

Review Article: COVID-19 And Liver Disease

Mr. Vikrant Mankar¹, *Clinical Instructor – Child Health Nursing, Datta Meghe College of Nursing, Wanadongri, Nagpur, Maharashtra, India 441110*

Ms. Madhavi Narayane², *Clinical Instructor- Medical Surgical Nursing, Datta Meghe College of Nursing, Wanadongri, Nagpur, Maharashtra, India 441110*

Mr. Amit Dhengre³, *Asst-Professor Medical Surgical Nursing Datta Meghe College of Nursing, Wanadongri, Nagpur, Maharashtra, India 441110*

Dr. Anjalee Chivane *Professor Dept. of Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences Sawangi (Meghe) Wardha*

Address for Correspondence

Mr. Vikrant Mankar,
*Clinical Instructor – Child Health Nursing,
Datta Meghe College of Nursing,
Wanadongri, Nagpur, Maharashtra, India 441110
M: 8806815379 Email: vikrantmankar143@gmail.com*

Abstract

Background:- Severe acute respiratory syndrome coronavirus 2 the causative pathogen of coronavirus disease 2019 became a global threat to human health. Liver impairment had been frequently reported as a common manifestation and clinical significance is still unclear particularly in patients with underlying chronic liver disease. **Aims:-** The summarise the changes in liver function tests during Severe acute respiratory syndrome corona virus 2 infection and its impact of COVID-19 in patients with Chronic Liver Disease. **Methods:-** A literature review using online database Pub Med was done using the search terms “SARS-CoV-2”, “COVID-19”, “liver”, “cirrhosis” and “liver transplantation”. **Conclusion:-** COVID-19 is frequently associated with different degrees of abnormal liver function tests most notably transaminases which are usually transitory and of mild degree. This Available evidence suggests that liver injury may have result from direct pathogenic effect by the virus and systemic inflammation or toxicity from commonly used drugs in this subset of patients. Severe acute respiratory syndrome corona virus 2 infections in children is associated with minimal or no increase in liver enzymes thus the presence of abnormal liver function tests should trigger evaluation for underlying liver diseases. It seems that patients with Chronic Liver Disease are not at greater risk for acquiring the infection these are cirrhosis, hepatocellular carcinoma, non-alcoholic fatty liver disease, autoimmune liver diseases or liver transplant may has a greater risk for severe COVID-19.

Keywords: COVID-19, liver disease, hepatocellular carcinoma, cirrhosis, liver injury

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), initially reported in Wuhan, China, but it's rapidly spread around

the world and caused a serious threat to global public health. Similar to SARS-CoV and SARS-CoV-2 mainly affects the respiratory system with fever; cough and dyspnoea being the most frequently reported symptoms.

2. COVID-19 AND HEPATIC INJURY

There are several studies have shown different degrees of elevated serum liver biochemistries in COVID-19 patients it mainly indicated by abnormal alanine aminotransferase and aspartate aminotransferase levels accompanied by slightly elevated total bilirubin levels. In fact, the incidence of elevated ALT and AST ranged from 2.5%-50.0% to 2.5%-61.1% respectively. With regard to TB, studies have reported increased levels in 0%-35.3% of cases. Relevant elevations of alkaline phosphatase and gamma-glutamyl transferase levels have not been reported in most studies. He examined 202 patients with confirmed COVID-19. 37.6% with non-alcoholic fatty liver disease and showed that elevated GGT levels portend a more severe course of the disease.

It remains unclear whether these laboratory test alterations are associated with a worse prognosis. In fact the literature has shown different results. In a large cohort including 1099 patients from 552 hospitals Guan and colleagues observed elevated levels of AST in 112 (18.2%) of patients with non-severe disease and 56 (39.4%) of patients with severe disease. Moreover the proportion of abnormal ALT in severe cases (28.1%) was higher than in mild cases (19.8%). Similarly Huang et al reported that the proportion of liver injury of intensive care unit (ICU) patients (61.5%) was higher than non-ICU patients (25.0%).

Other studies showed that reported conflicting results. For example, Wu et al showed no significant differences in liver function tests when compared mild/moderate patients with severe patients. Furthermore Wang and colleagues analysed 339 elderly COVID-19 patients and reported that there were no evident differences in ALT levels between survival and death. In addition cases of severe acute liver injury have rarely been described. There will be most recent studies argue that the COVID-19-related liver injuries are usually transitory and mild degree with small clinical significance. Hence it was recommended close monitoring and no specific treatment is required.

