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Sahar Hassan Abd-Allah

*Resident Physician in Internal Medicine Diseases, Al-Azhar University Hospital - Assiut,
peacemaker2551994@gmail.com*

Ashraf Mohammad Elkabeer

Assistant Professor of Internal Medicine Diseases, Faculty of Medicine, Al-Azhar University, Assiut

Ahmed Mohamed Mostafa

Lecturer of Internal Medicine Diseases, Faculty of Medicine, Al-Azhar University, Assiut

Ayman Abd Elaziz Abd Elrhman

Assistant Professor of Internal Medicine Diseases, Faculty of Medicine, Al-Azhar university, Assiut

Ebtisam Showky Ahmed Hassanin

Department of Clinical pathology Faculty of Medicine, New valley university

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Liver Biochemical Abnormalities Among COVID-19 Patients

Sahar Hassan Abd-Allah ^{a,*}, Ashraf Mohamad Elkabeer ^b, Ahmed Mohamed Mostafa ^b,
Ayman Abd Elaziz Abd Elrahman ^b, Ebtisam Showky Ahmed Hassanin ^c

^a Al-Azhar University Hospital, Assiut, Egypt

^b Al-Azhar University, Assiut, Egypt

^c Department of Clinical Pathology, Faculty of Medicine, New Valley University, Egypt

Abstract

Background: The severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) is a novel Corona virus that causes Corona virus disease 2019 (COVID-19). Except for respiratory symptoms, COVID-19 patient often develop different degrees of liver injury. Notably, COVID-19 patients with pre-existing liver diseases, especially liver cirrhosis, have higher incidence of liver biochemical abnormality, liver injury, and even hepatic decompensation event.

Aim: To determine the liver biochemistry changes in COVID-19 patients.

Patients and methods: In this retrospective study was conducted in quarantine department, Assuit Chest Hospital was conducted on 761 COVID-19 patients. Patients were divided into 2 groups: hepatic and non-hepatic groups.

Results: Hepatic patients showed significant elevation in AST and ALT compared to non hepatic patients. There was statistically significant difference between COVID-19 patients with normal and altered liver function regarding treatment. Patients with altered liver function tests showed significant elevation in INR compared to patients with normal liver function tests. There was no statistically significant difference between COVID-19 patients with normal and altered liver function regarding mortality. There was no statistically significant difference between them regarding pH, PCO₂, HCO₃, SO₂, Na and K.

Conclusion: Liver biochemical abnormality is more common in COVID-19 patients with liver cirrhosis. However, liver cirrhosis patients without COVID-19 have more hepatic decompensation events, so they should not be delayed from their hospitalization management during the COVID-19 pandemic. The presence of abnormal liver tests on admission was not associated with COVID-19 severity and mortality.

Keywords: COVID-19, Liver, SARS-COV-2

1. Introduction

The severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) is a novel Corona virus that causes Corona virus disease 2019 (COVID-19) which first appeared in Wuhan city in Hubei province in central China, It is highly contagious and is rapidly spreading around the world.¹ (see [Tables 1–25](#))

The clinical severity of COVID-19 varies from asymptomatic to fatal. Some cases are only accompanied by mild respiratory symptoms without fever and recover spontaneously.²

In contrast, others suffer from systemic symptoms including fever, chest pain, myalgia, shortness of breath and coughing associated with pneumonia, which contribute in part to the development of severe complications such as acute respiratory distress syndrome, and even death.³

Except for respiratory symptoms, COVID-19 patient often develop different degrees of liver injury. Notably, COVID-19 patients with pre-existing liver diseases, especially liver cirrhosis, have higher incidence of liver biochemical abnormality, liver injury, and even hepatic decompensation events.⁴

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* Corresponding author.
E-mail address: Peacemaker2551994@gmail.com (A.A.E.A. Elrahman).

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Table 1. Demographic characteristics among the studied groups.

		Non-hepatic patients (n = 472)		Hepatic patients (n = 28)		Total COVID-19 patients (n = 500)		Test value	P-value
		n	%	n	%	n	%		
Gender	Male	252	53.4%	15	53.6%	267	53.4%	X ² = 0.00	0.995
	Female	220	46.6%	13	46.4%	233	46.6%		
age (years)	Mean ± SD	63.34 ± 11.92		67.71 ± 7.44		63.58 ± 11.75		^Z MWU = 1.873	0.061
	Range	20.0–94.0		54.0–81.0		20.0–94.0			

Therefore; this study aim to determine the liver biochemistry changes in COVID-19 patient.

