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Original Article

Study of Liver Function in Coronavirus Disease-19 Patients Presenting with Mild Symptoms – Observational Study

Srinivasa Rao Gopisetty[1], N Anuradha[2], K M Vignesh[1], Patel Harshvardhan Anil Bhai[1]

[1]Post Graduate, Department of General Medicine, Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India, [2]Associate Professor, Department of General Medicine, Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India

Abstract

Introduction: Lung injury is the main outcome of coronavirus disease-19 (COVID-19) infection; however, damage can occur in other organs, including the liver. The liver is the vital organ in the human body and its exposure to the viral particles might be an additional concern for COVID-19 patients. Although the lung is the main target organ of severe acute respiratory syndrome coronavirus-2 infection, damage can occur in multiple organs.

Aim: This was to study liver function tests in COVID-19 positive patients with mild symptoms.

Materials and Methods: This observational study was conducted from the period of June 2020 to July in patients with mild symptoms, infected with coronavirus diseases. Excluded. Patients with any comorbids, severe COVID-19 cases. A total of 115 positive cases of COVID-19 were included in this study. Liver function test was performed at the time of admission and data were analyzed.

Results: Mean value of prothrombin time in male is 13.01 and in females is 13.08, international normalized ratio in males is 1.16 and in females is 1.16, total bilirubin in males is 0.62 and in females is 0.42, direct bilirubin in males is 0.32 and in females is 0.19, mean value of protein in males is 6.80 and in females is 7.09, albumin in males is 4.17 and in females is 4.15, serum glutamic oxaloacetic transaminase in males is 37.27 and in females is 24.23, serum glutamic pyruvic transaminase in males is 38.67 and in females is 27.06, and gamma-glutamyl transferase in males is 49.09 and in females is 32.96.

Conclusion: In patients presented with mild symptoms shown no abnormalities in liver function.

Key words: Coronavirus disease-19, Liver function test, Mild symptoms, Risk factor

INTRODUCTION

The coronavirus disease-19 (COVID-19) epidemic expanded in early December from Wuhan, China's 7th most populous city, throughout China and was then exported to a growing number of countries. The first confirmed case of COVID-19 outside China was diagnosed on January 13, 2020, in Bangkok (Thailand).[1] On March 2, 2020, 67 territories outside mainland China had reported 8565 confirmed cases of COVID-19 with 132 deaths, as well as significant community transmission occurring in several countries worldwide, including Iran and Italy. It was declared a global pandemic by the World Health Organization on March 11, 2020.[2] The number of confirmed cases is continuously increasing worldwide. After Asian and European regions, a steep increase in cases is currently (March 31, 2020) being observed in low-income countries.[3] It is problematic to quantify the exact size of this pandemic as it would be necessary to count all cases, including not only severe and symptomatic cases but also mild ones.[4] Unfortunately, to date, there is not a global and standard response to the pandemic, and each country is facing a crisis based on their possibilities, expertise, and hypotheses. Thus, there are different criteria for testing,

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Corresponding Author: Dr. N Anuradha, Department of General Medicine, Sree Balaji Medical College and Hospital, Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

hospitalization, and estimating of cases making it difficult to calculate the number of people affected by the epidemic.

According to Worldometer,[5] up to date total, positive cases all over the world were 43,323,390 among that deaths include 1,158,807 and recovered from the coronavirus diseases includes 31,897,086. In current state, active cases are 10,267,497 in that 10,189,749 (99%) were in mild condition and 77,748 (1%) were in critical and serious condition, closed cases includes 33,055,893 among that 31,897,086 (96%) were recovered and discharged and 1,158,807 (4%) were died. All over the world, America is the first in the majority of the people affected by coronavirus diseases, followed by India, Brazil, Russia, France, and Spain. In India, the total people affected by coronavirus diseases are 7,909,049 among that number of people deaths includes 119,030, recovered from coronavirus diseases includes 7,133,993 and active cases are 656,026. Eight thousand nine hundred forty-four peoples are in serious or critical condition and India total people tested are 102,523,469. In India, Maharashtra was the first state in people affected by coronavirus diseases includes 1638961, followed by Andhra Pradesh, where people affected are 804026 followed by Karnataka people affected are 798378 and in Tamil Nadu people affected includes 706136.

