International Journal Dental and Medical Sciences Research
Volume 3, Issue 5, Sep-Oct 2021 pp 995-1000 www.ijdmsrjournal.com ISSN: 2582-6018

A Profile of Liver Function Test (LFT) in COVID-19 Positive Patients

[1]Dr. Phurailatpam Uma Devi, [2]Dr. R.K. Vidyabati Devi [3]Dr. Suchitra Chongtham[*]

[1]*PGT, Department of Biochemistry, Jawaharlal Nehru Institute of Medical Sciences, Imphal*
[2]*Assoc. Prof., Department of Biochemistry, Jawaharlal Nehru Institute of Medical Sciences, Imphal*
[3] *Assoc. Prof., Department of Biochemistry, Jawaharlal Nehru Institute of Medical Sciences, Imphal*
[*]*Corresponding Author: Dr. Suchitra Chongtham*

Submitted: 10-10-2021 Revised: 20-10-2021 Accepted: 22-10-2021

ABSTRACT: Coronavirus disease 2019(COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has attracted enormous worldwide attention. The system usually associated is respiratory tract related ranging from mild common cold to severe acute respiratory syndrome. COVID-19 infection can involve multiple body organs other than respiratory tract and lung. The knowledge of pathogenesis of COVID-19 continues to evolve and limited data exist, especially in this part of this country, about the engagement of the tissues like liver which is involved in the metabolism and excretion. This cross-sectional hospital based is study conducted in Biochemistry Department, JNIMS, Imphal for a period of 8 months from March, 2020 to October, 2020 with the aim to study the profile of liver function test in COVID-19 patients in an adult population in Manipur, India. The parameters considered were Total bilirubin (T.bil), Direct bilirubin (D.bil), Alkaline phosphatase (ALP), Alanine amino transferases (ALT), Aspartate amino transferases (AST), Total protein (TP), Albumin and Globulin in a total of 233 patients. Abnormal liver function test was defined as increased level of liver enzymes or parameters. Statistical analysis was performed using SPSS Software version 21 and the values were expressed as mean±SD.

Out of 233 patients, 74(31.8%) were female and 159(68.2%) were male. The liver parameters AST and ALT were found to be raised with a mean value 83.93±91.63 U/L and 70.18±91.80 U/L respectively as compare to their normal values. AST and ALT were found to be more in male as compared to female. AST was found to be highest at the age group (45-59) years. ALT was increased in age group (45-59) years followed by ≥ 60 years age group. Abnormal LFT profiles are associated with a range of health outcomes. The study is taken up to describe the profile of COVID-19 related liver dysfunction that might help in facilitating future prevention and management of COVID-19.

KEYWORDS: Liver function test; COVID-19; Alkaline phosphatase (ALP); Alanine amino transferases (ALT); Aspartate amino transferases (AST)

I. INTRODUCTION

The ongoing pandemic of coronavirus disease (COVID-19) is caused by Severe Acute Respiratory Coronavirus 2 (SARS-Cov-2) leading to global health crisis [1]. The pathogen causes infection from mild to severe ranges [2]. The system usually associated is respiratory tract with symptoms ranging from mild fever, dry cough, to severe condition like acute respiratory distress syndrome [3]. COVID-19 infection can involve multiple body organs other than the respiratory tract like cardiovascular, digestive and nervous systems [4]. The virus has been reported to attach to and enter the cells through angiotensin converting enzyme (ACE2) receptors through the process of endocytosis. This receptor is found in the different organs of the human body and involved in the dysfunction of the vital organs, for instance, liver dysfunction [5]. There have been reports of abnormal liver function in COVID -19 patients [6-8]. The knowledge and pathogenesis of COVID-19 continues to evolve and limited data exist, especially in this part of the country, about the engagement of the tissues like liver which is involved in the metabolism and excretion.

The current study aims to study the profile of liver function test in COVID-19 patients in an adult population in Manipur, India.

II. MATERIALS AND METHODS

This cross-sectional hospital based study was conducted at the Biochemistry Department of Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur. The study was conducted for a

International Journal Dental and Medical Sciences Research
Volume 3, Issue 5, Sep-Oct 2021 pp 995-1000 www.ijdmsrjournal.com ISSN: 2582-6018

period of 8 months from March, 2020 to October, 2020 in a total of 233 patients aged above 18 year. The study was conducted on consecutive COVID-19 patients whose blood samples were sent at the Department of Biochemistry for routine blood test. A total of 233 COVID-19 positive patients undergoing treatment in JNIMS Hospital constitute the study population.

