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Original Article

COVID-19-Associated Variations in Liver Function Parameters: A Retrospective Study

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Abstract

Introduction: The coronavirus disease (COVID-19) was declared as pandemic disease by the World Health Organization. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mainly affects the respiratory system. The common symptoms of COVID-19 are fever, cough, fatigue, shortness of breath, expectoration, rhinorrheas, sore throat, diarrhea, loss of smell and taste, etc. In SARS-CoV-2 infection, multi-organ involvement of heart, kidney, pancreas, and liver are also reported. The fundamental aim of the study was to describe clinical characteristics of COVID-19 patients admitted with moderate to severe pneumonia and to find out their relation to the liver parameters.

Methods: This was a descriptive cross-sectional study in 253 COVID-19 patients (157 males and 96 females) with the age range of 20–60 years, which was conducted at Government Medical College, Baramulla from September 2021 to January 2022. Data collection includes recording of demographic parameters (age, gender, and sex). Blood samples of the patients were taken to measure serum liver function parameters.

Results: The result shows elevated levels of alanine transaminase in 24.11% patients, aspartate transaminase in 16.20% patients, total bilirubin in 12.65% patients, total protein in 16.21% patients, albumin in 3.95% patients, and alkaline phosphatase in 16.60% patients. However, reduced globulin levels were found in 3.95% in COVID-19 female patients but were normal in COVID-19 male patients.

Conclusion: This study shows the role of other factors like previous intake of medications; other undiagnosed liver diseases should be established. However, the continue follow-ups and serial estimation of liver function test in COVID-19 affected patients are required to derive a conclusive evidence of chronicity of this viral liver disease.

Key words: Expectoration, Rhinorrheas, Severe acute respiratory syndrome coronavirus 2, Shortness of breath, Sore throat

INTRODUCTION

An outbreak of coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially started in December 2019 in the Wuhan province of china and on March 11, 2021, the World Health Organization declared COVID-19 as a global pandemic disease.[1] SARS-CoV-2 mainly affects the respiratory system.[2] Patients can experience a range of clinical manifestations, from no symptoms to critical illness. The common symptoms of COVID-19 are fever, cough, fatigue, shortness of breath, expectoration, rhinorrheas, sore throat, diarrhea, loss of smell and taste, etc. According to illness severity, SARS-CoV-2 infection was grouped into mild, moderate, and severe categories.[3,4] In SARS-CoV-2 infection, multi-organ involvement of heart, kidney, pancreas, and liver are reported.[5,6] Abnormal liver function test (LFT) results might be due to liver damage by SARS-CoV-2. Angiotensin-converting enzyme 2 receptor is expressed on cholangiocytes of liver as well as in the hepatocytes, but its expression is much higher in cholangiocytes which may act as potential gate of entry for the virus in the liver leading to dysregulation of liver function. SARS-CoV-2-induced hepatic damage can also be explained by immune mediated inflammation such as cytokine

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storm, pneumonia, associated hypoxia, hypotension, and drug hepatoxicity.[1,5] A study of postmortem liver biopsy in COVID-19 patient revealed moderate microvascular steatosis, mild lobular, and portal activity.[7,8] Multiple studies suggest that though mild derangements of liver function may be experienced by the most COVID-19 patients, but significant liver injury is not common. The effect of abnormal liver biochemistry of COVID-19 is still unclear. Some studies have found that there is a significant association between elevated aspartate transaminase (AST) and alanine transaminase (ALT) with disease severity and mortality, whereas other researchers did not find it.[1] Profoundly, a little data involving liver enzyme derangements and its clinical implications on the COVID-19 patients are available.

