

Rapid Communications

Surveillance of COVID-19 Patients with Pre-Existing Liver Diseases: Need to Address

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1. Abstract

Nearly 60% of the patients with the novel virus have elevated liver enzymes. Liver inflammation can be hypothesized to the immune mediated process such as cytokine storm and pneumonia associated hypoxia that may lead to liver enzyme abnormalities or liver failure in critically ill patients with COVID-19. When assessing patients of COVID-19 with elevated liver biochemistries one must be consider for other etiologies unrelated to COVID-19, particularly hepatitis A, B and C & drug intakes. Various conditions like NASH, viral hepatitis, liver transplant candidates and autoimmune hepatitis that may put the COVID patients on high risk. We should avoid imaging unless there is a concern for biliary obstruction or venous thrombosis. There should be continued usage of personal protection measures against COVID-19 and continue surveillance in COVID patients with search of preexisting live pathologies for an early diagnosis and treatment.

2. Introduction

Novel corona virus pandemic started December 2019 from Wuhan, China and spread to more than 200 countries. Globally, there are more than 3 million confirmed cases of COVID-19 with more than 0.2 million mortality [1]. Currently, India has nearly thirty thousand cases with nearly one thousand deaths [2]. Liver pathologies are not uncommon in the world either. Infectious disease causes being dominant with 57% of deaths from liver cirrhosis and 78% of primary liver cancer are attributable to HBV and HCV infections [3].

Novel corona virus is a positive-stranded RNA virus with a crown-like appearance under an electron microscope due to the presence of spike glycoproteins on the envelope and shares more than 85% of the genome with SARS CoV and bat corona virus. The novel corona virus binds to the target cells through Angiotensin converting enzyme-2 receptors. The receptors are found abundantly in liver and biliary cells; liver becomes one of the potential target for infection [4].

The liver enzyme abnormalities are reported in nearly 60% of the patients with the novel virus. Various studies have documented that the clinical features of the patients with COVID-19 had liver co-morbidities. It was found that 2-11% of the patients with novel corona virus had liver comorbidities. Severity of the novel corona virus has been associated with abnormal liver enzymes. Previously it has been found that 16.1% - 53.1% of the patients with novel corona virus infection had abnormality of liver enzymes as the disease progressed [4-8]. Hence the patients with COVID -19 should have continuous surveillance for liver enzymes.

3. COVID-19 with Preexisting Liver Disease Liver Diseases

Hepatitis is mild and transient in majority of the cases of novel corona virus and may return to normal without any special treatment. Liver inflammation can be hypothesized to the immune mediated process such as cytokine storm and pneumonia associated hypoxia that may lead to liver enzyme abnormalities or liver failure in critically ill patients with COVID-19. Liver protection drugs were usually being administered in the Chinese patients when severe liver damage occurred. The data is limited but chronic hepatitis HBV and HCV may be more susceptible

to liver damage from novel corona virus as was the case with SARS CoV. It is still doubtful whether novel corona virus increases the cholestasis, in auto immune diseases such as Primary sclerosing cirrhosis; cholangitis or autoimmune hepatitis or primary biliary cirrhosis. Drug therapy in patients with tuberculosis, hepatitis B, C, HIV or Cancer may also lead to hepatotoxicities, which may explain some of the variation in the various studies. However the general and specific considerations have been delineated but the individual management of the patients strongly is dependent on the local COVID-19 burden and official implement rules and regulations (Table 1).

The presence of abnormal liver biochemistries should not be a contraindication to using investigational or off-label therapeutics for COVID-19 (e.g., remdesivir, tocilizumab, chloroquine, hydroxychloroquine, statins), although AST or ALT levels >5x ULN may exclude patients from consideration of some investigational agents. Regular monitoring of liver biochemistries should be performed in all COVID-19 patients, particularly those treated with remdesivir or tocilizumab, regardless of baseline values. Evaluation should be done for all children with elevated AST or ALT for underlying liver diseases and coexisting infections as COVID-19 is not commonly associated with abnormal liver biochemistries in children [9-11].

Table 1: Recommendations of the COVID-19 with Liver disease according to the condition of the patient. 9-11

Condition of patient	General Considerations	Disease	Specific Considerations
Compensated Chronic Liver disease	1. Telemedicine / visits by phone wherever possible.	Viral hepatitis	1. No increased risk of a severe course of COVID-19 2. Follow up prescriptions through telemedicine or refill of the medications 3. Continue treatment for hepatitis B and hepatitis C if already on treatment. 4. Consider delaying initiation of treatment for hepatitis C in patients with or without COVID-19
	2. Routine laboratory test may be conducted on the basis of teleconsultation locally.		
	3. Visit to the hospital may be avoided.		
	4. Diagnostic invasive procedures may be delayed unless required on emergency basis.		
	5. Routine variceal surveillance and screening may be avoided.		
	6. Individualized and non-invasive risk assessment should be applied.		
	7. With cancellation of the elective / non urgent endoscopy primary prophylaxis with beta blocker may be considered with significant portal hypertension or high risk of decompensation.		
	8. Provide prescriptions for 90- day supplies instead of 30-day supplies.		
		Non Alcoholic Fatty liver Disease/ Non alcoholic steato hepatitis:	1. They may have metabolic disorders such as diabetes, obesity putting them at increased risk of severity of the diseases 2. Serial liver enzyme testing is recommended
		Autoimmune disease	1. No need to reduce the immunosuppressive drugs except in consultation with specialist 1. SARS-CoV-2 routine testing be done before transplantation in both donor and recipients, acknowledging that negative test cannot rule out infection 2. Consent for diagnostic and therapeutic procedures related to transplantation should include the potential risk for nosocomial COVID-19 3. Living donor transplantations should be considered on a case to case basis.
Decompensated Liver disease	1. Care should continue as per guidelines.	Candidates for liver transplants	
	2. Minimal exposure to the medical staff, by using telemedicine / visits by phone wherever possible i.e. avoid admission		
	3. Shorten the hospital stay with necessary evaluation only.		
	4. Vaccination of Streptococcus pneumonia and influenza.		
	5. Prophylaxis of Spontaneous bacterial peritonitis and hepatic encephalopathy should be followed.		
	6. Testing of SARS-CoV-2 in patients with acute decompensating or acute chronic liver failure.		
	7. Provide prescriptions for 90- day supplies instead of 30-day supplies.		
Hepatocellular Carcinoma	1. Care should be maintained according to guidelines including continuing systemic treatments and evaluation for liver transplantations. (arbitrary delay of 2 months is reasonable)		
	2. Minimal exposure to medical staff, by using telemedicine and phone wherever possible to avoid admission.		
	3. If COVID-19 positive, early admission is recommended.		
Liver transplant	1. Care should continue as per guidelines.		
	2. Minimal exposure to the medical staff, by using telemedicine / visits by phone wherever possible i.e. avoid admission		
	3. Shorten the hospital stay with necessary evaluation only.		
	4. Vaccination of Streptococcus pneumonia and influenza.		
	5. No need to reduce the immunosuppressive drugs except in consultation with specialist.		

4. Conclusion

When assessing patients of COVID-19 with elevated liver biochemistries one must be consider for other etiologies unrelated to COVID-19, particularly hepatitis A, B and C & drug intakes. Further, avoid imaging unless there is a concern for biliary obstruction or venous thrombosis. There should be continued usage of personal protection measures against COVID-19 and continue surveillance in pre existing liver diseases for elevated liver enzymes to search for novel corona virus.

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