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Correlation of Hepatic Enzymes and Inflammatory Markers with Severity of Covid-19

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Abstract

Background: Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus, which has now become a pandemic. COVID-19 has a wide variety of clinical features, ranging from asymptomatic infection to moderate to severe pneumonia. Different laboratory measures get changed in these individuals and are, therefore valuable as biomarkers to detect disease development and identify patients who may present a severe and/or fatal clinical condition. The objective of the study was to find the correlation between the biochemical parameters along with the severity of the disease.

Methods: An observational descriptive cross-sectional study was carried out from May 2021 to May 2023 in the Father Muller Medical College Hospital's Department of Clinical Biochemistry in Mangalore, India. A total of 150 data on COVID-19 were collected, both clinical history and biochemical values. Statistical analysis of the collected data was analyzed by mean, standard deviation, chi-square test, and comparison done by Mann-Whitney test.

Results: In our study population, out of 150 COVID-19 cases, 74 cases were mild, 42 cases were moderate and 34 were severe. Affected patients were slightly male preponderance. As the severity of COVID -as increased, biochemical liver markers (AST & ALT) and inflammatory markers (CRP, Ferritin & LDH) were increased.

Conclusion: The liver parameters and inflammatory markers are good tests for differentiation of severity of COVID-19. Since these tests (AST, ALT, CRP, Ferritin, and LDH) are basic, they can be used for the early differentiation of severe infections.

Keywords: Blood Biochemical Parameters; COVID-19; SARS-CoV-2; Liver Disease; CRP

Abbreviations: WHO: World Health Organisation; ARDS: Acute Respiratory Distress Syndrome; LDH: Lactate Dehydrogenase; ALT: Alanine Transaminases; AST: Aspartate Transaminase; CRP: C-Reactive Protein; TNF: Tumour Necrosis Factor; FMIEC: Father Muller Institutional Ethics Committee

Introduction

In December 2019, a cluster of pneumonia cases of unclear etiology was identified in Wuhan city of Hubei province in China [1]. In January 2020, temporarily it was labeled as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), then changed to Coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) in February 2020 as the disease spread worldwide [2]. In March 2020, the WHO officially declared the COVID-19 outbreak as a global pandemic as the number of infected individuals from all continents continued to grow daily [3].

Coronaviruses belong to the family Coronaviridae, which possess a single-strand, positive-sense RNA genome. The virus bears club-shaped spike projections emanating from the surface which are responsible for the coronavirus's characteristic look, resembling a solar corona [4]. Coronaviridae is known to cause both respiratory and intestinal diseases in various animal species and humans and is transmitted from person to person through close contact, respiratory droplets, and aerosols [5]. COVID-19 has also been observed to spread from patients to health staff and flight attendants who had close contact with the affected patients. As per CDC, following viral exposure, the incubation period is 2-14 days [6]. Most infected individuals are asymptomatic or present non-specific, flu-like symptoms, such as fever, headache, fatigue, dry cough nausea, asthenia, diarrhoea, and myalgia which can

evolve into severe respiratory disease, sepsis, septic shock, acute respiratory distress syndrome (ARDS), multi-organ failure and leading to death [7,8].

Liver dysfunction has also been described as a common symptom, though the clinical relevance of this is still unknown [9]. The severity of the disease is higher in old age, male sex, and patients with comorbidities, such as obesity, hypertension, cancer, type 2 diabetes, cardiovascular disease, and immune-compromised individuals [6]. In this era of an unprecedented health crisis, research is happening at immense speed, to date, no effective drugs or vaccines have been developed to treat or prevent COVID-19. Clinical laboratory professionals were looking for dependable biomarkers related to COVID-19 disease development to develop fast and accurate diagnostic assays [10]. COVID-19 shows several laboratory abnormalities like a high rise in lactate dehydrogenase (LDH), D-dimer, cardiac troponin I, procalcitonin, ferritin, Alanine transaminases (ALT), Aspartate transaminase (AST), bilirubin, and lower lymphocyte count along with elevated inflammatory markers like C-reactive protein (CRP), tumour necrosis factor (TNF), and interleukin-6 (IL-6) [11].

