A RETROSPECTIVE STUDY OF LIVER FUNCTION TEST IN COVID-19 PATIENTS IN TERTIARY CARE HOSPITAL RAIGARH, CHHATTISGARH

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Abstract
Introduction: The Covid-19 pandemic is currently causing a worldwide public health emergency of significant concern. The coronavirus has been observed to be linked with the impairment of multiple organs, beyond respiratory afflictions. The evaluation of liver function in Covid-19 patients holds considerable significance as it serves as a crucial diagnostic tool for determining the severity and prognosis of the disease. Therefore, the current investigation aims to analyse the biochemical parameters for monitoring patients with Covid-19, with the objective of identifying critically ill patients and reducing the mortality rate.
Material and Methods: The present study was conducted retrospectively on a cohort of 200 COVID-19 patients at Late Shri Lakhiram Agrawal Memorial Government Medical College Raigarh (C.G). The liver function test was performed using the MISPA CLINIA AGGAPE fully automatic biochemistry analyzer.
Results: The study findings indicate that male and female patients exhibited elevated levels of serum AST, ALT, and ALP. A decrease in total protein levels was observed in COVID-19 patients of both genders. The study found a statistically significant increase ($P<0.05$) in the levels of ALP, TP, and ALB in both male and female patients diagnosed with COVID-19.
Conclusion: The findings of this study indicate that the proportion of serum TB and DB levels were within normal to slightly higher ranges, while AST, ALT levels were higher, and ALP, TP, and ALB levels were significantly higher ($P<0.05$) in both male and female patients diagnosed with COVID-19.
Keyword: liver function test, corona virus, mortality.

The following abbreviations are commonly used in the medical field: TB, which stands for Total Bilirubin; DB, which stands for Direct Bilirubin; AST, which stands for Aspartate

Transaminase; ALT, which stands for Alanine Transaminase; ALP, which stands for Alkaline phosphatase; TP, which stands for Total Protein; and ALB, which stands for Albumin.

Introduction:

The World Health Organisation declared the Covid-19 pandemic as a matter of international concern for public health in March 2020 [1]. A research investigation was carried out in China, which revealed that patients who had pre-existing hepatitis B infection exhibited a higher incidence of severe COVID-19 infections, with 32.1% of such patients being affected, as compared to 15.7% of patients who did not have hepatitis B [2]. The coronavirus has been observed to be linked with the malfunctioning of multiple organs, apart from respiratory ailments. SARS-CoV2, a highly pathogenic virus, primarily targets the respiratory system. However, recent research has shed light on its potential to cause organ dysfunction and induce multisystem organ inflammation, as evidenced by various published studies [3,4]. Several studies have reported a correlation between increased liver enzymes and COVID-19 infection, suggesting that it may lead to liver dysfunction through direct hepatotoxic injury caused by the viral infection, drug toxicity, or an immune-mediated response. According to previous reports, the incidence of liver damage among patients affected by the SARS epidemic was 60% [5]. Given that SARS-CoV-2 is classified within the coronavirus family, it is postulated that it has the potential to induce hepatic damage. The biliary epithelium exhibits the presence of the angiotensin-converting enzyme (ACE-2) receptor, which serves as the point of attachment for SARS-CoV-2 [6]. Patients diagnosed with COVID-19 exhibit significant alterations in various biochemical tests. According to previous research, there were significant levels of alanine aminotransferase (ALT) observed in patients who were admitted to the intensive care unit with COVID-19 [7]. Deng and colleagues observed elevated levels of ALT and AST in specific patient cohorts, accompanied by a reduction in total bilirubin levels below the established normal range. According to a study by [8], a total of 13% of patients diagnosed with COVID-19 exhibited elevated levels of both creatinine and creatine phosphokinase. Additionally, Wu et al. [9] observed alterations in the levels of various liver function biomarkers, including ALB, GGT, AST, ALT, TBIL, and ALP. A study was conducted to analyse the biochemical parameters of 200 patients diagnosed with Covid-19. Limited data is currently available regarding the biochemical findings of patients with COVID-19. The biochemical assessment of Covid-19 patients holds significant importance as it serves as a crucial tool in determining the severity and prognosis of the disease. Therefore, the current investigation aims to analyse the biochemical parameters for monitoring patients with Covid-19, with the goal of identifying those who are critically ill and reducing the mortality rate.