2. Patients and methods

In this retrospective study was conducted in quarantine department, Assuit Chest Hospital was

conducted on 761 COVID-19 patients was carried out in the period from January to July 2021 (3rd Wave) & from August to October 2021 (4th Wave). Patients were divided into 2 groups: hepatic and non-hepatic groups. All patients subjected to the following: Full history taking, Laboratory data was

Table 2. Clinical history among the studied groups.

		Non-hepatic patients (n = 472)		Hepatic patients (n = 28)		Total COVID-19 patients (n = 500)		Test value	P-value
		N	%	N	%	N	%		
DM	No	268	56.8%	15	53.6%	283	56.6%	X ² = 0.111	0.739
	Yes	204	43.2%	13	46.4%	217	43.4%		
Hypertension	No	235	49.8%	12	42.9%	247	49.4%	X ² = 0.508	0.476
	Yes	237	50.2%	16	57.1%	253	50.6%		
Hepatic disease	No	472	100.0%	0	0.0%	472	94.4%	X ² = 27.2	<0.001
	Cirrhosis	0	0.0%	8	28.6%	8	1.6%		
	Fatty liver	0	0.0%	2	7.1%	2	0.4%		
	HCV	0	0.0%	18	64.3%	18	3.6%		

P ≤ 0.05 is considered statistically significant, P ≤ 0.01 is considered high statistically significant, SD = standard deviation, comparison between groups done by Mann–Whitney test and Chi-square test.

Table 3. Clinical presentation among the studied groups.

		Non-hepatic patients (n = 472)		Hepatic patients (n = 28)		Total COVID-19 patients (n = 500)		Test value	P-value
		N	%	N	%	N	%		
Dyspnea	No	19	4.0%	0	0.0%	19	3.8%	X ² = 1.17	0.279
	Yes	453	96.0%	28	100.0%	481	96.2%		
Cough	No	56	11.9%	3	10.7%	59	11.8%	X ² = 1.86	0.395
	Dry	173	36.7%	7	25.0%	180	36.0%		
Fever	Productive	243	51.5%	18	64.3%	261	52.2%	X ² = 0.850	0.356
	No	62	13.1%	2	7.1%	64	12.8%		
Chest Pain	Yes	410	86.9%	26	92.9%	436	87.2%	X ² = 3.59	0.058
	No	418	88.6%	28	100.0%	446	89.2%		
L.L. edema	No	54	11.4%	0	0.0%	54	10.8%	X ² = 1.49	0.222
	Yes	458	97.0%	26	92.9%	484	96.8%		
Other symptoms	Yes	14	3.0%	2	7.1%	16	3.2%	X ² = 8.96	0.441
	Fatigue	69	14.6%	1	3.6%	70	14.0%		
	Loss of smell/taste	52	11.0%	2	7.1%	54	10.8%		
	Vomiting	37	7.8%	2	7.1%	39	7.8%		
	Loss of appetite	29	6.1%	4	14.3%	33	6.6%		
	Bone ache	27	5.7%	2	7.1%	29	5.8%		
	Diarrhea	14	3.0%	2	7.1%	16	3.2%		
	Headache	9	1.9%	0	0.0%	9	1.8%		
	Sore throat	6	1.3%	0	0.0%	6	1.2%		
	Shortness of breath	4	0.8%	0	0.0%	4	0.8%		
	Dizziness/drowsiness	3	0.6%	0	0.0%	3	0.6%		

Table 4. Comparison between the studied groups regarding vital signs.

	Non-hepatic patients (n = 472)				Hepatic patients (n = 28)				Mann–Whitney U test	
	Mean	± SD	Range		Mean	± SD	Range		Test value	P-value
Systolic BP (mm/Hg)	122.91	13.94	80.0	180.0	127.14	20.34	90.0	180.0	0.949	0.343
Diastolic BP (mm/Hg)	77.72	10.27	10.0	100.0	77.86	11.66	50.0	100.0	0.144	0.885
Heart rate (beats/min)	92.06	14.42	44.0	207.0	91.79	17.85	62.0	140.0	0.852	0.394
Respiratory rate	25.91	2.64	21.0	33.0	25.21	2.28	21.0	30.0	1.212	0.225
Temperature (°C)	38.24	.76	36.40	40.0	38.37	.79	37.0	40.0	0.748	0.454

Table 5. Comparison between the studied groups regarding CBC in 3rd wave.

