Evaluation of Liver Function in Symptomatic and Asymptomatic COVID-19 Patients

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Abstract
Background: The biochemical analysis of COVID-19 patients exhibited the abnormality of liver enzymes level. Patients with severe COVID-19 seem to have higher rates of hepatic dysfunction. The aim of the study was to evaluate the abnormality in the liver function test (LFT) in COVID-19 patients admitted at Pacific Institute of Medical Sciences Hospital, Udaipur, Rajasthan (India) and its association with the disease severity. The present study involved 208 symptomatic and 205 asymptomatic COVID-19 patients, who were admitted to Pacific Institute of Medical Sciences (PIMS) Hospital, Udaipur, Rajasthan.
Materials and Methods: The case records of 208 symptomatic and 205 asymptomatic COVID-19 patients were evaluated at the biochemistry laboratory, PIMS, Udaipur, Rajasthan. Various pathology tests were performed, and data were analysed. The liver function tests (LFT) including Bilirubin Total, Bilirubin Direct, Bilirubin Indirect, Total Protein, Albumin, SGOT (AST), SGPT (ALT) and Alkaline Phosphatase values were recorded for define the liver dysfunction of patients using automated analyser (Erba EM 200 and EM 300).
Results: From March 2021 to December 2021, a total of 208 symptomatic and 205 asymptomatic COVID-19 patients were selected for the study. Both symptomatic, as well as asymptomatic patients showed elevation comparative to the normal reference range in the following LFT parameters including Bilirubin Total, Bilirubin Direct, Bilirubin Indirect, SGOT (AST), SGPT (ALT) and Alkaline Phosphatase with results was significant according to p value (< 0.01).
Conclusions: Hepatic damage is a common symptom in symptomatic or asymptomatic COVID-19 patients. The pathogenetic mechanisms for abnormal LFT in COVID-19 patients are not fully understood therefore the biochemical analysis of LFT parameters is useful to unfold the pathogenetic mechanisms. The effects of COVID-19 on underlying chronic liver disease require detailed study to develop the base for drug designing and vaccine development for new strains.

Keywords: COVID-19, Liver function, Symptomatic, Asymptomatic.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the ongoing COVID-19 (coronavirus disease 2019) global public health emergency. The novel coronavirus was first reported from Wuhan city, China in 2019 [1].

The SARS-CoV-2 is the member of family of *Coronaviridae*. Coronaviruses are enveloped, single-stranded RNA viruses that RNA genomes size

905

ranging approximately from 26 to 32 kb [2,3,4]. SARS-CoV-2 spike (S) glycoprotein binds to the cell membrane protein receptor angiotensin-converting enzyme 2 (ACE2) to enter human cells [5,6].

The COVID-19 patient infected with SARS-CoV-2 may be asymptomatic or symptomatic and often show suspected sign e.g., cough, flulike symptoms, fever etc [7]. Symptomatic patients are with suspected COVID-19 signs e.g., initial respiratory signs including sore throat without shortness of breath, fever, cough, muscle ache, headache, and RT-PCR positive patients. The asymptomatic patients are RT-PCR positive but not show any symptoms included in study.

Hepatic injuries reported in patients with COVID-19 infection, mainly in those with moderate to severe illness. The mechanisms involved in liver injury of COVID-19 patients are still not clearly understood [8]. The injury may be caused by either SARS-CoV-2 infection or drug-induced liver injury [9]. A few COVID-19 cases reported disorder of liver enzymes during disease progression [10, 11]. Patients with severe COVID-19 had higher rates of hepatic dysfunction [12, 13, 14]. The hepatic dysfunction is reported in 14-53% of patients with COVID-19 especially in severe cases [15].

In the present study, we evaluated the changes in the liver function test in COVID-19 patients admitted at Pacific Institute of Medical Sciences (PIMS) Hospital, Udaipur, Rajasthan, India, and its association with the severity of the disease. The study involving 208 symptomatic and 205 asymptomatic patients.

Materials and Methods

The liver dysfunction was defined as any parameter having more than the upper limit of normal value. The blood sample of 208 symptomatic and 205 asymptomatic COVID-19 patients were collected and examined by using automated analyser (Erba EM 200 and EM 300) of biochemistry lab, Pacific Institute of Medical Sciences (PIMS) hospital, Udaipur, Rajasthan, India, and all experimental data were analysed. The result / values of following liver function tests (LFT) were recorded as percentages and frequency e.g., Bilirubin Total, Bilirubin Direct, Bilirubin Indirect, Total Protein, Albumin, SGOT (AST), SGPT (ALT) and Alkaline Phosphatase.