The major aim of study was to describe the clinical characteristics of COVID-19 patients admitted with moderate-to-severe pneumonia in the Government Medical College and Associated Hospital, Baramulla, and to find out their relation to the liver parameters.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted at Government Medical College Baramulla, from September 2021 to January 2022. The study proposal was approved by the Institutional Ethics Committee. The confirmed COVID-19 cases on the basis of RT-PCR of nasopharyngeal and oropharyngeal swab samples, admitted in dedicated COVID-19 ward during the period, were included in the study.[4] The moderate cases presented with features of fever, cough, dyspnea, hypoxia, (SpO_2 <94%), and respiratory rate of 24 or more. The patients with severe pneumonia or adult respiratory distress syndrome with SpO_2 <90% on room air, respiratory rate of more than 30 breaths per minute and chest X-ray infiltrates and occurrence of respiratory or other organ failure. The patients with underlying liver disease, including chronic hepatitis B and C, alcoholic or non-alcoholic fatty liver disease by less were excluded from the study. The patients with fever of any other infections' etiology such as malaria, dengue, and human immunodeficiency virus were excluded from study. Detailed medical history was taken from all the cases to assess the presence of comorbid complications in corona affected patients. Informed consent was taken and venous blood samples were collected aseptically in plain vials from each case after 12 h of fasting. Serum separated following centrifugation was analyzed using a biochemistry auto analyzer kenelsg. All samples were loaded and assayed in a blind fashion by an investigator who was unaware of participants clinical status in both study and catral groups. Serum levels of total bilirubin was estimated by Diazo method.[9] Liver enzymes ALT and AST were measured by IFCC method,[10] while alkaline phosphatase (ALP) level determination was done using AMP Buffer. Total protein and albumin were assayed using Biuret and Bromo cresol green reagents, respectively.[11] Statistical analysis was performed using BM statistical package for the social sciences. Software version 20 windows (IBM, New York USA) and inferences were drawn. All values were expressed as mean (+,−) standard deviation comparison of continuous variables between groups were evaluated using analysis of variance test. Categorical variables were compared using Pearson's Chi-squared test (χ^2) test.

RESULTS

The average baseline characteristics of the entire population are summarized in Table 1. Table 1 depicts the comparative status of LFT parameters in the study. Total bilirubin level was raised in the study population. The primary liver enzyme ALT was also raised in this study population. ALP and AST were also out of range. Serum total protein levels were out of their physiological limits in study population. Sr. Albumin level was also high. However, reduced serum globulin was observed. Out of 96 females, 6 (6.25%) patients were having elevated total bilirubin, 13 (13.54%) patients were having high total protein level, 1 (1.04%) patient was having high albumin level, 1 (1.04%) patient was having reduced globulin level, 14 (14.58%) patients were having high ALP levels, 8 (8.33%) patients were having high AST levels, and 12 (12.5%) patients were having high ALT levels. Out of 157 males, 26 (16.56%) patients were having elevated total bilirubin, 28 (17.83%) patients were having high total protein level, 9 (5.73%) patients were having high albumin level, all patients were having normal globulin level, 28 (17.83%) patients were having high ALP levels, 33 (21.02%) patients were having high AST levels, and 49 (31.21%) patients were having high ALT levels [Figures 1-7].

Table 1: Analysis of biochemical parameters of COVID-19 patients

Parameters	Average	SD
Total bilirubin	0.94 g/dL	0.6395
Total protein	7.87 g/dL	0.441
Albumin	4.99 g/L	2.557
Globulin	3.04 g/L	0.343
ALP	125.94 U/L	60.331
AST	37.86 U/L	22.34
ALT	48.49 U/L	37.79

ALP: Alkaline phosphatase, AST: Aspartate transaminase, ALT: Alanine transaminase

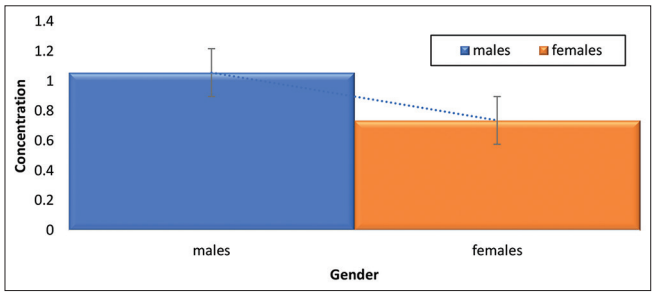

Figure 1: Average aspartate transaminase concentration in COVID-19 males and females

