Effect of SARS-COV-2 Infection on Liver Functions

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Abstract

Background: **Liver function abnormality has been reported in cases with severe acute respiratory syndrome corona virus -2 (SARS-Cov-2) infection. Based on clinical severity, cases infected with SARS-CoV-2 can exhibit a variety of clinical manifestations, ranging from asymptomatic to severe disease.** ***Aim of work:*** **Assessment of the effect of SARS-Cov-2 infection on liver function test according to the severity of the disease.** ***Subjects & methods*****: across sectional study was conducted, where data from 105 patients was collected, then we compared Liver function test among different severity groups (mild - moderate-severe) of SARS-CoV-19 infection.** ***Result:*** **Over half (53.3%) of the studied Corona virus disease -2019 (COVID -19) population had liver function test abnormalities. cases had severe COVID-19 infection had significantly higher Aspartate aminotransferase (AST) and Alanine transaminase (ALT) levels compared to mild/moderate disease severity (p=0.004 & p=0.048 correspondingly). Abnormal Liver Function Tests (LFTs) were significantly associated with comorbidities and severe COVID-19 infection. Also a significant relation was noted among abnormal LFTs and Computed Tomograghy scan (CT) of chest involvement, which was more common in 50-75% of patients. The mortality rate was significantly related with older age (p<0.001), multiple comorbidities (p=0.002), higher LFTs (ALT, AST and Prothrombin time) (p<0.001), & severe COVID-19 infection (p<0.001). no significant variance was found in hospital stay duration among cases with moderate & severe COVID-19 infection (mean 7.80 ± 3.579 days vs 8.54 ± 5.249 days).** ***Conclusion*****: Infection with COVID-19 and anti-COVID-19 treatments have an impact on liver function that must be evaluated in great detail**

Key words: SARS-COV-2, Liver Functions.

Introduction:

Cases with SARS-Cov-2 infection have been found to exhibit liver function abnormalities. cases infected with SARS-CoV-2 can exhibit a variety of clinical signs, ranging from being asymptomatic to experiencing severe illness, depending on the intensity of the infection. Typically, adults who have contracted SARS-CoV-2 can be classified into several levels of disease severity. However, the specific criteria for each category may differ between clinical guidelines and trials, and a patient's condition may alter over time. [1]

Through the analysis of liver biopsies, researchers have identified pathological alterations as microvesicular steatosis, as well as lobular & portal activity. Consequently, it is critical to understand the pattern of liver damage associated with SARS-Cov-2 infection. The direct cytotoxic effect of the virus, an uncontrolled immune reaction, peritonitis, or drug-induced liver injury may all contribute to hepatic involvement in SARS-Cov-2 infection. The liver constitutes a prospective target for SARS-CoV-2 due to the

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elevated expression of angiotensin converting enzyme -2 (ACE2) receptors in cholangiocytes. [2]

Furthermore, COVID-19 has the potential to exacerbate pre-existing chronic liver disease, resulting in acute-on-chronic liver failure & hepatic decompensation, which are associated with increased mortality. [3]

This study, aimed to assess the pattern of liver function test abnormalities in cases with SARS-COV-2 infection according to its severity. And comparing between cases with normal and abnormal liver function tests.

Patients & Methods

A cross-sectional study was conducted of patients confirmed to be infected with COVID 19 with variable severity admitted to isolation department in Suez Canal University Hospital, Ismailia, Egypt, after of ethical committee approval at (18/1/2022) and consent assignment from participants. Clinical, biochemical & radiological data were collected throughout the period from the start of December 2021 to the end of March 2022. The study included 105 patients confirmed to be infected with COVID-19 by Polymerase chain reaction test (PCR) presented and admitted to the isolation department with variable severity of COVID 19 infection and excluded cases age less than 18 and cases with incomplete data.

Data collection

1. Patient-related data: Socio-demographic characteristics including: Patient's age, gender. Other clinical data: co-morbidities such as cardiac, pulmonary, diabetes, pre-existing liver disease. Medications: Protocol 1for moderate cases (ceftriaxone-remedisfer-dexamethazone- enoxaparin). Protocol 2 for severe cases (ceftriaxone-remedisfer-dexamethazone- enoxaparin - tocilizumab).