The continuous variables were recorded as mean and standard deviation. Student's t-test was applied on continuous variables. If the P value was < 0.05, then the difference between various parameters was considered statistically significant. All data were analysed with the software SPSS 26.0. Ethical clearance was obtained from the PIMS Institutional Ethical Committee before the start of the study.

Results

From March 2021 to December 2021, a total of 208 symptomatic and 205 asymptomatic COVID-19 patients were selected for the study; 58 were excluded due to either significant alcohol history or due to prior liver disease.

Table 1. Mean values of Liver function - Bilirubin Direct, Bilirubin Indirect, and Bilirubin Total

LFT Parameter	Symptomatic (Mean)	Asymptomatic (Mean)
Bilirubin Direct (mg/dl)	1.181	0.299
Bilirubin Indirect (mg/dl)	0.596	0.311
Bilirubin Total (mg/dl)	1.359	0.529

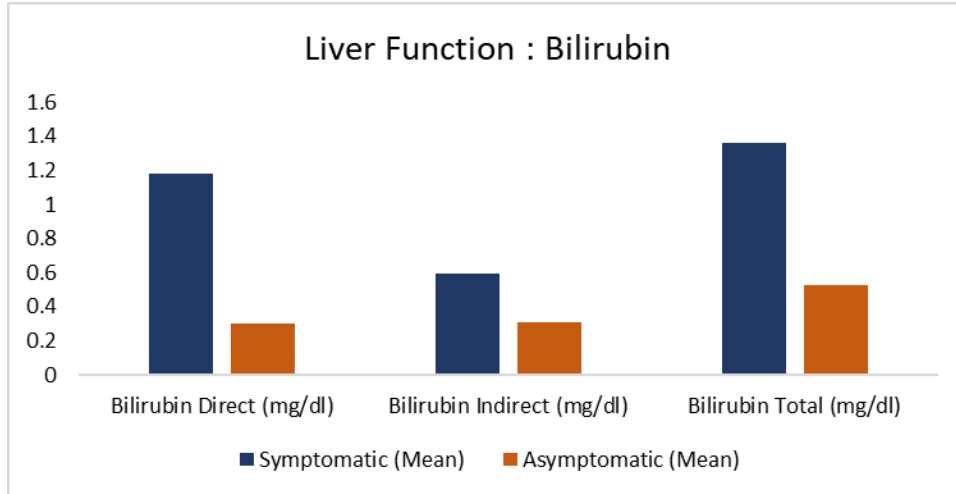**Fig 1. Liver function - Bilirubin Direct, Bilirubin Indirect, and Bilirubin Total**

Table 2. Mean values of Liver function - Total Protein and Albumin

LFT Parameter	Symptomatic (Mean)	Asymptomatic (Mean)
Total Protein (g/dl)	5.811	6.273
Albumin (g/dl)	2.743	3.182

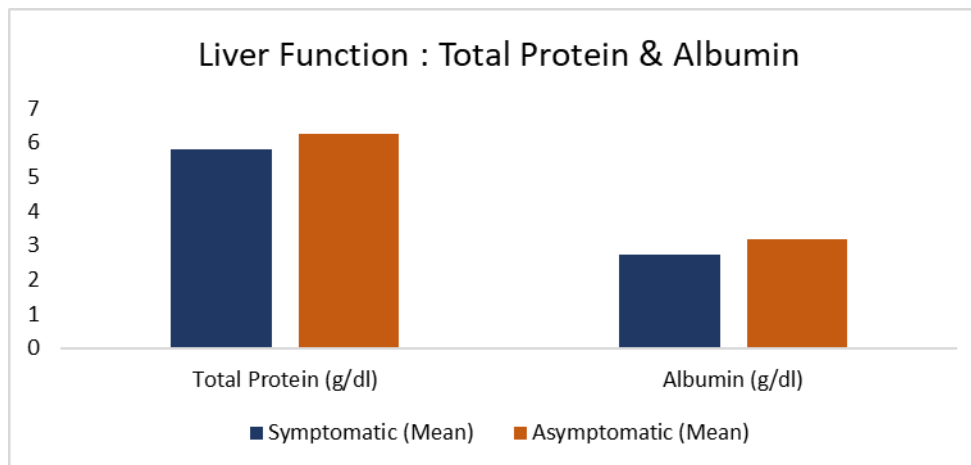**Fig 2. Liver function - Total Protein and Albumin**