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus is an enveloped, single-stranded virus, and the angiotensin-converting enzyme 2 (ACE2) receptor is thought to be a primary receptor for the viral spike protein and critical for infectivity.[6,7] The ACE2 protein is found at high levels in the colon, biliary system, and liver,[8] and ribonucleic acid shedding in the gastrointestinal (GI) tract is well described.[9] These data suggest that the SARS-CoV-2 may have tropism for the GI tract and liver and that these may be sites of active viral replication and either direct or indirect tissue injury. Liver injury in the setting of COVID-19-related illness poses a unique challenge to the clinician. First, there is often uncertainty, whether there is preexisting undiagnosed liver disease. Second, many of the medications used to treat moderate and severe illnesses have their profiles of liver toxicity. Finally, in the subset of patients who experience a critical condition, multiple factors may influence the trajectory of liver injury.

Aim

This was to study the liver function tests in COVID-19 positive patients with mild symptoms.

MATERIALS AND METHODS

This observational study was conducted from the period of June 2020 to July 2020 to evaluate the function of the liver in patients with mild symptoms infected with coronavirus diseases. A total of 115 positive cases of COVID-19 were included in this study. Inclusion criteria: Patients reported with positive reverse transcription-polymerase chain reaction with mild symptoms. Exclusion criteria: Patients affected with other comorbidities such as diabetes mellitus, blood pressure, liver problems, immunocompromised patients, hypoxia, and history of drinking alcohol and smoking habits. Written informed consent obtained from the patient. Liver function test was done in the admission. Parametri data were analyzed using one-way ANOVA and independent-sample *t*-test. Non-parametric data were analyzed using the Kruskal–Wallis test and Mann–Whitney test. Data were analyzed using SPSS version 21.

RESULTS

Out of 115 positive cases of COVID-19, 66 were male and 49 were female. Based on age group, 5 were in an age < 20, 23 patients between 21 and 30 years, 32 patients between 31 and 40 years, 19 patients between 41 and 50 years, 18 patients between 51 and 60 years, 10 patients between 61 and 70 years, and 8 patients > 70 years [Figures 1 and 2].

Out of 115 positive cases of COVID-19, 66 were male and 49 were female.

Mean prothrombin time/international normalized ratio (PT/INR) value of the patients presented with mild symptoms was 13.03 ± 0.82, mean total bilirubin (T-Bil) was 1.06 ± 0.10, mean protein was 6.92 ± 0.85, mean albumin was 4.15 ± 0.40, mean serum glutamic oxaloacetic transaminase (SGOT) was 31.78 ± 26.21, mean serum glutamic pyruvic transaminase (SGPT) was 33.78 ± 26.34, mean alkaline phosphatase (ALP) was 74.96 ± 44.5, and mean gamma-glutamyl transferase (GGT) was 42.23 ± 28.54. There is no correlation between study patient age and liver parameters [Figures 3-12].

Mean value of PT in male is 13.01 and in females is 13.08, INR in males is 1.16 and in females is 1.16, T-Bil in males is 0.62 and in females is 0.42, direct bilirubin (D-Bil) in males is 0.32 and in females is 0.19, mean value of protein in males is 6.80 and in females is 7.09, albumin in males is 4.17 and in females is 4.15, SGOT in males is 37.27 and in females is 24.23, SGPT in males is 38.67 and in females is 27.06, and GGT in males is 49.09 and in females is 32.96.

The *P*-value for prothrombin time and age group is 0.203, for INR is 0.12, for T-Bil is 0.787, for D-Bil is 0.383, for protein is 0.439, for albumin is 0.242, for SGOT is 0.017, for SGPT is 0.036, and for ALP is 0.308 which is not statistically significant. The *P*-value for GGT and age group is 0.004, which is < 0.005, which is statistically significant [Table 1].

The *P*-value for prothrombin time and gender is 0.709, for INR is 0.903, for protein is 0007, for albumin is 0793, for SGPT IS 0.008, and for ALP is 0.398, which are not statistically significant. The *P*-value for T-Bil and gender group is less than 0.0001, for D-Bil is 0.0001, for SGOT is 0002, and for GGT is 0.002, which are < 0.0001, which is statistically significant [Table 2].

DISCUSSION

In our study, the majority of the patients were males. The higher number of peoples affected by coronavirus diseases were in the age group between 31 and 40 years followed by 21–30 years, and least no of people were in the age group between <20 years.

