



Liver enzymes as a predictor of mortality in patients with COVID-19? A cross-sectional study

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ABSTRACT

Liver injury in patients with COVID-19 infection may directly result from viral infection of liver cells, immune-mediated inflammation such as cytokine storm, and hypoxia resulting from pneumonia. Additionally, liver injury may occur due to drug toxicity and may lead to liver failure in critically ill COVID-19 patients. Given the significance of the liver and its vulnerability in COVID-19 patients, this study aimed to investigate the correlation of serum liver enzymes with the prognosis of hospitalized COVID-19 patients at Imam Khomeini Hospital in Urmia. This descriptive-analytical study involved hospitalized COVID-19 patients at Imam Khomeini Hospital in Urmia. Patient data were extracted from medical records and recorded in checklists, including demographic characteristics (age and gender), serum levels of Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST), and patient outcomes (recovery and mortality). Subsequently, the serum levels of AST and ALT in recovered and discharged patients were compared with those of deceased patients. The mean AST level was higher in deceased patients compared to recovered and discharged patients, and this difference was statistically significant ($P < 0.033$). Therefore, overall, higher AST levels in COVID-19 patients may indicate a worse prognosis. Similarly, the mean ALT level was higher in deceased patients compared to recovered and discharged patients, and this difference was statistically significant ($P < 0.015$). Thus, higher ALT levels in COVID-19 patients may generally indicate a worse prognosis. Continuous monitoring of liver enzymes in patients with a poor prognosis can lead to early identification and, to the extent possible, prevention of complications and mortality through enhanced care.

1. Introduction

The evidence indicates that COVID-19 patients with more severe symptoms also have higher liver dysfunction [1]. Liver impairment in individuals with COVID-19 is common, and some studies have shown that 60% of patients with SARS (a type of coronavirus) have experienced this impairment [2]. However, liver dysfunction in some of these patients can be somewhat attributed to the administration of effective drugs for treating the disease [1]. Nonetheless, studies have demonstrated that liver damage in COVID-19 patients may directly result from viral infections of liver cells, immune-mediated inflammation such as cytokine storms, and hypoxia resulting from pneumonia. Furthermore, liver damage can occur due to drug toxicity and may lead to liver failure in critically ill COVID-19 patients [3].

According to available evidence, 2–11% of COVID-19 patients develop liver diseases, and 14–53% exhibit abnormal levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) during the course of the disease [4]. Liver damage in mild cases of COVID-19 is usually transient and can return to normal without specific treatment [5]. However, it appears that patients with severe COVID-19 may have higher levels of liver dysfunction [6]. Taking into account the prevalence of the Omicron variant during this period and its worse prognosis compared to the Delta variant, along with the significance of the liver and its vulnerability, and the limited resources related to liver damage in COVID-19 patients, the present study was conducted to investigate the correlation of serum liver enzymes with the prognosis of hospitalized COVID-19 patients at Imam Khomeini Hospital in Urmia. The objectives of the research were:

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1. Determining the demographic characteristics (age and gender) of COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.
2. Assessing the serum level of AST in COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.
3. Evaluating the serum level of ALT in COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.
4. Identifying the prognosis (mortality rate) of COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.
5. Establishing the correlation between the serum level of AST and mortality in COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.
6. Establishing the correlation between the serum level of ALT and mortality in COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.

2. Methods

2.1. Study design

This study is a descriptive-analytical study in which COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia were examined. Patient data were extracted from medical records and recorded in checklists. Data were gathered from patients who were hospitalized with confirmed diagnoses of COVID-19, involving both the Delta and Omicron variants, at Imam Khomeini Hospital in Urmia between September 2022 and March 2023.

2.2. Participants

A purposive convenient sampling technique was employed to select participants for this study.

2.2.1. Inclusion criteria

COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.

2.2.2. Exclusion criteria

Patients with underlying malignant diseases and other clinical conditions that increase AST and ALT levels, except for COVID-19, exposure to toxins, and lack of consent to participate in the study.

