# Clinical Outcome and Risk Assessment in Hospitalized COVID-19 Patients with Elevated Transaminases and Acute Kidney Injury: A Single Center Study

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## *Abstract*

**Objectives:** Initial reports indicate a high incidence of abnormal aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels in the corona virus disease 2019 (COVID-19) and possible association with acute kidney injury (AKI). We aimed to investigate clinical features of elevated transaminases on admission, its association with AKI and outcomes in patients with COVID-19.

**Methods:** A retrospective analysis of the register of patients with laboratory-confirmed COVID-19 and assessment of the AST and ALT was performed. Multinominal logistic regression was used to determine factors associated with community-acquired AKI (CA-AKI) and hospital-acquired AKI (HA-AKI).

**Results:** 828 patients were included. 51% were male, the mean age - 65±16 years, 70% had anamnesis of hypertension, 26% – of diabetes mellitus, 8% – of chronic kidney disease (CKD). In-hospital mortality was 21%. At admission 41% of patients had hypertransaminasemia. These patients were younger, had higher levels of inflammatory markers, d-dimer, poorer outcomes. AKI incidence in study population was 27%. The higher frequency of AKI was seen in patients with hypertransaminasemia (33% vs 23%, p=0.003). Patients with predominant elevated AST were more likely to have adverse outcomes, AKI, than patients with elevated ALT. Multinomial logistic regression found that hypertension, CKD, elevated AST and hematuria were shown to be associated with CA-AKI, and age over 65 years, hypertension, malignacy, elevated AST and hematuria were predictors of HA-AKI.

**Conclusions:** Elevated transaminases on admission are associated with AKI and poor outcomes. Patients with elevated AST were more likely to have adverse outcomes. Elevated AST on admission was associated with CA-AKI and was a predictor of HA-AKI.

**Key words**: COVID-19, clinical outcome, liver injury, AKI, ALT, AST

Abbreviations:

ADHF - acute decompensated heart failure

AKI - acute kidney injury

ALT - alanine aminotransferase

AST - aspartate aminotransferase

CA-AKI - community-acquired acute kidney injury

CAD - coronary artery disease

CKD - chronic kidney disease

COVID-19 - corona virus disease 2019

CRP - C-reactive protein

CT - computer tomography

DBP – diastolic blood pressure

DM - diabetes mellitus

HA-AKI - hospital-acquired acute kidney injury

Hb – haemoglobin

ICU - intensive care unit

LDH - lactate dehydrogenase

MV - mechanical ventilation

RRT - renal replacement therapy

Sat02 - pulse oxygen saturation

SBP – systolic blood pressure

sCr - serum creatinine

WBC - white blood cells

## Introduction

Initially, corona virus disease 2019 (COVID-19) was considered as a predominantly respiratory infection, mortality from which is associated with progression of respiratory failure [1]. Currently, various extrapulmonary manifestations of the disease have been described, in addition, multi-organ involvement is confirmed by the detection of the viral RNA not only in the respiratory epithelium, but also in other tissues [2, 3]. One of the common extrapulmonary manifestations of COVID-19 is liver injury**[4, 5].** A meta-analysis of liver injury in COVID-19 by R. Mayo et al. showed elevated alanine aminotransferase (ALT), on average, in 18% of cases (4 to 40%), aspartate aminotransferase (AST) in 21% of cases (4 to 53%), total bilirubin in 6% of cases (1 to 18%), and decreased albumin in 6% (3 to 11%) of cases [5]. It has been previously demonstrated that hypertransaminasemia was associated with more frequent admission to the intensive care unit (ICU), the need for mechanical ventilation (MV), and an increase in hospital mortality in patients with COVID-19 [6, 7, 8, 9, 10].

Acute kidney injury (AKI) is also a risk factor for severe COVID-19 and a poor prognosis [11, 12]. Data for the Russian Federation are limited, but they also confirm an increased risk of in-hospital mortality in patients with AKI [13]. In addition, some patients with AKI require renal replacement therapy (RRT), which significantly increases the

cost of their treatment. Considering the above, determination of risk factors for AKI may help to identify a group for more aggressive therapy and frequent monitoring and adjustment of treatment.

Previously, there have been reports of a possible association between liver and kidney injuries in COVID-19 [8, 14]. According to Piano et.al, the prevalence of AKI was 22% and 11% in the group with and without abnormal liver function test results ($p = 0.004$, respectively). Another study by Huang H. et.al reported a higher serum creatinine (sCr) level (88.5 vs 70 mmol/L, $p = 0.02$) in patients with ischemic hepatitis compared with patients without it [15].

The origin of this relationship is not completely clear and requires further investigation, since data on the prevalence and prognostic value of combined liver and kidney injury in COVID-19 are limited. We aimed to investigate clinical features of elevated transaminases on admission, its association with the prevalence, risk of development, course of AKI, poor outcomes and mortality in patients with COVID-19.