When compared to patients with mild or moderate conditions, the levels in severe individuals are higher. As a result, it's critical to comprehend how these laboratory anomalies might be utilized to predict illness prognosis [12]. The present study will attempt to determine the biochemical parameters and inflammatory markers to differentiate the severity of COVID-19 patients.

Materials and Methods

An Observational descriptive cross-sectional study conducted in Department of Clinical Biochemistry at Father Muller Medical College Hospital, Mangalore, India, from May 2021 to May 2023. The ethical approval was granted by Father Muller Institutional Ethics Committee (FMIEC) with the Ref No: FMIEC/CCM/420/2021. All of the enrolled patients were over the age of 18 years, and were confirmed as SARS-CoV-2 RNA positive based on oro-nasopharyngeal swab specimens obtained using RT-PCR. Patient's IP number, age, sex, and clinical data of RT-PCR positive patients were collected from Medical Record Department, and data from the same patient's biochemical tests ALT, AST, LDH, CRP, and Ferritin were gathered from the Biochemistry Central Lab's laboratory test registers. The biochemical test was performed using Roche Cobas 6000 analyzer. The COVID-19 patients were divided into three main groups, being those with mild, moderate, and severe. Severe pneumonia was defined as 'the presence of Respiratory distress, in the resting state mean oxygen saturation is ≤90%, HRCT score >7, Severe metabolic acidosis (pH↓, bicarbonate↓, hypoxia).

Inclusion criteria

1) Laboratory confirmed (by RT-PCR) COVID-19 positive patients

2) Both male and female, age group of 19 to 60 years.

3) Moderate: with fever, cough, cold, diarrhoea, body pain, seizure, imaging shows pneumonia, in the resting state, mean oxygen saturation ≤94%, oxygen required.

4) Severe: symptoms meet any of the following:

a) Respiratory distress

b) In the resting state, mean oxygen saturation is ≤90%

c) HRCT score >7

d) Severe metabolic acidosis (pH↓, bicarbonate↓, hypoxia)

Exclusion Criteria

1) Children below 18 years with RT-PCR positive.

2) Pregnant women with RT-PCR positive.

Sample size

$$N = \left[2(Z\alpha + Z\beta)\frac{2}{C2}\right] + 3$$

Where: $Z\alpha = 1.96$ *at* 95% *C.I,*

$Z\beta = 1.281$ *at* 90% *power*

$$C = 0.5\ Ln\left(\frac{1+r}{1-r}\right)$$

$r = 0.548$ *(between severity and LDH)* [13]

$Therefore, N = 150$ *Cases*

Statistical Analysis

Collected data were entered in Microsoft Excel and computerized statistical analysis was performed using SPSS (Statistical Package of Social Sciences) version 23. The correlation between biochemical parameters in relation to the severity of COVID-19 disease was analyzed by the chi-square test (Fischer's exact test). Mann Whitney test for analyses of the differences in the incidence among multiple groups. The level $P<0.05$ was considered a cut-off value or significance. Categorical data were described using frequencies, percentages, Mean with Standard deviation & median with interquartile range.

Results

Demographics and General Information of 150 COVID-19 Patients

Of the 150 patients included in the study from 18-60 years, 80 were males (53.3%) and 70 (46.7%) were females, with a mean age of 40.48 ± 13.70 years. There were 74 cases in the mild group, 42 cases in moderate and 34 cases in the severe group. A total of 45(30%) patients had comorbidities like diabetes, hypertension, and acute kidney disease. Furthermore, 8 out of 150 patients (5.33%) were non-survivors and 142(94.66%) were survivors.