2. Disease-related data: Symptoms of the patient. Hypoxia. need oxygen support. type of the lung ventilation.

3. Laboratory data: Complete blood count including: hemoglobin level (HGB), total leukocyte count (TLC), and differential and platelets. Liver function tests: ALT, AST, Bilirubin, Albumin, Prothrombin Time (PT), INR, C-reactive protein (CRP), D-dimer and serum ferritin

4. Radiographic data: The percentage of CT chest affection of the COVID-19 imaging findings. Used CT chest is a 16-slice scanner, activation 16 model TSX2012 with standard accessories (Toshiba Medical System). CT scan done as follows: in cranio-caudal direction with breath holding manner, starting from the apex of the lung to the Costo-phrenic sulci, slice thickness =1mm. the process was analyzed by multiplatform software application for medical imaging competing. The affection percentage of the involved both lungs were subdivided to 4 main categories estimated by percentages which had been used for the classification of the involvement according to the clinical practice during work at the hospital, they were: 0 % -30%, 30 %- 50 % ,50 % -75 %, more than 75 %. **5. Oxygen saturation:** assessed at patient first presentation, directs the physician about the condition of the patient, need for further assessment, and need for admission and follow up. In addition to, determine the patient's oxygen need and the type of oxygen support.

6- Outcome after COVID-19 infection: Mortality rate, recovery according to severity of the disease (mild- moderate-severe) and hospital stay duration.

-**Adults with SARS-CoV-2 infection were grouped into the following severity of illness categories:**

Asymptomatic or Pre-symptomatic Infection: Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but who have no symptoms that are consistent with COVID-19.

Mild Illness: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do

not have shortness of breath, dyspnea, or abnormal chest imaging.

Moderate Illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have oxygen saturation (SpO2) ≥94% on room air at sea level.

Severe Illness: Individuals who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%.

Critical Illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction. [1]

Statistical analysis: All statistical analyses were conducted utilizing version 25 of the SPSS statistical package for social science. Numerical descriptive statistics, as means, standard deviations, or percentages, were utilized to characterize the quantitative variables. When applicable, diagrammatic & tabular formats will be utilized to depict the qualitative variables. The significance of correlations among variables was assessed by applying the Chi-square test to categorical variables & the Student (t) test/ANOVA to continuous variables containing data that followed a normal distribution. The Chi-square test was employed to examine non-normally distributed data for categorical variables, while the Mann-Whitney U/Kruskal Wallis test was utilized to analyze continuous variables. To establish statistical significance, outcomes were deemed to have a p-value of 0.05 or less.

Results

Table 1 summarizes the laboratory characteristics of the studied cases. The average hemoglobin was 12.03 ±1.90 g/dl, while the mean TLC was 9418.5 ±4870.4 cells/ cmm. About 94.3% of the patients had lymphopenia. Regarding liver function test, the mean AST was 77.03 ±169.73 IU/l while the mean ALT was 64.59 ±108.97 IU/l. Regarding inflammatory markers, the mean serum ferritin was 251.68 ±289.06 mg/dl while the mean D-dimer was 444.80 ±277.37 ng/mL.

Table 1. Laboratory parameters for the studied patients

Variables	mean ±SD
Hemoglobin (g/dl)	12.03 ±1.90
TLC (cells/ cmm)	9418.5 ±4870.40
Lymphocytes, n (%)	
Normal	6 (5.7)
Lymphopenia	99 (94.3)
Platelet count (x 10^3)	247.20 ±113.31
AST (IU/l)	77.03 ±169.73
ALT (IU/l)	64.59 ±108.97
Total bilirubin (mg/dl)	0.66 ±0.34
Albumin (g/dl)	3.341 ±0.55
PT (sec)	14.34 ±2.13
INR	1.10 ±0.19
Serum ferritin (mg/dl)	251.68 ±289.06
D-dimer (ng/mL)	444.80 ±277.37
CRP (mg/L)	116.45 ±104.33

Table 2 shows the relation between normal and abnormal liver enzymes regarding some parameters that showed that abnormal LFTs is significantly associated with presence of co-morbidities as cardiac patients (p = 0.003) and CKD patients (p=0.044), and the severe form of COV-19 infection. Also, there is significant relation between abnormal LFTs and CT chest involvement being more common among patients with CT. Chest

affection is about 50% -75%), and those treated with protocol 2 of treatment(ceftriaxone-remedisfer-dexamethasone-enoxaparin-tocilizumab).