	Non-hepatic patients (n = 472)				Hepatic patients (n = 28)				Mann–Whitney U test	
	Mean	± SD	Range		Mean	± SD	Range		Test value	P-value
Hemoglobin (g/dL)	12.2	1.7	5.6	19.9	12.9	4.0	3.9	23.4	1.188	0.235
Platelets count (10 ⁹ /L)	283.14	98.25	70.0	803.0	105.36	37.83	37.0	163.0	8.581	<0.001
WBCs (10 ⁹ /L)	9.83	4.99	.10	28.20	14.03	23.83	2.50	129.50	0.815	0.415
Lymphocytes	1.4	.9	.1	7.3	1.2	.8	.4	3.5	1.426	0.154
Monocytes	.48	.41	.00	3.20	1.11	3.53	.10	19.00	0.402	0.688
Neutrophils	8.5	6.4	.1	81.0	7.7	6.6	.5	27.5	1.665	0.096

P ≤ 0.05 is considered statistically significant, P ≤ 0.01 is considered high statistically significant, SD = standard deviation, comparison between groups done by Mann–Whitney U test.

Table 6. Comparison between the studied groups regarding renal function tests, ABG and serum electrolytes.

	Non hepatic patients (n = 472)				Hepatic patients (n = 28)				Mann–Whitney U test	
	Mean	± SD	Range		Mean	± SD	Range		Test value	P-value
Serum urea (mg/dl)	122.91	13.94	80.00	180.00	127.14	20.34	90.00	180.00	0.788	0.431
Serum creatinine (mg/dl)	55.37	31.02	18.00	222.00	63.96	44.38	25.00	186.00	0.062	0.951
pH	1.57	4.33	.30	91.00	1.40	.75	.70	3.40	0.202	0.840
PCO2	7.45	.16	4.49	7.63	7.47	.06	7.35	7.59	0.664	0.507
HCO3	35.11	11.67	3.90	135.00	32.89	7.89	16.00	51.00	0.860	0.390
SO2	24.96	7.38	4.10	93.00	23.82	6.47	9.00	39.00	0.223	0.824
Na	86.45	14.72	9.30	100.00	89.00	8.55	56.00	100.00	1.287	0.198
k	137.55	8.73	104.00	193.00	135.32	6.99	121.00	155.00	−0.1410	0.159

Table 7. Comparison between the studied groups regarding inflammatory markers.

	Non-hepatic patients (n = 472)				Hepatic patients (n = 28)				Mann–Whitney U test	
	Mean	± SD	Range		Mean	± SD	Range		Test value	P-value
Random blood sugar (mg/dl)	250.31	121.52	40.00	644.00	277.32	147.88	109.00	582.00	0.579	0.563
Ferritin	3.18	.30	2.60	3.70	3.16	.34	2.60	3.70	0.176	0.860
D. dimer	529.09	560.98	19.00	4918.00	479.10	329.83	60.00	1440.00	0.089	0.929
CRP	3.05	27.83	.01	361.00	.62	.54	.03	2.30	1.261	0.207

Table 8. Urine analysis among the studied groups.

		Non-hepatic patients (n = 472)		Hepatic patients (n = 28)		Total COVID-19 patients (n = 500)		Test value	P-value
		n	%	n	%	n	%		
		Acetone	Negative	443	93.9%	24	85.7%		
	Positive	29	61.4%	4	14.3%	33	6.6%		
Albuminuria	No	460	97.5%	25	89.3%	485	97.0%	X2 = 3.58	0.058
	Yes	12	2.5%	3	10.7%	15	3.0%		

Table 9. Comparison between the studied groups regarding liver function in 3rd wave.

	Non-hepatic patients (n = 472)			Hepatic patients (n = 28)			Mann–Whitney U test	
	Mean	± SD	Range	Mean	± SD	Range	Test value	P-value
AST	29.56	18.10	5.00–186.00	62.64	58.36	5.00–325.00	4.759	<0.001
ALT	28.01	14.92	7.00–112.00	67.18	32.25	14.00–132.00	6.147	<0.001
Albumin	3.15	.49	.30–5.00	2.95	.52	2.10–4.20	–1.822	.068

$P \leq 0.05$ is considered statistically significant, $P \leq 0.01$ is considered high statistically significant, SD = standard deviation, comparison between groups done by Mann–Whitney U test.