## Methods

For this single-center retrospective analysis of the register patients were recruited from April 13 to June 30, 2020 at Moscow City Hospital. The study was approved by the local Ethics Committee of the RUDN University (No. 07- 20) and the written informed consent from the patients was not required. The study included patients over 18 years of age with laboratory-confirmed COVID-19 and assessment of AST and ALT levels within the first 48 hours after hospitalization. The exclusion criteria were: readmission, acute surgical pathology, with duration of hospitalization less than 48 hours, history of chronic liver disease, continuous RRT, a single measurement of serum creatinine (sCr) per hospitalization.

On admission, all patients underwent standard clinical laboratory tests and an imaging investigation, including a complete blood count, urinalysis, blood chemistry test on admission and in dynamics, a chest computer tomography (CT) scan.

Abnormality in aminotransferases was defined as ALT and/or AST >40 U/L according to local laboratory documents. Definition and staging of AKI was based on KDIGO 2012 criteria [16]. Baseline sCr was determined as the minimum sCr value during hospitalization, or if available last sCr in the previous 6 months before hospitalization. Patients admitted to the hospital with AKI or those who developed AKI during the first 48 hours, were denoted as having community-acquired AKI (CA-AKI). Hospital-acquired AKI (HA-AKI) was defined as any AKI documented after 48 hours of hospital admission. Hematuria was defined as the presence of more than three erythrocytes in the field of view, proteinuria as the level above 0.3 g/L. We assessed the degree of lung injury by chest CT. The $1^{st}$ stage was defined as below 25% lung injury, the $2^{nd}$ - 26-50%, the $3^{rd}$ - 51-75% and the $4^{th}$ – more than 75%. The term acute decompensated heart failure (ADHF) is used to describe patients with previously history of chronic stable heart failure with the typical symptoms and/or signs of decompensation of HF during hospitalization.

### *Statistical Analysis*

Mathematical and statistical analysis of the results was performed using the Stata 13.0 for Mac OS software packages (StataCorp, College Station, TX, USA). Continuous variables were described as mean and standard deviation ($M \pm SD$) for normally distributed data or median and interquartile range (IQR) values for non-normal distribution. Qualitative parameters were presented as frequencies and percentages. The means of continuous variables were compared using independent t-tests. The ratios of qualitative variables were compared using the $\chi 2$ test. A multinomial logistic regression was performed to explore the potential predictors of CA-AKI and HA-AKI. Covariates in the model included variables at admission: age over 65 years (yes or no), sex (male or female), hypertension (yes or no), coronary artery disease (CAD) (yes or no), ADHF (yes or no), history of chronic kidney disease (CKD) (yes or no), diabetes mellitus (DM) (yes or no), history of cancer (yes or no), haemoglobin < 120 g/L in females and <130 g/L in males (anemia) (yes or no), white blood cells (WBC) < $4x10^9$/L (leukopenia) (yes or no), lymphocytes < $1.2x10^9$/L (lymphopenia) (yes or no), thrombocytes < 150 x $10^9$/L (thrombocytopenia) (yes or no), oxygen saturation less than 93% on admission with room air breathing (yes or no), C-reactive protein (CRP) > 75 g/L (yes or no), albumin < 35 g/L (yes or no), total bilirubin > 21 μmol/L (yes or no), AST > 40 U/L (yes or no), ALT > 40 U/L (yes or no), hematuria (yes or no) and proteinuria (yes or no). Relative risk ratios (RRRs) were calculated with 95% confidence intervals (CIs). P value <0.05 was considered statistically significant.

## Results

### *Demographics*

At the start of our study, 1204 patients hospitalized with COVID-19 were included in the registry. We excluded 376 patients (Figure 1).

