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THE CLINICAL EFFECTS OF COVID-19 ON LIVER ENZYMES AND FERRITIN PROTEIN LEVEL IN IRAQI PATIENTS

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Abstract

In 2019 has seen a lot of critical attention focused on patients with coronavirus illness who have liver damage. However, it is unclear whether the presence of a high rate of liver enzymes is a result of the viral infection or the underlying undetected liver illness. From July 2020 to September 2021, we used polymerase chain reaction to retrospectively investigate 1280 patients who had SARS-CoV-2 at our particular medical facility. The 48 hours following admission were used to acquire all laboratory tests. In the cities of Baghdad and Al-Basrah, patients hospitalized with COVID-19 disease had a notably high rate of liver impairment. More patients who had liver failure and high ferritin protein levels at the time of their admission needed intensive care and mechanical ventilation. The present results referred that the total ALT level mean was significantly increased in COVID-19 patients compared to the normal value according to the Iraqi Health Ministry normal values of the clinical diagnostics tests (41.72 ± 1.29 vs. 30.0 IU/L). The ALT level mean was high in males compared to females in the COVID-19 patients' group (44.09 ± 1.80 vs. 38.72 ± 1.84 IU/L). The results were also shown significant aspartate transaminase elevation (45.56 ± 1.54 *vs.* 40 IU/L, $P < .001$) in those with pneumonia compared to those without. Elevated liver enzymes were seen in patients with higher temperature (38.5 ± 0.9) and higher serum ferritin (240 ± 274 vs 165 ± 198 ng/ml, $P = .002$). While, the results of AST level mean were not significantly increased in males compared to females in COVID-10 patients' group (47.91 ± 2.14Vs. 42.59 ± 2.21) These patients were more likely to require intensive care and mechanical ventilation. In addition, the results of alkaline phosphatase (ALP) appeared a significant increasing level mean of ALP in the total COVID-19 patients group compared with the normal values of ALP according to the Iraqi Health Ministry normal values of the clinical diagnostics tests (118.01 ± 2.51 vs. 50 – 160IU/L). A significant increase in ferritin levels was noted in patients with severe disease, compared to patients with mild disease. Elevated ferritin level seems to be related to the severity of infection with confirmed COVID-19 virus.

Despite the fact that COVID-19 infection was relatively moderate, abnormal liver enzyme levels were common, linked to more severe illness. Future research should

look into whether those with a history of liver disease are more likely to develop COVID-19 disease.

Keywords: Liver injury, Statistical analysis, Coronavirus, Liver enzymes and Ferritin

Introduction

Coronaviruses belongs to Coronaviridae family and the order Nidovirales [1]. In terms of epidemic, there are three epidemics that have been recognized epidemic viruses, severe acute respiratory syndrome (SARS)- CoV, Middle East respiratory syndrome (MERS)-CoV, and covied or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Currently, COVID-19 is considered a new viral disease. The first case of this disease was discovered in December 2019 in Wuhan, China. The most dangerous thing about this disease is its rapid spread as it spread to 19 countries within one month, which led to the outbreak of a pandemic, which is called 2019-nCoV or COVID-19 [2-4].

The SARS-CoV virus is considered a systemic infection that affects multiple organs involved, heart, kidneys, pancreas, and liver. Liver dysfunction can be caused by a complication of covid-19 infection or by a severe pharmacological reaction to the antibiotics used to treat the infection. The surface of cholangiocytes in the liver and bile contains a very high number of ACE2 receptors. Apparently, duct cells increase SARS-COV-2 entrance into the cells, resulting in liver enzyme dysregulation [5, 6].

Numerous investigations [7,8] have described the connection between COVID-19 and abnormal liver function tests (LFTs). However, the data on liver enzymes in patients with SARS-CoV-2 infection from recent epidemiological and clinical research is mostly ambiguous and contradictory [9,10,11]. With a focus on the prevalence of abnormal liver enzymes among COVID-19 patients based on clinical severity and disease mortality, several systematic reviews and meta-analyses have recently been published [12].

Ferritin has been recognized as a discriminative, predictive, or prognostic marker in patients with liver disorders since it is an acute-phase protein that can be produced in the presence of systemic inflammation [13]. Ferritin is receiving more and more attention in the fight against the COVID-19 pandemic as a risk factor in the classification or prognosis of COVID-19 [14]. Even while clinical observation has shown that severe COVID-19 patients have aberrant ferritin levels, its value has yet to be fully understood.

In order to provide guidelines for future clinical management, this study evaluated the hepatic enzyme activity in COVID19 patients, the ability of ferritin to distinguish between liver injury and severe sickness upon admission, as well as the potential of outcome prediction. With order to better understand the mechanism of liver disease and effectively manage liver damage in COVID-19 patients, on the day of admission to a hospital in Baghdad.