It remains unclear but liver injury is caused by the virus or reflects a severe inflammatory response with liver damage. SARS-CoV-2 may directly infect liver cells as the receptor of the virus and angiotensin-converting enzyme is expressed by liver and bile duct cells. Data from two independent cohorts revealed ACE2 expression in 2.6% of hepatocytes and 59.7% of cholangiocytes. He suggested that SARS-CoV-2 might directly bind to ACE2-positive cholangiocytes to dysregulate liver function. Liver biopsies in patients with SARS-associated coronavirus infection showed a significant increase in mitotic cells and ballooned hepatocytes, suggesting that it may induce apoptosis of liver cells.

These changes are nonspecific and may be caused by SARS-CoV-2 infection, hypoxemia or drug-induced liver injury. It is important to note that in none of these samples intranuclear or intracytoplasmic viral inclusions were identified.

3. COVID-19 AND CLD

Patients with CLD, particularly those with autoimmune liver diseases or post-transplant patients under immunosuppressive therapy are at increased risk of infection because of their altered immune function. The interaction between underlying CLD and COVID-19 has not been studied. Patients with cirrhosis are at increased risk of decomposition or development of acute-on-chronic liver failure when with bacterial, fungal or virus infection. However, the incidence of complications in COVID-19 patients, including hepatic encephalopathy, upper gastrointestinal

bleeding and liver failure has not been reported and needs to be assessed in large-cohort clinical studies. The paucity of data contributing the confirmed cases to the international given the expression of the ACE2 receptor in cholangiocytes, SARS-CoV-2 infection could aggravate cholestasis in patients with primary biliary cholangitis or primary sclerosing cholangitis. There are no data about exacerbations in these patients.

Immunosuppressive drugs have impact innate and adaptive immune responses. It will be increasing the risk for more severe or complicated infections caused by common viral agents (eg influenza). In that coronavirus infection the host response is an important contributor to the disease process. In fact, dysregulated and excessive innate immune responses to infection can result in tissue damage and cellular compromise. Surprisingly, it will be infection of immunocompromised host occurs, it leads to protected by a weaker immune response against the infectious agent. This statement is corroborated by the experience made so far on corona viruses' outbreaks. The outbreak of SARS caused by SARS-CoV in 2002-2003, characterised by atypical acute community-acquired pneumonia, caused a total of 8096 patients infected and 774 fatalities in over 30 countries. Transplant patients were expected to have poor outcomes, however, at the end of the outbreak, no such case has been recorded. Middle East Respiratory Syndrome (MERS) is another lethal zoonosis caused by the coronavirus named MERS-CoV, most occurring in Saudi Arabia in 2018. Several risk factors were identified for poor outcomes including advanced age, male sex and presence of co morbidities. These are immunosuppressed status was not considered a risk factor. In what concerns to COVID-19, the Hospital Papa Giovanni XXIII in Bergamo hosts one of the largest European centers for pediatric liver transplantation and is located in the "red zone" for the Italian outbreak. The report was around two hundred transplant recipients including ten current inpatients, none of them have developed clinical pulmonary disease despite three tested positive for SARS-CoV-2. Thus, immunosuppressed patients may not have an increased risk of severe complications by COVID-19 when compared to the general population. The effects of immunosuppression on COVID-19 are not well established that's why it is urgent that clinics share their experience with immunocompromised patients.

4. COVID-19-RELATED LIVER DAMAGE IN CHILDREN

All ages are susceptible people of SARS-CoV-2 infection. However they are infected children appear to have a milder disease course and a better prognosis than adults. In fact, children have a special immune response system with distinct clinical features in COVID-19.

Qiu et al analysed 36 paediatric patients (aged 0-16 years) with laboratory-confirmed COVID-19 in three hospitals in Zhejiang and they recorded and only 2 children with elevated liver enzymes. Wang et al studied 31 cases of SARS-CoV-2 infection in children from six provinces in northern China and reported 22.2% of patients with elevated transaminases levels, being the highest value registered of ALT and AST 68 U/L and 67 U/L respectively. Moreover Zhu et al analysed the clinical features and outcomes of 10 neonates born to mothers with COVID-19 pneumonia and reported only two patients with abnormal liver function tests. Since COVID-19 in children is associated with minimal or no increase in ALT and AST levels, American Association for the Study of Liver Diseases suggests evaluating all children with abnormal liver enzymes for underlying liver diseases and do not assume COVID-19.