All the RTPCR COVID-19 positive patients, who were aged 18 years and above, both male and female, whose blood sample were received at the Biochemistry Department for liver function test were included in the study. Those known case of carcinoma or malignancy, hepatitis B and C, HIV infected patients, pregnant woman and patients on hepatotoxic drugs like anti tubercular, allopurinol, etc. were excluded from the study.

Informed consents were taken from patients who have participated in the study. Under proper aseptic precaution, 2ml of blood was drawn from the antecubital vein from the selected subjects/ participants. The blood sample was then transferred to plain vial. It was then centrifuged at 3000 Revolutions per Minute (RPM) for 10 minutes in a centrifuge machine and serum was collected. The serum was processed immediately.

The liver function test parameters were estimated using IFCC (The International Federation of Clinical Chemistry and Laboratory Medicine) approved method. Total protein and Serum Albumin were estimated using Biuret [9] and Bromocresol Green method [10]. Total Bilirubin and Direct Bilirubin were estimated based on Azobilirubin and Dual WL spectrophotometric [11]. Transaminases (AST & ALT) were estimated using Kinetic with Pyridoxal-5-phosphate [12, 13]. Alkaline phosphatase method is based on pNPP/AMP buffer [14].

Abnormal liver function tests was defined when the Total Bilirubin ≥ 1.3 mg/dL and/ or Total Protein < 6.3g/dL and/ or Albumin < 3.5 g/dL and/or Globulin > 3.5 g/dL and/or AST > 46 IU/L and / or ALT > 69 IU/L and/ or ALP > 126 IU/L. These values are consistent with the upper or lower limits of normal established by reference laboratory for the area**.**

III. STATISTICAL ANALYSIS

The data obtained was analysed using SPSS version 21. Results were expressed as mean ± standard deviation (SD).

IV. RESULT

During the period from March, 2020 to October, 2020, the blood samples of a total of 233 patients were collected at the Department of Biochemistry for the liver function test including 74 (31.81%) females and 159 (68.2%) males.

The average age of the patients was 49 years. The male patients have high value of mean age (51.67±14.51 years) as compared to the female (44.33±17.01 years). The liver parameters AST and ALT were found to be raised with a mean value of 83.93 ± 91.63 U/L and 70.18 ± 91.80 U/L respectively as compared to their normal values.

AST and ALT were found to be more in male with respective values of 97.18±104.88 U/L and 84.09±106.36U/L as compared to female (Table 1).

AST was found to be highest (98.19±100.51 U/L) at age group (45-59) years. ALT was increased in age group (45-59) years with a value of 80.48 ± 94.29 U/L followed by ≥ 60 years age group with a value of 73.47 ±112.74 U/L (Table 2).

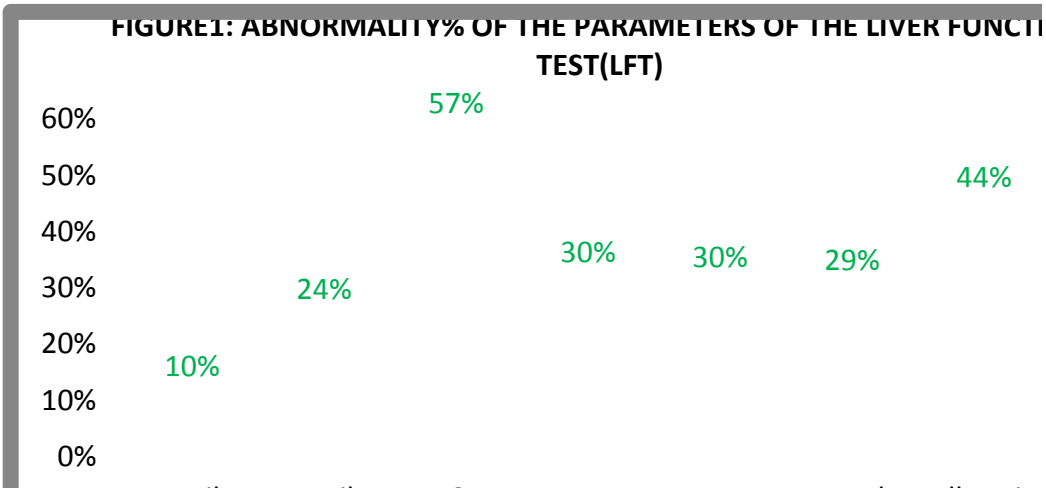
In this study, serum AST value was found to be abnormal in 57% of the cases. Serum albumin, serum ALT,ALP, total protein, T.Bil were found to be deranged in 44%, 30%, 30%, 29% , 10% respectively (FIGURE1)