A study conducted by Chen *et al.*[10] stated that in his research, the median age group was 33 years, which shows consistent with our studies. Similarly, other studies also show that males were commonly affected compared to females, which also shows similarity with our reviews.[10-12]

In our study, no deaths have occurred; all the patients were recovered and discharged, but the research conducted by

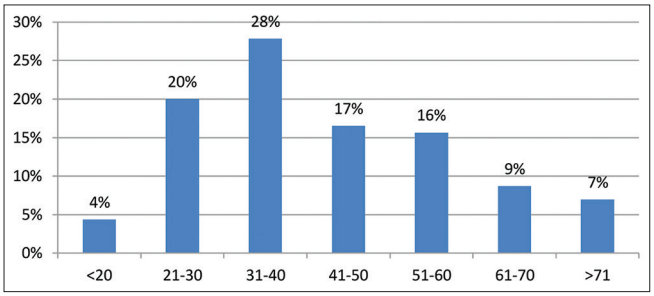

Figure 1: Age distribution

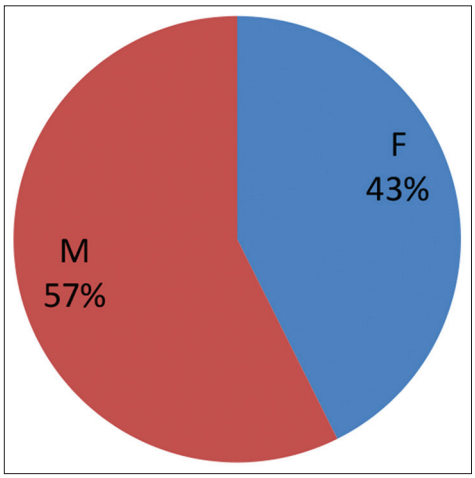

Figure 2: Gender distribution

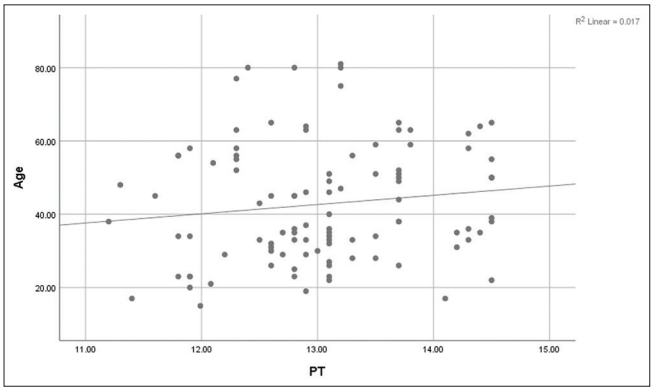

Figure 3: Correlation of age with prothrombin time

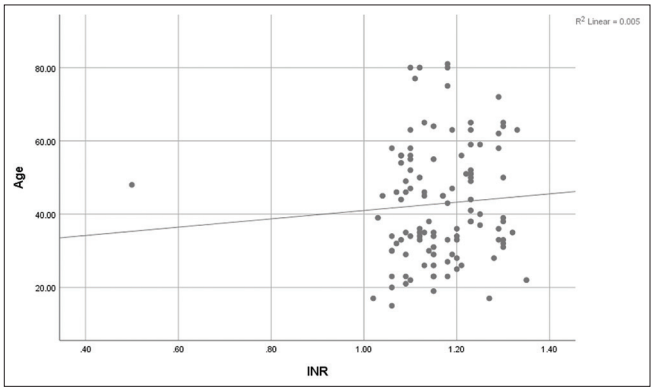

Figure 4: Correlation of age with international normalized ratio

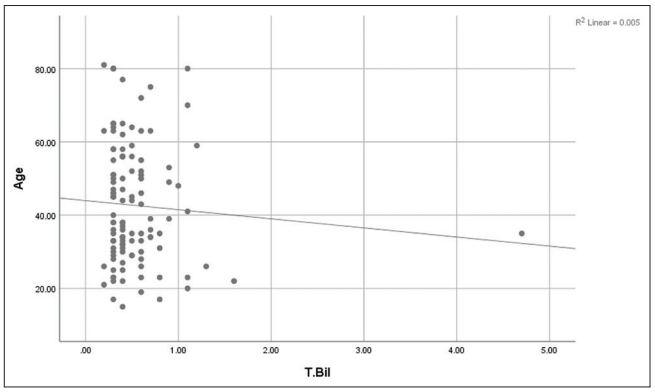

Figure 5: Correlation of age with total bilirubin

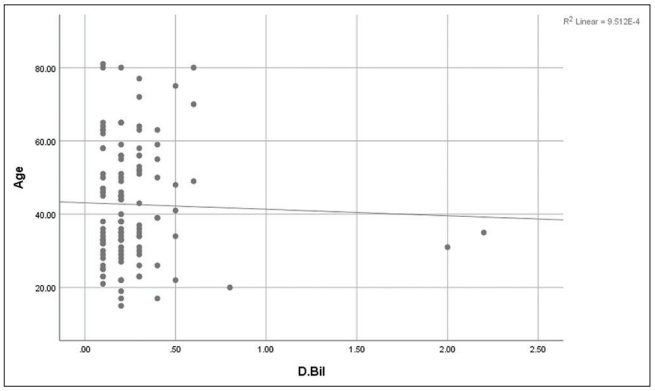

