality were serum albumin, total leukocyte count and respiration rate in our investigation. Blood albumin is a known acute-phase reactant. When exposed to high levels of oxidative stress, it may undergo irreversible oxidation, increasing the risk of cellular harm. [26] Serious illness, ICU admission, and ventilator support necessitated lower blood albumin levels in the seriously ill group than in the mild-to-moderately afflicted population (3.4 vs. 3.9, P value = 0.013). A rise in direct bilirubin was seen in our research population's nonsurvivors (0.15 vs 1.35 p = 0.001), which is indicative of acute liver damage. Type II alveolar cells and cholangiocytes both express ACE-2 receptors, however hepatocytes have a 20-fold lower level of ACE-2 receptor expression [27], as shown by Chai et al. [27].

CONCLUSION

COVID-19 affects several systems. COVID-19 causes liver damage through cytokine-induced inflammation. Liver function enzymes may be used as surrogates to predict COVID-19 severity based on the degree of liver damage.

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