2.3. Sample size

Based on the available pool of patients, a total of 136 individuals were part of this research (see Fig. 1). Following Küçükceran et al.'s study [7], with a confidence interval of 95% and 80% power, G*Power 3.1 [8] was used to calculate a minimum sample size of 130. Accounting for a 5% attrition rate, the final sample size was set at 136 participants. Our study adhered to the STROCSS criteria [9].

$$n = \frac{z_{1-\alpha/2}^2 \times p(1-p)}{d^2}$$

2.4. Data collection

Information for this investigation was obtained by reviewing the medical records of patients admitted to Imam Khomeini Hospital in Urmia. The research team extracted pertinent details from the medical records of all patients diagnosed with COVID-19 and affected by the Delta and Omicron variants during the specified timeframe. Patient data were extracted from medical records and recorded in checklists. The necessary information included demographic characteristics (age and gender), serum levels of AST and ALT, and patient outcomes (recovery and mortality). Subsequently, the serum levels of AST and ALT in recovered and discharged patients were compared with those of deceased patients. Patient data were coded, entered into Excel, and analyzed using SPSS version 27.

2.4.1. Study population

COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.

2.4.2. Unit characteristics

COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.

2.4.3. Data collection tool

Checklists.

2.4.4. Data analysis method

Patient characteristics will be presented in tables and frequency distributions, and descriptive statistics including mean and standard

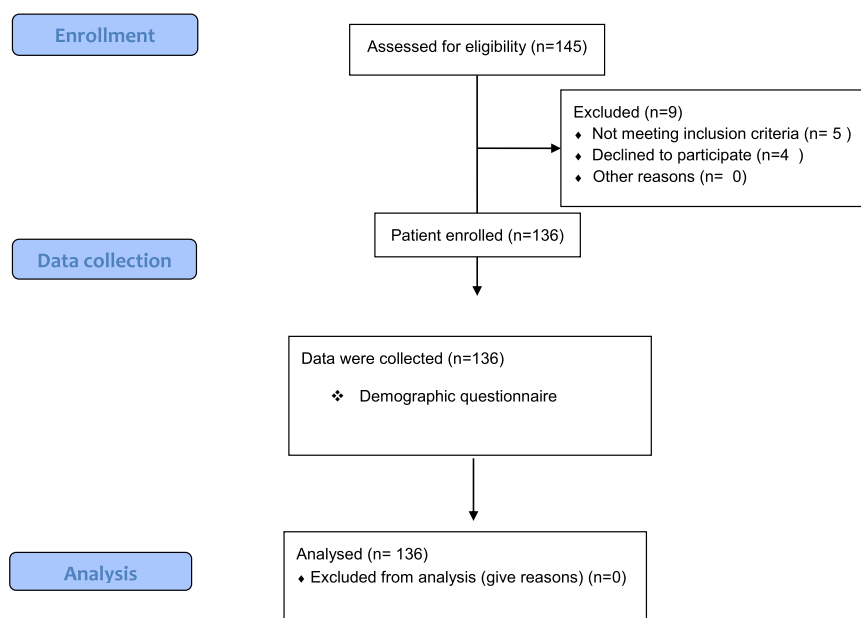


Fig. 1. Flow diagram of entering subjects in the study.

deviation will be utilized. Normality of liver enzyme levels will be assessed using the Kolmogorov-Smirnov test. Comparison of liver enzyme levels based on the outcomes under study will be conducted using independent t-tests (Mann-Whitney U test, if necessary). Data will be analyzed using SPSS version 27. A significance level of 0.05 will be considered for all tests.

2.4.5. Ethical considerations

- 1. Ethical approval was obtained from the university’s ethics committee (IR.UMSU.HIMAM.REC.1402.058)
- 2. Coordination with hospital authorities was carried out.
- 3. Patient sample information was kept confidential.
- 4. Information was used solely for research purposes.

3. Findings

This study involving 136 patients, of which 80 (58.8%) were female and 56 (41.2%) were male. The gender distribution is depicted in [Chart 1](#). It is evident that there are more female patients than male patients in the study.

The serum AST levels of the patients ranged from 10 to 237 mg/dl, with a mean of 40.40 ± 45.54 mg/dl and a median of 46 mg/dl ([Chart 2](#)).