Table 10. CT among the studied groups.

		Non hepatic patients (n = 472)		Hepatic patients (n = 28)		Total COVID-19 patients (n = 500)		Test value	P-value
		n	%	n	%	n	%		
CT chest	Normal	173	36.7%	7	25.0%	180	36.0%	X2 = 1.558	0.212
	Ground glass appearance	299	63.3%	21	75.0%	320	64.0%		

Table 11. Management among the studied COVID-19 groups in 3rd wave.

		Non-hepatic patients (n = 472)		Hepatic patients (n = 28)		Total COVID-19 patients (n = 500)		Test value	P-value
		n	%	n	%	n	%		
Management	Clexane	331	70.1%	20	71.4%	351	70.2%	X2 = 13.7	0.033
	Dexamethasone	263	76.9%	15	53.6%	278	55.6%		
	Meronem	106	22.5%	13	46.4%	119	23.8%		
	Ceftriaxone	215	45.6%	7	25.0%	222	44.4%		
	Solu-Medrol	26	5.5%	1	3.6%	27	5.4%		
	Levofloxacin	16	3.4%	0	0.0%	16	3.2%		
	Averozolid	42	8.9%	6	21.4%	48	9.6%		

$P \leq 0.05$ is considered statistically significant, $P \leq 0.01$ is considered high statistically significant, SD = standard deviation, comparison between groups done by Chi-square test.

Table 12. Severity of COVID-19 among the studied groups.

		Non-hepatic patients (n = 472)		Hepatic patients (n = 28)		Total COVID-19 patients (n = 500)		Test value	P-value
		n	%	n	%	n	%		
Severity	Mild to moderate	222	47.0%	13	46.4%	235	47.0%	X2 = 0.004	0.950
	Severe	250	53.0%	15	53.6%	265	53.0%		

included; CBC, C-reactive protein, albumin, ALT, AST, serum creatinine & urea serum sodium & potassium, prothrombin time, international normalized ratio (INR), and activated partial thromboplastin time (APTT), ABG, RBG, serum

ferritin and D. dimer and Imaging were included; CT chest and pelviabdominal US. Patients with laboratory confirmed COVID-19 infection by nasopharyngeal swab for SARS-CoV-2 more than 18 year were included criteria, while; Age less than 18

Table 13. Outcome of COVID-19 among the studied groups.

		Non-hepatic patients (n = 472)		Hepatic patients (n = 28)		Total COVID-19 patients (n = 500)		Test value	P-value
		n	%	n	%	n	%		
Outcome	Survived	303	64.2%	16	57.1%	167	64.0	X2 = 0.305	0.581
	Died	169	35.8%	12	72.9%	94	36.0		

Table 14. Demographic characteristics among the studied groups.

		Non-hepatic patients (n = 241)		Hepatic patients (n = 20)		Total COVID-19 patients (n = 261)		Test value	P-value
		n	%	n	%	n	%		
Gender	Male	111	46.1%	11	55.0%	122	46.7%	X ² = 0.593	0.441
	Female	130	53.9%	9	45.0%	139	53.3%		
age (years)	Mean ± SD	61.64 ± 13.53		63.55 ± 10.93		61.79 ± 13.34		^Z MWU = 0.623	0.533
	Range	19.0–90.0		37.0–81.0		19.0–90.0			

Table 15. Clinical history among the studied groups in 4th wave.

		Non-hepatic patients (n = 241)		Hepatic patients (n = 20)		Total COVID-19 patients (n = 261)		Test value	P-value
		N	%	N	%	N	%		
DM	No	152	63.1%	18	90.0%	170	65.1%	X ² = 5.88	0.015
	Yes	89	36.9%	2	10.0%	91	34.9%		
Hypertension	No	131	54.4%	14	70.0%	145	55.6%	X ² = 1.83	0.176
	Yes	110	45.6%	6	30.0%	116	44.4%		

P ≤ 0.05 is considered statistically significant, P ≤ 0.01 is considered high statistically significant, SD = standard deviation, comparison between groups done by Chi-square test

Table 16. Clinical presentation among the studied groups in 4th wave.