Methods

Subjects

The current study is a cross-sectional study, the clinical information was collected from 1280 patients infected with Coronavirus that received health care in AL-Muanee General Hospital, Basra province, Iraq and Al-Shifa Specialized Center, Medical City, Baghdad, Iraq in the period from July 2020 – until the end of September 2021. The age range of the patients in the present study is between 18 to 86 years old. The clinical data collected from these hospitals included the age, gender, and liver function test in addition to molecular detection of COVID-19 to ensure the positivity of those patients. The data were statistically analyzed using the IBM SPSS computer program version 28.0 [15] to calculate the mean, standard deviation for the parametric data, and the probability was calculated by using Student's t-test or ANOVA table. For the nonparametric data, Pearson's chi-square was used to calculate the probability. The probability was considered significant when it was < 0.05.

Results

The present results referred that 55.2% of the 1280 COVID-19 patients included in this study were males, while 43.8% were females positive for COVID-19 (Figure 1).Additionally, the present results referred that the total ALT level mean was significantly increased in COVID-19 patients compared to the normal value according to the Iraqi Health Ministry normal values of the clinical diagnostics tests (41.72 ± 1.29 *vs.* 30.0 IU/L) (Table 1), such results referred that the ALT level mean was high in males compared to females in COVID-19 patients' group (44.09 ± 1.80 *vs.* 38.72 ± 1.84 IU/L), (Table 1).

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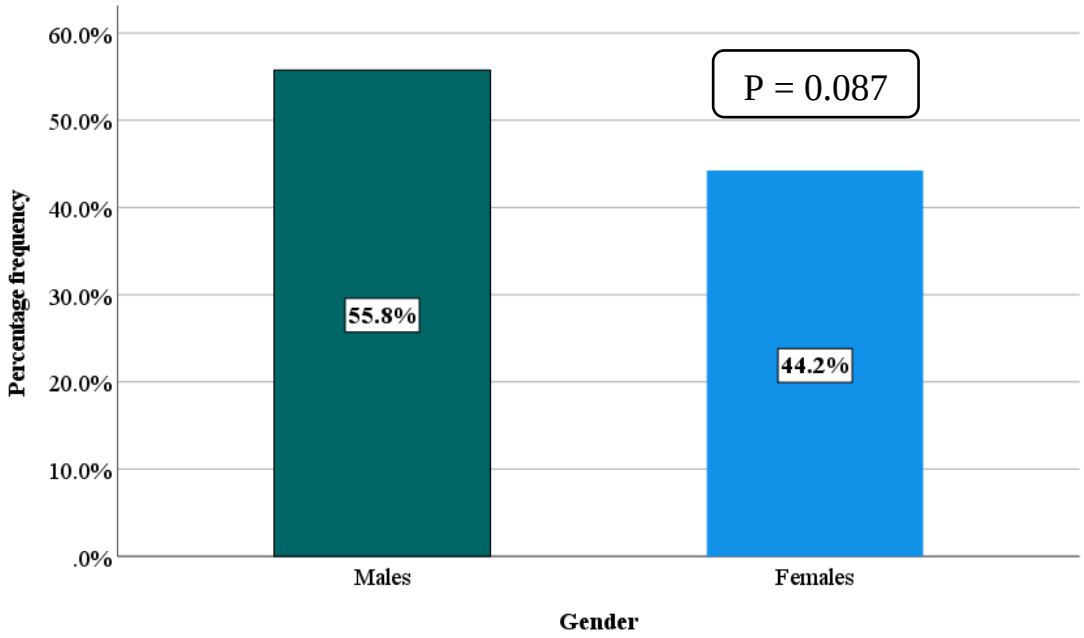

Figure 1: the percentage frequency distribution of COVID-19 infections according to gender

Table 1: ALT test levels among the COVID-19 patients' group

Groups	GOT (ALT) level mean ± SE (IU/ml)	Probability
Males	**44.09 ± 1.80**	**P < 0.05**
Females	**38.72 ± 1.84**	
Total	**41.72 ± 1.29**	**P < 0.001**

Additionally, according to results mention in table 2, the level mean of AST in COVID-19 patients was significantly higher than the level mean in the COVID-19 patients group as a whole, as measured by the normal values of the clinical diagnostic tests as established by the Iraqi Health Ministry (45.56 1.54 vs. 40 IU/L) (Table 2). While the mean AST levels in the COVID-10 patients' group were not significantly higher in males than in females (47.91 2.14 Vs. 42.59 2.21) (Table 2).