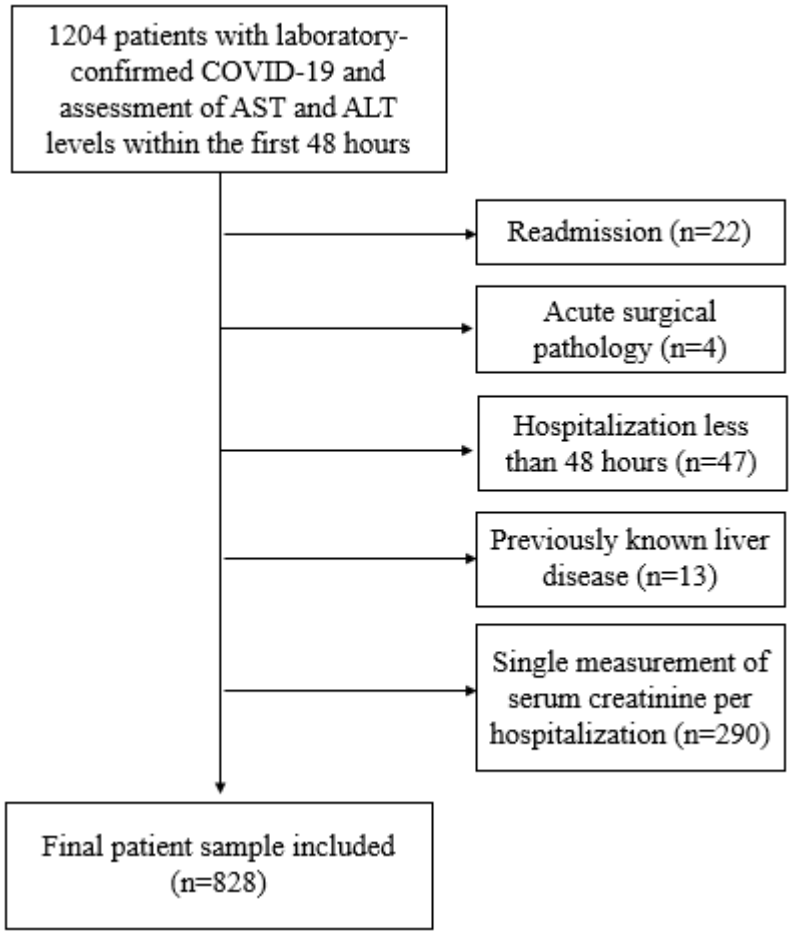



**Figure 1**: Flow chart of study population.

Anthropometric data on admission were available for 513 patients, urinalysis was performed within 48 hours after admission in 772 patients, lactate dehydrogenase (LDH), ferritin and d-dimer were measured within 48 hours after admission in 308, 263, 624 patients, respectively.

The study included 828 patients (Table 1). 51% were male, the average age was 65 ± 16 years. The most common comorbidity was hypertension (70%). More than a half of patients had obesity (51%). 49% of patients had the oxygen saturation decreased to <93% while the patients were breathing ambient air. The mean length of stay was 12 [9; 15] days, 25% of patients spent at least one day in the ICU, the mean length of stay in the ICU was 5 [2; 9] days. In-hospital mortality was 21%. Elevated aminotransferase levels on admission were noted in 41% of patients (Table 1).

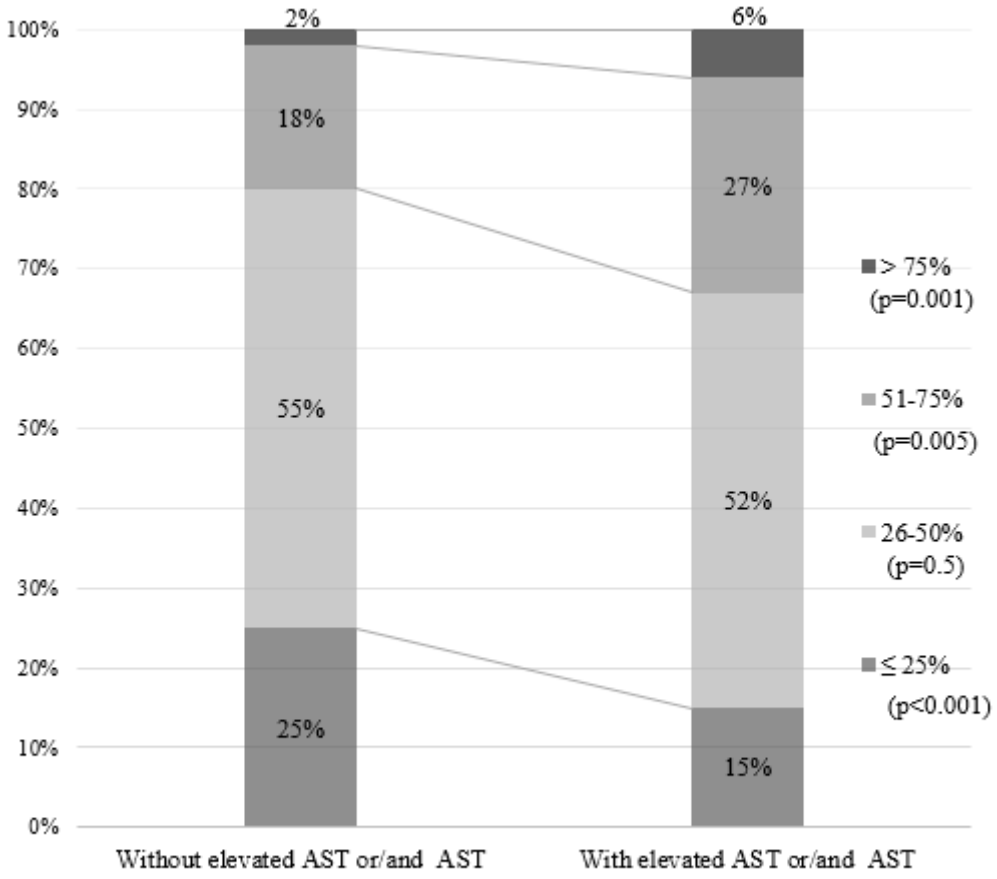
**Table 1:** Clinical characteristics of study patients.