[Charts 3 and 4](#) shows the serum ALT level of the patients included in the study. The serum ALT level of the patients included in the study was in the range of 8–160 mg/dl. The mean serum ALT level of all patients was 44.78 ± 30.46 mg/dl and the mean serum ALT level of the patients was 45.5 mg/dl.

The outcomes of the patients treated at Imam Khomeini Hospital in Urmia are summarized in [Table 1](#). Out of the 136 patients studied, 118 (86.8%) recovered and were discharged, while 18 (13.2%) passed away. Most of the studied patients were in the recovered and discharged category.

The comparison of serum AST levels in discharged and deceased COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia is depicted in [Table 2](#). According to the independent t-test results, the mean AST level in patients who passed away was higher than in those who recovered and were discharged, and this difference is statistically significant (p-value < 0.001). Therefore, in general, higher AST levels in COVID-19 patients may indicate a worse prognosis.

The comparison of serum ALT levels in discharged and deceased COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia is presented in [Table 3](#) and [Chart 5](#). According to the independent t-test results, the mean ALT level in patients who passed away was higher than in those who recovered and were discharged, and this difference is statistically significant (p-value < 0.015). Therefore, in general, higher ALT levels in COVID-19 patients may indicate a worse prognosis.

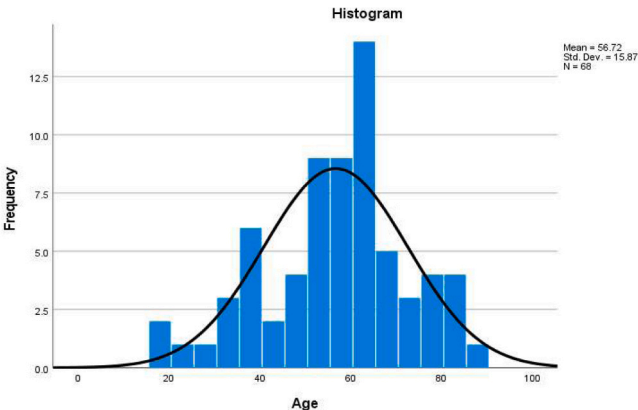


Chart 1. The gender distribution of the enrolled patients.

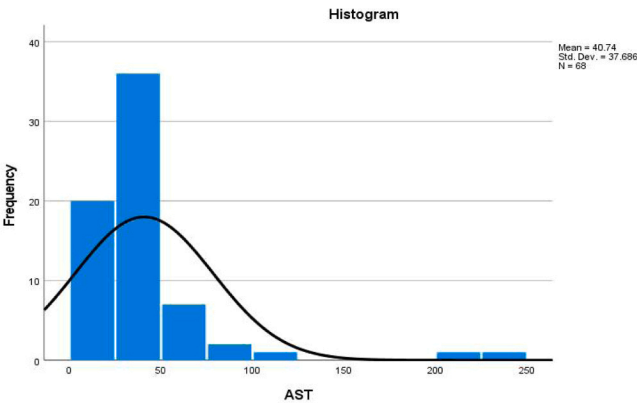


Chart 2. Serum AST level of patients included in the study.

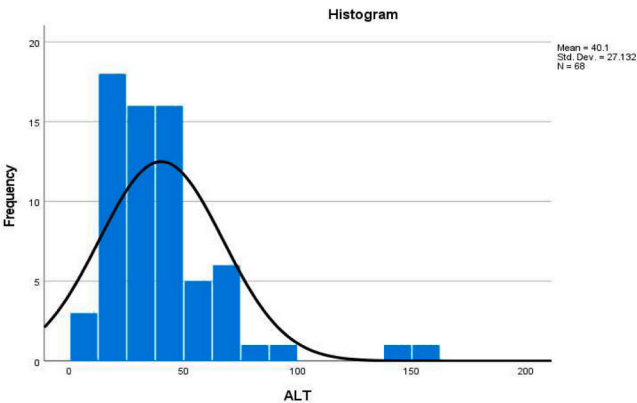


Chart 3. Serum ALT level of patients included in the study.

