A study on hepatic dysfunction in Covid 19 patients

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ABSTRACT

Background and Objectives - Covid -19 is a pandemic, which is known to be a multi organ disease with complex clinical manifestations. Covid 19 virus has predilection for lung involvement but can also cause hepatic dysfunction. This study aims to analyze the significance of abnormal liver function tests in SARS- COV2 positive patients.

METHOD- This retrospective study, involved 150 patients (75 MALES, 75 FEMALES) who tested positive for SARS COV2. After obtaining clearance from the ethical committee, clinical and biochemical data were collected retrospectively from patient records, for a period of six months. They were segregated into severe and non severe SARS COV2 infected individuals. liver function test were compared among patients between these 2 groups.

RESULTS-

Of the 150 covid- 19 positive patients, 75 were males and 75 were females. The mean age was 50±5 years. 95 patients belonged to the non severe covid-19 category (22 hypoxic and 73 non hypoxic patients), who were admitted in the ward. 55 patients belonged to the severe covid -19 category (hypoxic patients who required NIV/ ventilator support), admitted in the ICU.

Severe hypoalbuminemia 63% , was observed in the severe category, compared to 6.32% in the non- severe category. Raised transaminases were observed in 60% in the severe category, compared to 23.15% in the non severe category.

The incidence of death observed in the ICU in our study was 25.45%, of which 35% were female patients and 64.28% were male patients.

CONCLUSION- Hypoalbuminemia, raised transaminases and bilirubin were observed in covid-19 patients admitted in the ICU, indicating, they could be considered as a poor prognostic factor.

Keywords – hepatic dysfunction, Liver Function Test, Covid 19

INTRODUCTION

Covid -19 is a global pandemic, which is known to be a multi organ disease with complex clinical manifestations. (1) Though atypical pneumonia was the primary symptom of covid-19, liver impairment was also commonly observed among covid-19 affected patients.(2). SARS COV2, apart from affecting the lung causes other organ dysfunction like the gastrointestinal system. It binds to ACE2 receptor in the cholangiocytes and hepatic endothelial cells, thereby causing liver injury by means of inducing systemic inflammatory response. In a study by Guan et al. 1099 patients with confirmed covid-19 status in China, in which he observed 21.3% and 22.2% of the patients presented with raised ALT and AST, respectively, indicating liver injury to be very common among patients with Covid-19. (3).Prediction of duration of hospital stay, need for ICU admission, or prognosis, their

association has not been interpreted in these studies. Our study aimed to explore these parametrs.

MATERIALS AND METHODS

This retrospective study involved 150 patients (75 male,75 females) on an average aged 50±5years, tested positive for SARS COV2. Retrospectively we collected the data ,from patient records in the covid 19 isolation wards of Saveetha medical college and hospital during a period of six months.Patients irrespective of gender, aged more than 18 years and who tested positive for SARS COV 2 were included in the study. Exclusion criteria consisted of patients with chronic liver disease like cirrhosis, viral hepatitis (hepatitis B surface antigen positive, HCV RNA positive), pregnant women, history of chronic alcohol consumption. The study protocol was accepted by the ethical committee and retrospectively collected clinical and biochemical data from the patient records. Clinical information and vital parameters like saturation, status, pulse rate, respiratory rate, blood pressure and biochemical information such as complete blood count, liver function test, d-dimer, serum ferritin, coagulation profile. Sars cov2 RNA recognition was obtained by performing swabbing of both the nostrils and oropharyngeal specimens were obtained by swabbing the posterior pharynx, determination done based on a quantitative real time polymerase chain reaction .Severity of sars cov2 was analysed based on vital parameters and depending on finding obtained from HRCT, and patients were segregated according as severe and non severe(mild/moderate cases).

Patients with pulse rate of 60-100, SBP > 120mmHg DBP > 80mmHg ; RR-18-24/min. Pao2/Fio2 300-500. Without changes or with findings such as small patchy ground glassing opacities, in the lung peripheries and under the pleura or on HRCT chest or CT severity score <8/25,were considered to be non severe.

The presence of one or more of the following features was considered to be severely infected sars cov2- RR>24/min, pulse rate > 120/min, oxygen saturation in room air, on rest < 92% ,Pao2/Fio2 <300mmhg, HRCT chest revealing ground glassing opacities involving more than 50% lung or CT severity score >10/25.