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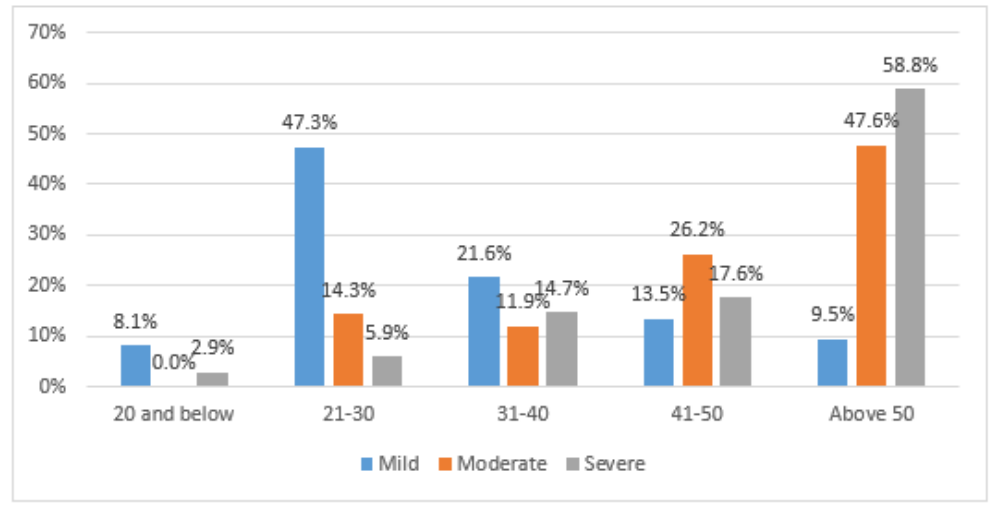

Figure 1: Graphical representation of the age-wise distribution of severity of COVID-19.

Age-Wise Distribution of COVID-19

The age of patients ranged from 18 to 60 years with a mean age of 40.48 years. Severity of the disease was more seen in patients above 50 years [20 cases (58.8%)] and was least severe in age below 18 years [1 case (2.9%)] as shown in (Figure 1).

Distribution According to Clinical History

With respect to the clinical history of the patients, the maximum number (74 cases, 49.3%) were mild, followed by moderate (42 cases, 28.0%) and severe (34 cases, 22.7%) as shown in Table 1.

Table 1: Grading of the severity of COVID-19.

Severity of disease	Frequency (%)
Mild	74 (49.3%)
Moderate	42 (28%)
Severe	34 (22.7%)

Table 2: Correlation of AST with the severity of COVID-19.

AST	N	Median (IQR)	P-value	Mild-Moderate	Mild-Severe	Moderate-Severe
Mild	74	22(17.75-35)				
Moderate	42	41(27.25-65)	<0.001 HS	<0.001, HS	<0.001, HS	0.289, NS
severe	34	33(27.25-52.75)				

Table 3: Correlation of ALT with the severity of COVID-19.

ALT	N	Median (IQR)	P-value	Mild-Moderate	Mild-Severe	Moderate-Severe
Mild	74	20.5(14.75-30.25)				
Moderate	42	34.5(22.75-55.75)	<0.001 HS	<0.001, HS	0.607, NS	0.084, NS
severe	34	21.5(15-41.5)				

Table 4: Correlation of CRP with the severity of COVID-19.

CRP	N	Median (IQR)	P-value	Mild-Moderate	Mild-Severe	Moderate-Severe
Mild	74	6.61(2.14-30.3375)				
Moderate	42	26.47(6.8675-78.095)	<0.001 HS	<0.001, HS	<0.001, HS	0.354, NS
Severe	34	34.56(11.845-127.0325)				

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Table 5: Correlation of Ferritin with the severity of COVID-19.

Ferritin	N	Median (IQR)	P-value	Mild-Moderate	Mild-Severe	Moderate-Severe
Mild	74	98.12 (41.7-198.125)				
Moderate	42	609.5(334.725-956.45)	<0.001 HS	<0.001, HS	<0.001, HS	0.794, NS
severe	34	507.05(250.325-1339.5)				

Table 6: Correlation of LDH with the severity of COVID-19.