Table 1: Liver profiles in COVID-19 patients(in mean±SD)

	TOTAL	MALE	FEMALE
Age(years)	**49.37±15.68**	**51.67±14.51**	**44.43±17.01**
T.bil(mg/dl)	0.86±0.81	0.97±0.94	0.63±0.32
D.bil(mg/dl)	0.34±0.39	0.39±0.46	0.24±0.16
AST(U/L)	**83.93±91.63**	**97.18±104.88**	**55.45±40.93**
ALT(U/L)	**70.18±91.80**	**84.09±106.36**	40.30±31.13
ALP(U/L)	114.61±74.36	118.14±76.53	107.00±69.35
Total protein(g/dl)	6.65±0.76	6.67±0.77	6.59±0.73
Albumin(g/dl)	3.60±0.56	3.63±0.55	3.56±0.59
Globulin(g/dl)	3.06±0.57	3.08±0.60	3.03±0.48

International Journal Dental and Medical Sciences Research
Volume 3, Issue 5, Sep-Oct 2021 pp 995-1000 www.ijdmsrjournal.com ISSN: 2582-6018

Table 2: Age-wise liver profiles in COVID-19 patients(in mean±SD)				
	<30years	**30-44years**	**45-59years**	**>=60years**
Age(years)	25.04±3.49	36.10±4.14	51.85±4.03	66.45±5.91
T.bil(mg/dl)	0.696±0.45	0.685±0.37	0.972±1.00	1.010±1.00
D.bil(mg/dl)	0.268±0.29	0.266±0.21	0.383±0.42	0.418±0.50
AST(U/L)	**54.28±45.35**	**83.11±0.92**	**98.19±100.51**	**81.27±94.93**
ALT(U/L)	52.24±36.31	64.83±74.95	**80.48±94.29**	**73.47±112.74**
ALP(U/L)	99.44±66.16	114.96±82.37	114.26±70.89	119.10±72.32
Total protein(g/dl)	6.772±0.84	6.569±0.83	6.685±0.72	6.665±0.70
Albumin(g/dl)	3.904±0.73	3.661±0.56	3.567±0.58	3.500±0.47
Globulin(g/dl)	2.908±0.44	2.921±0.60	3.113±0.59	3.194±0.52



V. DISCUSSION

In the current study, out of 233 COVID-19 cases, 159 were male and 74 were female. The mean age of patients was 49.37 ±15.68 years. Grouping with age interval of around 15 years, age group of 45-59 years and ≥ 60 years were found to have abnormal liver function test. Although the mechanism is not clear, a study of Feng G. et al also mentioned about the association of liver dysfunction in COVID-19 patients with older age [15].

Males have higher LFT profiles than female which is in co-ordination with others study [16-18]. The AST value was higher in male (97.18 ±104.880 U/L) as compared to female (55.45 ±40.939U/L). The result is in accordance with other studies where the AST values were higher in men as compared to female [18-22].

Also, in this present study, ALT value was higher than that of female. The higher values of the LFT profiles in case of male than female may be attributed by the sex-based immunologic and/or hormonal differences [23]. These higher values of the liver parameter throw a light on the hypothesis that infected males may be predisposed to develop COVID-19 related liver dysfunction as compared to female.

Again, in the present study serum AST value was found to be abnormal in 57% of the cases. Serum albumin, serum ALT, ALP, total protein, T.Bil were found to be deranged in 44%, 30%, 30%, 29%, 10% respectively. The finding of our study contradicts the findings reported by Kuller et al. [24] where the abnormalities percent for AST was lower than that of ALT. In their study AST was found to be abnormal in 21% and ALT in 24% of the cases.

There are certain limitations of our study. In this cross sectional survey, our knowledge on the etiologic factors associated with the COVID-19 patients is limited. We failed to collect the proper detailed history of the patients due to hindrances by COVID-19 management protocol. There is limited liver profile data of the patients prior to COVID-19 infection. The history of prior intake of drugs like oral contraceptive pills, or hormone replacement

therapy or of alcohol abuse could not be collected. Also, we were unable to obtain the clinical features and treatment received by the patients enrolled in our study which limited us in explaining the phenomenon caused by SARS-CoV-2.