Liver function test abnormalities consisted of serum bilirubin > 1.2mg/dl, ALT > 35 units/l, AST >50 units/l, serum albumin <3.5 mg/dl, INR> 1.2, Acute liver injury- ALT/AST ratio 3 times more than the upper limit of normal.

Other parameters: D-dimer(> 300ng/l), Serum ferritin (>464ng/ml- male, >137ng/ml-females) were also recorded. All the date were collected and analysis were done.

RESULTS

Of the 150 covid- 19 positive patients, 75 were males and 75 were females. The mean age was 50±5 years. 95 patients belonged to the non severe covid-19 category (22 hypoxic and 73 non hypoxic patients), who were admitted in the ward. 55 patients belonged to the severe covid -19 category (hypoxic patients who required NIV/ ventilator support), admitted in the ICU.

On comparing the compiled data, (FIGURE 1 &2) we observed that 63% had severe hypoalbuminemia (35 out of 55), was observed in the severe category, compared to 6.32% (6 out of 95) in the non- severe category.

Raise in AST 3 x ULN was observed in the severe category as high as 806 IU/l. Raised transaminases were observed in 60% (33 out of 55) in the severe category, compared to

23.15% (22 out of 95) in the non severe category. D-dimer was observed to be exponentially raised in patients admitted in the ICU.

In the non- severe category, out of 95 patients (FIGURE 3), (45 females, 50 males)- liver dysfunction was observed in 28.88% (13 out of 45) female patients, and 40% (22 out of 55) male patients, and was no death reported.

Among patients admitted in the ICU (FIGURE 4) 88% (22 out of 25) female patients and 96.6% (29 out of 30) male patients were observed to have liver dysfunction. The incidence of death observed in the ICU in our study was 25.45% (14 out of 55) of which 35% (5 out of 14) were female patients and 64.28% (9 out 14) were male patients.
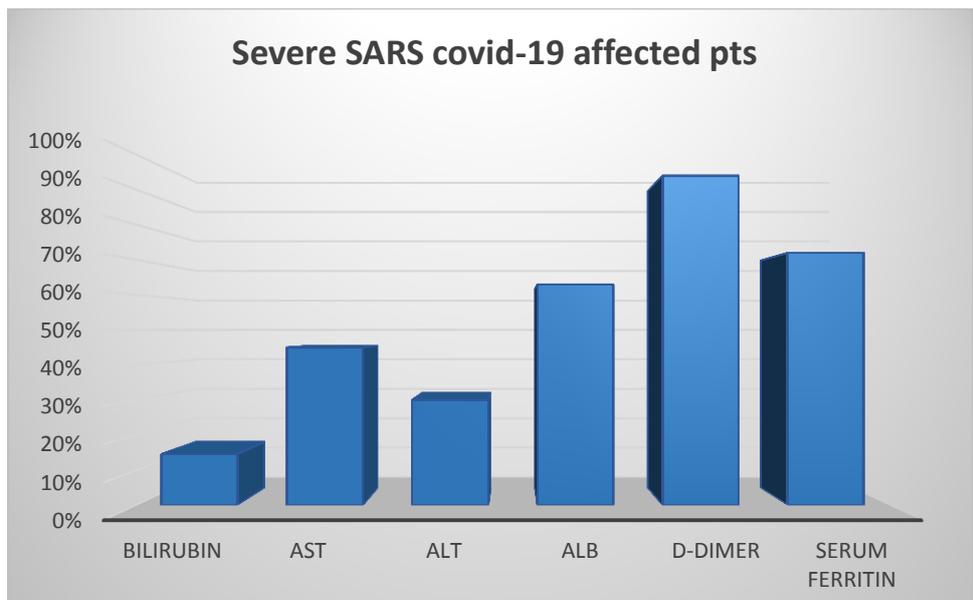

