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# Correlation of Liver Enzymes with Severity of Covid19 and Mortality

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***Abstract***
***Introduction:***
*Data on the global COVID19 pandemic suggests that liver injury could be a manifestation of the disease, and that liver disease could also be related to a worse prognosis. Various studies have shown AST/ALT ratio > 1 was associated with severe course and increased mortality. Previous studies show abnormal AST was associated with the highest mortality compared with other indicators of liver injury.*
***Aim:***
*We aimed to investigate the independent predictive factors for the severity and survival of COVID19 disease from routine blood parameters, characteristics of patients who required invasive mechanical ventilation (IMV) were compared with stable hospitalized patients who did not require invasive ventilation .*
***Methodology:***
*Ours was a hospital record based, retrospective observational study which included a total of 400 cases admitted at Kempegowda Institute of Medical Sciences Bengaluru. The cases were categorized into non-severe which included WHO category A and B and severe which included WHO category C. Demographic and laboratory parameters were analysed. Statistical analysis was done*
***Results :***
*Liver enzyme levels were higher in severe cases of COVID19. The levels corelated with mortality. Higher levels of AST and AST/ALT of more than 1 were associated with poor outcome.*
***Conclusion :***
*Monitoring liver enzymes can be a useful method to predict outcome of COVID19*

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## I. INTRODUCTION

At the end of 2019, a novel corona virus was identified as the cause of a cluster of pneumonia cases in Wuhan. In February 2020, WHO designated the disease COVID19. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for the current pandemic, can have multi-organ impact.The body's hyperinflammatory response and the plausible direct effects of SARS-CoV-2 on multiple organs via angiotensin-converting enzyme 2 (ACE2), has been associated with complications of the disease, SARS, heart failure, renal failure, liver injury, shock, and multi-organ failure have led to death.

The clinical presentation of Coronavirus disease 2019 (COVID-19) might range from mild symptoms to critical illness requiring respiratory support including invasive mechanical ventilation

Recent studies show that liver involvement could be a common manifestation of COVID-19, with up to 76.3% of patients having abnormal liver test results. The presence of abnormal liver test results is more pronounced during the first 2 weeks of hospitalization. Patients with abnormal liver test results characterized by hepatocellular injury or mixed injury have higher odds of progressing to a severe disease course. There are many potential contributing etiologies to elevated liver enzymes in patients with SARS-CoV-2 including direct liver injury, associated inflammatory responses, congestive hepatopathy, hepatic ischemia, drug-induced liver injury (DILI), and muscle breakdown.

Although most studies have showed that liver injury is more prevalent in severe cases of COVID-19 cases, its relationship with mortality has not been clearly demonstrated. In addition, the prognostic value of aminotransferases in predicting severe clinical outcomes in patients with COVID-19 remains uncertain. Therefore, the aim of this study was to assess the prognostic value of aminotransferases levels at hospital admission to predict all-cause mortality in hospitalized patients withCOVID-19.

## II. MATERIALS AND METHODS

This was a retrospective hospital based observational study that included 400 patients admitted at Kempegowda Institute of Medical Sciences, Bengaluru between April 2021 to July 2021. Diagnosis of COVID 19 was confirmed by RTPCR swab from oropharynx and nasopharynx. The cases were categorized into WHO Category A, B (non-severe) and C (severe).

Demographic and laboratory parameters including complete hemogram, liver enzymes, inflammatory markers like ferritin, CRP, LDH were collected. Statistical analysis was done using Kruskal Wallis test followed by Dunn's post hoc test. p value of less than 0.001 was considered statistically significant. Multivariate logistic regression analysis was conducted using SPSS software.

| CATEGORY | TYPE OF PATIENTS TREATED |
|---|---|
| GROUP A | Asymptomatic/Patients with mild symptoms<br>RR<24/m & SpO2>94% in room air |
| GROUP B | Symptomatic patient with mild to moderate Pneumonia with no signs of severe disease<br>RR:24 - 30/m & SpO2 : 90-94% in room air |
| GROUP C | Symptomatic patient with severe pneumonia<br>RR > 30/min (or) SPO2 < 90% at Room Air (or) less than 94% with oxygen, ARDS, septic shock |

RTPCR confirmed cases of COVID19 aged >18 years were included in the study.
Patients with chronic liver disease, hepatitis, alcoholism, pregnant women and patients on hepatotoxic drugs were excluded from the study.

## III. RESULTS

Out of 400 cases, 235 were men ,165 were women.