The liver dysfunction may be a complication of COVID-19 infection or can be due to adverse drug reactions used to control the infection like lopinavir-ritonavir [25]. Acetaminophen is frequently used for COVID-19 symptom relief and can cause alterations in aminotransferases even at therapeutic doses [26]. AST is found primarily in the heart, liver, skeletal muscle, and kidney, ALT is found primarily in the liver and kidney, with lesser amounts in heart and skeletal muscle [27]. Although the value of ALT is more specific than AST for determining the liver function test, it is found to be affected by body mass index (BMI) and triglyceride levels [28-30]. Total cholesterol levels and alcohol consumption among men have a positive correlation, whereas smoking , physical activity and age were reported to have a negative correlation with ALT levels [31-32]. But in our study, the increase is more significant in case of AST. Hence, further investigation is necessary to determine the cause of raised liver enzymes in order to rule out the confounding factors or effect modifiers contributing to the raised liver parameters like that of cardiovascular dysfunctions, etc.

VI. CONCLUSION

Abnormal LFT profiles are associated with a range of health outcomes. The mechanism of hepatic injury is not well understood yet and seems to be multifactorial. The patients with remarkably altered LFT are at higher risk of progression to more serious disease contributing to its mortality and morbidity. This descriptive cross-sectional study is taken up to describe the profile of COVID-19 related liver dysfunction that might help in facilitating future management and prevention of fatal COVID-19 complications and to throw some light that might help in generating hypothesis of liver function abnormalities and specific impending COVID-19 complications to reduce morbidity and mortality.

REFERENCES

[1]. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–20.

[2]. Rezasoltani S, Hatami B, Yadegar A, Asadzadeh Aghdaei H, Zali MR. How Patients With Chronic Liver Diseases Succeed to Deal With COVID-19? Front Med (Lausanne). 2020 Jul 10;7:398. doi: 10.3389/fmed.2020.00398. PMID: 32754608; PMCID: PMC7381291.

[3]. Larsen JR, Martin MR, Martin JD, Kuhn P and Hicks JB (2020) Modeling the Onset of Symptoms of COVID-19. Front. Public Health 8:473. doi: 10.3389/ fpubh.2020.00473

[4]. Dong M, Zhang J, Ma X, Tan J, Chen L, Liu S, Xin Y, Zhuang L. ACE2, TMPRSS2 distribution and extrapulmonary organ injury in patients with COVID-19. Biomed Pharmacother. 2020 Nov;131:110678. doi: 10.1016/j.biopha.2020.110678. Epub 2020 Aug 24. PMID: 32861070; PMCID: PMC7444942.

[5]. Hwaiz R, Merza M, Hamad B, HamaSalih S, Mohammed M, Hama H. Evaluation of hepatic enzymes activities in COVID-19 patients. Int Immunopharmacol. 2021 Aug;97:107701. doi: 10.1016/j.intimp.2021.107701. Epub 2021 Apr 21. PMID: 33930704; PMCID: PMC8059948.

[6]. C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, L. Zhang, et al., Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395 (2020) 497–506.

[7]. Fan Z, Chen L, Li J, Cheng X, Yang J, Tian C, Zhang Y, Huang S, Liu Z, Cheng J. Clinical Features of COVID-19-Related Liver Functional Abnormality. Clin Gastroenterol Hepatol. 2020 Jun;18(7):1561-1566. doi: 10.1016/j.cgh.2020.04.002. Epub 2020 Apr 10. PMID: 32283325; PMCID: PMC7194865.

[8]. H. Shi, X. Han, N. Jiang, Y. Cao, O. Alwalid, J. Gu, Y. Fan, et al., Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study, Lancet Infect. Dis. 20 (2020) 425–434.

[9]. Kingsley G.R. The direct biuret method for determination of serum proteins as applied to photoelectric and visual colorimetry. J. Lab. Clin. Med. 1942;27:840–845

[10]. Peters T. All about albumin: Serum Albumin- Biochemistry, genetics and Medical Applications. Washington D.C.: American Association of Clinical Chemistry Press; 1996.