Table 3. Mean values of Liver function - Alkaline Phosphates, SGOT (AST), SGPT (ALT)

LFT Parameter	Symptomatic (Mean)	Asymptomatic (Mean)
Alkaline Phosphates (U/L)	152.387	138.265
SGOT (AST) [U/L]	90.469	48.986
SGPT (ALT) [U/L]	70.005	41.142

Fig 3. Liver function - Alkaline Phosphates, SGOT (AST), SGPT (ALT)
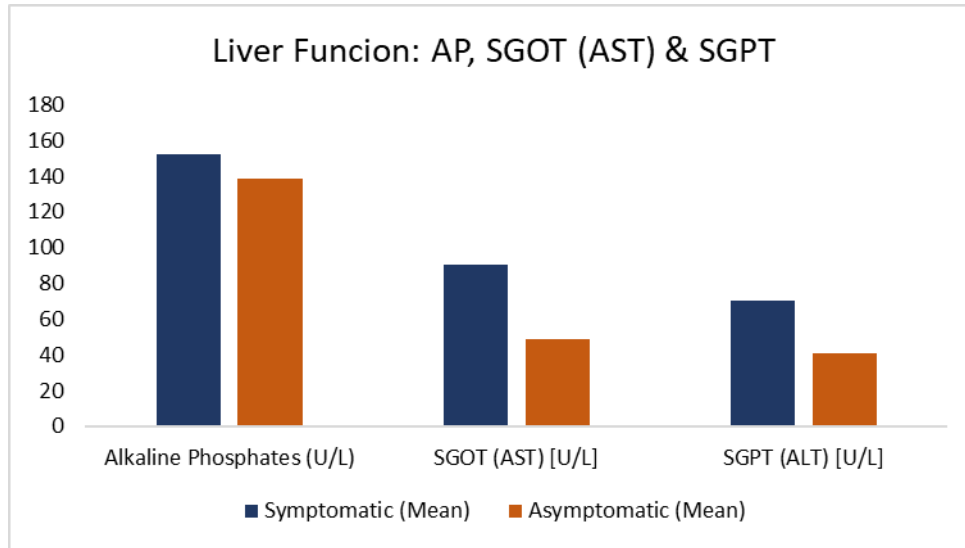

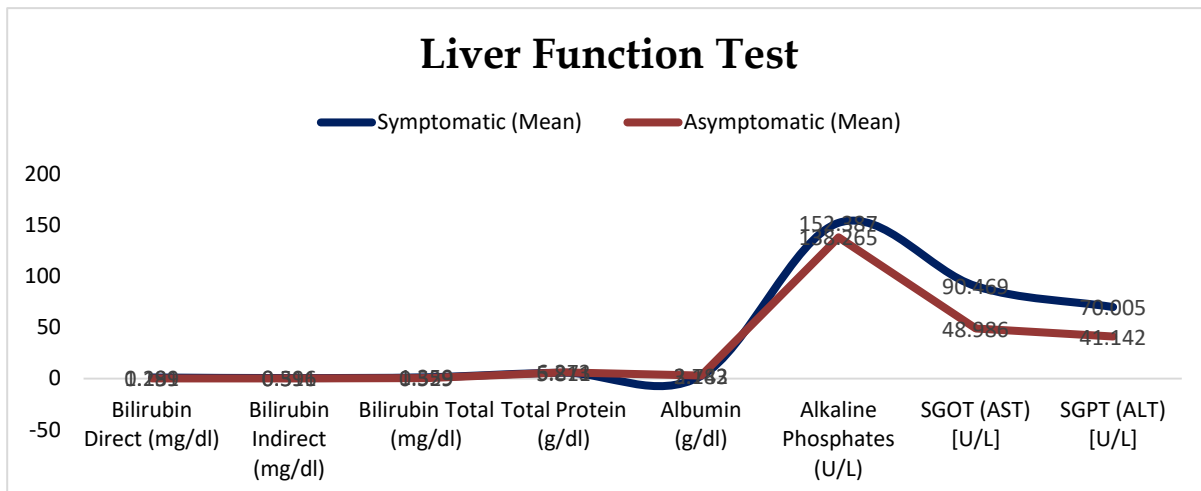**Fig 4. Comparative all Liver function test of symptomatic and asymptomatic patients**