| **Variables** | **Study population (n=828)** | **With elevated AST or/and AST (n=338)** | **With normal AST or/and AST (n=490)** | **p*** |
|---|---|---|---|---|
| Age, M±SD | 65±16 | 63±16 | 66±16 | 0,006 |
| Male, n (%) | 426 (51) | 156 (46) | 270 (55) | 0.01 |
| Day of illness at admission, Me [IQR] | 6 [3;8] | 6 [3;8] | 5 [3;8] | 0.07 |
| Comorbidities, n (%) | | | | |
| Hypertension | 582 (70) | 232 (69) | 350 (71) | 0.4 |
| Diabetes mellitus | 215 (26) | 87 (26) | 128 (26) | 0.9 |

| | | | | |
|---|---|---|---|---|
| CAD | 141 (17) | 54 (16) | 87 (18) | 0.5 |
| Malignacy | 84 (10) | 30 (9) | 54 (11) | 0.3 |
| CKD | 70 (8) | 24 (7) | 46 (10) | 0.2 |
| ADHF | 120 (14) | 48 (14) | 72 (15) | 0.8 |
| Obesity | 271 (51) | 118/220 (54) | 153/307 (50) | 0.4 |
| SBP/DBP, mmHg, M±SD | 126±16/80±10 | 126±16/ 80±11 | 126±16/80±10 | 0.9/0.8 |
| Sat02 on room air, %, Me [IQR] | 94 [92;95] | 93 [91;94] | 94 [92;95] | 0.0007 |
| Laboratory parameters, Me [IQR] | | | | |
| AST, U/L | 34 [25;50] | 55 [44;72] | 26 [21;32] | - |
| ALT, U/L | 24 [17;40] | 44 [32;64] | 18 [14;24] | - |
| sCr, mmol/L | 91 [77;114] | 93 [77;119] | 89 [76;112] | 0.04 |
| WBC, $x10^9$/L | 6.1 [4.4;8.3] | 6.2 [4.5;8.8] | 6 [4.4;8.1] | 0.2 |
| WBC <4 $x10^9$/L, n (%) | 142 (17) | 54 (16) | 88 (18) | 0.5 |
| Lymphocytes, $x10^9$/L | 1 [0.7;1.4] | 1 [0.7;1,3] | 1 [0.7;1.4] | 0.7 |
| Lymphocytes <1.2$x10^9$/L, n (%) | 506 (61) | 207 (61) | 299 (61) | 0.9 |
| Platelets, $x10^9$/L | 191 [151;252] | 195 [153;247] | 191 [148;256] | 0.9 |
| Platelets <150$x10^9$/L, n (%) | 204 (25) | 77 (23) | 127 (26) | 0.3 |
| Hb, g/L | 130 [119;144] | 133 [122;146] | 129 [117;142] | 0.002 |
| Anemia, n (%) | 216 (26) | 75 (22) | 141 (29) | 0.03 |
| C-reative protein, mg/L | 74 [28;125] | 91 [37;146] | 65 [24;109] | <0.0001 |
| LDH, U/L | 361 [265;539] | 454 [333;660] | 301 [234;412] | <0.0001 |
| Total bilirubin, mmol/L | 10 [7.3;13.8] | 11 [8;15] | 9.5 [7;13] | 0.0008 |
| Ferritin, µg/L | 495 [253;676] | 627 [404;747] | 420 [192;618] | <0.0001 |
| Albumin, g/L | 34 [31;37] | 34 [30;37] | 34 [31;38] | 0.3 |
| D-dimer, µg/L | 311 [164;593] | 325 [192;592] | 293 [147;593] | 0.02 |
| Fibrinogen, g/L | 5.9 [4.9;6.9] | 6 [5;7.1] | 5.8 [4.8;6.8] | 0.2 |
| Hematuria, n (%) | 124/772 (16) | 48/311 (15) | 76/461 (16) | 0.7 |
| Proteinuria, n (%) | 254/772 (33) | 129/311 (41) | 125/461 (27) | <0.001 |
| AKI, n (%) | 224 (27) | 110 (33) | 114 (23) | 0.003 |
| CA-AKI, n (%) | 129 (16) | 71 (21) | 58 (12) | <0.001 |
| HA-AKI, n (%) | 95 (11) | 47 (14) | 57 (12) | 0.3 |