[11]. Doumas B.T., Perry B.W., Sasse E.A., et al. Standardisation in bilirubin assays: Evaluations of selected methods and stability

of bilirubin solutions. Clin. Chem. 1973;19:984–993.
[12]. Saris N.E. Revised IFCC method for aspartate aminotransferase. Clin. Chem. 1978;24:720–721.
[13]. Bergmeyer H.U., Scheibe P., Wahlefeld A.W. Optimization of methods for aspartate aminotransferase and alanine aminotransferase. Clin. Chem. 1978;24:1–1.
[14]. Lamb EJ, Browne M, John WG, Price CP. Alkaline phosphatase activity measurement in the UK by AMP-buffered methods: an appraisal of current practice. Ann Clin Biochem. 1998 Jan;35(Pt1):120-7.doi: 10.1177/000456329803500117. PMID: 9463750.
[15]. 9.Feng G, Zheng KI, Yan QQ, Rios RS, Targher G, Byrne CD, Poucke SV, Liu WY, Zheng MH. COVID-19 and Liver Dysfunction: Current Insights and Emergent Therapeutic Strategies. J Clin Transl Hepatol. 2020 Mar 28;8(1):18-24. doi: 10.14218/JCTH.2020.00018. Epub 2020 Mar 30. PMID: 32274342; PMCID: PMC7132016.
[16]. Z. Fan, L. Chen, J. Li, X. Cheng, J. Yang, C. Tian, Y. Zhang, et al., Clinical features of COVID-19-Related liver functional abnormality, Clin. Gastroenterol. Hepatol.18 (2020) 1561–1566.
[17]. L. Fu, J. Fei, S. Xu, H.-X. Xiang, Y. Xiang, Z.-X. Tan, M.-D. Li, et al., Acute liver injury and its association with death risk of patients with COVID-19: a hospital based prospective case-cohort study, Med. Rxiv 2020 (2020), 2004.2002.20050997.
[18]. 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;395:507–513. doi: 10.1016/S0140-6736(20)30211-7.
[19]. 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;368:m606. doi: 10.1136/bmj.m606.
[20]. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Zhonghua Jie He He Hu Xi Za Zhi 2020;43:E005. doi: 10.3760/cma.j.issn.1001-0939.2020.0005.
[21]. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020;12:8. doi: 10.1038/s41368-020-0074-x.
[22]. Chai X, Hu L, Zhang Y, Han W, Lu Z, Ke A, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. bioRxiv 2020(v1). doi: 10.1101/2020.02.03.931766.
[23]. Pirola CJ, Sookoian S. COVID-19 and ACE2 in the Liver and Gastrointestinal Tract: Putative Biological Explanations of Sexual Dimorphism. Gastroenterology. 2020 Oct;159(4):1620-1621. doi:10.1053/j.gastro.2020.04.050. Epub 2020 Apr 26. PMID: 32348773; PMCID: PMC7194954.
[24]. Kullar R, Patel AP, Saab S. Hepatic Injury in Patients With COVID-19. J Clin Gastroenterol. 2020 Nov/Dec;54(10):841-849. doi: 10.1097/MCG.0000000000001432. PMID: 32976196.
[25]. Cai Q, Huang D, Yu H, Zhu Z, Xia Z, Su Y, et al. COVID-19: abnormal liver function tests. J Hepatol 2020 Apr 13. https://doi.org/10.1016/j.jhep.2020.04.006.
[26]. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012–. PMID: 31643176.
[27]. Mauro P and Renze B. In: Tietz textbook of clinical chemistry and molecular diadnostics**.** 6th edition. Rifai N, Horvath AR, Wittwer C, editors. Elsevier; 2018. Serum Enzymes; p. 404-34.
[28]. Siest G, Schiele F, Galteau M, Panek E, Steinmetz J, Fagnani F, et al. Aspartate aminotransferase and alanine aminotransferase activities in plasma: statistical distributions, individual variations and reference values. Clin Chem 1975; 21:1077-1087.
[29]. Salvaggio A, Periti M, Miano L, Tavenelli M, Mazurati D. Body mass index and liver enzyme activity in serum. Clin Chem 1991; 37:720-723.
[30]. Piton A, Poynard T, Imbert-Bismut F, Khalil L, Delattre J, Pelissier E, et al. Factors associated with serum alanine transaminase activity in healthy subjects: consequences for the definition of normal values, for selection of blood donors, and for patients with chronic hepatitis C. MULTIVIRC

Group. HEPATOLOGY 1998;27:1213-1219.

[31]. Nuttall F, Jones B. Creatinine kinase and glutamic oxoloacetic transaminase activity in serum: kinetics of change with exercise and effect of physical conditioning. J Lab Clin Med 1968; 51:257-261.

[32]. Dufour D. Effects of habitual exercise on routine laboratory tests. Clin Chem 1998; 44:136.