5. NEW THERAPIES AND LIVER DISEASE

Presently, there no therapies or vaccines have yet demonstrated to be effective in treating or preventing COVID-19. The several drugs are now under investigation. It is important to keep in mind that therapeutic agents may be hepatotoxic, especially in patients with underlying CLD. Moreover patients with certain immunosuppressive therapies should be closely monitored due to drug interactions. American Association for the Study of Liver Diseases recommends that

patients with COVID-19 and elevated liver tests should still be considered for investigational therapeutics.

Lopinavir/ritonavir, an antiretroviral protease inhibitor, it can cause transient and usually asymptomatic elevations in serum aminotransferase levels. The risk of Lopinavir-associated hepatotoxicity in patients with very advanced liver disease is low, however Lopinavir plasma trough levels are increased and so it should be used with caution. In hepatitis B virus and hepatitis C virus coinfecting patients, highly active antiretroviral therapy with Lopinavir may result of an exacerbation of the underlying chronic hepatitis B or chronic hepatitis C.

Hydroxychloroquine is an antimalarial agent has not been suggesting for liver abnormalities and is an extremely rare cause of clinically apparent acute liver injury. Dose adjustments are not necessary in patients with hepatic impairment. Hydroxychloroquine should be used with caution since there continues to be no high-quality clinical data showing a clear benefit of these agents for COVID-19 and it has the potential to cause harm including serious cardiac side effects.

6. CONCLUSIONS

The COVID-19 epidemic has spread globally and raised many questions public health challenges. SARS-CoV-2 infection is frequently associated with different degrees of abnormal liver function tests, most notably that, transaminases, which are usually transitory and of mild degree. The little data are available concerning the incidence of SARS-CoV-2 infection in immunosuppressed patients; however it seems that those with CLD are not at greater risk for acquiring the infection. In the other hand, patients with cirrhosis, NAFLD, HCC and autoimmune liver diseases or liver transplant may have a greater risk for severe COVID-19. It is suggested to keep close surveillance and identify potential ways to prioritise the care of these patients in times of limited healthcare resources especially in the elderly and those with other comorbidities. Further research should focus on the effect of existing liver-related comorbidities on treatment and outcome of COVID-19.

REFERENCES

1. Del Rio C, Malani N. 2019 novel coronavirus—important information for clinicians. *JAMA*. 2020; 323: 1039.
2. Guan W-J, Ni Z-Y, Hu YU, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020; 382: 1708- 1720.
3. Jin XI, Lian J-S, Hu J-H, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. *Gut*. 2020; 69: 1002- 1009.
4. Ji D, Qin E, Xu J, et al. Implication of nonalcoholic fatty liver diseases (NAFLD) in patients with COVID-19: a preliminary analysis. *J Hepatol*. 2020. <https://doi.org/10.1016/j.jhep.2020.03.044>
5. Hossain, M., & Pasha, T. “PREVALENCE OF LOW BACK PAIN AND ITS ASSOCIATED FACTORS AMONG THE NURSES OF A SELECTED HOSPITAL AT DHAKA. *Journal of Medical Research and Health Sciences*, (2020), 3(11), 1110-1113. <https://doi.org/10.15520/jmrhs.v3i11.293>
6. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020; 395: 497- 506.
7. L, He W, Yu X, et al. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. *J Infect*. 2020; 80: 639– 645.
8. Mzezewa, S., Setati, M., Netshiongolwe, T., & Sinoamadi, V. “Prevalence of breast cancer in reduction mammoplasty specimens, in women of African origin: preliminary histology results at Mankweng and Polokwane hospitals. *Journal of Medical Research and Health Sciences*, (2020), 3(10), 1109-1113. <https://doi.org/10.15520/jmrhs.v3i10.264>

