

**Issue 1**  
April 2020

# Hepatology Today

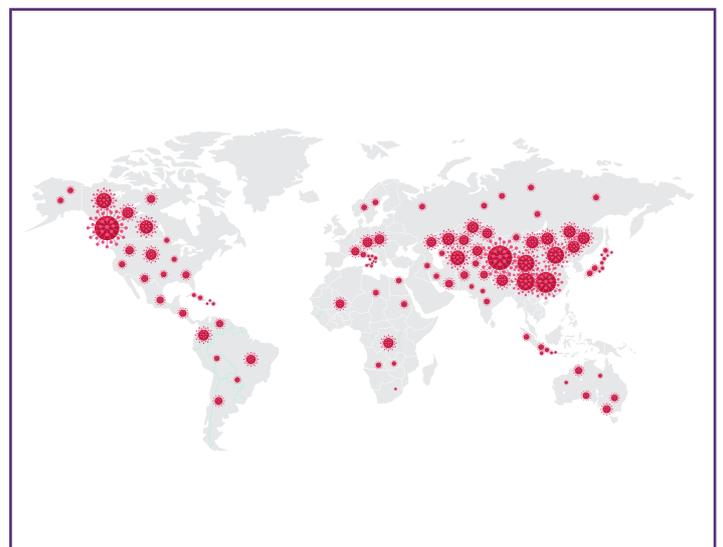
## *An Insight to Viral Hepatitis*

Viral Hepatitis and COVID-19

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### **Viral Hepatitis During COVID-19 Pandemic: An Insight**



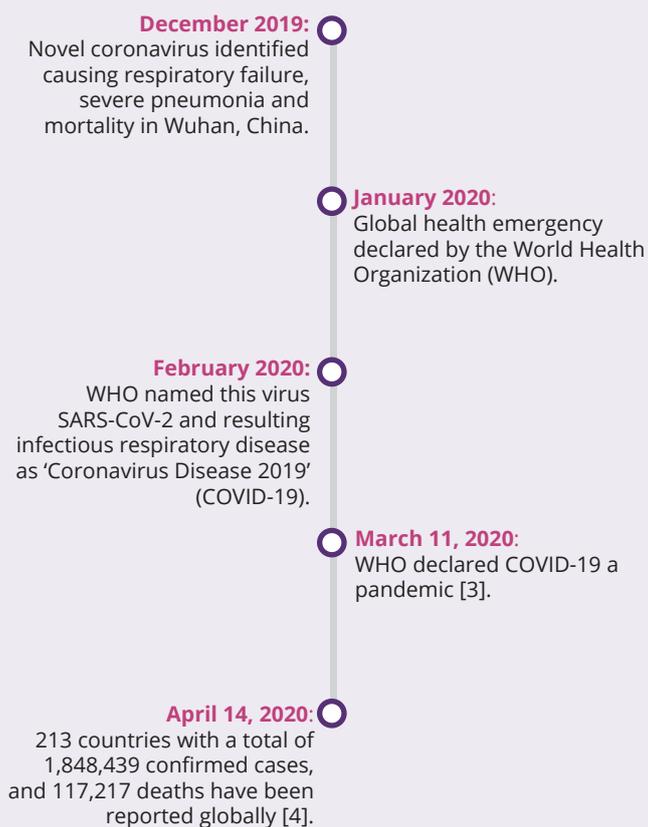
# COVID-19 – A Pandemic

Coronavirus disease 2019 (COVID-19) caused by the novel coronavirus, named as Severe Acute Respiratory Syndrome – Coronavirus 2 (SARS-CoV-2), is on the spread globally. A surge is anticipated in many nations and the health-care providers are on the run to prepare their patients and settings to mitigate the transmission of COVID-19.

In December 2019, a virus sharing 82% genetic homology with the virus SARS-CoV (cause of SARS in 2002) and 50% homology with Middle Eastern Respiratory Syndrome (MERS)-CoV (cause of MERS in 2012) was identified to be the cause of infectious respiratory disease in Wuhan, China [1]. The novel coronavirus is an enveloped RNA betacoronavirus that transmits through exposure to respiratory droplets of an infected person [2].

Nations worldwide are implementing and executing public health measures to contain the viral transmission and assure appropriate clinical care capacity to provide care and treatment for patients.