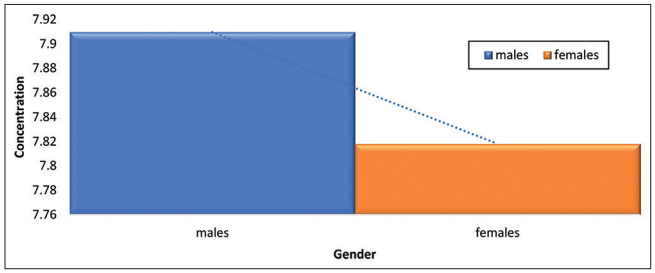

Figure 2: Average total protein concentration in COVID-19 males and females

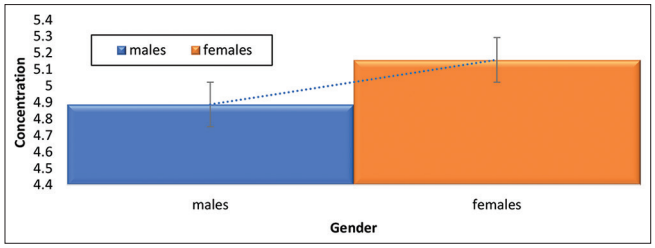

Figure 3: Average albumin concentration in COVID-19 males and females

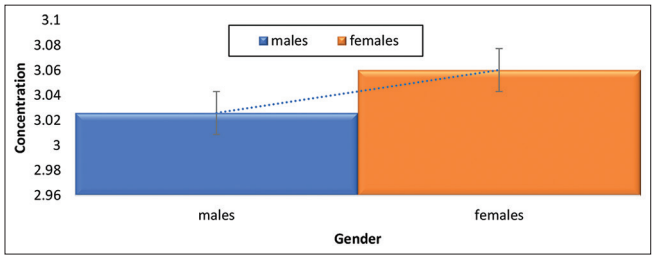

Figure 4: Average globulin concentratio in COVID-19 males and females

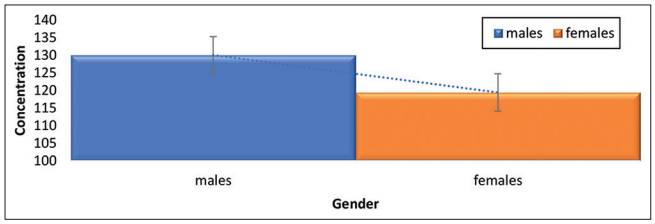

Figure 5: Average alkaline phosphatase concentration in COVID-19 males and females

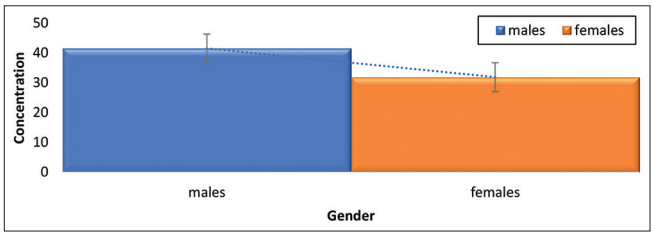

Figure 6: Average aspartate transaminase concentration in COVID-19 males and females

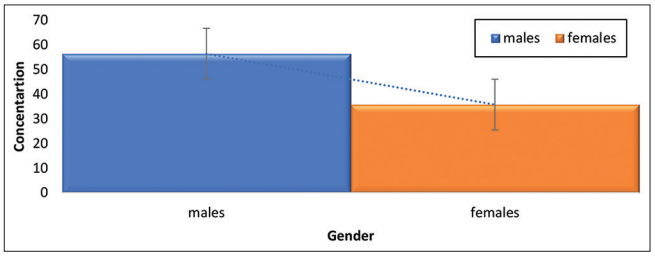

Figure 7: Average aspartate transaminase concentration in COVID-19 males and females

DISCUSSION

In patients admitted with COVID-19, liver dysfunction may be common. It is more in severe cases of COVID-19.[5,12] Abnormal liver enzymes in COVID-19 patients were first reported by (Chen *et al.*) from Wuhan. He had reported an increase in serum levels of ALT, AST, and lactate dehydrogenase in 43.4% of cases.[13] In a study from china, Average aspartate transaminase concentration in COVID-19 males and females it has been reported that there is higher elevation of ALT and AST in severe diseases (28.1%) compared to mild cases (19.8%).[14] Xu *et al.*, all in their recent study from Wuhan, found abnormal AST in severe cases (18.2%) and the incidence of liver injury in severe cases was also markedly higher (36.2%) than mild patients (9.6%).[15] Another study from Northern Italy revealed alteration of LFT in 62.4% of patients. In half of these patients, AST, ALT, and GGT were elevated, but reduced serum albumin levels were seen in 93.5% of cases.[16] The present study results are showing elevation of total bilirubin, total protein, ALT, AST, ALP, albumin levels, and reduced globulin levels. Elevated levels of ALT, AST, total bilirubin, total protein, albumin, and ALP were noted in 24.11%, 16.20%, 12.65%, 16.21%, 3.95%, and 16.60% and reduced level of Globulin was observed in 3.95% patients. The upper level of normal studies from South East Asia like those from Kaushik *et al.* in their study in Uttar Pradesh, India showed that 59.04% of admitted COVID-19 patients had abnormal LFT with elevated AST in 45.71% and elevated ALT in 25.21% cases.[17] A similar study from Palestine by (Asghar *et al.*) found elevated levels of liver enzymes, but they