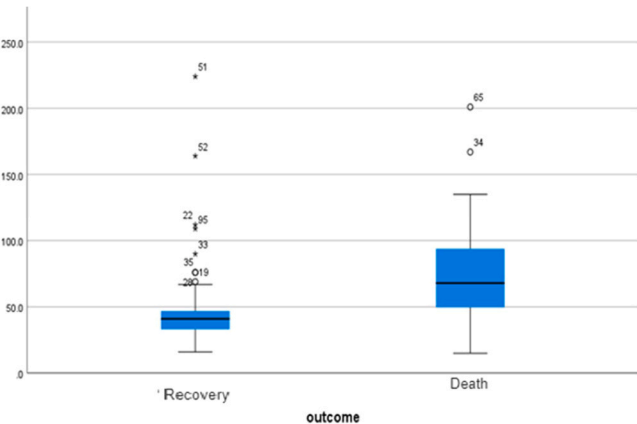


Chart 4. Comparison of serum AST levels between discharged and deceased patient.

Table 1		
Prognosis of hospitalized patients with COVID-19 at Imam Khomeini Hospital in Urmia.		
Patient treatment outcomes	Frequency	Percentage
Recovery	118	86.8
Death	18	13.2

Table 2
Comparison of serum AST levels between discharged and deceased patients.

Patient treatment outcomes	AST Mean ± Standard Deviation	Minimum	Maximum	Results
Recovery	39.59 ± 3.10	10	125	<0.001
Death	84.56 ± 4.71	48	237	<0.001
Total	45.54 ± 4.40	10	237	<0.001

Table 3
Comparison of serum ALT levels between discharged and deceased patients hospitalized with COVID-19.

Patient treatment outcomes	ALT Mean ± Standard Deviation	Minimum	Maximum	Results
Recovery	38.73 ± 2.18	8	160	<0.015
Death	86.44 ± 3.68	45	161	<0.015
Total	44.78 ± 3.46	8	161	<0.015

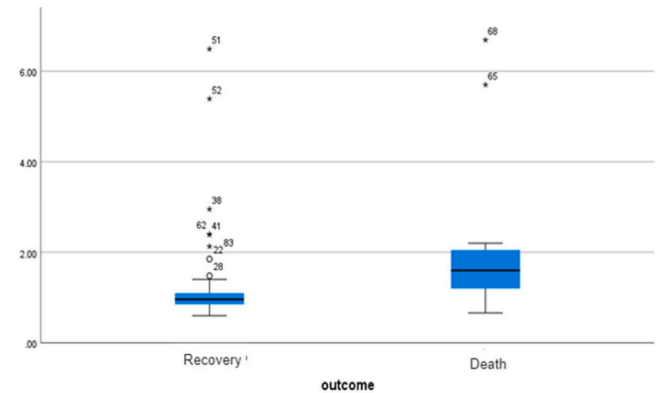


Chart 5. Comparison of serum ALT levels between discharged and deceased patients.

4. Discussion

The Based on the available evidence from previous studies, 2–11% of COVID-19 patients experience liver diseases, and 14.5–53% exhibit abnormal levels of ALT and AST during the course of the disease. Liver damage in mild COVID-19 cases is often transient and can return to normal without specific treatment. However, it seems that patients with severe COVID-19 may have higher liver dysfunction. Liver damage in COVID-19 patients may directly result from viral liver cell infection, immune-mediated inflammation such as cytokine storm, and hypoxia due to pneumonia. Additionally, liver damage may occur due to drug toxicity and may progress to liver failure in critically ill COVID-19 patients. Given the liver’s importance and vulnerability in COVID-19 patients, our study aimed to investigate the correlation between serum liver enzyme levels and the prognosis of COVID-19 patients hospitalized at Imam Khomeini Hospital in Urmia.

According to our study, and in line with the independent t-test results, the mean AST level was higher in patients who passed away compared to those who recovered and were discharged, and this difference was statistically significant (p-value < 0.033). Therefore, in general, higher AST levels in COVID-19 patients may indicate a worse prognosis. Similarly, according to the independent t-test results, the mean ALT level was higher in patients who passed away compared to those who recovered and were discharged, and this difference was statistically significant. Hence, in general, higher ALT levels in COVID-19 patients may indicate a worse prognosis.