## The Progression of SARS-CoV-2



## People at Higher Risk [5]

-  Age 65 or older
-  People with chronic lung disease or those with moderate to severe asthma
-  People with serious heart conditions
-  Immunocompromised patients
-  People living in nursing home and long-term care settings
-  People with other comorbid conditions, such as morbid obesity, renal failure, patients on dialysis, diabetes, liver diseases, and those who have undergone organ transplantation

A study by Center for Disease Control and Prevention (CDC) reported that in the United States (US), people with underlying health conditions were at greater risk of hospitalization or admission to intensive care. Among patients  $\geq 19$  years, the non-ICU hospitalization was higher in those with underlying health conditions (27%-30%) as compared to those without any conditions (7%-8%). Higher cases in ICU were recorded among those with underlying conditions (13%-14%) than others with COVID-19 (2%).

Diabetes mellitus (11%), chronic lung disease (9%), and cardiovascular disease (9%) were among the most reported conditions as underlying health conditions in COVID-19 patients in ICU and non-ICU hospitalizations [6].

Table 1 represents the correlation of comorbid conditions and fatality rate in COVID-19, as reported to China's Infectious Disease Information system as of February 11, 2020 [7].

Comorbid Condition	Confirmed Cases	Deaths	Fatality Rate
Overall	44,672	1,023	2.3%
Hypertension	2,683	161	6.0%
Diabetes	1,102	80	7.3%
Cardiovascular Disease	873	92	10.5%
Chronic Respiratory Disease	511	32	6.3%
Cancer (any)	107	6	5.6%
None	15,536	133	0.9%
Missing	23,690	617	2.6%

**Table 1:** The association of comorbidities and fatality rate in COVID-19 as per China Infectious Disease Information system (as of 11.02.2020)

# COVID-19 in the Middle East

Table 2 represents the spread of COVID-19 in the Middle East as of April 15, 2020.

Countries	Coronavirus Cases	Deaths
Bahrain	1,528	7
Cyprus	662	17
Egypt	2,190	164
Iran	74,877	4,683
Iraq	1,400	78
Israel	11,235	110
Jordan	391	7
Kuwait	1,355	3
Lebanon	641	21
Oman	813	4
Palestine	287	2
Qatar	3,428	7
Saudi Arabia	5,369	73
Syria	25	2
Turkey	61,049	1,296
United Arab Emirates	4,521	25
Yemen	1	0

**Table 2:** COVID-19 pandemic in Middle eastern countries

Source: Coronavirus (COVID-19) Pandemic situation dashboard. World Health Organization (As accessed on April 15, 2020)

## Cases in the United Arab Emirates

Figures 1, 2 and 3 illustrate the total number of cases, deaths and active cases, respectively, in the United Arab Emirates during the COVID-19 pandemic.