		Non-hepatic patients (n = 241)		Hepatic patients (n = 20)		Total COVID-19 patients (n = 261)		Test value	P-value
		N	%	N	%	N	%		
Dyspnea	No	16	6.6%	2	10.0%	18	6.9%	X ² = 0.012	0.912
	Yes	225	93.4%	18	90.0%	243	93.1%		
Cough	No	41	17.0%	6	30.0%	47	18.0%	X ² = 1.32	0.250
	Yes	200	83.0%	14	70.0%	214	82.0%		
Fever	No	77	32.0%	5	25.0%	82	31.4%	X ² = 0.154	0.694
	Yes	164	68.0%	15	75.0%	179	68.6%		
Sore throat	No	226	93.8%	12	60.0%	238	91.2%	X ² = 3.59	0.058
	Yes	15	6.2%	8	40.0%	23	8.8%		
Diarrhea	No	234	97.1%	12	60.0%	246	94.3%	X ² = 40.3	<0.001
	Yes	7	2.9%	8	40.0%	15	5.7%		
chest pain	No	239	99.2%	20	100.0%	259	99.2%	X ² = 0.856	0.355
	Yes	2	0.8%	0	0.0%	2	0.8%		
Los of taste/smell	No	240	99.6%	20	100.0%	260	99.6%	X ² = 0.856	0.355
	Yes	1	0.4%	0	0.0%	1	0.4%		

P ≤ 0.05 is considered statistically significant, P ≤ 0.01 is considered high statistically significant, SD = standard deviation, comparison between groups done by Chi-square test.

year, Any advanced malignancy, Patient under treatment of chemotherapy, Pregnancy & lactating female and Liver biochemical examination was not available during hospitalization were excluded

criteria. Confidentiality maintained during all stages of the assessment. Approval of the ethical committee of Al-Azhar faculty of medicine in Assiut will be obtained. The collected data will be, tabulated, and

Table 17. Distribution of the studied patients as per vital signs.

	Non-hepatic patients (n = 241)			Hepatic patients (n = 20)			Mann–Whitney U test			
	Mean	± SD	Range	Mean	± SD	Range	Test value	P-value		
Systolic BP (mm/Hg)	119.95	16.92	14.00	170.00	122.75	16.34	100.00	160.00	–.600-	.549
Diastolic BP (mm/Hg)	75.93	10.46	50.00	100.00	75.00	12.77	60.00	100.00	–.452-	.651
Heart rate (beats/min)	93.23	15.16	37.00	170.00	93.00	14.25	54.00	110.00	–.544-	.587
Respiratory rate	25.67	4.27	15.00	45.00	26.15	5.27	19.00	40.00	–.009-	.993
Temperature (°C)	37.79	.77	36.00	41.00	37.61	.70	36.50	38.90	–.876-	.381

Table 18. Comparison between the studied groups regarding CBC in 4th wave.

	Non-hepatic patients (n = 241)				Hepatic patients (n = 20)				Mann–Whitney U test	
	Mean	± SD	Range		Mean	± SD	Range		Test value	P-value
Hemoglobin (g/dL)	12.29	2.11	6.00	20.10	11.91	2.22	6.40	14.70	–.533-	.594
Platelets count (10 ⁹ /L)	256.27	100.45	50.00	700.00	201.21	142.28	24.00	473.00	–2.876-	.004
WBCs (10 ⁹ /L)	10.29	5.68	1.70	45.70	13.69	7.05	4.60	27.60	–2.055-	.040
Neutrophils	8.28	4.82	1.00	36.80	11.56	6.72	3.20	26.10	–2.124-	.034
Lymphocytes	1.31	1.02	.20	8.60	1.38	.82	.30	3.80	–.788-	.431

P ≤ 0.05 is considered statistically significant, P ≤ 0.01 is considered high statistically significant, SD = standard deviation, comparison between groups done by Mann–Whitney U test.

Table 19. Comparison between the studied groups regarding renal function tests, ABG and serum electrolytes.

	Non-hepatic patients (n = 241)				Hepatic patients (n = 20)				Mann–Whitney U test	
	Mean	± SD	Range		Mean	± SD	Range		Test value	P-value
Serum urea (mg/dl)	57.51	32.81	18.00	213.00	70.20	42.08	19.00	177.00	–1.468-	.142
Serum creatinine (mg/dl)	1.51	.88	.50	6.20	1.77	1.09	.60	4.00	–.771-	.441
pH	7.43	.11	6.63	7.91	7.43	.13	7.11	7.58	–.770-	.441
PCO2	36.07	11.95	15.40	106.00	36.99	12.98	20.10	68.00	–.320-	.749
HCO3	25.28	16.30	7.00	254.00	24.65	7.36	16.60	44.00	–.794-	.427
SO2	59.47	25.16	19.00	200.00	68.50	29.28	28.90	156.00	–1.571-	.116
Na	142.48	9.16	116.00	187.00	142.99	14.20	123.00	186.70	–.248-	.804
k	3.72	.82	1.50	6.30	3.75	.56	2.50	4.60	–.551-	.582

Table 20. Comparison between study group regarding other lab in 4th wave.