LDH	N	Median (IQR)	P-value	Mild-Moderate	Mild-Severe	Moderate-Severe
Mild	74	218.5(179.75-300.25)				
Moderate	42	316.5(223.5-386)	<0.001 HS	<0.001, HS	<0.001, HS	0.608, NS
severe	34	371.5(237-508.25)				

The Table 2 shows the correlation between AST and the severity of COVID-19 analysed by the Mann-Whitney test. The P-value < 0.001 in AST was found to be statistically significant for mild-moderate and mild to severe cases.

The Table 3 shows the correlation between ALT and the severity of COVID-19 analyzed by the Mann-Whitney test. The P-value < 0.001 in AST was found to be statistically significant for mild-moderate cases.

The Table 4 shows the correlation between CRP and the severity of COVID-19 analysed by Mann-Whitney test. The P-value < 0.001 in CRP was found to be highly significant for severe cases with mean of 309.29 and S.D 98.88.

The Table 5 shows the correlation between ferritin and the severity of COVID-19 analysed by Mann-Whitney test. The P-value < 0.001 in ferritin was found to be highly significant for moderate and severe cases with mean (S.D) of 877.31(1055.46) and 1214.38(1690.72) respectively.

The Table 6 shows the correlation between LDH and the severity of COVID-19 analysed by Mann-Whitney test. The P-value < 0.001 in LDH was found to be statistically significant for mild, moderate and severe cases. In this study, the serum biochemical markers show a significant correlation with severity of COVID-19 patients.

Discussion

Today, COVID-19 is a serious public health problem that has an impact on patient health as well as related medical expenses. For this, clinical laboratories can help establish biomarkers that would enable grading of the risk of patients developing more serious illnesses and help accelerate clinical decision-making. This study explored the changes in liver-related enzymes and inflammatory markers and addressed the importance of these in the classification and diagnosis of COVID-19. Our study showed significant differences with regard to the biochemical markers ALT, AST, CRP, Ferritin, and LDH among mild, moderate, and severe COVID-19 cases. The result indicates the increase of ALT, AST, CRP, Ferritin, and LDH during COVID and the study demonstrates a significant correlation between liver enzymes and inflammatory markers and the severity of COVID-19.

In order to assess the impact of SARS-CoV-2, we evaluated AST & ALT as liver enzymes indicating liver damage, LDH for tissue damage, and Ferritin and CRP are acute-phase proteins that may reflect SARS-CoV-2-induced hyper-inflammation. Although liver enzymes did not significantly differ across the mild, moderate, and severe COVID-19 individuals, we saw a significant change in inflammatory markers. But all parameter levels were significantly above the biological reference ranges provided for a healthy population. In line with our result, the study conducted by Chen et al which included 99 confirmed cases of COVID-19, also showed the ALT and AST values that were higher than the reference range [14].

In accordance with previous study reported by Zhou C et.al, our study showed the quantity of ferritin was increased in the severe group than in other groups(P<0.001) [8]. Data gathered by Smilowitz N R. et al. also shows patients with simultaneous elevations in CRP and D-dimer had a significantly greater mortality rate (39.8%, P<0.001) than those with low CRP and D-dimer readings [15]. Previously Henry B. M et.al showed, there was a significant correlation with the severity of COVID-19 patients (P-value <0.001) corresponding to our values [16].

These data support the existing evidence of correlation of liver enzymes and inflammatory markers with poor clinical outcomes in COVID-19. Liver function test abnormalities and inflammatory markers might be utilized as a predictor for the severity of the disease because they are regular investigations performed at the time of admission. This is aligned with another study that found that individuals with severe COVID-19 have significantly higher levels of the inflammatory biomarkers CRP, LDH, serum ferritin, D-dimer, IL-2, and IL-6.