Table 2. Comparison between patients with normal LFTs and abnormal LFTs according to different parameters

	Normal (n = 49)		Abnormal (n = 56)		Test of sig.	p
	No.	%	No.	%		
Gender						
Male	21	42.9	23	41.1	χ^2= 0.034	0.853
female	28	57.1	33	58.9		
Age						
Min. – Max.	18.0 -84.0		17.0 -92.0		t= 1.224	0.224
Mean ± SD.	54.0 ±17.27		57.91 ±15.47			
Median (IQR)	54.0(42.0-69.0)		57.50 (47.0 - 69.5)			
Co-morbidities						
Cardiac diseases	0	0.0	9	16.1	8.613*	^{FE}p =0.003*
Chronic kidney disease (CKD)	4	8.2	0	0.0	4.752*	^{FE}p=0.044*
Chronic liver disease (CLD)	3	6.1	4	7.1	0.044	^{FE}p=1.000
Diabetes mellitus (DM)	23	49.9	31	55.4	0.741	0.389
Hypertension (HTN)	20	40.8	33	58.9	3.430	0.064
End-stage renal disease (ESRD)	1	2.0	0	0.0	1.154	^{FE}p=0.467
Pre- existing liver disease						
No	46	93.3	51	91.1	0292	^{FE}p= 0.721
Yes	3	6.1	5	8.9		
Type of CLD						
Hepatitis virus C+ve	2	66.7	4	80.0	0.178	^{FE}p= 1.000
Hepatitis virus B+ve	1	33.3	1	20.0		
Severity						
Mild	17	34.7	18	32.1	11.327*	0.003*
Moderate	23	46.9	12	21.4		
severe	9	18.4	26	46.4		
Hospital stay duration						
No	17	34.7	18	32.1	χ^2= 0.077	0.782
Yes	32	65.3	38	67.9		
Min. – Max.	2.0 – 21.0		2.0 – 21.0		U= 598.50	0.910
Mean ± SD.	8.09 ± 4.26		8.24 ± 4.70			
Median (IQR)	7.0 (5.0–10.0)		7.0 (5.0–10.0)			
Ct. chest involvement						
Free	9	18.4	2	3.6	χ^2= 11.710*	0.020*
<30	19	38.8	18	32.1		
30 – 50	12	24.5	11	19.6		
>50 – 75	6	12.2	18	32.1		
>75	3	6.1	7	12.5		
Hypoxia						
Non	17	34.7	18	32.1	0.077	0.782
Hypoxic	32	65.3	38	67.9		
O2 support						
Room air	17	34.7	18	32.1	χ^2= 12.318	^{MC}p= 0.053
O2 mask	10	20.4	3	5.4		
Nasal	6	12.2	2	3.6		

Venture	3	6.1	5	8.9		
Reservoire	5	10.2	12	21.4		
C-pap	2	4.1	8	14.3		
Intubated	6	12.2	8	14.3		
Outcome						
Died	10	20.4	16	28.6	χ^2=0.935	0.334
Recovery	39	79.6	40	71.4		
Stay						
Outpatient	17	34.7	18	32.1	χ^2=2.124	0.346
Isolation	23	46.9	21	37.5		
ICU	9	18.4	17	30.4		
Medication	(n = 32)		(n = 38)			
Protocol 1	23	71.9	12	31.6	χ^2= 11.283*	0.001*
Protocol 2	9	28.1	26	68.4		

*χ^2: **Chi square test*** *MC: **Monte Carlo*** ***U: Mann Whitney test***

p: p value for comparing among the examined groups

: Statistically significant at p ≤ 0.05

***Protocol 1:** ceftriaxone-remedisfer-dexamethasone- enoxaparin*

***Protocol 2:** ceftriaxone-remedisfer-dexamethasone- enoxaparin – tocilizumab*

Table 3. summarizes the laboratory characteristics of the patients with abnormal LFTs. The average hemoglobin level was (11.67 ± 1.99 g /dl), while the average TLC was (10485.7±6062.2 cells /cumm). The mean platelet level was (392.5 ± 1029.7). Regarding LFTs the mean level of AST and ALT was (124.9 ± 224.7, 101.3 ± 140.5) respectively and the mean serum level of bilirubin, albumin and PT was (0.7 ± 0.37, 3.2 ± 0.59, 14.8 ± 2.56) respectively. and finally, regarding the inflammatory markers, the mean serum ferritin level was (268.8 ± 313.8 mg/dl), while the mean D. dimer level was (492.2 ± 305.8 ng/ml), and the mean CRP level was (110.0 ± 100.6110 IU/ml).