	Non-hepatic patients (n = 241)				Hepatic patients (n = 20)				Mann–Whitney U test	
	Mean	± SD	Range		Mean	± SD	Range		Test value	P-value
Random blood sugar (mg/dl)	3.15	.49	.30	5.00	2.95	.52	2.10	4.20	–1.102-	.270
INR	1.39	.50	1.00	4.80	1.60	.42	1.20	2.40	–1.996-	.046
D. dimer	2.85	4.22	.11	25.00	4.08	3.95	.40	9.80	–1.178-	.239

P ≤ 0.05 is considered statistically significant, P ≤ 0.01 is considered high statistically significant, SD = standard deviation, comparison between groups done by Mann–Whitney U test.

Table 21. Distribution of the studied patients as per liver functions.

	Total COVID-19 patients (n = 261)			
	Mean	± SD	Min.	Max.
AST	31.24	22.17	5.00	325.00
ALT	29.2	15.5	7.00	112.00
Albumin	3.13	.49	.30	5.00

statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 26.0, Microsoft Excel 2016 and MedCalc program

Table 22. CT among the studied groups.

		Non-hepatic patients (n = 241)		Hepatic patients (n = 20)		Total COVID-19 patients (n = 261)		Test value	P-value
		n	%	n	%	n	%		
		CT chest (GGO)	Normal	1	0.4%	0	0.0%		
	CORAD1	3	1.2%	0	0.0%	3	1.1		
	CORAD2	76	31.5%	9	45.0%	85	32.6		
	CORAD3	77	32.0%	4	20.0%	81	31.0		
	CORAD4	59	24.5%	3	15.0%	62	23.8		
	CORAD5	25	10.4%	4	20.0%	29	11.1		

software version 19.1. The level of significance was taken at P value < 0.05 is significant, otherwise is non-significant. The p-value is a statistical measure for the probability that the results observed in a study could have occurred by chance.

3. Results

This retrospective study was conducted on 761 patients (500 patients in third wave & 261 patients in

Table 23. Severity of COVID-19 among the studied groups.

Severity		Non-hepatic patients (n = 241)		Hepatic patients (n = 20)		Total COVID-19 patients (n = 261)		Test value	P-value
		n	%	n	%	n	%		
		Mild to moderate	23	9.5%	4	20.0%	27		
Severe	218	90.5%	16	80.0%	234	89.7%			

Table 24. outcome of COVID-19 among the studied groups.

Outcome		Non-hepatic patients (n = 241)		Hepatic patients (n = 20)		Total COVID-19 patients (n = 261)		Test value	P-value
		n	%	n	%	n	%		
		Survived	155	64.3%	12	60.0%	167		
Died	86	35.7%	8	40.0%	94	36.0			

Table 25. Comparison between 3rd and 4th waves regarding liver function.

		Patients with normal liver function tests			Patients with altered liver function tests			Test value	P-value
		Mean	± SD	Range	Mean	± SD	Range		
		AST	3rd wave	29.56	18.10	5.00	186.00		
	4th wave	38.98	27.04	11.00	229.00	32.00	48.89	32.66	13.00
	Test value	5.13			1.11				
	P-value	<0.001			0.266				
ALT	3rd wave	28.01	14.92	7.00	112.00	67.18	32.25	14.00	132.00
	4th wave	38.55	24.22	9.00	185.00	60.21	85.64	11.00	391.00
	Test value	5.95			0.076				
	P-value	<0.001			0.940				
Albumin	3rd wave	3.15	.49	.30	5.00	2.95	.52	2.10	4.20
	4th wave	3.17	.37	.30	5.00	3.12	.40	2.10	4.20
	Test value	1.309			2.066				
	P-value	0.190			0.039				

In patients with altered liver function tests, albumin was significantly higher in 4th wave compared to results in 3rd wave ($p = 0.039$). In patients with normal liver function tests, AST & ALT were significantly higher in 4th wave compared to results in 3rd wave ($p < 0.001$).