** - We compared groups with elevated and normal transaminases. Abbreviations: AST–aspartate transaminase, ALT – alanine transaminase, ADHF- acute decompensated heart failure, CAD – coronary artery disease, CKD – chronic kidney disease, SBP – systolic blood pressure, DBP – diastolic blood pressure, Sat02 - pulse oxygen saturation, sCr - serum creatinine, WBC - white blood cells, Hb – haemoglobin, LDH – lactate dehydrogenase, – AKI – acute kidney injury, CA-AKI – community-acquired acute kidney injury, HA-AKI –hospital-acquired acute kidney injury.*

Elevated AST was more common than ALT (37% (304) vs 25% (208), respectively). There were no differences in concomitant pathology, statins and antibacterial drugs intake before hospitalization (10% vs 12%, p = 0.4, 49% vs 47%, p = 0.6, in the groups with and without abnormal level of transaminases, respectively). Patients with elevated transaminases on admission were younger, more often female, had higher levels of inflammatory markers and d-dimer. The length of stay did not differ between the groups (11 [9; 15] vs 12 [9; 16] days, p = 0.4, respectively). The AKI incidence was higher in patients with elevated AST and/or ALT levels on admission. There was a greater degree of lung injury according to chest CT in patients with abnormal transaminase level (Figure 2).




Abbreviations: AST–aspartate transaminase, ALT – alanine transaminase

**Figure 2:** Lung injury by chest CT scan in patients stratified by ALT or/and AST at admission.

### *Elevated transaminases and outcomes*

Patients with elevated ALT and/or AST on admission were more frequently hospitalized in the ICU and needed MV. In addition, AKI rates and in-hospital mortality were higher in the group with elevated ALT and/or AST (Figure 3). There were no significant differences in the incidence of thrombosis.

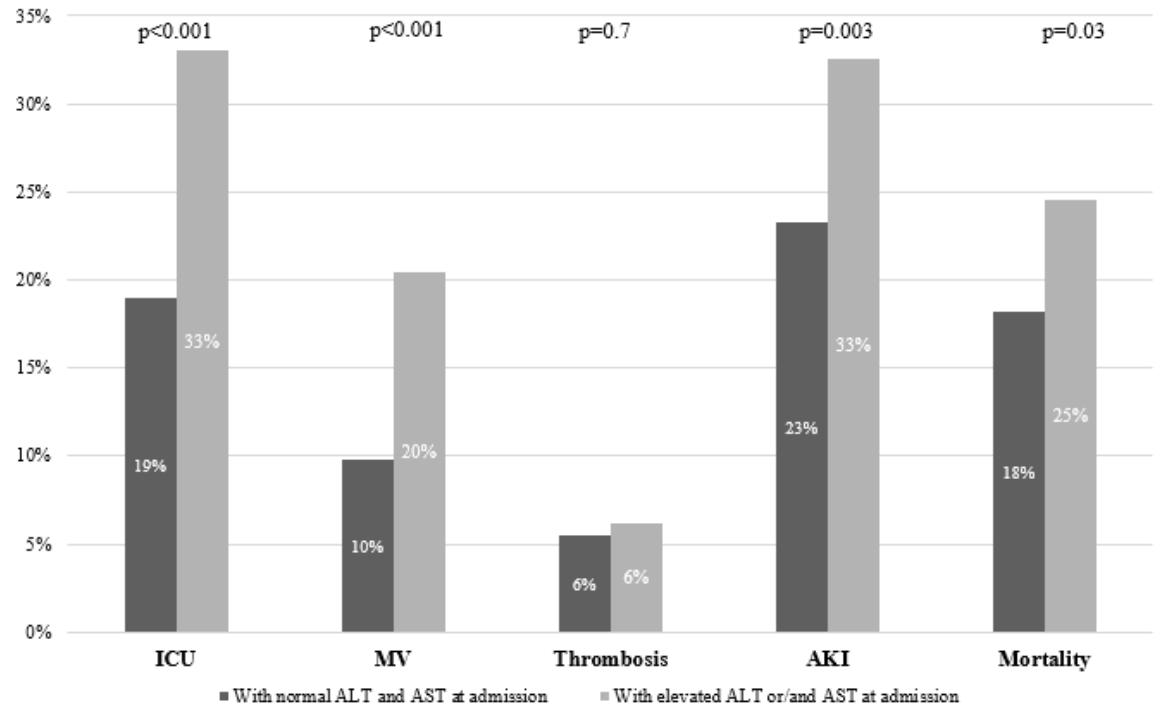



**Figure 3:** Outcomes in patients stratified by ALT or/and AST at admission.

Further, the analysis was performed with division into the groups with predominant elevated ALT and AST. Patients with predominant elevated AST on admission had significantly worse outcomes, such as transfer to the ICU, need for MV, progression of lung injury by CT, mortality, and the AKI incidence (Figure 4).