Table 4. Liver function test of symptomatic and asymptomatic patients

Liver Function Test								
	Symptomatic COVID-19 Patients			Asymptomatic COVID-19 Patients				
Parameter	Mean	SD	CV	Mean	SD	CV	t-Value	P-Value

Parameter								
Bilirubin Total	1.36	3.28	241.65	0.529	0.36	68.07	-2.512	0.0128
Bilirubin Direct	1.18	3.41	288.88	0.299	0.16	56.69	-5.164	0.0105
Bilirubin Indirect	0.31	0.22	69.84	0.596	1.14	192.68	-3.449	0.0006
Total Protein	6.27	0.76	12.08	5.811	0.84	14.55	5.754	< 0.0001
Albumin	2.74	0.44	16.22	3.182	0.41	12.86	-10.272	< 0.0001
SGOT (AST)	90.47	100.18	110.74	48.986	24.09	49.18	5.694	< 0.0001
SGPT (ALT)	79.01	73.53	93.07	41.142	25.80	62.71	6.872	< 0.0001
Alkaline Phosphatase	152.39	168.03	110.26	138.26	566.54	409.75	-0.239	0.8114

Among the 413 patients, 196 patients had liver dysfunction while 217 patients had a normal liver function. Most patients showed symptomatic as well as asymptomatic patients shown an improvement in their liver function tests after discharge (Table 1, 3, 4 and Fig 1,3,4). Both symptomatic as well as asymptomatic patients shown elevation comparative to normal reference range in following LFT parameters including Bilirubin Total, Bilirubin Direct, Bilirubin Indirect, SGOT (AST), SGPT (ALT) and Alkaline Phosphatase with results was significant according to p value (< 0.01).

It's observed that the mean values of Total Protein and Albumin mean decreased more in symptomatic COVOD-19 patients than the asymptomatic COVID-19 patients comparative to reference range of parameters and results were significant (Table 2; Fig 2, 4). The symptomatic patients show more increase/ decrease in LFT parameter comparatively to asymptomatic COVID-19 patient. The mean values of albumin decreased more in symptomatic COVID-19 patients than the asymptomatic COVID-19 patients and the mean values of total protein decreased more in asymptomatic COVID-19 patients than the symptomatic COVID-19 patients comparative to reference range of parameters and results were significant (Table 4).

Discussion

The research studies explain that patients with COVID-19 show raised level of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) during the progression of the illness [16]. The research findings correlate between the severity of SARS-CoV-2 infection and the degree of liver enzyme increase [17]. A significant increase in serum bilirubin and liver enzymes observed in severe COVID-19 patients and gradually the liver parameters became normal with the recovery of patients [18].

The severity of COVID-19 increases the level of ALT, AST, total bilirubin, and alkaline phosphatase (ALP), and the level of albumin reduces [19], its also associated with severe disease and increased inflammatory markers. The degree of liver injury may also increase in proportion to the severity of

COVID-19. Present research finding explain that both symptomatic as well as asymptomatic patients shown elevation comparative to normal reference range in following LFT parameters including Bilirubin Total, Bilirubin Direct, Bilirubin Indirect, SGOT (AST), SGPT (ALT) and Alkaline Phosphatase with results was significant according to p value (< 0.01).

The mean values of total protein and albumin mean decreased more in symptomatic COVOD-19 patients than the asymptomatic COVID-19 patients comparative to reference range of parameters and results were significant [20]. Present research findings explain that the mean values of albumin decreased more in symptomatic COVID-19 patients than the asymptomatic COVID-19 patients and the mean values of total protein decreased more in asymptomatic COVID-19 patients than the symptomatic COVID-19 patients comparative to reference range of parameters and results were significant

Conclusion

Both symptomatic as well as asymptomatic patients shown elevation in following LFT parameters including Bilirubin Total, Bilirubin Direct, Bilirubin Indirect, SGOT (AST), SGPT (ALT) and Alkaline Phosphatase with results were significant according to p value (< 0.01). COVID-19 associated hepatic dysfunction observed in severe cases and is associated with fatal outcome. The pathogenetic mechanisms for abnormal LFT in COVID-19 patients are not fully understood therefore the biochemical analysis of LFT parameters useful to unfold the pathogenetic mechanisms. The effects of COVID-19 on underlying chronic liver disease require detailed study to develop the base for drug designing and vaccine development for new strains.