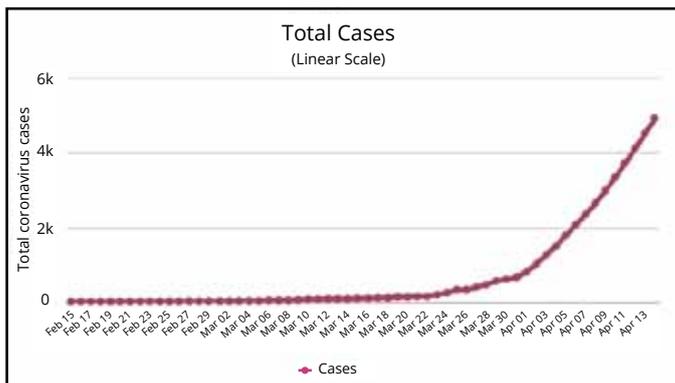


Figure 1: Total coronavirus cases in the United Arab Emirates

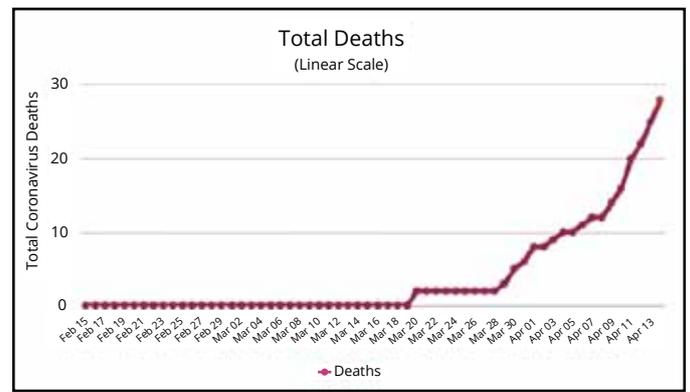


Figure 2: Total deaths in the United Arab Emirates due to COVID-19

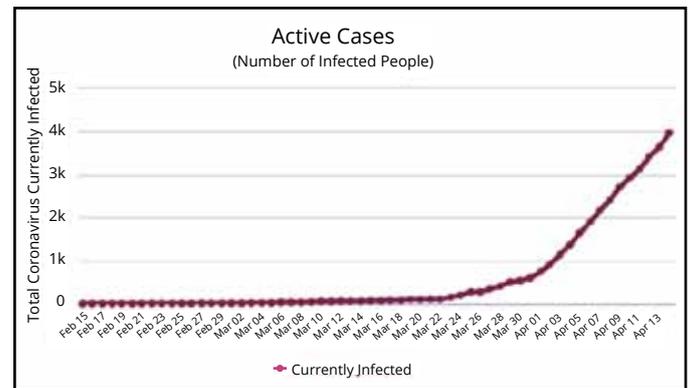


Figure 3: Active cases in the United Arab Emirates

Source (Images): <https://www.worldometers.info/coronavirus/country/ united-arab-emirates/>

## COVID-19 Pandemic and Liver Diseases

SARS-CoV-2 is found to bind to the cells through angiotensin-converting enzyme 2 (ACE2). ACE2 is also present in liver and biliary epithelial cells. Thus, the liver is a potential target for SARS-CoV-2 infection [8].

As per the reports, patients above 60 years of age, or with cirrhosis, advanced liver disease, autoimmune hepatitis, or taking immunosuppressive drugs, or pre and post-transplant fall into the category of vulnerable patient cohorts and have an increased risk of severe illness if infected with COVID-19 [9].

The data suggest approximately 15% to 45% of COVID-19 patients have shown signs of liver injury during the disease course, and patients with severe COVID-19 cases are more likely to develop liver dysfunction when compared to non-severe cases [10].

The serum liver biochemistries in 14% to 53% hospitalized patients with COVID-19 have shown elevated aspartate aminotransferase (AST) and alanine transaminase (ALT), slightly

increased bilirubin levels, and low serum albumin levels [10]. However, it cannot be confirmed yet whether the increase in liver biochemistry is due to the coronavirus infection or the resulting complications, or due to the medications causing the hepatotoxicity, such as statins, remdesivir, and tocilizumab [8].

For patients with hepatocellular carcinoma (HCC), the risks are unknown, but cancer patients are more likely to have severe outcomes of COVID-19 [7].

Table 3 below is a summarized results of different studies performed on patients with COVID-19 with liver disease and liver dysfunction [10].

Studies	Patients with COVID-19 infection	Patients with pre-existing liver conditions	Patients with abnormal liver function	Findings
Guan et al [11]	1099	23 (2.3%)	Abnormal AST (22.2%)	Increased AST level in 112 (18.2%) out of 615 patients with non-severe disease and 56 (39.4%) of 142 patients with severe disease. Increased ATL level were found in 120 (19.8%) of 606 patients with non-severe disease and 38 (28.1%) of 135 patients with severe disease.
Huang et al [12]	41	1 (2.0%)	15 (31.0%)	Patients with severe disease were observed with increased abnormal liver function. Increased AST level in 8 (62%) of 13 patients in the ICU and 7 (25%) of 25 patients not requiring ICU admission.
Chen et al [2]	99	NA	43 (43.0%)	Severe liver function damage was observed in one patient.
Wang et al [13]	138	4 (2.9%)	NA	
Shi et al [14]	81	7 (8.6%)	43 (53.1%)	Patients who were diagnosed with COVID-19 by CT scan in the subclinical phase had significantly lower rate of incidence of abnormal AST levels as compared to patients diagnosed after the onset of symptoms.
Xu et al [15]	62	7 (11.0%)	10 (16.1%)	
Yang et al [16]	52	NA	15 (29.0%)	No difference was found in the incidences of abnormal liver function between survivors (30%) and non-survivors (28%).

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ICU, Intensive care unit  
Adapted from: Zhang C, Shi L, Wang FS. Liver Injury in COVID-19: Management and Challenges. *Lancet Gastroenterol Hepatol*. 2020.

**Table 3:** Correlation of comorbid conditions with liver disease in COVID-19 patients

## COVID-19 and Viral Hepatitis

Till now, patients with viral hepatitis, majorly hepatitis B virus (HBV) and hepatitis C virus (HCV) haven't been found to be more susceptible to severe illness due to SARS-CoV-2 unless they have an underlying condition, such as hypertension, cardiovascular disease, diabetes, or advanced liver disease [17].