**Table 1: Age and gender distribution of study patients**

| Age and Gender distribution among study patients | | | |
|---|---|---|---|
| Variable | Category | n | % |
| Age | 20-40 yrs. | 133 | 33.3% |
| | 41-60 yrs. | 102 | 25.5% |
| | 61-80 yrs. | 143 | 35.8% |
| | > 80 yrs. | 22 | 5.5% |
| | | Mean | SD |
| | Mean & SD | 52.28 | 18.49 |
| | Range | 20 - 83 | |
| Gender | Males | 235 | 58.8% |
| | Females | 165 | 41.3% |

142 cases belonged to Cat A, 166 to Cat B, 92 cases were Cat C.

**Table 2: Distribution of study patients based on severity of COVID19**

| Distribution of study patients based on severity of COVID-19 | | | |
|---|---|---|---|
| Variable | Category | n | % |
| Severity | Category A | 142 | 35.5% |
| | Category B | 166 | 41.5% |
| | Category C | 92 | 23.0% |

136 cases had ICU admission while 264 were non-ICU cases. 60 cases succumbed to the disease.

**Table 3: Distribution of study patients based on ICU admission**

| Distribution of ICU Admissions among study patients | | | |
|---|---|---|---|
| Variables | Category | n | % |
| ICU Admission | Yes | 136 | 34.0% |
| | No | 264 | 66.0% |

**Table 4: Distribution of mortality among study patients**

| Distribution of Mortality rate among study patients | | | |
|---|---|---|---|
| Variables | Category | n | % |
| Mortality | Non-survivor | 60 | 15.0% |
| | Survivor | 340 | 85.0% |

Liver Enzyme levels were higher in Cat C compared to Cat B and Cat A. Mean AST value in Cat A was 30.44 , Cat B 61.86 and 90.95 in Cat C. Similarly ALT values were higher in Cat C (73.84) compared to Cat B(50.96) and Cat A(22).

**Table 5: Table showing comparison of mean SGOT(AST) values**

| Comparison of mean OT values based on the severity of the disease using Kruskal Wallis Test followed by Dunn's Post hoc Test | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Severity | N | Mean | SD | Min | Max | P-Value [a] | Sig. Diff | P-Value [b] |
| Category A | 142 | 30.44 | 9.69 | 16.0 | 70.0 | <0.001* | A vs B | <0.001* |
| Category B | 166 | 61.86 | 26.95 | 18.0 | 167.0 | | A vs C | <0.001* |
| Category C | 92 | 90.95 | 23.20 | 30.0 | 156.0 | | B vs C | <0.001* |

* - Statistically Significant

**Note:** a. p-value derived by Kruskal Wallis Test; b. p-value derived by Dunn's post hoc Test

**Table 6: Table showing comparison of mean SGPT(ALT) values**

| Comparison of mean PT values based on the severity of the disease using Kruskal Wallis Test followed by Dunn's Post hoc Test | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Severity | N | Mean | SD | Min | Max | P-Value [a] | Sig. Diff | P-Value [b] |
| Category A | 142 | 22.00 | 10.74 | 7.0 | 90.0 | <0.001* | A vs B | <0.001* |
| Category B | 166 | 50.96 | 21.36 | 7.0 | 120.0 | | A vs C | <0.001* |
| Category C | 92 | 73.84 | 24.22 | 20.0 | 137.0 | | B vs C | <0.001* |