had quoted significantly elevated levels of GGT and ALP, while, in contrast, we encountered normal levels of ALP with elevation of AST/ALT. The pathogenic mechanism of altered LFTs are not clear but most likely it seems multifactorial including hepatocytes and/or cholangiocyte infection, microthrombotic endothelialitis, immune dysregulation, drug-induced liver injury, and hepatic ischemic related to hypoxia and ICU related infections. The liver injury seems to be self-limiting and specific treatment is not necessary.[5,8] Abnormal LFT in COVID-19 is transient and simultaneously combined with increased enzymes from heart and muscle and it return to normal without any liver related morbidity and mortality.[13] Aminotransferase elevation in COVID-19 may be also due to myositis similar to severe influenza infection. A recent study had hypothesized that SARS-COV-2 binds directly to cholangiocytes demonstrating angiotensin-converting enzyme 2 (ACE) receptor and cause liver damage.[18] This explains partially the contribution of SARS-COV-2 infection to liver dysfunction in our patients.

Limitations

The limitation of this study is that the role of other factors like previous intake of medications, other undiagnosed liver diseases were not established. Continue follow-ups and serial estimation of LFT in COVID-19 affected patients is required to derive a conclusive evidence of chronicity of this viral liver disease.

CONCLUSION

Present study shows the role of other factors like previous intake of medications; other undiagnosed liver diseases should be established. However, the continued follow-ups and serial estimation of liver function test in COVID-19 affected patients are required to derive conclusive evidence of chronicity of this viral liver disease.

REFERENCES

1. Ridruejo E, Soza A. The liver in times of COVID-19: What hepatologists should know. Ann Hepatol 2020;19:353-8.
2. Weekly Epidemiological Update-17 November 2020 Data as Received by WHO from National Authorities, as of 10 am CEST 15 November 2020.
3. Centers for Disease Control and Prevention. Clinical Presentation of People with SARS-CoV-2 Infection. Available from: https://www.coronavirus.gov [Last accessed on 2020 Oct 09].
4. Government of India Ministry of Health and Family Welfare. Clinical Management Protocol: Covid-19. Version 3. Government of India Ministry of Health and Family Welfare Directorate General of Health Services (EMR Division); 2020.
5. Ghoda A, Ghoda M. Liver injury in COVID-19 infection: A systematic review. Cureus 2020;12:e9487.
6. Bzeizi K, Abdulla M, Mohmmad N, Alqamish J, Jamshidi N, Broering D. Effect of COVID-19 on liver abnormalities: A systematic review and meta-analysis. Sci Rep 2021;11:10599.
7. Cai Q, Huang D, Yu H, Zhu Z, Xia Z, Su Y, *et al.* COVID-19 abnormal liver function tests. J Hepatol 2020;73:566-74.
8. Bertolini A, van de Peppel IP, Bodewes FA, Moshage H, Fantin A, Farinati F, *et al*. Abnormal liver function tests in patients with COVID-19: Relevance and potential pathogenesis. Hepatology 2020;72:1864-72.
9. Pearlman PC, Lee RT. Detection and measurement of total bilirubin in serum, with use of surfactants as solubilizing agents. Clin Chem 1974;20:447-53.
10. Thomas L. Alanine aminotransferase (ALT), Aspartate aminotransferase (AST). In: Thomas L, editor. Clinical Laboratory Diagnostics. Frankfurt am Main: TH-Books Verlagsgesellschaft; 1998.
11. Tietz NW, editor. Text Book of Clinical Chemistry. Philadelphia, PA: WB Saunders; 1986. p. 579-89.
12. Zhang C, Shi L, Wang FS. Liver injury in COVID-19 management and challenges. Lancet Gastroenterol Hepatol 2020;5:428-30.
13. Li J, Fan JG. Characteristics and mechanism of liver injury in 2019 coronavirus disease. J Clin Transl Hepatol 2020;8:13-7.
14. Guan W, Ni Z, Hu Y, Liang WH, Ou CQ, He JX, *et al*. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-20.
15. Xu L, Liu J, Lu M, Yang D, Zheng X. Liver injury during highly pathogenic human coronavirus infections. Liver Int 2020; 40:998-1004.
16. Lenti MV, Andries FB, Pelligrino I, Klersy C, Merli S, Miceli E, *et al*. Impact of COVID-19 on liver function: Results from an internal medicine unit in Northern Italy. Intern Emerg Med 2020;15:1399-407.
17. Kaushik A, Wani SN, Baba MA, Agrawal AK. Prevalence of abnormal liver function tests in COVID-19 patients at a tertiary care centre. J Assoc Physicians India 2020;68:73-5.
18. Chai X, Hu L, Zhang Y, Han W, Lu Z, Ke A, *et al*. Specific ACE expression in cholangiocytes may cause liver damage after 2019-nCoV infection. Bio Rxiv 2020;2020-02.

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