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Original Article,

ALT and AST- new prognostic markers of COVID-19 in India

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Abstract:

Introduction: The second wave of the COVID-19 pandemic has affected India ruthlessly, and high mortality has been observed in all age groups. The city of Lucknow was severely affected, and many patients were admitted to our hospital during the second wave, which occurred from April to May 2021. In the present study, we investigated the association between the level of ALT (Alanine Aminotransferase) and AST (Aspartate Aminotransferase) with the other biomarkers (serum CRP, ferritin, and D-dimer) COVID-19 patients' mortality.

Method: Clinical and laboratory data from 80 consecutive cases meeting inclusion criteria were obtained from the records of patients with SARS CoV-2 infection admitted to Neuro ICU Medanta Hospital Lucknow. Patients were divided into two groups. The first group had data from patients who were discharged (control group), and the second group had data from patients who succumbed to death (case group). The data was analyzed by independent-sample t-test using IBM SPSS Statistics Version 20 software.

Result: It was observed that clinical features and co-morbidity were similar in both groups except for diabetes, which was more prevalent in the deceased group (p 0.01). A study of investigated biomarker levels (CRP, FERRITIN, D-DIMER, ALT, AST) in two groups revealed that raised ALT and AST levels (> 1000 u/l) were very frequent in the deceased group and the difference was statistically very significant ALT (P< 0.001), AST (P<0.005). A similar pattern was found in other biomarkers. So ALT and AST > 1000 u/L can be used as biomarkers for high mortality. It is economical, easy to perform, and widely available too.

Keywords: COVID-19, ALT, AST, Liver injury, Poor prognostic markers

Introduction:

The disease COVID-19, caused by a novel corona virus called SARS-CoV-2, was first reported by WHO on December 31st, 2019 in Wuhan, People's Republic of China. The rapid transmission of this virus has been seen from human to human since then. The World Health Organization (WHO) declared this as a public health emergency of international concern and called it a global pandemic (*Huang Ian 20201*)[1]. The COVID-19 pandemic has impacted health sector around the world. Many hospitals had scaled back or postponed non-emergency services. The health and social systems across the globe were struggling to cope. Every part of the health care system came under pressure to meet the needs of the community while responding to additional COVID-19 case loads and readjusting their care priorities. Due to the crisis, our hospital's beds had been converted to COVID-care beds. COVID-19 patients were admitted in neuro ICU for more than one month. While testing COVID-19 patients in the neuro ICU, it had been observed that liver function tests were significantly deranged in COVID-19 patients who were critically ill. During review literature it has been found that significant of ALT and AST as a biomarker as a prognostic biomarker was not emphasized too much. So we planned an observational study by using the method of statistical T-test and random sampling technique.

Aims and objective

To investigate the association of ALT and AST with very poor prognosis (mortality) along with the other biomarkers, e.g. serum C-reactive protein (CRP), D-Dimer, serum ferritin,

Materials and methods:

Location of the study: It is a retrospective observational study carried out at the Department of Neuroscience of Medanta Hospital in Lucknow, Uttar Pradesh, India**.** The study was carried out between April and May, during the second wave. Records of patients were studied to obtain consecutive (N = 40) discharged patient groups A and consecutive (N = 40) deceased patient groups B.

Statistical analysis: The statistical analysis was done using IBM SPSS Statistics Version 20, software. The value was expressed as a percentage. To test the significance of two meanings, the student "t" test was used. To compare between-group variances amongst the studied groups.p values of less than 0.05 were considered statistically significant

Table- 1 Criteria for classify biomarker level are given

Biomarker Level	ALT	AST	CRP	D-DIMER
Normal	21-72u/l	17-59u/L	0.0-5.0mg/L	>50mg/L
High	85u/l	>65u/L	>10mg/L	>50mg/L
Critical high	>1000u/l	>1000u/L	>50mg/L	>500ng/L
Critical high	>1000u/l	>1000u/L	>50mg/L	5000ng/L

Table-2 per cent distribution of patient as per gender

Gender	Total N=80	Group A N=4	Group B N=40
Male	53 (68.75%)	25 (62.5%)	28 (70.0%)
Female	27 (33.75%)	15 (37.5%)	12 (30.0%)

Results:

From April to May 2021, a total of 120 patients with a diagnosis of laboratory-confirmed COVID-19 were admitted to the Neuro ICU at Medanta Hospital, Lucknow, U.P. Table 2 demonstrates the male-to-female ratio in the study. In the 80 patients studied, 68.75% were male and 33.8% were female. In group A (n = 40), 62.5% of male and 37.5% of female patients were there, while 70.0% of male and 30.0% of female were in group B (n = 40). The age distribution of patients in different categories is given in fig. 1. Group A (n = 40) had 27.5% of patients who were younger than 40 years old, 12.5% of patients who were 40-50 years old, 17.5% of patients who were 50-60 years old, 32.5% of patients who were 60-70 years old, and 10.0% of patients who were more than 70 years old. Similarly, in Group B (n = 40), 10.0% of patients were less than 40 years old, 12.5% of patients were aged 40–50 years, 22.5% were aged 50–60 years, 37.5% of patients were aged 60–70 years, and 17.5% of patients were more than 70 years old. Elderly people were more likely to be among the deceased than among the aged.

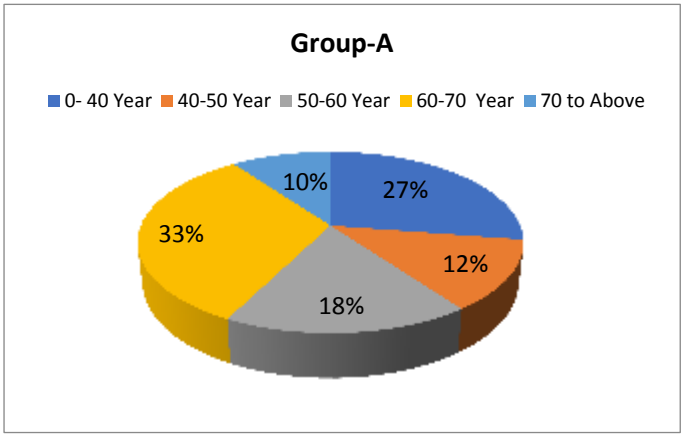


Fig-1 per cent distribution of patient as percentage

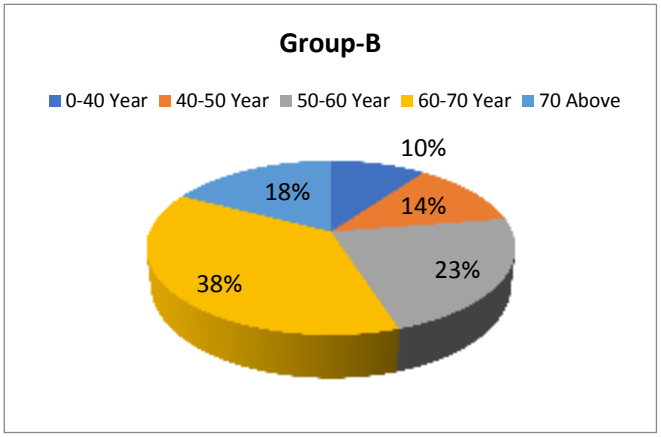
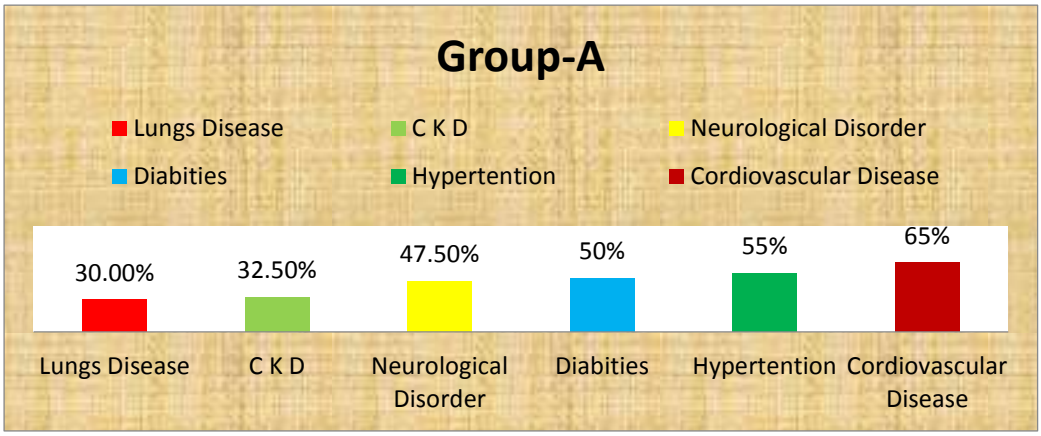
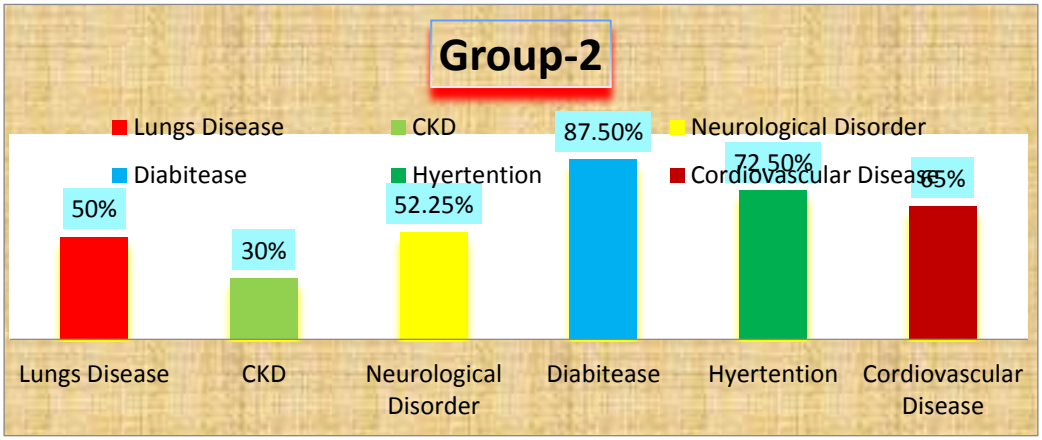


