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COVID -19 ASSOCIATED VARIATIONS IN LIVER PARAMETERS – A RETROSPECTIVE STUDY.

Biochemistry

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ABSTRACT

Recent data on the coronavirus disease 2019 (COVID-19) pandemic that has affected millions across the globe has begun to shine light on the impact of the disease on the liver besides affecting other organs. We evaluated the clinical characteristics of COVID-19 in patients with abnormal liver test results to demonstrate its effects on liver tissue.A retrospective cross sectional study was done among Covid-19 positive cases(RT-PCR confirmed) admitted in GMCH for a period of 4 months from April 2021 to July 2021(4 months). Laboratory reports of diagnosed 500 COVID -19 patients admitted in GMCH was taken up for the study from Central Clinical Laboratory Biochemistry and patient clinical data collected from the clinical files of the patients stored in the MRD office **Results:** Of 500 patients with COVID-19, 285 (57%) had normal liver test results,215(43%) had raised liver enzymes at the time of admission. The presence of raised liver tests became more pronounced during hospitalization within 2 weeks, with 85 patients having severe liver injury where 20 (23.5%), 35(41.1%), 30 (35.2%) patients have alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase levels elevated to more than 3× the upper limit of normal, respectively **Summary and conclusion:** We observed a high prevalence of liver test abnormalities and liver injury in 215 patients with COVID-19 admitted to our referral center, and the injury increased substantially during hospitalization. The presence of abnormal liver tests and liver injury were associated with the raised inflammatory marker CRP.

KEYWORDS

AST, ALT, ALKP, CRP

INTRODUCTION:

Coronaviruses are a family of viruses that are known to cause both respiratory and intestinal diseases in various animal species and humans[1] These viruses tend to target the upper respiratory tract, causing from moderate to severe illnesses, such as fever, cold or in extreme cases, pneumonia.

While most COVID-19 cases had been identified as mild, more extreme diagnoses have led to respiratory failure, septic shock, and/or multiple organ dysfunction.[2] It is known that the primary organ targeted in SARS is the lung, however, other organ dysfunctions, included gastrointestinal symptoms, abnormal liver functions.

These occurrences reflected widespread immuno pathology or extrapulmonary dissemination and replication of SARS-coronavirus. [3] The pathological changes could be attributed either to the direct cytotoxic effect by local replication of the virus or indirectly due to immune response induced by the viral infection.[4].

A study found the binding of SARS-CoV-2 virus to Angiotensin Converting Enzyme-2 (ACE2) on cholangiocytes leading to its dysfunction, which led to liver injury through inducing a systemic inflammatory response.[5] Several hospital-based studies had reported liver damage in patients with COVID-19 in terms of elevated levels of liver enzymes like aspartate aminotransferase (AST) ,alanine aminotransferase (ALT) and alkaline phosphatase. [6,7,8]

OBJECTIVES:

1)To study the liver test abnormalities in patients with Covid -19 at the time of admission and during hospitalization and to observe the progression of patients with liver injury to severe disease and its correlation with the inflammatory marker(C-reactive protein)

MATERIALS AND METHOD:

Retrospective cross sectional study done among 500 Covid-19 positive cases(RT-PCR confirmed) above 18 years of age admitted in GMCH for a period of 4months from April 2021 to July 2021(4 months). Laboratory reports of diagnosed COVID -19 patients admitted in GMCH was taken up for the study from Central Clinical Laboratory Biochemistry and patient clinical data collected from the clinical files of the patients stored in the MRD office

Patients suffering from chronic liver diseases, alcoholism, hepatitis, pregnant women and children (below 18 years) were excluded from the study.

Estimation of Liver function tests and CRP was carried out in Vitros 5600 fully Automated Analyser. After all the calculations and the biochemical estimations, the results obtained were statistically analyzed and compared between different groups of the study. Baseline characteristics of the study participants were expressed in mean ± SD (standard deviation).

Results considered significant when the probability (p value) < 0.05 % .Statistical analysis done using GraphPad InStat version 3.00. All the statistical graphs were prepared using Microsoft Excel 2007.

RESULTS:

Out of total 500 COVID 19 pateints 321 were male and 179 were female subjects.We categorised the study population into three different age groups and the highest number of cases were found in the 40-60 years group. Amongst the study group 285 (57%) had normal liver test results, while 215(43%) had raised liver enzymes at the time of admission.