Figure 6: Correlation of age with direct bilirubin

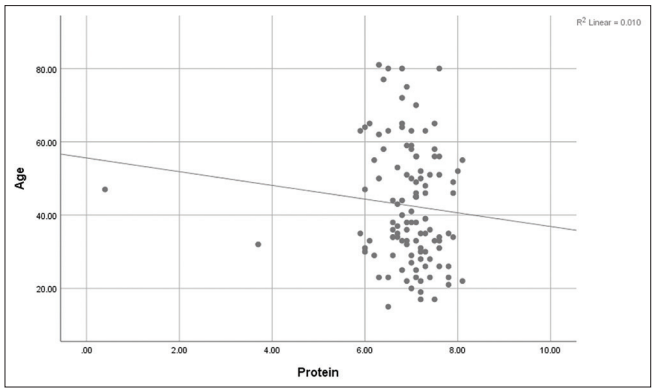

Figure 7: Correlation of age with protein

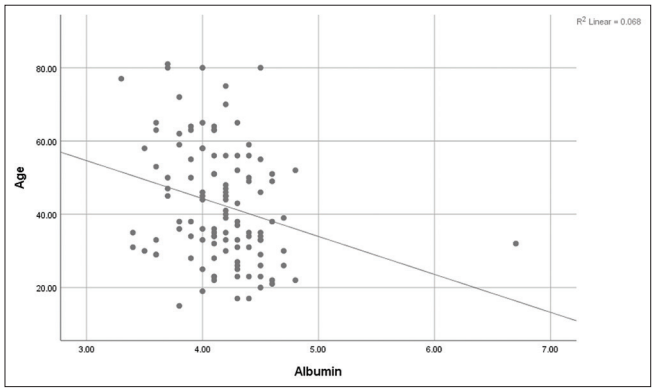

Figure 8: Correlation of age with albumin

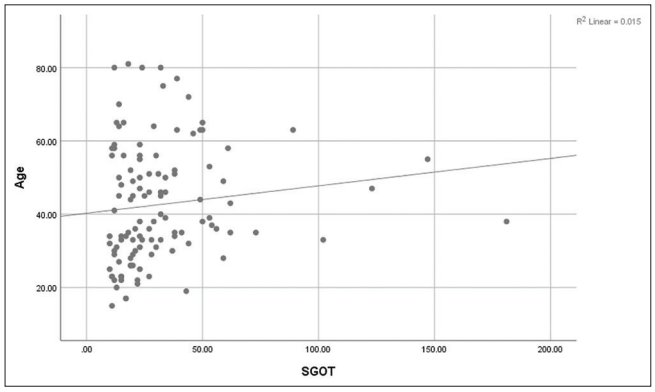

Figure 9: Correlation of age with serum glutamic oxaloacetic transaminase

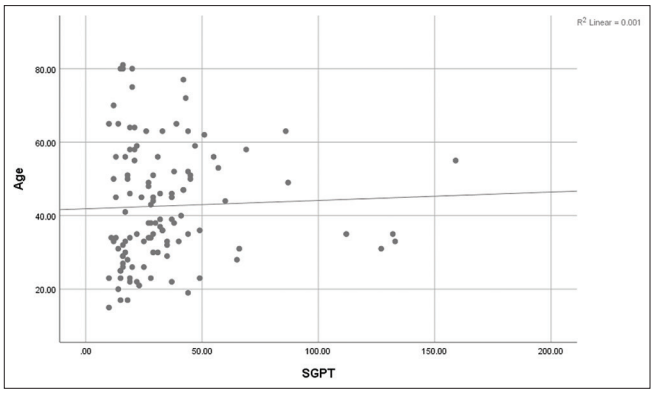

Figure 10: Correlation of age with serum glutamic pyruvic transaminase

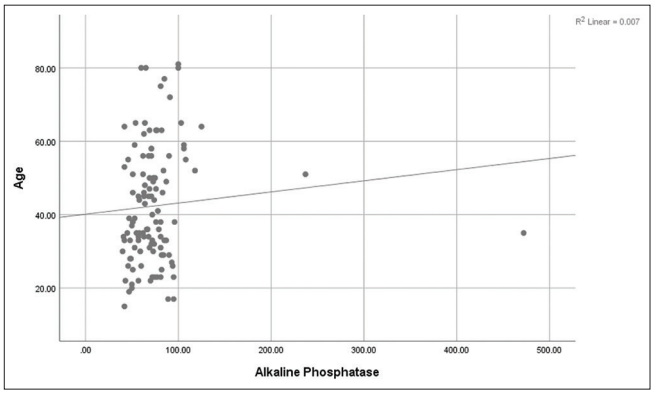

Figure 11: Correlation of age with alkaline phosphatase

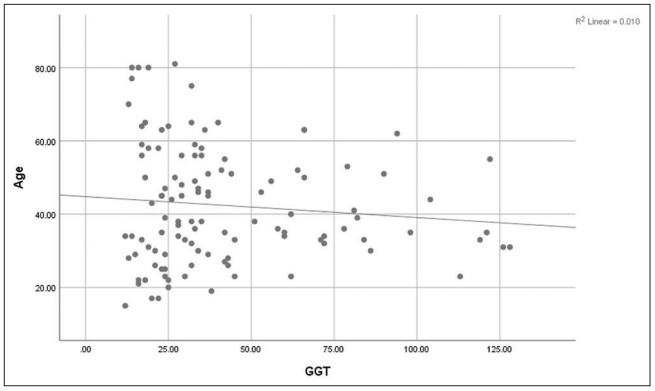

Figure 12: Correlation of age with gamma-glutamyl transferase

Wu *et al.*[13] reported in his studies that mortality rate was 2.3%.

Huang *et al.*[14] and Guan *et al.*[15] in his study revealed that aspartate aminotransferase enzymes and alanine aminotransferase enzymes are elevated in COVID-19 positive patients. Zheng *et al.*,[16] Zhang *et al.*,[17] and Fan *et al.*[18] in his studies reported that GGT was elevated in COVID-19 positive patients was about 13–45% which obeys our study also. In our study, T-Bil was elevated, which is similar to the survey done by Cai *et al.*[19] in his research, shows that 1–18% shows elevated T-Bil.[16]

Liver damage in COVID-19 patients may be caused by the virus directly infecting liver cells. In the study by Greenough *et al.*, 90% of the patients infected with SARS-CoV had decreased lymphocytes, 25% had diarrhea, and 66% had elevated plasma liver enzyme concentration.[20] Attention should be paid to the elevation in liver enzymes and liver lesions in these patients.

In the current pandemic, hepatic dysfunction has been seen in 14–53% of patients with COVID-19, particularly in those with severe disease. Cases of acute liver injury have been reported and are associated with higher