Table 2: AST test levels among the COVID-19 patients' group

Groups	GPT (AST) level mean ± SE (IU/ml)	Probability
Males	**47.91 ± 2.14**	**P > 0.05**
Females	**42.59 ± 2.21**	
Total	**45.56 ± 1.54**	**P < 0.001**

In table 3, the results of alkaline phosphatase (ALP) appeared a significant increasing level mean of ALP in the total COVID-19 patients group compared to the normal values of ALP according to the Iraqi Health Ministry normal values of the clinical diagnostics tests (118.01 ± 2.51 *vs.* 50 – 160IU/L). Furthermore, there was a significantly increased level mean of ALP in males compared to females in COVID-19 patients' group (123.87 ± 3.84 *Vs.* 110.60 ± 2.93) (Table 3).

Table 3: ALP test levels among the COVID-19 patients' group

Groups	ALP level mean ± SE (IU/ml)	Probability
Males	**123.87 ± 3.84**	**P < 0.05**
Females	**110.60 ± 2.93**	
Total	**118.01 ± 2.51**	**P < 0.001**

In addition, the results of ferritin level mean in total COVID-19 patients' group were significantly increased level mean in the total COVID-19 patients' group compared to the normal range of the normal values according to the Iraqi Health Ministry normal values of the clinical diagnostics tests (206.80 ± 5.89 *vs.* 44 -147 IU/L) (Table 4). While, there was no significantly increased level mean of ferritin in males compared to females in COVID-19 patients' group (216.27 ± 8.35 *vs.* 195.49 ± 8.19) (Table 4).

Table 4: Ferritin levels among COVID-19 patients

Groups	Ferritin level mean ± SE ()	Probability
Males	216.27 ± 8.35	P > 0.05
Females	195.49 ± 8.19	
Total	206.80 ± 5.89	P < 0.001

Discussion

The age range of the groups in this study was 18 to 86 years, and the results showed that men were more frequently observed than women (55.8% vs. 44.2%). The age range of the COVID-19 infected individuals was between 20 and 80 years old, and the present results were in agreement with prior findings that showed that more men than women were infected on average [16].. Such the liver function tests (ALT, AST, and ALP) appeared significantly increasing levels in COVID-19 patients' group compared to the normal values according to the Iraqi Health Ministry normal values of the clinical diagnostics tests (Table 1, 2

and 3). The present results were compatible with Bertolini etal. (2020), that they recorded mildly increased LFTs in the sera of patients infected with COVID-19, but these increases did not refer to hepatocyte damage or liver failure [17]. Moreover, Kullar et al. (2020) referred that liver injury is the more prevalent organ in COVID-19 patients outside the respiratory system [18]. Hepatocellular injury brought on by changes in the hemodynamics and oxygen delivery mechanisms may result in COVID-19 infections, which have noticeably higher amounts of LFTs. In the presence of cardiac failure, pulmonary failure, or shock, hypoxic hepatitis may result in abrupt elevations in aminotransferases [19].In acute cardiac failure, which occurs in severe COVID-19 patients, the systemic arterial pressure decreases suddenly, resulting in a dropping in the hepatic arterial perfusion and hepatocellular hypoxia [20]. The pathogenesis comprises besides the hepatic ischemia, the hepatic venous congestion because of the high central venous pressure, which predisposes the hepatocytes to be a more significant hypoxic damage [21]. Whether these hemodynamic variations can change the LFTs is unclear [22].

There are diverse hypotheses of COVID-19 action mechanism and LFTs abnormalities [23, 24]. The more important hypotheses are that the COVID-19 virus can provoke immune-mediated liver injury in certain individuals who develop severe liver dysfunction related to an exaggerated cytokine storm, eventually leading to multiple organ failure and severe respiratory distress syndrome [25]. or the injury occurs via the ischemic process related to hypoxia. There are many reports suggesteing the increasing rate of liver function tests elevation (26-29). In addition, the current findings demonstrated that COVID-19 patients had significantly higher ferritin levels than average. The amount of ferritin was dramatically raised in the serum of COVID-19 patients, according to other reports that concur with the current findings [13, 14, 30-32].

Conclusion

Increased ferritin levels were linked to higher levels of liver enzymes on their own. That, in addition to systemic inflammation, potential coagulopathy is linked to liver harm caused by microvascular thrombosis. COVID19 patients with liver failure are more likely to develop systemic coagulopathy, which increases their risk of developing severe illness. Furthermore, our findings suggest that early ferritin testing could be a useful technique for detecting liver impairment, the severity of the illness, and poor prognosis in COVID-19 patients. The processes of SARS-CoV-2 infection-induced liver damage are mostly unclear. According to current knowledge, infection with a highly pathogenic human coronavirus might result in liver injury due to virus-induced cytopathology and immunopathology caused by excessive inflammatory responses.

Additionally, we found from our cross-sectional study results that the liver function tests and ferritin serum level were highly elevated in COVID-19 remarkably when it compared to the normal values of these tests, and males' group also had remarkably higher levels compared to females in COVID-19 patients' group.

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