The presence of raised liver tests became more pronounced during hospitalization within 2 weeks of stay with 85 subjects progressing to severe liver injury where 20(23.5%), 35(41.1%),and 30 (35.2%) patients had alanine aminotransferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALKP) levels elevated to more than 3× the upper limit of normal (ULN) respectively.On doing Pearson Correlation, the raised liver enzymes had a statistically significant positive correlation with the inflammatory marker C-reactive protein (CRP)

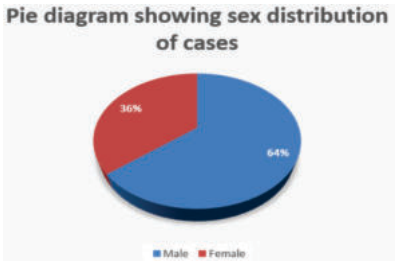

Fig1: Pie diagram showing sex distribution of cases

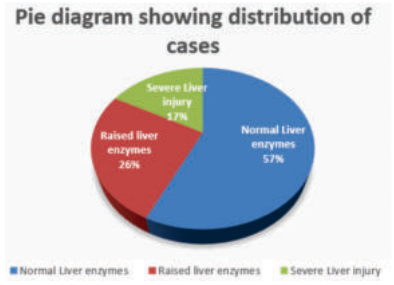

Fig 2:Pie diagram showing distribution of cases

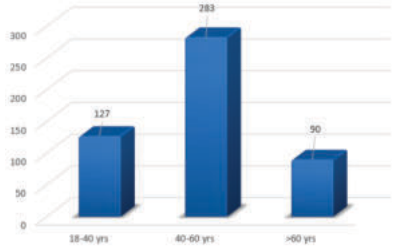

Fig 3: Bar diagram showing age distribution of cases

Table 4: Showing mean ± SD of different liver enzymes depending on liver injury.

Parameters	Patient with normal liver enzymes(mean ±SD)	Patient with raised liver enzymes (mean ± SD)	Patient with severe liver injury(mean± SD)	P value
AST	28.15±10.32	67.19±13.21	157.36±31.12	<0.0001
ALT	24.64±14.30	62.8912.02	176.32±40.91	
ALKP	98.14±18.51	151.19±16.08	286.25±39.71	

Table 5: Showing pearson correlation between CRP and liver enzymes.

Parameter	r	r 2	P
AST	0.257	0.066	0.031
ALT	0.388	0.151	0.001
ALKP	0.419	0.175	0.003

DISCUSSION:

Since various studies have suggested the involvement of liver damage due to systemic inflammatory response generated by SARS CoV-2 virus ,a deranged liver function test was expected. Male population was affected more than the female population and the frequency of cases was highest in the age group of 40-60 years .Cases presenting with raised liver enzymes at the time of admission progressed to severe liver injury with AST,ALT,ALKP rising 3X ULN(upper level normal). Liver injury was more prevalent in severe COVID-19 cases (e.g. ICU admission) than mild cases, so liver function could be considered as an indicator of disease progression.[9]

The liver injury could be due to a direct effect of SARS-CoV-2, or an indirect effect following septic shock, multiorgan dysfunction, drug-related toxicity, immune-related hepatitis, or a systemic inflammatory responses (cytokine release or storm) of the COVID-19 syndrome. A recent study showed that SARS-CoV-2 might directly bind to ACE2 positive cholangiocytes and cause liver damage,[10]explaining the contribution of SARSCoV- 2 infection to the liver test dysfunction in the patients.Moreover, the use of ACE-inhibitors could have also affected liver tests. Hypertensive patients in our case group using ACE inhibitors at admission, may have influenced their abnormal liver tests.

We found a positive correlation of raised liver enzymes with the inflammatory marker CRP which supported the basis of profound inflammatory response seen in COVID-19 and might have played a central role in liver injury. Data published from a few recent studies suggest that mitochondrial proteins may directly interact with the virus, [11] that provided a potential explanation for the AST-dominant injury profile. Moreover, congestive hepatopathy might have occured as a consequence of an acute cardiomyopathy which was thought to be a common complication of COVID -19 and associated with elevations in aminotransferases. [12,13] Alkaline phosphatase elevation occuring late in COVID-19 disease progression could reflect the cholestasis of sepsis, critical illness, or medication effect.[14]

CONCLUSION:

As liver function tests are routine investigations carried out at the time of admission, liver function test abnormalities could, have been used as a predictor for the severity of the disease. It is now postulated that the SARS-CoV-2 virus was not only highly transmissible, but also caused severe multi-organ dysfunction in humans. Through this study we could put some insight into the extrapulmonary damage caused by SARS Cov-2 which is still a major cause of morbidity and mortality in the affected individuals.

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