Despite numerous ongoing studies, the pathogenicity of the Coronavirus is still not fully understood, these routine laboratory testing may help with symptom-based treatment and aid in a

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better understanding of the disease. These outcomes may give insight on how liver function tests and inflammatory markers affect COVID-19 prognosis and offer potential for improvement in patient care during the on-going outbreak. Limitation of this study is a retrospective observational study design that was performed by using information gathered from a single centre and few parameters were only considered. To establish these parameters as prognostic indicators of COVID-19, more research with bigger sample sizes connecting liver enzymes and inflammatory markers with disease severity are necessary.

Conclusion

This study concluded that the biochemical parameters like liver enzymes and inflammatory markers will help to differentiate the COVID-19 disease severity. Similarly, CRP and ferritin can also be helpful to the clinicians in differentiating moderate from severe covid as they are highly raised in severe conditions. Early differentiation of COVID-19 severity will help to reduce the mortality rate.

References

1. Boregowda U, Aloysius MM, Perisetti A, Gajendran M, Bansal P, et al. (2020) Serum activity of liver enzymes is associated with higher mortality in COVID-19: a systematic review and meta-analysis. Frontiers in medicine 7: 431.
2. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A (2020) The role of biomarkers in diagnosis of COVID-19-A systematic review. Life sciences 254: 117788.
3. WHO (2020) Coronavirus disease 2019 (COVID-19): situation report, 99.
4. Khan M, Adil SF, Alkhathlan HZ, Tahir MN, Saif S, et al. (2021) COVID-19: A Global Challenge with Old History, Epidemiology and Progress So Far. Molecules (Basel, Switzerland) 26(1): 39.
5. Cai Q, Huang D, Yu H, Zhu Z, Xia Z, et al. (2020) COVID-19: Abnormal liver function tests. Journal of hepatology 73(3): 566-574.
6. Das B, Bhatia SY, Pal PM (2021) Evaluation of the role of routine laboratory biomarkers in COVID-19 patients: perspective from a tertiary care hospital in India. Indian Journal of Clinical Biochemistry 36(4): 473-484.
7. Mardani R, Vasmehjani AA, Zali F, Gholami A, Nasab SDM, Kaghazian H, et al. (2020) Laboratory parameters in detection of COVID-19 patients with positive RT-PCR; a diagnostic accuracy study. Archives of academic emergency medicine 8(1): 43.
8. Zhou C, Chen Y, Ji Y, He X, Xue D (2020) Increased serum levels of hepcidin and ferritin are associated with severity of COVID-19. Medical science monitor: international medical journal of experimental clinical research 26: 926178.
9. Ahmed S, Ghani F (2020) Trend analysis of lab tests requisitions of COVID-19 prognostic biomarkers at a clinical chemistry reference laboratory-an observational study. Annals of Medicine Surgery 60: 522-525.
10. Dashatan NA, Koushki M, Ghorbani F, Naderi N (2020) Increased inflammatory markers correlate with liver damage and predict severe COVID-19: a systematic review and meta-analysis. Gastroenterology hepatology from bed to bench 13(4): 282-291.
11. Nepal G, Maitreyee DS, Aroor AR, Shivashankara AR (2021) Cytokine profile as biomarker of COVID-19 and its correlation with liver function enzymes and other markers of inflammation. Biomedicine 41(4): 747-751.
12. Dhama K, Khan S, Tiwari R, Sircar S, Bhat S, Malik YS, et al. (2020) Coronavirus disease 2019–COVID-19. Clinical microbiology reviews 33(4): e00028-20.
13. Gong J, Dong H, Xia QS, Huang ZY, Wang DK, et al. (2020) Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19: a retrospective study. BMC infectious diseases 20(1): 963.
14. Chen N, Zhou M, Dong X, Qu J, Gong F, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet infectious diseases 395(10223): 507-513.
15. Smilowitz NR, Kunichoff D, Garshick M, Shah B, Pillinger M, et al. (2021) C-reactive protein and clinical outcomes in patients with COVID-19. European heart journal 42(23): 2270-2279.
16. Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, et al. (2020) Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. The American journal of emergency medicine 38(9): 1722-1726.

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