Table 3. Descriptive analysis of the patients with abnormal liver function test according to different lab data (n = 56)

	Min. – Max.	Mean ± SD.
HGB	7.50 – 16.0	11.67 ± 1.99
TLC	2800.0 – 30000.0	10485.7±6062.2
Platelet (×10^3)	16.0 – 7900.0	392.5 ± 1029.7
AST	47 – 1110	124.9 ± 224.7
ALT	15 – 684	101.3 ± 140.5
Bilirubin	0.2 – 1.9	0.7 ± 0.37
Albumin	1.6 – 4.5	3.2 ± 0.59
PT	13 – 22	14.8 ± 2.56
S.ferritin	10.0 – 1212.0	268.8 ± 313.8
D-dimer	45.0 – 1460.0	492.2 ± 305.8
CRP	2.0 – 500.0	110.0 ± 100.6

IQR: Inter quartile range SD: Standard deviation

Table 4 summarizes the liver function of the studied patients in each group. cases suffered from severe COVID-19 infection had statistically significant greater levels of AST & ALT in comparison to mild and moderate grades (p=0.004) & (p=0.048).

Table 4. Comparison between the severity of the SARS COV-2 patients in regard to liver function tests				
Variables	Mild (n= 35) mean ±SD	Moderate (n= 35) mean ±SD	Severe (n= 35) mean ±SD	p-value
AST	42.1 ± 23.0	41.1 ± 31.5	147.8 ± 280.7	0.004*
ALT	51.4 ± 43.8	34.5 ± 20.2	107.8 ± 175.9	0.048*
Total bilirubin	0.72 ± 0.34	0.64 ± 0.41	0.62 ± 0.26	0.413
Albumin	3.46 ± 0.40	3.33 ± 0.48	3.22 ± 0.71	0.082
PT	13.8 ± 1.04	14.1 ± 2.39	15.1 ± 2.53	0.042
INR	1.05 ± 0.07	1.11 ± 0.266	1.14 ± 0.17	0.125
[a] p-values are based on as Chi-square test. Statistical significance at P < 0.05 [c] p-values are based on as Fisher Exact test. Statistical significance at P < 0.05				

Table 5 summarizes the association between mortality and clinical characteristics of the sample studied. Mortality was statistically significantly related to higher age (p<0.001), presence of multiple comorbidities (p=0.002) as cardiac (0.016*) and liver diseases (0.003*). Moreover, Mortality was statistically significantly associated with cases had cough and shortness of breath

Table 5. comparison between survivors and non-survivors in regard to their Clinical Characteristics			
Variables	**Outcome**		**p-value**
	Recovery (n= 79)	**Death (n= 26)**	
Age, mean ± SD	50.37±13.345	70.38±13.888	**<0.001*[c]**
Sex, n (%)			
Male	37 (46.8)	11 (42.3)	0.162[a]
Female	42 (53.2)	15 (57.7)	
Comorbidities, n (%)			
Absent	32 (40.5)	2 (7.7)	**0.002*** [c]
Present	47 (59.5)	24 (92.3)	
Diabetes mellitus	34 (43)	16 (61.5)	0.117[b]
Hypertension	35 (44.3)	13 (50)	0.613 [b]
Chronic kidney disease	2 (2.5)	1 (3.8)	0.727 [c]
Cardiac disease	6 (7.6)	7 (26.9)	**0.016***
Liver disease			**0.003***
Absent	77 (97.5)	20 (76.9)	
Present	2 (2.5)	6 (23.1)	
Complaint at presentation, n (%)			
Fever	38 (48.1)	14 (53.8)	0.611 [a]
Cough	66 (83.5)	14 (53.8)	**0.002*** [a]
Malaise	8 (10.1)	0 (0)	0.091 [c]
Headache	6 (7.6)	0 (0)	0.148 [c]
Diarrhea	4 (5.1)	0 (0)	0.242 [c]
Dyspnea	29 (36.7)	24 (92.3)	**<0.001*** [a]
Anosmia	1 (1.3)	0 (0)	1.000[c]
Hospital stay duration	4.90 ±5.4	7.12 ±1.48	0.065[c]
[a] p-values are based on as Chi-square test. Statistical significance at P < 0.05 [b] p-values are based on as Fisher Exact test. Statistical significance at P < 0.05 [c] p-values are based on as Mann Whitney test. Statistical significance at P < 0.05			

Table 6 shows that no significant variance was found among patients with moderate & severe grade COVID-19 infection regarding hospital stay duration (7.80 ± 3.579 vs 8.54 ± 5.249). On the other hand, there was no hospital admission among patients with mild disease form