Authors' Contributions

Data collection, interpretation and drafting of manuscript: Rajneesh Prajapat and Manish K Vaishnav.

Concept design of project and editing of article: Suman Jain and Sandeep Bhatnagar.

Ethical Issues

The research project is the part of Ph.D research work. Research project approved by the ethics committee of Pacific Institute of Medical Sciences, Sai Tirupati University, Udaipur- 313003, Rajasthan, INDIA.

Acknowledgements

References

1. Prajapat R, Jain S, Bhatnagar S. *In Silico* Molecular Modeling and Docking Analysis of SARS-CoV-2 Helicase (YP_009725308) as Drug Target. IJMSCR 2022; 5 (2): 418-427.

2. Song Z, Xu Y, Bao L. From SARS to MERS: thrusting coronaviruses into the spotlight. Viruses 2019; 11 (1): 59. doi: 10.3390/v11010059.

3. Anand K, Ziebuhr J, Wadhwani P, Mesters JR, Hilgenfeld R. Coronavirus main proteinase (3CLpro) structure: basis for design of anti-SARS drugs. Science 2003; 300 (5626): 1763–1767. doi: 10.1126/science.1085658.

4. Prajapat R, Jain S. *In Silico* Molecular Docking Study for Inhibitor Designing Against SARS-CoV-2 Spike Protein. IJMSCR 2022; 5(1): 877-885.

5. Li W, Moore MJ, Vasllieva N, Sui J, Wong SK, Berne MA *et al*. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature 2003.

6. Tai W, He L, Zhang X, Pu J, Voronin D, Jiang S *et al*. Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine. Cellular and Molecular Immunology. 2020.

7. Colafrancesco S, Alessandri C, Conti F, Priori R. COVID-19 gone bad: A new character in the spectrum of the hyperferritinemic syndrome? Autoimmun Rev 2020;19 (Suppl 7):102573.

8. Zghal M, Bouhamed M, Mellouli M, Triki M, Kallel R, Ayedi L, Boudawara TS, Makni S. Liver injury in COVID-19: pathological findings. Pan Afr Med J 2022; 41:56.

9. Zhe X, Lei S, Yijin W, Jiyuan Z, Lei H, Chao Z *et al*. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020; 8(4):420–422.

10. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y *et al*. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet 2020; 395:507–13.

11. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020; 323:1061–9.

12. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J *et al*. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. Lancet Infect Dis 2020; 4:425–34.

13. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL *et al*. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: Retrospective case series. BMJ 2020; 2020:368.

14. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H *et al*. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. Lancet Respir Med 2020; 8:475–81.

15. Isabel FM, Siraj El JM, Paniz-Mondolfi A, Ronald EG, Jason R, Jela B *et al*. Findings of severe hepatic severe acute respiratory syndrome Coronavirus-2 infection. Cell Mol Gastroenterol Hepatol 2021;11(3): 763–770.

16. Deidda S, Tora L, Firinu D, Del Giacco S, Campagna M, Meloni F *et al*. Gastrointestinal coronavirus disease 2019: Epidemiology, clinical features, pathogenesis, prevention, and management Expert Rev Gastroenterol Hepatol 2021; 15:41–50.

17. Singhai A, Pavan GS, Panda S. Evaluation of liver function in symptomatic COVID-19 patients. J Family Med Prim Care 2021;10 (9):3252-3256.

18. Cai Q, Huang D, Ou P, Yu H, Zhu Z, Xia Z *et al*. COVID-19 in a designated infectious disease Hospital Outside Hubei Province, China Allergy 2020; 75:1742–52.

19. Ghoda A, Ghoda M. Liver injury in COVID-19 infection: A systematic review. Cureus 2020;12: e9487.

20. Jothimani D, Venugopal R, Abedin MF, Kaliamoorthy I, Rela M. COVID-19 and the liver. J Hepatol 2020;73 (5):1231-1240.