Material and Methods: The present investigation was a retrospective study that involved the analysis of liver function test results from a cohort of 200 patients diagnosed with COVID-19. The study was conducted at Late Shri Lakhiram Agrawal Memorial Government Medical College Raigarh (C.G). The Biochemistry fully automatic analyzer, specifically the MISPA CLINIA AGGAPE, was utilised to analyse the liver function test results.

The inclusion criteria for this study are patients who have been diagnosed with Covid-19.

The exclusion criteria for this study encompass patients with diabetes and liver disease.

For the purpose of sample collection, a total of five millilitres of venous blood were obtained from the antecubital vein using a plain vial. The procedure was conducted under aseptic conditions. The blood sample underwent centrifugation at a rate of 4000 revolutions per minute for a duration of 5 minutes, following which the serum was extracted. The serum

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underwent assessment of various parameters using a fully automated analyzer, specifically the MISPA CLINIA AGGAPE.

The methods employed for the determination of various biochemical parameters were as follows: Diazotized Sulphanilic Acid method [10] was used for the measurement of Total Bilirubin and Direct Bilirubin, IFCC Kinetic UV Test [11] was employed for the estimation of AST and ALT, while ALP was determined using IFCC Kinetic UV Test [12]. Total Protein was quantified using the Biuret method [13] . Albumin and Bromocresol green (BCG) were utilised in the study [14] .

RESULT: The present investigation involved a cohort of 200 individuals diagnosed with COVID-19, and the clinical biochemistry laboratory at Late Shri Lakhiram Agrawal Memorial Government Medical College was utilised to perform biochemical analyses. The primary aim of this study was to assess various biochemical parameters in patients with IPD COVID-19. The study's notable discovery is that among 200 COVID-19 patients, **Table 1** illustrates the distribution of age and sex, while **Graph 1** interprets the results. The data suggests that the majority of male patients affected by COVID-19 fall within the 61-70 age group. In contrast, the age bracket of 21-30 exhibited the greatest number of female individuals. Upon combining the patient population of both genders, it was observed that the majority fell within the age range of 21 to 30 years. The study determined that the average age of male patients was 49.20 years, while the average age of female patients was 39.86 years. The arithmetic average age of the combined male and female population was 44.53 years, while the ratio of males to females was 1.89:1. The study observed elevated levels of Serum TB (N=9, 6.87%), DB (N=2,1.52%), AST (N=66,50.38%), ALT (N=38, 29.00%), and ALP (N=10, 7.23%) in male patients (N=131) and female patients with COVID-19 (N=69). Similarly, elevated levels of Serum TB (N=5, 7.24%), DB (N=2,2.89%), AST (N=33,47.82%), ALT (N=16, 23.18%), and ALP (N=12,17.39%) were observed in female patients with COVID-19 (N=69) **(Table-2)**. The study revealed a decrease in total protein and albumin levels in both genders, as presented in **Table 3**. Additionally, **Table 4** indicates a statistically significant increase ($P<0.05$) in the proportion of ALP, TP, and ALB among male and female patients diagnosed with COVID-19.

The present study presents Table 1, which displays the distribution of age and sex among a sample of 200 individuals diagnosed with COVID-19.

Age	Male (N=131)		Female (N=69)		Total N=200	
	N	%	N	%	N	%
≤10	0	0	3	4.3	3	1.5
11-20	05	3.8	05	7.2	10	5
21-30	16	12.4	23	33.3	39	19.5
31-40	25	19.0	07	10.3	32	16
41-50	26	19.8	11	15.9	37	18.5
51-60	18	13.7	09	13.0	27	13.5
61-70	28	21.4	09	13.0	37	18.5
>70	13	9.9	02	2.9	15	7.5
Total	131	100	69	100	200	100