* - Statistically Significant

**Note:** a. p-value derived by Kruskal Wallis Test; b. p-value derived by Dunn's post hoc Test

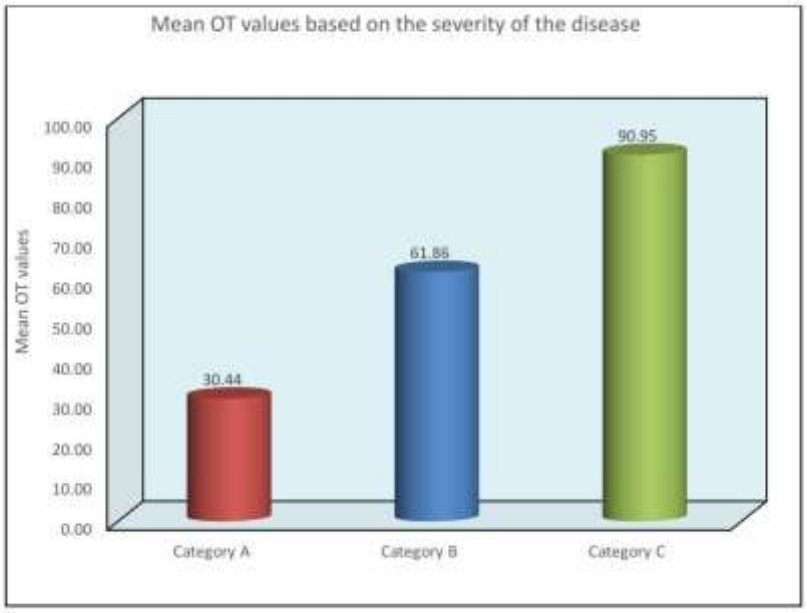


**Figure 1: Bar diagram showing SGOT(AST) levels based on disease severity**

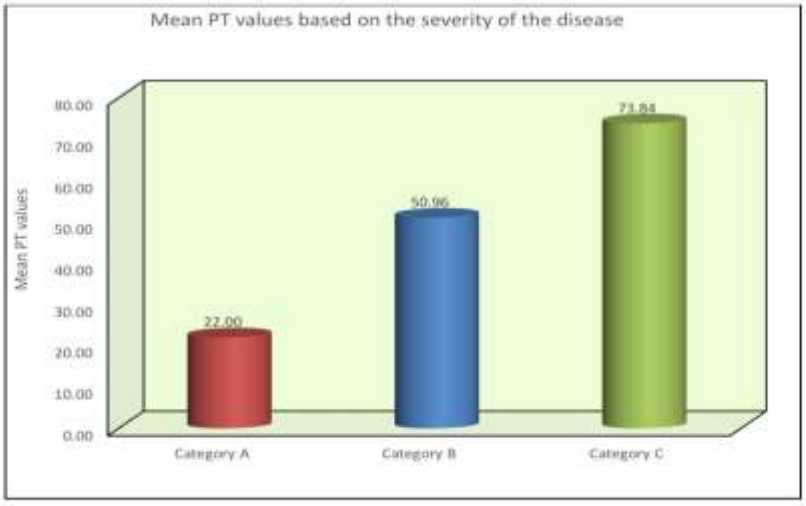


**Figure 2: Bar diagram showing SGPT(ALT) levels based on disease severity**

**Table 7: Table showing comparison of study parameters based on ICU admission**

| Comparison of mean values of different study parameters based on ICU admission using Mann Whitney Test | | | | | | |
|---|---|---|---|---|---|---|
| Parameter | ICU Admission | N | Mean | SD | Mean Diff | p-value |
| OT | Yes | 136 | 81.99 | 26.61 | 37.25 | <0.001* |
| | No | 264 | 44.73 | 25.57 | | |
| PT | Yes | 136 | 66.04 | 25.28 | 30.46 | <0.001* |
| | No | 264 | 35.59 | 22.45 | | |
| Ferritin | Yes | 136 | 489.63 | 400.01 | 261.36 | <0.001* |
| | No | 264 | 228.26 | 208.83 | | |
| CRP | Yes | 136 | 6.29 | 4.96 | 2.60 | <0.001* |
| | No | 264 | 3.69 | 3.86 | | |

* - Statistically Significant

**Table 8: Table showing comparison of study parameters based on mortality**

| Comparison of mean values of different study parameters based on Mortality status using Mann Whitney Test | | | | | | |
|---|---|---|---|---|---|---|
| Parameter | Mortality | N | Mean | SD | Mean Diff | p-value |
| OT | Non-survivor | 60 | 86.47 | 28.52 | 34.20 | <0.001* |
| | Survivor | 340 | 52.27 | 28.97 | | |
| PT | Non-survivor | 60 | 70.42 | 28.05 | 28.79 | <0.001* |
| | Survivor | 340 | 41.62 | 25.09 | | |
| Ferritin | Non-survivor | 60 | 494.97 | 424.92 | 209.22 | <0.001* |
| | Survivor | 340 | 285.74 | 278.62 | | |
| CRP | Non-survivor | 60 | 5.83 | 5.17 | 1.47 | 0.02* |
| | Survivor | 340 | 4.36 | 4.26 | | |

* - Statistically Significant

Mean AST value was 81.99 among ICU admission cases compared to 44.73 in non ICU cases. Mean ALT value was 66.04 among ICU admission cases.
Mean AST value in non-survivors were 86.47 compared to 52.27 in survivors. Similarly higher ALT values were seen in non-survivors compared to survivors (70.42 vs 41.62)
Higher enzyme levels were associated with mortality and higher levels of CRP,ferritin, LDH.