Table 6. Comparison between the severity of the SARS COV-2 cases in regard to hospital stay duration

Variables	Mild (n= 35)	Moderate (n= 35)	Severe (n= 35)	p-value
hospital stay duration				
mean± SD	-	7.80 ± 3.579	8.54 ± 5.249	0.789
median (range)	-	7 (3 -19)	7 (2- 21)	

[a] p-values are based on Mann Whitney U test. Statistical significance at P < 0.05

Discussion

In the current study, the socio-demographic data of the examined population showed that the average age of the studied cases was 55.32±15.97 years, about 67.6% of the patients had comorbidities, where the most frequent was diabetes mellitus (47.6%), and hypertension (45.7%), moreover, the most frequent presentations were cough (76.2%), dyspnea (50.5%) and fever (49.5%), while diarrhea was less common, which represented (3.8%).

On other hand, **Wang et al.** [4] found that the predominant signs seen at the beginning of the disease were fever (136 [98.6%]), tiredness (96 [69.6%]), dry cough (82 [59.4%]), myalgia (48 [34.8%]), & dyspnea (43 [31.2%]). Headache, dizziness, stomach discomfort, diarrhea, nausea, & vomiting were Less common signs.

Sun et al. [5] have verified the pattern of signs & symptoms. The researchers discovered that the prevalence of fever was 89 percent, the prevalence of cough was 72 percent, & the prevalence of fatigue was 42 percent.

Regarding the laboratory features of the studied patients, it showed that lymphocytopenia was occurred in (94.3%) of patients, elevated mean serum level of AST and ALT were (77.03 ±169.73 IU/l, 64.59 ±108.97 IU/l) respectively, also prolonged PT time (14.34 ±2.13) seconds, mean s. ferritin level was (251.68 ±289.06), D. dimer was (444.80 ±277.37) and CRP was (116.45 ±104.33).

In the same context of laboratory findings, Wang et al. found that lymphocytopenia (lymphocyte count, 0.8 × 109/L [interquartile range {IQR}, 0.6-1.1]) occurred in 97 patients (70.3%), prolonged prothrombin time (13.0 seconds [IQR, 12.3-13.7]) in 80 patients (58%), and elevated lactate dehydrogenase (261 U/L [IQR, 182-403]) in 55 patients (39.9%), also this is Consistent with findings by Jiang et al. he stated that cases diagnosed with COVID-19 exhibited abnormal laboratory findings, as reduced lymphocyte & platelet counts, as well as increased levels of procalcitonin, CRP, transaminase, cardiac enzymes, creatinine, & D-dimer in their blood serum.

Regarding radiological data of the population studied, showed that the approximate rate of abnormal CT chest findings was (89.5%), indicating that about (10.5%) of chest CTs was normal. The most common outcomes were ground glass opacity, consolidation and bilateral patches.

This aligns with the 8.4 percent occurrence rate of normal chest CT scans reported in recent research conducted by Zhu J, et al. [6]

A further meta-analysis conducted by Sun P. et al. [5] revealed that 96.6 percent of COVID-19 cases exhibited abnormal chest CT results. These findings were characterized by the presence of bilateral patchy shadows

or ground glass opacity in the lungs of all cases.

In a study conducted by Weijie Guan et al. [7], it was discovered that cases with SARS-CoV-2 infection commonly showed ground-glass opacity & bilateral patchy shadowing on chest CT scans.

Upon admission, our study revealed that 53.3% (56 out of 105) of COVID-19 infected cases exhibited abnormalities in their LFTs. Previous investigations have demonstrated that the occurrence of abnormalities in LFTs varied between 37 percent & 69 percent Cai, Fanz, Bloom P, et al. [8]

This study, reveales that The abnormal LFTs showed the highest levels of AST & ALT to be 1110 IU/l and 684 IU/l, respectively. Conversely, the lowest levels were 47 IU/l for AST & 15 IU/l for ALT.

Chen et al. [9] observed that the AST & ALT levels reached their peak values at 1445 IU/l & 7590 IU/l, correspondingly.

This study showed that the mean serum level of AST, ALT & PT were higher in severe COVID-19 cases (147.8 ± 280.7 IU/l, 107.8 ± 175.9 IU/l) (15.1 ± 2.53 sec.). respectively, than those with mild severity (42.1 ± 23.0 IU/l, 51.4 ± 43.8 IU/l) (13.8 ± 1.04 sec.) respectively, and this is agreed with study by Zhang et al. [10] who stated that the average level of ALT, AST & total bilirubin in severe COVID-19 cases were greater than that in mild patients (37.87 ± 32.17 vs 21.22 ± 12.67; 38.87 ± 22.55 vs 24.39 ± 9.79; 14.12 ± 6.37 vs 10.27 ± 4.26).