fourth wave) with laboratory confirmed COVID-19 infection by nasopharyngeal swab for SARS-CoV-2 more than 18 year under the observation of quarantine department, Assuit Chest Hospital. There was no statistically significant difference between the two groups regarding age and gender ($p > 0.05$) in the third and fourth wave. No statistically significant difference between COVID-19 patients in hepatic and non-hepatic groups regarding Laboratory examination in third and fourth wave ($p > 0.05$). No statistically significant difference between COVID-19 patients in hepatic and non hepatic groups regarding clinical presentation ($p > 0.05$). No statistically significant difference between COVID-19 patients in hepatic and non hepatic groups regarding heart rate, respiratory rate and temperature in third and fourth wave ($p > 0.05$). No statistically significant difference between them

regarding pH, PCO₂, HCO₃, SO₂, Na and K ($p > 0.05$). DM was significantly higher in non-hepatic patients compared to hepatic patients ($p = 0.015$). No statistically significant difference between the two groups regarding hypertension in third and fourth wave ($p > 0.05$). No statistically significant difference between the two groups regarding other clinical presentation ($p > 0.05$). no statistically significant difference between the two groups regarding CT findings ($p > 0.05$). No statistically significant difference between the two groups regarding severity of COVID-19 ($p > 0.05$). No statistically significant difference between the two groups regarding mortality ($p > 0.05$). Significantly higher in 4th wave compared to results in 3rd wave ($p = 0.039$). Normal liver function tests, AST & ALT were significantly higher in 4th wave compared to results in 3rd wave ($p < 0.001$).

3.1. Third wave

Third wave was carried out in the period from January to July 2021 and conducted on 500 Patients.

3.2. Fourth wave

Fourth wave was carried out in the period from August to October 2021 and conducted on 261 Patients.

4. Discussion

Liver injury in SARS-CoV-2 infection may be caused by either systemic inflammation response or drug hepatotoxicity, which is supported by the first autopsy pathological analysis of a COVID-19 patient showing moderate microvesicular steatosis and mild lobular and portal activity in the liver tissue.⁵

Regarding in our study, No statistically significant difference between the hepatic (n = 20) and non-hepatic (n = 241) groups regarding age, gender and hypertension.

The current results were supported by Wang et al.,⁶ who compared 64 (41%) patients with COVID-19 and elevated aminotransferases versus 92 (59%) patients with COVID-19 and normal aminotransferases, the study found that was no statistically significant difference between the studied groups regarding age, gender, and comorbidities. The most common comorbidities were DM and hypertension.

In our study, at third and fourth wave, no statistically significant difference between hepatic and non hepatic groups regarding clinical presentation (p > 0.05).

Our results were supported by An et al.,⁷ who revealed that there was no statistically significant difference between COVID-19 patients with normal and altered liver function regarding clinical presentation (p > 0.05). The most common symptoms were fatigue, fever, cough and shortness of breath. The same was reported by Garrido et al.,⁸

In our study, third and fourth waves showed significant decrease in platelets count compared to non hepatic patients (p < 0.001). No statistically significant difference between hepatic and non hepatic groups regarding Hb., WBCs, lymphocytes in third and fourth waves (p > 0.05).

In agreement with the current study An et al.,⁷ revealed that Patients with altered liver function tests showed significant decrease in platelets count compared to patients with normal liver function tests (p < 0.001), but other CBC results and

inflammatory markers were comparable between the studied groups.

In harmony with our results Voiosu et al.,⁹ who enrolled 1207 patients, 134 patients (11%) with abnormal liver functions test. Patients with altered liver function tests showed significant decrease in platelets count compared to patients with normal liver function tests (p < 0.001). Meanwhile, there was no statistically significant difference between COVID-19 patients with normal and altered liver function regarding Hb and WBC.

In the current study, during the third and fourth wave, no statistically significant difference between hepatic and non hepatic groups regarding serum urea and creatinine (p > 0.05). No statistically significant difference between them regarding pH, PCO₂, HCO₃, SO₂, Na and K (p > 0.05).

In agreement with the current study An et al.,⁷ reported that there was no statistically significant difference between the studied groups regarding creatinine, sodium, and potassium.

Furthermore, Garrido et al.,⁸ reported that there was no statistically significant difference between COVID-19 patients with normal and altered liver function groups regarding creatinine, Alkaline phosphatase and Sodium.