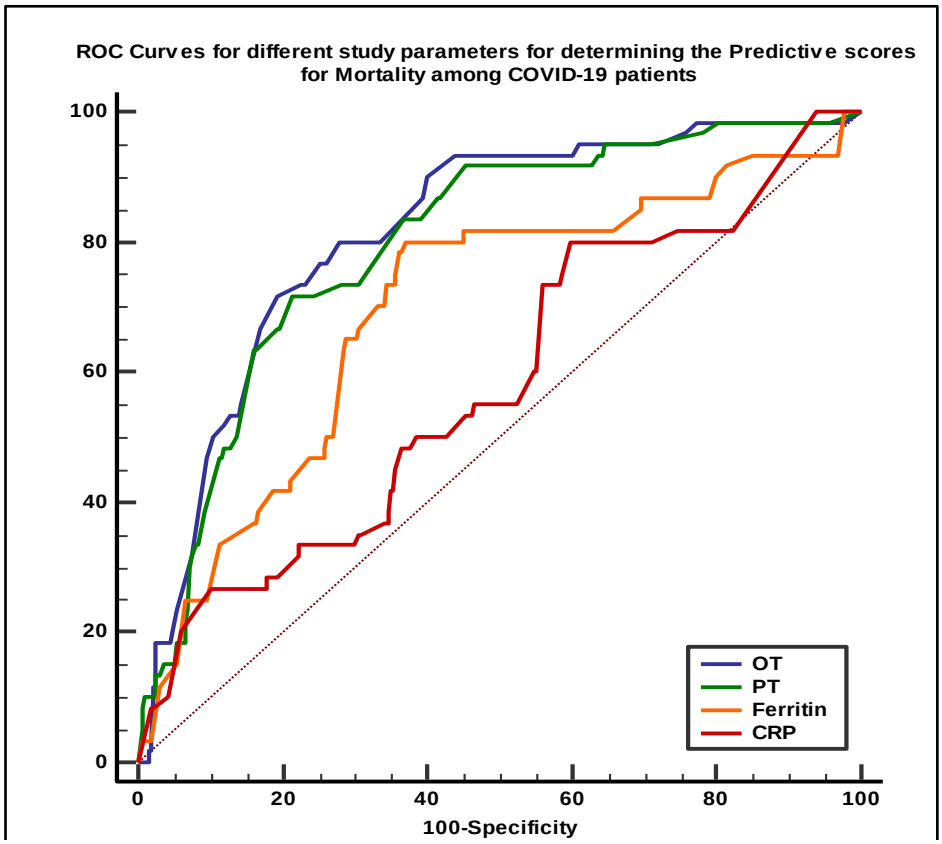


**Figure 3: ROC curves for different study parameters**

## IV. DISCUSSION

The current study highlighted that elevated aminotransferases levels at admission predicted in-hospital all-cause mortality in patients with severe COVID-19. . Mean AST value in Cat A was 30.44, Cat B 61.86 and 90.95 in Cat C. Similarly ALT values were higher in Cat C (73.84) compared to Cat B(50.96) and Cat A(22).
Mean AST value was 81.99 among ICU admission cases compared to 44.73 in non-ICU cases. Mean ALT value was 66.04 among ICU admission cases.
Higher levels of AST and ALT were seen in non-survivors compared to survivors.
Our findings have implications for optimizing management of hospitalized patients with COVID-19 since measurement of ALT and AST levels could be useful simple parameters to identify patients at high risk of mortality. The prevalence of significant elevated aminotransferases (≥ 2 × ULN) at hospital admission reported in the present study was similar to those previously described.
Despite the pathways for liver injury in COVID-19remains unclear, this might be explained by direct viralinfection, high expression of liver angiotensin-convertingenzyme-2 (ACE-2) receptor, muscular injury, presence ofsteatosis, microthrombosis, and the use of hepatotoxic drugs. Elevation of aminotransferases, especially at hospital admission, seems to be the liver expression of severeSARS-CoV-2 infection.
The main limitations of the study remain the lack ofprior history of chronic liver disease or use of hepatotoxic medications and the relatively high number ofpatientsexcludeddue to missing aminotransferases levelsat hospital admission. Viral hepatitis serologies, historyof alcohol intake or co-medications use prior to hospitaladmission were not available.

## V. CONCLUSION

Elevated aminotransferases levels at hospital admission could predict in-hospital all-cause mortality in patients with COVID-19, especially in those with severe disease at hospital admission. The use of these simple

and worldwide available parameters can help identify patients with severe COVID-19 at high risk of worse prognosis during hospitalization. The measurement of aminotransferases levels at hospital admission should be integrated into the care of patients with COVID-19.

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