In the Omrani et al. study in 2020, AST (P) > 0.001), ALT (P) >

0.001), and ALP (P) > 0.001) levels were higher in COVID-19 patients compared to the control group. The most common liver failure events were an increase in direct bilirubin, ALT, AST, ALP, and total bilirubin. Mortality rates significantly increased with elevated AST levels (P=0.023) [10]. Our study also showed a correlation between AST and ALT levels and the mortality rate of COVID-19 patients.

In the study by Medetalibeyoglu et al. in 2020, the mortality rate and the need for intensive care units were higher in individuals with high ALT-AST levels, which was statistically significant (0.001). The rate of poor prognosis in the cholestatic pattern group was 26.5%, the mixed pattern group was 36.1%, and the hepatocellular pattern group was 30% (0.001) [11]. Our study also found a correlation between mortality rates and the AST and ALT levels of patients.

In the study by Singhai et al. in 2021, patients with severe COVID-19 were more likely to experience liver dysfunction than those with mild cases. The average hospital stay for patients with liver dysfunction was longer than for those with normal liver function [12]. In our study, patients with more severe COVID-19 who passed away had higher AST and ALT levels and more liver dysfunction.

In the case-control study by Shaveisi-Zadeh et al. in 2022, COVID-19 patients showed increased AST, ALT, WBC, neutrophils, NLR, and PLR levels, and decreased platelet and lymphocyte counts compared to the control group. However, high levels of AST, ALT, NLR, PLR, and LMR were not associated with mortality [13]. Contrary to their results, our study found a correlation between higher AST and ALT levels and mortality in COVID-19 patients.

In the systematic review and meta-analysis by Zahedi et al. in 2021, the prevalence of increased ALT and AST in non-severe COVID-19 patients was 30% and 21%, respectively, and in severe cases, it was 38% and 48%. Patients with severe COVID-19 infection had a 4.22, 4.96-, and 4.13-times higher likelihood of having increased AST, ALT, and lactate dehydrogenase (LDH) levels. Liver function test abnormalities were more common in severe COVID-19 patients than in non-severe cases [14]. Similarly, in our study, patients with severe COVID-19 who passed away had higher AST and ALT levels.

In the study by Liu et al. in 2021, elevated AST (p=0.035), elevated ALT (p=0.023), and a higher AST/ALT ratio (p=0.002) were associated with the progression of COVID-19. They concluded that increased AST, ALT, and AST/ALT ratios are related to the severity of COVID-19 and mortality [15]. Our study also found a correlation between increased AST and ALT levels and the mortality of COVID-19 patients.

The COVID-19 pandemic has significantly impacted the education and training of nurses. As frontline healthcare workers, nurses have faced unprecedented challenges during this global health crisis [16–18]. The pandemic has underscored the critical need for nurses to possess advanced skills in infection control, patient care, and crisis management [18]. Educational institutions and nursing programs have had to adapt rapidly, implementing virtual learning environments, simulation-based training, and revised clinical experiences to ensure that nurses receive comprehensive education while minimizing exposure to the virus [19–21]. Furthermore, the pandemic has emphasized the importance of ongoing education and professional development for nurses to effectively respond to dynamic healthcare demands [22–24]. As a result, educational strategies and curricula have evolved to address these evolving needs, ultimately shaping a more resilient and adaptable nursing workforce [25,26].

5. Conclusion

In conclusion, it is recommended to conduct a more comprehensive investigation with a larger number of patients, not only at a specific university center but also in various hospitals and medical facilities. This will help in identifying the relationship between liver enzymes and the prognosis of COVID-19 patients. Continuous monitoring of liver enzymes in patients with a worse prognosis can lead to earlier identification and, to the best extent possible, prevention of complications and

mortality through increased care.

CRedit authorship contribution statement

Hamid Reza Mehryar: Visualization, Resources. **Babak Choobi Anzali:** Visualization, Formal analysis. **Mansour Abbasi:** Visualization, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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