In a webinar conducted by American Association for the Study of Liver Diseases (AASLD) COVID-19 Working Group Members, a discussion on chronic HBV and HCV patients with COVID-19 concluded that treatment for coronavirus disease is of prime importance. The antiviral therapy against HBV and HCV does not have any known activity against COVID-19 therapy. Patients who are on HBV and HCV therapy or have just started the treatment should continue with their treatment. The treatment

for viral hepatitis in COVID-19 patients may also help produce a protective effect by reducing enzymes and thus improving outcomes of COVID 19 therapy [18].

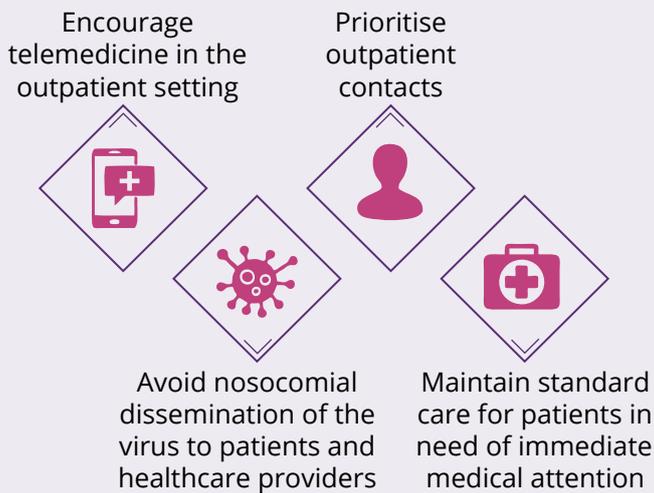
Based on present indications, patients with chronic liver disease and viral hepatitis should be considered as at-risk patient cohorts and at an increased risk of developing comorbid complications during the COVID-19 course [1].

## Challenge for Healthcare Providers

The present scenario questions the impact of this pandemic and deviated medical care and resources on the patients with chronic liver disease who need critical medical attention. The hepatologists and healthcare providers (HCPs) are now facing a gruelling task to provide immediate treatment and care to the

patients in need while assuring the safety of patients and healthcare workers amid this pandemic. If the spread is not contained, the capacity of healthcare facilities can become overwhelming with reduced availability of intensive care unit (ICU) beds, ventilators, and healthcare workers [8].

### Need of the Hour [8]



## Recommendations for COVID-19 and Viral Hepatitis [8,9]

AASLD, CDC and European Association for the Study of the Liver (EASL), recommend considerations to prioritize patients as per their current requirement, protect them as well as communities and healthcare workers from the pandemic.

### General Recommendations

- The protection of vulnerable patient cohorts from individuals with potential SARS-CoV-2 exposure or infection is important. The benefits of patient care should outweigh the risk of infection.
- Limit the number of patients coming to the clinic for transplant evaluations. Maximize the use of telemedicine alternatives.

- Practice restrictions on direct patient care. Replace the examinations with virtual visits where applicable. This will help reduce the unnecessary personal protective equipment (PPE) utilization and use of hospital supplies.
- Limit the team members addressing the patients, i.e., staff and healthcare professionals, as much as possible and promote virtual conferencing.
- Obtain labs and imaging only as clinically necessary.
- Ensure availability of essential medications and refills for patients.
- Limit direct inpatient care, especially for HCPs at higher risk (above 70 years, immunocompromised or with underlying disorders).
- Avoid patients and/or caregivers' congregation in rooms or waiting areas. Ensure proper social distancing and disinfection of all the areas.
- Avoid delivering patient education with multiple patients in a single room. Consider internet-based sessions for patients, family members and caregivers.
- Limit the visitors or company in the healthcare setting. Promote the use of phone or video for critical caregivers.
- Consider phone visits or telemedicine against in-person visits, if not urgent.
- Instruct patients to avoid attending community recovery support meetings.
- Limit the transport of patients within and between healthcare facilities.
- Advise patients not to travel.