Another study by Guan et al. [7] showed that Around eighteen percent of cases with non-severe COVID-19 illness & around fifty-six percent of cases with severe COVID-19 infection exhibited elevated blood levels of AST. Based on logistic regression analysis of possible risk factors for LFT abnormalities in our patients, we discovered that co-morbidities (p. 0.003) & elevated serum ferritin levels (p. <0.001) might potentially contribute to the development of LFT abnormalities.

Furthermore, Bangash et al. [11] have reported that there is a correlation between liver dysfunction & elevated levels of ferritin & serum hemoglobin. Serum ferritin serves as both an indicator of iron storage and a potent sign of inflammation. Therefore, we can clearly deduce that the excessive release of inflammatory cytokines is significantly involved in causing abnormalities in LFT.

Regarding factors associated with increasing mortality rate, our results found that the mortality rate amongst COVID-19 patients were statistically significantly associated with higher age (P 0.001), presence of co-morbidities (P 0.002) as cardiac (P 0.016) and CLD (P 0.003), elevated LFTs (P <0.001), higher serum ferritin level (p<0.001), severity of COVID-19 infection (p<0.001*) and higher percentage of lung affection on CT chest (p<0.001).

Li et al [12] documented the clinical features of 25 cases who died with COVID-19. The clinical profile of these cases revealed that the primary risk factors for mortality were advanced age & pre-existing medical conditions. The most often documented underlying conditions related with mortality were chronic hypertension, followed by diabetes mellitus, chronic heart disorders, cerebral infarction, & renal disease.

Guan et al. [7] noted that Prevalence of circulatory & endocrine co-morbidities was high amongst cases with COVID-19.

Zhou, et al. [13] observed that non-survivors had a notable increase in the blood level of ferritin in comparison with survivors throughout the clinical phases of the disease, & this elevation was observed as the cases deteriorated.

Cao et al. [14] revealed that The presence of ground-glass opacity was related to a higher mortality rate, being found in 41.2 percent of individuals who died compared to 12.9 percent of those who survived.

Regarding hospital stay duration, the mean hospital stay duration for the studied

population was (5.45±5.317) days, and for those with severe grade of infection was (8.54±5.249) days. While in study by Oksuz, et al. [15] the mean hospital stay duration was 9.1 days, another research by Fadel, et al. [16] on cases admitted for severe covid-19 infection, mean ICU and hospital stay duration were (7.4, 13.9) days respectively.

And finally, this current study revealed a significant difference between elevated liver enzymes and medication protocol, being more common among those treated with Protocol 2 (ceftriaxone-remedisfer-dexamethazone- enoxaparin - Tocilizumab) (P 0.001), than other Protocol 1, which doesn't involve tocilizumab (TCZ).

The study findings can be attributed to the severity of cases, that need TCZ as an additional therapy, or to the drug – induced liver injury (DILI) than can be associated with TCZ, as that observed by Gao, et al. [17] where 67.01% of patient treated with TCZ showed elevated liver enzymes the 1st four days after receiving TCZ therapies.

In contrast, Serviddio et al. [18] found that after TCZ administration to patients who had all elevated liver enzymes at baseline, before TCZ administration, and All cases had no prior medical history of liver or pulmonary illness & were taken to the hospital owing to severe hypoxemic respiratory failure, dyspnea, & fever caused by bilateral pneumonia from COVID-19. It was seen that their clinical condition improved quickly and their liver function test results returned to normal within three weeks of treatment. TCZ has shown potential efficacy in treating severe cases of COVID-19, including those with high liver function tests.

Conclusion:

During a severe infection, COVID-19 not only impacts the respiratory system but also leads to cardiac & hepatic complications, which can be responsible for serious complications &, in some cases, of fatal outcomes. Further comprehensive investigations with extended duration of observation are required to delineate the magnitude of hepatic injury in COVID-19 and its associated clinical consequences. Furthermore, a severe COVID-19 patient is a multifaceted individual who may undergo pharmacological polypharmacy, which carries a heightened risk of liver damage. Comprehensive assessment is necessary to examine the impact of COVID-19 infection & therapies for COVID-19 on liver function.

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