In the current study the third and fourth wave, no statistically significant difference between hepatic and non hepatic groups regarding random blood sugar, ferritin, D-dimer and CRP (p > 0.05).

In agreement with the current study An et al.,⁷ reported that there was no statistically significant difference between COVID-19 patients with normal and altered liver function regarding Fasting Blood Glucose, and CRP. Patients with altered liver function tests showed significant elevation in INR compared to patients with normal liver function tests (p < 0.001).

Furthermore, Garrido et al.,⁸ reported that there was no statistically significant difference between COVID-19 patients with normal and altered liver function groups regarding CRP, D-dimer, Ferritin and INR.

At the third wave, hepatic patients showed significant elevation in AST and ALT compared to non hepatic patients (p < 0.001). No statistically significant difference between the two groups regarding serum albumin (p > 0.05). Results still the same during the fourth wave.

Our results were supported by An et al.,⁷ who revealed that elevated AST (23.50% versus 0.00%, P=.033) and AKP (35.30% versus 0.00%, P=.007) were significantly more common in COVID-19 patients with liver cirrhosis than those without liver cirrhosis.

As well, Ferreira et al.,¹⁰ revealed that patients with altered liver function tests showed significant increase in AST compared to patients with normal liver function tests. There was no statistically significant difference between COVID-19 patients with normal and altered liver function regarding ALT and serum albumin ($p > 0.05$). The disagreement regarding ALT was due to the difference in inclusion criteria.

During the third wave, clexan was the most frequent drug used in 70.2% patients followed by dexamethasone in 55.6% patients then ceftriaxone in 44.4% patients. There was statistically significant difference between hepatic and non hepatic groups regarding treatment ($p = 0.033$).

The study by Mendizabal et al.,¹¹ revealed that a higher proportion of patients presenting abnormal liver biochemistry parameters on admission were under antibiotic treatment ($P < .0001$). During hospitalization, specific COVID-19 treatment was prescribed in 43.8% of the cohort ($n = 705$) and was more commonly administered to patients with abnormal liver tests on admission ($p < 0.0001$). Other drugs frequently used for hospitalized patients with COVID-19, were also significantly more commonly prescribed to patients who presented abnormal liver biochemistry values on admission.

In our study, ground glass appearance was present in 64% patients for the third waves and 99.6% patients for the fourth waves. No statistically significant difference between the two groups regarding CT findings for third and fourth waves ($p > 0.05$).

An Egyptian review by Hefeda,¹² stated that CT plays a pivotal role in the diagnosis and management of COVID-19 pneumonia. The typical appearance of COVID-19 pneumonia is bilateral patchy areas of ground glass infiltration, more in the lower lobes. The appearance of other signs like consolidation, air bronchogram, crazy pavement appearance, and air bubble signs appear during the course of the disease.

Regarding third wave, 47% patients had mild to moderate symptoms while 53% of them had severe manifestation, during the fourth wave 10.3% patients had mild to moderate symptoms while 89.7% of them had severe manifestation. No statistically significant difference between the two groups regarding severity of COVID-19 for third and fourth waves ($p > 0.05$).

In agreement with our results Garrido et al.,⁹ revealed that there was no statistically significant difference between COVID-19 patients with normal and altered liver function regarding severity of COVID-19 ($p > 0.05$).

Also, Marín-Dueñas et al.,¹³ there was no statistically significant difference between COVID-19 patients with normal and altered liver function regarding severity of COVID-19 ($p > 0.05$).

Regarding, No statistically significant difference between hepatic and non hepatic groups regarding mortality during third and fourth waves ($p > 0.05$).

In agreement with our results Garrido et al.,⁹ revealed that there was no statistically significant difference between COVID-19 patients with normal and altered liver function regarding mortality ($p > 0.05$). The total mortality rate was 22.8%.

5. Conclusion

Liver biochemical abnormality is more common in COVID-19 patients with liver cirrhosis. However, liver cirrhosis patients without COVID-19 have more hepatic decompensation events, so they should not be delayed from their hospitalization management during the COVID-19 pandemic. The presence of abnormal liver tests on admission was not associated with COVID-19 severity and mortality. Further well-designed large-scale studies should be necessary to validate these findings and establish the strategy for managing patients with SARS-CoV-2 infection and liver cirrhosis.

Conflict of interest

There is no conflict of interest.

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