## Recommendations for Patients with Viral Hepatitis

- Check the temperature and screen all patients for COVID-19 symptoms or recent exposure before they enter the clinic (over phone call 24 hours prior to visit) and then at the entry gate in the setting. Patients with fever (>100 °F) should be referred to the hospital's protocol for symptomatic patients.
- Serologic testing for HBV and HCV should be carried out in COVID-19 patients with abnormal liver biochemistries.
- Limit outpatients visits to those with urgent issues (e.g., jaundice, elevated ALT or AST >500 U/L, hepatic decompensation onset).
- Patients with HCC or those patients with severe disease and high Model for End-stage Liver Disease (MELD) scores who are likely to benefit from immediate liver transplant listing should be attended.
- Do not evaluate COVID-19 patients with symptoms in the hepatology/liver transplant clinic.
- Surveillance imaging should be continued in patients with cirrhosis, HCC, HBV and HCV. A delay of 2 months is reasonable, depending on the circumstances of patients or facility.
- Liver biopsy for grading/staging should be deferred in chronic viral hepatitis patients without COVID-19 (Recommendation depends on the COVID-19 burden and the patient's indication for histological assessment).
- Advanced imaging such as ultrasound, magnetic resonance imaging (MRI), etc. to be avoided unless necessary as in case of cholangitis, biliary obstruction, or venous thrombosis.
- Bronchoalveolar lavage fluid specimens are the most sensitive (93%), followed by nasal swabs (63%) and pharyngeal swabs (32%). Taking and testing samples from

multiple sites can improve sensitivity and reduce the chances of false negative results.

- Off-label therapies such as remdesivir, tocilizumab, chloroquine, hydroxychloroquine, statins should not be contraindicated in COVID-19 patients with elevated liver biochemistries.
- Liver biochemistries should be performed regularly in all COVID-19 patients, especially in those being treated with remdesivir or tocilizumab.
- For patients under viral hepatitis therapy, consider the use of telemedicine/local laboratory testing for follow-up visits, and send follow-up-prescriptions by mail.
- Evaluate patients with liver disease experiencing new onset encephalopathy for COVID-19.
- Evaluate children with increased levels of AST or ALT for any underlying liver diseases and/or coexisting infections as COVID-19 is not likely to be associated with abnormal liver enzymes in children.
- When performing procedures, use of standard PPE (gloves, gown, eyewear) headwear and masks for those with a risk of exposure to droplets is recommended.
- Confirm the availability of ICU beds, PPE, ventilators, and supply of blood products.
- Stress on the importance of vaccination for *Streptococcus pneumoniae* and influenza
- Follow guidance in the clinical study protocol and/or by the Food and Drug Administration, US (FDA) for monitoring of liver functions and discontinuation of study drug used to treat COVID-19.
- Follow recommendations by CDC for cleaning and disinfection of rooms and/or areas visited by suspected or confirmed COVID-19 patients.

## Take-Home Message

- Nations worldwide are implementing and executing public health measures to contain the transmission of pandemic coronavirus disease 2019 or COVID-19 infection caused by a novel coronavirus, named as SARS-CoV-2, and assure clinical care capacity to provide care and treatment for patients.
- People at higher risk:
  - ✓ Age 65 or older
  - ✓ People with chronic lung disease or those with moderate to severe asthma
  - ✓ People with serious heart conditions
  - ✓ Immunocompromised patients
  - ✓ People living in nursing home & long-term care settings
  - ✓ People with other comorbid conditions, such as morbid obesity, renal failure, patients on dialysis, diabetes, liver diseases, and those who have undergone organ transplantation
- Patients above 60 years of age, with cirrhosis, advanced liver disease, or autoimmune hepatitis, or taking immunosuppressive drugs, or pre and post-transplant fall into the category of vulnerable patient cohorts and have an increased risk of severe illness if infected with COVID-19.
- As per the reports, approximately 15% to 45% COVID-19 patients have shown signs of liver injury during the disease course, and patients with severe COVID-19 cases are more likely to develop liver dysfunction when compared to non-severe cases.
- Patients with viral hepatitis (majorly HBV and HCV) have not been found to be more susceptible to severe illness due to SARS-CoV-2 unless they have an underlying condition.
- AASLD, CDC and EASL recommend considerations to prioritize patients as per their current requirement, protect them as well as communities and healthcare workers from the pandemic.

## Recent Updates on Viral Hepatitis Related to COVID-19



AASLD Clinical Insights: Covid-19 and the Liver Webinar



COVID-19 Message from World Hepatitis Alliance President, Su Wang



WHA Member CATIE Webinar



National Viral Hepatitis Roundtable Webinar



UNODC Information on COVID-19

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Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals and patients are asked to report any suspected adverse reactions via the national reporting schemes as applicable. Adverse reactions may also be reported directly to the manufacturer of the suspected product. Adverse reactions related to Gilead products may be reported directly to Gilead via [Drugsafety.dubai@gilead.com](mailto:Drugsafety.dubai@gilead.com).

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