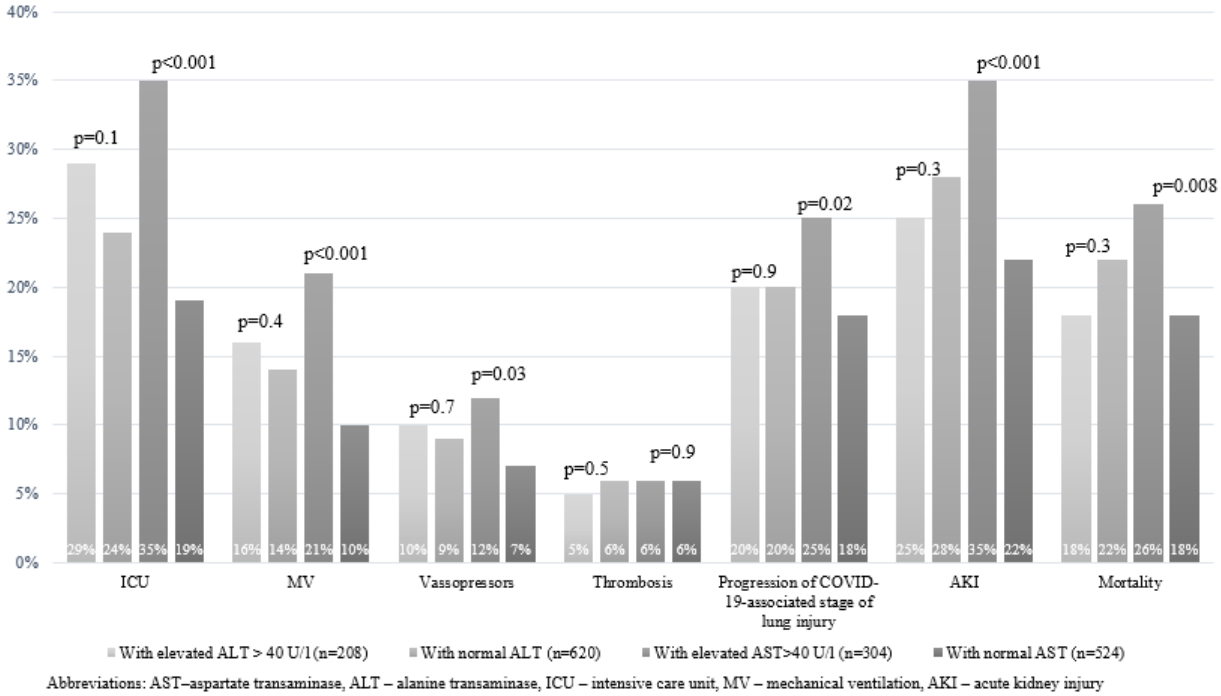



**Figure 4:** Outcomes in patients stratified by elevated ALT or AST at admission.

## *Risk factors for AKI*

Hypertension, history of CKD, elevated AST and hematuria on admission were independently associated with a significant risk of incidence of CA-AKI according to multinomial logistic regression. Age over 65 years, history of

hypertension, malignacy, elevated AST and hematuria on admission were predictors for HA-AKI (Table 2). Abnormal ALT level on admission was not associated with the incidence of CA-AKI and HA-AKI in this population.