9. Wu J, Li W, Shi X, et al. Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19). *J Intern Med*. 2020. <https://doi.org/10.1111/joim.13063>
10. Feng G, Zheng KI, Yan Q-Q, et al. COVID-19 and Liver dysfunction: current insights and emergent therapeutic strategies. *J ClinTranslHepatol*. 2020; 8: 18- 24.
11. Chai X, Hu L, Zhang Y, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. *bioRxiv*. 2020. <https://doi.org/10.1101/2020.02.03.931766>
12. Albillos A, Lario M, Álvarez-Mon M. Cirrhosis-associated immune dysfunction: distinctive features and clinical relevance. *J Hepatol*. 2014; 61: 1385- 1396.
13. Sarin SK. "Fast, faster, and fastest: science on the run during COVID-19 drama"- "do not forget the liver". *Hepatol Int*. 2020. <https://doi.org/10.1007/s12072-020-10042-0>
14. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol*. 2020; 5: 428- 430
15. Ordu J I, Chukwu A (2018) Kinetics And Stability Studies Of Formulated Micro/Nano Suspension Of Metronidazole *International Journal Of Scientific Research And Education*.06,03 (March-18) 7882-97
16. Waryana, SabarSantosa, J Supadi (2018) Integrated Community Service's Guideline Influences Communication Skill And Team Work On Solving Health Problem *International Journal Of Scientific Research And Education*.06,03 (March-18) 7877-81
17. Kaltsas A, Sepkowitz K. Community acquired respiratory and gastrointestinal viral infections: challenges in the immunocompromised host. *CurrOpin Infect Dis*. 2012; 25: 423- 430.
18. World Health Organization. Consensus document on the epidemiology of severe acute respiratory syndrome (SARS). <https://apps.who.int/iris/handle/10665/70863>. Accessed April 14, 2020.
19. Hui S, Azhar I, Kim J, Memish A, Oh D, Zumla A. Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission. *Lancet Infect Dis*. 2018; 18: e217- e227.
20. Lleo A, Invernizzi P, Lohse AW, Aghemo A, Carbone M. Highlights for management of patients with autoimmune liver disease during COVID-19 pandemic. *J Hepatol*. 2020. <https://doi.org/10.1016/j.jhep.2020.04.002>
21. Ludvigsson F. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *ActaPaediatr*. 2020; 109: 1088- 1095
22. Chen ZM, Fu JF, Shu Q. New coronavirus: new challenges for pediatricians. *World J Pediatr*. 2020. <https://doi.org/10.1007/s12519-020-00346-4>
23. I. Vinik, A., Perrot, S., Vinik, E., Pazdera, L., Stoker, M., Snijder, R., Ortega, E., & Katz, N. (2019). Repeat treatment with capsaicin 8% patch (179mg capsaicin cutaneous patch): Effects on pain, quality of life, and patient satisfaction in painful diabetic peripheral neuropathy: an open-label, randomized controlled clinical trial . *Journal of Current Medical Research and Opinion*, 2(12), 388-401. <https://doi.org/10.15520/jcmro.v2i12.242>
24. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *TranslPediatr*. 2020; 9: 51- 60.
25. American Association for the Study of Liver Diseases. Clinical insights for hepatology and liver transplant providers during the COVID-19 pandemic. <https://www.aasld.org/about-aasld/covid-19-resources>. Accessed April 14, 2020
26. Sulkowski MS. Drug-induced liver injury associated with antiretroviral therapy that includes HIV-1 protease inhibitors. *Clin Infect Dis*. 2004; 38: S90- S97.
27. Fries JF, Singh G, Lenert L, Furst DE. Aspirin, hydroxychloroquine, and hepatic enzyme abnormalities with methotrexate in rheumatoid arthritis. *Arthritis Rheum*. 1990; 33: 1611- 1619.
28. Meyerowitz EA, Vannier AGL, Friesen MGN, et al. Rethinking the role of hydroxychloroquine in the treatment of COVID-19. *FASEB J*. 2020; 34: 6027- 6037
29. Roshan Kumar Jha, DhrubaHariChandi, Dr.Ranjit S. Ambad. ENVIRONMENTAL AND DEMOGRAPHIC FACTOR: ASPECTS ON COVID-19 IN INDIAN POPULATION. *Journal of critical reviews*. Vol 7, Issue 10, 2020; 1-3. Scopus

30. KannamaniRamasamy, S. Jayakumar. The Trend of COVID-19 at Bengaluru: Prediction to Continue the Better Epidemic Management International Journal of Current Research and Review. Vol 12 Issue 13, July, 2020, 56-60