Graph 1: Age and Sex Distribution of COVID- 19 patients (N=200)
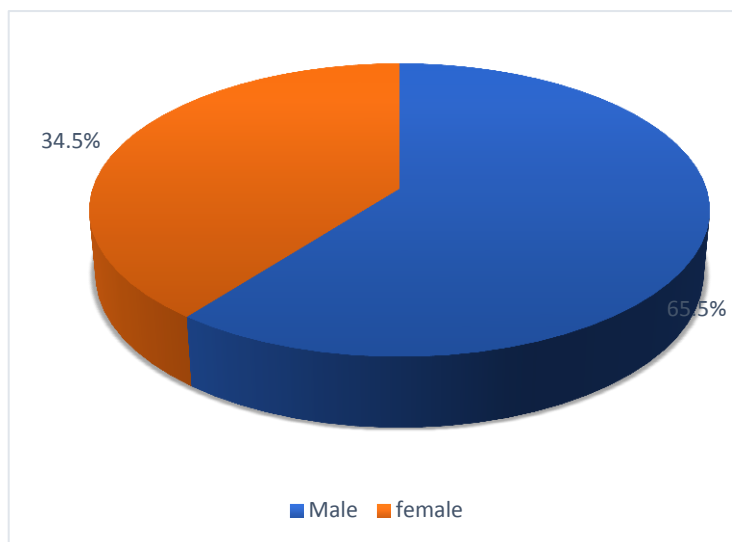
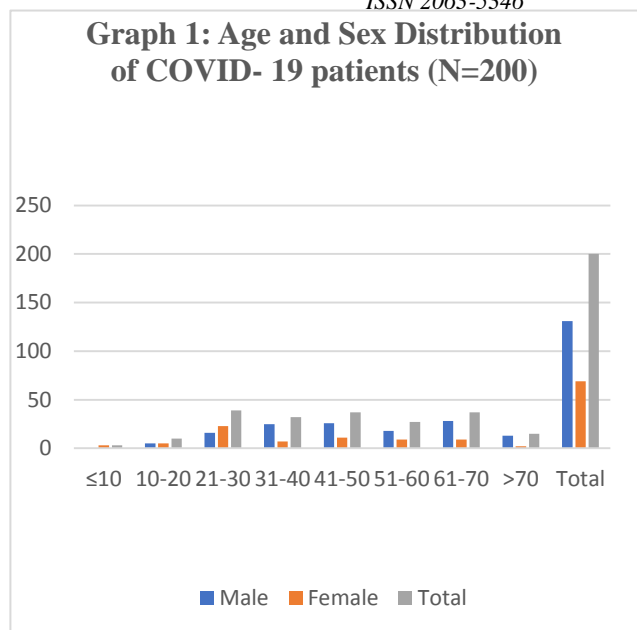**Graph 2** displays the relationship between age and sex ratio.

Table 2 displays the proportion and percentage of normal and high levels of various parameters of liver function test in a sample of 200 COVID-19 patients.

Gender	Liver function test	Reference range	Normal level	Percentage (%)	High level	Percentage
Male (N=131)	TB	0.1-1.2 mg/dl	**122**	**93.129771**	**9**	**6.87**
	DB	0.1-0.6 mg/dl	**129**	**98.4732824**	**2**	**1.52**
	AST	5-45 U/L	**65**	**49.6183206**	**66**	**50.38**
	ALT	5-50 U/L	**93**	**70.9923664**	**38**	**29.00**
	ALP	64-306 U/L	**121**	**92.3664122**	**10**	**7.63**
Female (N=69)	TB	0.1-1.2 mg/dl	**64**	**92.7536232**	**5**	**7.24**
	DB	0.1-0.6 mg/dl	**67**	**97.1014493**	**2**	**2.89**
	AST	5-45 U/L	**36**	**52.173913**	**33**	**47.82**
	ALT	5-50 U/L	**53**	**76.8115942**	**16**	**23.18**
	ALP	64-306 U/L	**57**	**82.6086957**	**12**	**17.39**

Table 3 displays the distribution of Total protein and Albumin among a sample of 131 individuals diagnosed with covid-19.