FIGURE 1- GRAPHICAL REPRESENTATION OF DERRANGED LIVER FUNCTION TEST AND INFLAMMATORY MARKERS IN SEVERE COVID-19 INFECTION (ICU)
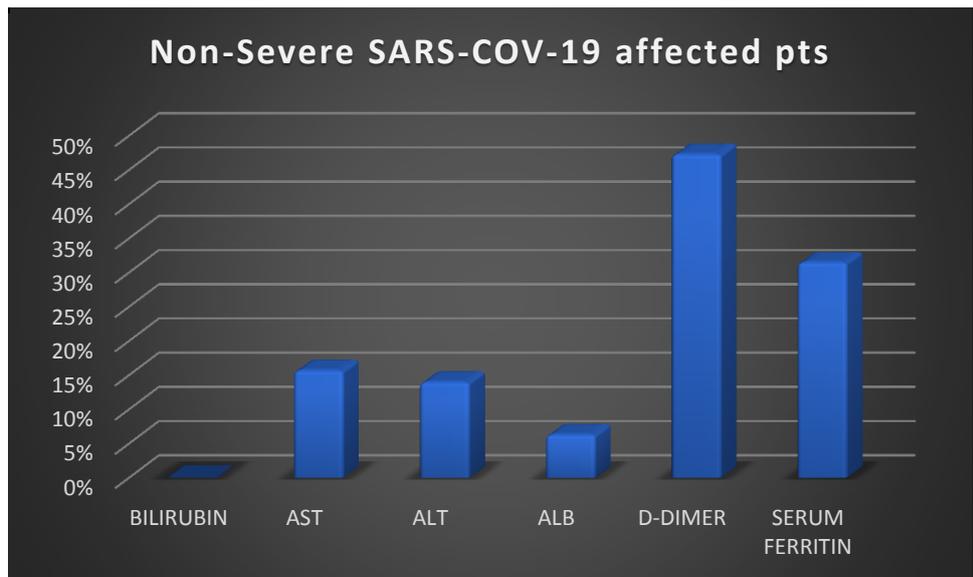

FIGURE 2- LIVER DYSFUNCTION AND RAISED INFLAMMATORY MARKERS IN NON- SEVERE (WARD) COVID 19 PATIENTS
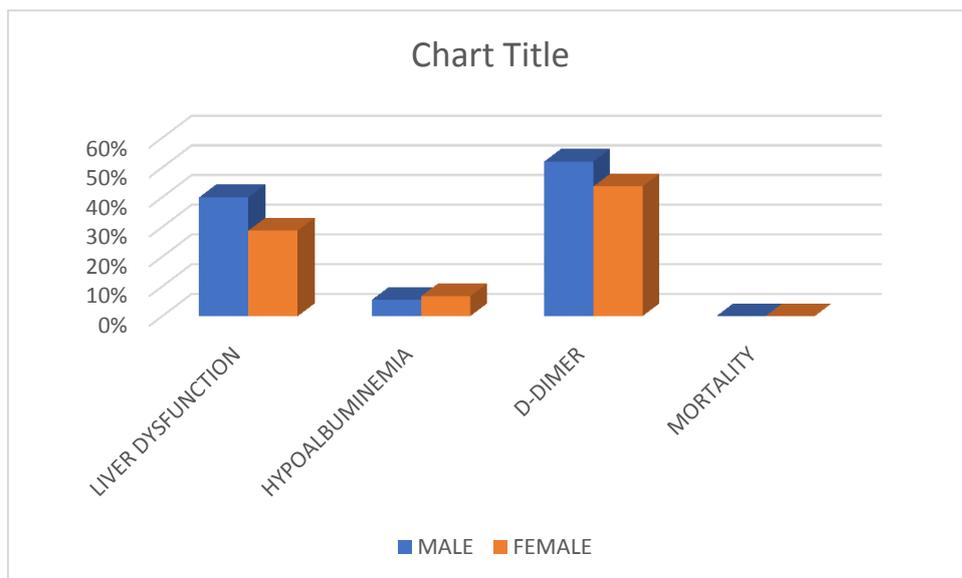
FIGURE 3- GENDER BASED DEPICTION OF ABNORMALITIES OBSERVED IN
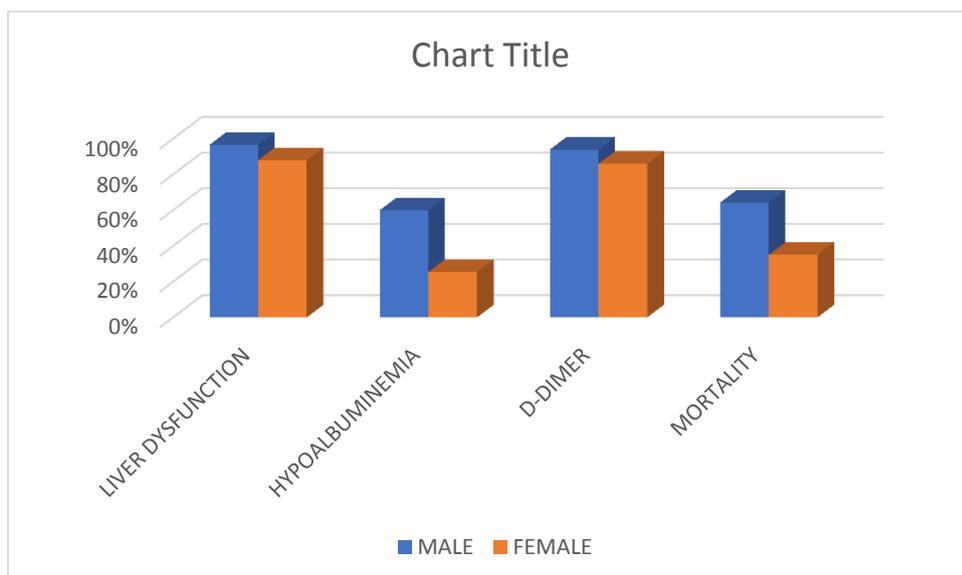COVID 19 PATIENTS ADMITTED IN THE WARD