Table 1: Clinical parameters

Liver parameters		Mean	Standard deviation	*P*-value
Prothrombin time	<20	12.46	1.07	0.203
	21–30	12.83	0.67	
	31–40	13.20	0.84	
	41–50	13.07	0.90	
	51–60	12.95	0.90	
	61–70	13.51	0.79	
	>71	12.85	0.42	
	Total	13.04	0.83	
International normalized ratio	<20	1.11	0.10	0.12
	21–30	1.15	0.07	
	31–40	1.19	0.09	
	41–50	1.12	0.17	
	51–60	1.16	0.08	
	61–70	1.23	0.08	
	>71	1.17	0.07	
	Total	1.16	0.10	
Total bilirubin	<20	0.64	0.32	0.787
	21–30	0.53	0.36	
	31–40	0.60	0.77	
	41–50	0.49	0.25	
	51–60	0.50	0.24	
	61–70	0.40	0.16	
	>71	0.59	0.36	
	Total	0.54	0.47	
Bilirubin	<20	0.36	0.26	0.383
	21–30	0.21	0.11	
	31–40	0.33	0.48	
	41–50	0.24	0.15	
	51–60	0.25	0.09	
	61–70	0.19	0.11	
	>71	0.34	0.21	
	Total	0.27	0.28	
Protein	<20	7.08	0.37	0.439
	21–30	7.11	0.54	
	31–40	6.88	0.76	
	41–50	6.68	1.59	
	51–60	7.19	0.51	
	61–70	6.62	0.55	
	>71	6.80	0.42	
	Total	6.92	0.85	
Albumin	<20	4.20	0.29	0.242
	21–30	4.25	0.36	
	31–40	4.23	0.55	
	41–50	4.14	0.26	
	51–60	4.15	0.34	
	61–70	3.94	0.23	
	>71	3.93	0.38	
	Total	4.16	0.40	
Serum glutamic oxaloacetic transaminase	<20	20.20	13.01	0.017
	21–30	20.13	10.68	
	31–40	38.63	32.80	
	41–50	33.53	26.03	
	51–60	33.82	32.50	
	61–70	39.50	23.14	
	>71	27.00	11.82	
	Total	31.78	26.21	
Serum glutamic pyruvic transaminase	<20	20.20	13.61	0.036
	21–30	24.17	12.68	
	31–40	41.78	34.45	
	41–50	32.89	17.81	
	51–60	41.47	34.46	
	61–70	34.30	22.49	
	>71	23.00	12.32	
	Total	33.78	26.35	
Alkaline phosphatase	<20	64.60	25.26	0.308
	21–30	68.26	17.87	
	31–40	77.47	73.39	
	41–50	69.26	9.00	
	51–60	85.06	45.49	
	61–70	75.50	23.96	
	>71	83.14	15.83	
	Total	74.96	44.56	
Gamma-glutamyl transferase	<20	23.40	9.48	0.004
	21–30	35.09	23.95	
	31–40	55.75	34.54	
	41–50	39.68	22.78	
	51–60	44.65	28.59	
	61–70	41.70	25.49	
	>71	19.29	7.39	
	Total	42.24	28.55	

Table 2: Correlation between gender and clinical parameters

Gender		Mean	Standard deviation	*P*-value
Prothrombin time	Male	13.01	0.85	0.709
	Female	13.08	0.80	
International normalized ratio	Male	1.16	0.12	0.903
	Female	1.16	0.07	
Total bilirubin	Male	0.62	0.58	<0.0001
	Female	0.42	0.22	
Direct bilirubin	Male	0.32	0.35	0.0001
	Female	0.19	0.11	
Protein	Male	6.80	1.04	0.007
	Female	7.09	0.45	
Albumin	Male	4.17	0.48	0.793
	Female	4.15	0.27	
Serum glutamic oxaloacetic transaminase	Male	37.27	30.79	0.002
	Female	24.23	15.49	
Serum glutamic pyruvic transaminase	Male	38.67	30.74	0.008
	Female	27.06	16.81	
Alkaline phosphatase	Male	78.98	56.25	0.398
	Female	69.52	19.23	
Gamma-glutamyl transferase	Male	49.09	31.13	0.002
	Female	32.96	21.66	

mortality. Hepatic involvement in COVID-19 could be related to the direct cytopathic effect of the virus, an uncontrolled immune reaction, sepsis, or drug-induced liver injury. The postulated mechanism of viral entry is through the host angiotensin-converting enzyme 2 (ACE2) receptors that are abundantly present in Type 2 alveolar cells. Interestingly, ACE2 receptors are expressed in the GI tract, vascular endothelium, and cholangiocytes of the liver.[21]

CONCLUSION

Available data suggest that shown no abnormalities in liver function in COVID-19. Patients may monitor for direct

effect by the virus, immune-mediated inflammation, or drug-induced toxicity.

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