Gender	Parameter	Reference range	No. of patients	Percentage
Male N=131	**TP**	6-8 g/dl	109	83.20
		>6-8 g/dl	0	0
		<6-8 g/dl	22	16.79
	ALB	3.5-5.2 g/dl	77	58.77
		>3.5-5.2 g/dl	0	0
		<3.5-5.2 g/dl	54	41.22
Female N=69	**TP**	6-8 g/dl	47	68.11
		>6-8 g/dl	0	0
		<6-8 g/dl	22	31.88
	ALB	3.5-5.2 g/dl	54	78.26
		>3.5-5.2 g/dl	0	0
		<3.5-5.2 g/dl	15	21.73

Table 4 presents a comparison of liver function test results between male and female Covid-19 patients, with a sample size of 200.

↓ Liver Function	Gender →	Male	Female	χ^2 Value	P value
TB	High	9	5	**0.0098**	**0.921052 (NS)**
	Normal	122	64		
DB	High	2	2	**0.4339**	**0.510058 (NS)**
	Normal	129	67		
AST	High	66	33	**0.1181**	**0.731126 (NS)**
	Normal	65	36		
ALT	High	38	16	**0.7765**	**0.378218 (NS)**
	Normal	93	53		
ALP	High	10	12	**4.3955**	**0.036035 (Significant)**
	Normal	121	57		
TP	low	22	22	**5.9974**	**0.014327 HS**
	Normal	109	47		
ALB	low	54	15	**7.5921**	**0.005866 HS**
	Normal	77	54		

The liver function test parameters were compared between male and female patients with COVID-19. The results indicated that there was no statistically significant difference, except for ALP. Statistical analysis revealed a significant difference (P<0.05) in the levels of ALP among male and female individuals diagnosed with covid-19, as presented in **Table 4.**

Discussion- The present investigation was carried out retrospectively on a sample of 200 COVID-19 patients at Late Shri Lakhiram Agrawal Memorial Government Medical College Raigarh (C.G). The study found that the average age of male patients was 49.20 years, while the average age of female patients was 39.86 years. The arithmetic average age of the combined male and female population was 44.53 years, while the ratio of males to females was 1.89:1. Zhou C's findings indicate a higher prevalence of elevated liver enzyme levels in males (67.4%) compared to females (46.03%). The increased likelihood of males being affected by the condition may be linked to the greater prevalence of ACE2 receptors in their bodies, as documented in a study conducted in Wuhan [15] . According to Ramadori G, patients exhibiting abnormal liver enzyme levels and liver injury demonstrated significantly diminished levels of albumin and total proteins (p<0.0001) in comparison to those patients with normal liver enzyme levels. The observed downregulation of albumin synthesis in the liver following the onset of COVID-19 may be attributed to poor nutritional intake and the role of cytokine storm, which leads to the release of major acute-phase cytokines. This has been suggested in previous studies. [16] . According to Wang JT's recent systematic review and meta-analysis, it was demonstrated that 33.3% of COVID-19 cases exhibited elevated AST, while 24.1% showed elevated ALT. [17]

The current liver profile of male patients (N=131) revealed elevated levels of Serum TB (N=9, 6.87%), DB (N=2, 1.52%), AST (N=66, 50.38%), ALT (N=38, 29.00%), and ALP (N=10, 7.23%). The study observed that male patients diagnosed with covid-19 exhibited total protein levels exceeding 6-8 g/dl (0%), as well as levels lower than 6-8g/dl (N=22,16.79%). Additionally, the albumin levels in these patients were found to be lower than <3.5-5.2 g/dl (N=54,41.22%). The sample size for this study was N=131. Elevated levels of Serum TB (N=5, 7.24%), DB (N=2,2.89%), AST(N=33,47.82%), ALT (N=16,

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23.18%), and ALP (N=12,17.39%) were observed in the cohort of 69 female patients diagnosed with covid-19. The study revealed that the total protein levels in COVID-19 patients were either above or below the range of 6-8 g/dl, with the latter being observed in 22 cases (31.88%). Additionally, the albumin levels were lower than the range of 3.5-5.2 g/dl in 15 cases (21.73%). Notably, both male and female COVID-19 patients exhibited a significantly higher proportion of ALP, TP, and ALB levels ($P<0.05$).

In conclusion, the findings of this study indicate that the proportion of serum TB and DB levels were within normal to slightly elevated ranges in both male and female COVID-19 patients. However, the levels of AST and ALT were higher, and the levels of ALP, TP, and ALB were significantly higher ($P<0.05$) in these patients.

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