**Table 2**: Independent predictors of CA-AKI and HA-AKI development from multinomial logistic regression.

| **Variables** | **CA-AKI** | | | **HA-AKI** | | |
|---|---|---|---|---|---|---|
| | **RRR** | **95% CI** | **p** | **RRR** | **95% CI** | **p** |
| Age ≥ 65 years | 1.40 | 0.82-2.39 | 0.2 | 3.09 | 1.52-6.29 | 0.002 |
| Sex | 0.89 | 0.56-1.41 | 0.6 | 0.98 | 0.58-1.67 | 0.9 |
| ADHF | 0.99 | 0.54-1.83 | 0.9 | 1.76 | 0.95-3.28 | 0.07 |
| CAD | 1.43 | 0.82-2.49 | 0.2 | 0.62 | 0.31-1.22 | 0.2 |
| Hypertension | 2.65 | 1.38-5.01 | 0.003 | 2.66 | 1.14-6.19 | 0.02 |
| CKD | 2.55 | 1.32-4.92 | 0.006 | 1.84 | 0.86-3.96 | 0.6 |
| Malignacy | 1.73 | 0.88-3.39 | 0.1 | 2.24 | 1.09-4.56 | 0.03 |
| Diabetes mellitus | 1.26 | 0.78-2.04 | 0.3 | 1.24 | 0.71-2.16 | 0.4 |
| Sat02<93% on room air | 1.24 | 0.79-1.95 | 0.4 | 1.29 | 0.76-2.16 | 0.3 |
| Anemia | 1.14 | 0.68-1.91 | 0.6 | 1.64 | 0.94-2.87 | 0.08 |
| Leukopenia | 0.53 | 0.27-1.04 | 0.06 | 0.82 | 0.40-1.66 | 0.6 |
| Lymphopenia | 1.32 | 0.80-2.17 | 0.3 | 1.52 | 0.82-2.84 | 0.2 |
| Thrombocytopenia | 1.63 | 0.97-2.75 | 0.07 | 1.45 | 0.79-2.64 | 0.3 |
| C-reactive protein>75 g\L | 0.96 | 0.60-1.55 | 0.9 | 1.63 | 0.93-2.86 | 0.09 |
| AST > 40 U/L | 2.51 | 1.46-4.31 | 0.001 | 2.13 | 1.17-3.88 | 0.01 |
| ALT > 40 U/L | 0.90 | 0.50-1.65 | 0.7 | 0.38 | 0.17-0.85 | 0.02 |
| Total bilirubin>21 mmol/L | 1.25 | 0.56-2.81 | 0.6 | 1.83 | 0.78-4.34 | 0.2 |
| Albumin < 35 g/L | 1.35 | 0.82-2.21 | 0.2 | 0.86 | 0.48-1.55 | 0.6 |
| Hematuria | 2.57 | 1.51-4.39 | 0.001 | 2.86 | 1.59-5.16 | 0.001 |
| Proteinuria | 1.36 | 0.85-2.17 | 0.2 | 1.43 | 0.83-2.45 | 0.2 |

*Abbreviations: CA-AKI – community-acquired acute kidney injury, HA-AKI –hospital-acquired acute kidney injury, RRR – relative risk ratios, CI – confidence interval, ADHF- acute decompensated heart failure, CAD – coronary artery disease, CKD – chronic kidney disease, Sat02 - pulse oxygen saturation, AST–aspartate transaminase, ALT – alanine transaminase.*

## Discussion

Our study with of 828 hospitalized patients with laboratory-confirmed COVID-19 and pneumonia showed that elevated transaminase levels were common and associated with a disease severity, which is consistent with the results of recent studies [7, 8, 9]. Thus, the systematic meta-analysis of 24 studies with 12882 included patients demonstrated a high prevalence of increased AST (41%) and ALT (29%). It has been shown that abnormal AST (odds ratio (OR) 2.98; with 95% CI: 2.35–3.77; p <0.00001) and, to a lesser extent, ALT (OR 1.85; with 95% CI: 1.49–2.29; p<0.00001) is associated with poor outcomes, such as hospitalization in the ICU, a decrease in oxygen saturation below 90%, initiation of MV or in-hospital mortality [7]. Another multicenter study from China found elevated ALT in 42% of hospitalized patients and elevation of AST in 48.5% of patients, hypertransaminasemia was statistically more frequent in patients with higher levels of inflammatory biomarkers and severe course of COVID-19, which also correlates with our findings [17].

In our work elevated AST and/or ALT did not correlate with comorbidities, age, which was noted in another study [8]. At the same time, associations with inflammatory markers prove a possible relationship with the severity of the disease, explaining the poor prognosis in this group of patients. Pathogenesis of elevated transaminases in COVID-19 is complex and not fully understood, since it can potentially include several factors: ischemic damage [18] as patients with elevated transaminase levels had lower saturation, damage due to systemic inflammation, similar to sepsis [19], as well as coagulation disorders, including micro- and macrovascular thrombosis.

The possible relationship between hypercoagulation and hypertransaminasemia were discussed in the work of A. Hamadé [20], which retrospectively shows a potential association between elevated transaminases and venous thrombosis. Our study found no similar associations, since lower extremity ultrasound was not performed routinely in our patients, but only for patients with clinical signs of thrombosis or a significant increase in d-dimer, which was

probably the reason for a low detection rate of thrombosis in the study population. On the other hand, our study had a greater statistical power since the study by A. Hamadé et.al. included 46 patients.

Earlier studies showed that elevated AST is more common in patients with COVID-19 than ALT, which correlates with our findings [4, 7, 14, 21, 22]. Moreover, in our study elevated AST is associated with a poor prognosis to a greater extent than elevated ALT. In a retrospective study of 2073 hospitalized patients from China, only elevated AST and direct bilirubin levels, among all liver parameters, were associated with in-hospital mortality (adjusted HR 1.61 (95% CI: 1.20–2.15, P = 0.001) and adjusted HR 1.57 (95% CI: 1.14–2.16, P = 0.006), respectively) [4]. Also. in analysis of 64 studies (11245 patients with COVID-19), elevated AST was more common in severe disease (45.5% vs 15%) [22]. Despite a large amount of data on the negative predictive value of elevated AST and the AST/ALT ratio compared to ALT in COVID-19, the reason for this difference is not completely clear and requires further investigation.