FIGURE 4- GENDER BASED DEPICTION OF ABNORMALITIES OBSERVED IN
COVID 19 PATIENTS ADMITTED IN THE ICU

DISCUSSION

In covid-19 patients, liver injury and abnormalities, have been reported even as a sequelae of
covid-19 in many patients post hospitalization.(4). In a study by Piano et al, they have found
that abnormal LFT is an independent predictor for admission in the intensive care unit.(5)
Although exact underlying mechanism for raise in LFT is unclear, several possible theories
have been hypothesized. The main hypothesis underlying respiratory involvement in covid-
19, is via the ace 2 receptors present in the lung tissue.(6)Ace2 receptors are also highly
expressed in the brush border of small intestinal enterocytes; to substantiate this SARS COV2
nucleocapsid have also been detected in the cytoplasm of intestinal biopsies of a patient with
covid-19 (7). This viral replication in the intestine, then enters the portal circulation and

reaches the liver, is another theory constituted upon understanding the effect of sars cov2 on the liver.

Altered LFTs could also be related to hypoxia, ischemic injury and the cytokine storm syndrome, wherein there will be excessive or uncontrolled release of proinflammatory cytokines that is associated with multiorgan failure (8). This can be substantiated by the extravasation of inflammatory cells and release of mediators causing disseminated intravascular coagulation, raised d-dimer, and altered coagulation profile. ACE2 receptors are expressed in hepatic bile duct cells.(9)In our study we observed, derangement in liver function test in the form of raised bilirubin and hypoalbuminemia in patients with severe covid-19, who were admitted in the ICU.

 Increased bilirubin (marker of cholangiocyte damage), elevation of ALT, decrease in albumin, are indices of high mortality (10). However, normal ALP, increased AST/ALT, doesn't support hypothesis of liver injury. (11). In Covid 19, coagulation dysfunction, thrombosis, high serum ferritin, are potential risk factor for liver dysfunction.

Studies have also reported that the use of multiple drugs during the covid 19 infection; such as antipyretic, acetaminophen, corticosteroids, antibiotics, antivirals are known to have some level of hepatotoxicity, resulting in liver dysfunction.(12,13)

Increased transaminases ,may not only be due to hepatocyte damage, myositis can also result in the same, which can be supported by increased creatinine, and lactate dehydrogenase and myoglobin that have been reported by patients with severe covid-19.(14,15). Deranged liver function test in the form of increased Bilirubin, AST, ALT, hypoalbuminemia is observed in covid-19 patients admitted in the ICU, and is also an indicator of poor prognosis and risk of mortality.(16), which was observed in our study.

The most consistent hemostatic abnormality observed in COVID-19 patients is thrombocytopenia and raised D-dimer levels, which is associated with increased risk of admission in the intensive care unit, need for mechanical ventilation, and increased risk of mortality, especially in elderly and with comorbidities.(17), which was also an observation made in our study.

CONCLUSION

Hypoalbuminemia, raised transaminases and bilirubin were observed in covid-19 patients admitted in the ICU, than patients who were treated under non severe category. It is important to give attention to hypoalbuminemia, and raised bilirubin, as they are early indicators of poor prognosis, and indicate the longer duration of course of stay in the hospital.

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