Fig 2: Distribution of patient according to Co-morbidity exhibited

In our study, Fig. 2 demonstrated that co-morbidities were more common in both groups. In Group-A (n = 40), the distribution of co-morbidities was as follows: lung disease (other than COVID pneumonia) 30.0%, chronic kidney disease 32.5%, neurological disorder 47.5%, diabetes 50.0%, hypertension 55.0%, and cardiovascular disease 62.5%. In Group-B (n = 40), the distribution of co-morbidities was chronic kidney disease 30.0%, lung conditions 50.0%, neurological disorders 52.25%, cardiovascular disease 65.0%, hypertension 72.5%, and a large proportion of the patients were diagnosed with diabetes 87.5%.





Discussion:

After analysis of data it has been found that co-morbidities were rampant among patient infected SARS COV-2. About 85.5% of patients diagnosed with diabetes. One possible explanation was that data at ICU patients with co-morbidities are more likely to be admitted to the ICU. In a study by *Sanyaolu, et.al.2020,*[2] *the* frequency of co-morbidities identified in COVID patients were hypertension (15.8%), cardiovascular and cerebrovascular conditions (11.7%), and diabetes (9.4%).

Our study results revealed that critical high levels of AST (P 0.05) and ALT (p 0.001) were associated with poor outcomes. Liu, *et.al. 2021*[3]studied the relationship between SARS coV-2 organotropism and receptor ACE2 distribution. Co-expression of the ACE2 receptor and virus antigen was observed in the lungs, trachea, small intestine, kidney, pancreas, and heart. In contrast, the ACE2 receptor was not expressed in the liver cells. *Bloom.P et.al*[4]. Reported that, early in the COVID-19 pandemic, there was significant disagreement among senior hepatologists with regard to the cause of abnormal liver biochemistry in a small group of SARS-CoV-2 infected patients, but consistency with regard to follow-up was recommended.

In a study conducted by *Liu Z et.al.*[5]at Leishenshan hospital, Wuhan, they also found similar findings and concluded that elevated levels of AST and levels may serve as biomarkers of

disease progression, poor prognosis, and mortality.

COVID-19 related liver injury is less evident in mild to moderate cases and this could be the reason behind the raised critical values of ALT and AST that were found only in sick patients. Other biomarker levels were compared to those found in other studies. Studies by *Leulseged et al. 2021* [6], *Huang I et al.* 2019 [1], *Madhusudan.S et al.* 2021)[7] and *Malik P et al.* 2020 [8] showed thatcritical high values CRP, D-dimer, and ferritin were also associated with poor outcomes very similar to our findings.

Conclusion:

In our study, we found that the critically high value of the biomarkers AST and ALT were statistically significantly and associated with poor outcomes including mortality. We attempted to find studies on the AST and ALT levels and poor outcomes, but discovered only a few studies that had emphasized this. AST and ALT tests are widely available and can be performed in a small setup while remaining cost-effective. Therefore, critical high values of ALT and AST can be useful markers for disease severity, poor outcome, and triaging COVID-19 patients.

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