In addition, in our study, an increase in AST over 40 U/L was associated with CA-AKI (RR 2.51, CI: 1.46-4.31, p = 0.001) and was a predictor of HA-AKI (RR 2.13, CI: 1.17-3.88, p = 0.01).

The relationship between CA-AKI and elevated AST indicate probable correlation with the disease severity at admission, since patients with community-acquired AKI were admitted in a more severe condition than those without AKI [23]. Also, the combination of involvement of various systems and organs once again confirms the multisystem injury in COVID-19. On the other hand, a the recent study by A. J. Martínez-Rueda et al. showed that patients with CA-AKI with COVID-19 more frequently have comorbidities as compared with HA-AKI, including CKD (10% vs 3%, p = 0.015) and hypertension (45% vs 25%, p <0.001), and the development of CA-AKI was associated with a history of CKD (OR 4.17, 95% CI: 1.53–11.3), hypertension (OR 1.55, 95% CI: 1.01–2.36), Charlson comorbidity index (OR 1.16, 95% CI 1.02–1.32) and the sequential organ failure assessment score (OR 2.19, 95% CI: 1.87– 2.57) [23]. The above data are consistent with ours, because in addition to elevated AST on admission, CA-AKI was statistically more common in patients with a history of hypertension and CKD, emphasizing the increased risks of adverse outcomes in the population of patients with COVID-19 and comorbidities.

Moreover, hypertension is a recognized risk factor for renal function impairment and AKI in COVID-19 and the most common comorbidity in our and more other studies [24, 25, 26]. According to the study by K. Parker et al., aimed to investigate a possible effect of continuous anticoagulant therapy before hospitalization on the prevention of AKI, the risk factors for AKI were CKD, hypertension and the male gender [25]. However, our study showed that a history of hypertension is a risk factor for not only CA-AKI, but also HA-AKI.

Hematuria on admission was also a predictor of both AKI forms in our study. Similar data were described in earlier studies, which have demonstrated that proteinuria and hematuria are predictors of poor prognosis and HA-AKI in patients with COVID-19 [27, 28]. It should be noted that the predictive role of urine changes for AKI development was known earlier [29].

In before COVID-19 times, two meta-analyses showed that the prognosis in HA-AKI was worse than in CA-AKI [30, 31]. However, the prognosis in various forms of AKI in COVID-19 is ambiguous. Thus, J. Pelayo et al. have shown that the mortality rate in HA-AKI in hospitalized patients with COVID-19 is higher than in patients with CA-AKI, as well as the need for vasopressor support and MV [32]. On the other hand, in a study carried out by Martínez-Rueda AJ et al. in Mexico, which included 1170 hospitalized COVID-19 patients, both forms of AKI were associated with a poor prognosis, with no statistically significant difference between CA-AKI and HA-AKI [23]. As data are limited and inconsistent, more epidemiological data on prognosis is needed in the future.

Our study showed for the first time that elevated AST was a common significant factor associated with the both phenotypes of AKI. The advantage of our study was the exclusion of patients with previously known liver diseases and the determination of transaminase levels on admission to the hospital, which allowed to reduce the probability of other causes of cytolysis [33, 34].

The retrospective nature of the study was a limitation, as a number of factors might have been left out. In many patients, the SCr and transaminases levels were missed before hospital admission. Therefore, it could lead to a decreased or increased incidence of AKI and CKD, in addition, patients with previously undiagnosed chronic liver disease could be included in the study. The definition of AKI did not include the urine volume-based criterion of <0.5 mL/kg/h for 6 h, which may have led to underestimation of AKI incidence. Another limitation of our study is the lack of data on the use of non-steroidal anti-inflammatory drugs in some patients before hospitalization since this group of drugs can lead to an increase in transaminase levels.

Further research is needed to prospectively analyze the predictive role of hypertransaminasemia in outcomes, including AKI, of COVID-19. Findings of a comprehensive assessment of the heart function in patients with and without elevated AST would be interesting.

## Conclusions

In conclusion, our study showed a high prevalence of elevated transaminases among patients hospitalized for COVID-19 in a large tertiary center in Moscow in the first half of 2020. Hypertransaminasemia at admission is associated with systemic inflammation, d-dimer level. Patients with elevated AST or/and ALT had the higher frequency of AKI (33% vs 23%, p=0.003) and in-hospital mortality (24.6% vs 18.2%, p=0.03). Patients with predominantly elevated AST were more likely to have adverse outcomes than those with predominant elevated ALT. Elevated AST above 40 U/L on admission was independently associated with development of CA-AKI and HA-AKI. Patients with increased levels of AST at admission should be closely followed up due to potential poorer outcomes.

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## Declarations of interest

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