Gastrointestinal And Hepatic Manifestations Of Coronavirus (COVID-19)

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Continuing Education Activity

COVID -19 is an acute viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 primarily affects the respiratory system; however, it can affect other major organ systems such as the gastrointestinal tract (GI) and the liver. This activity illustrates the incidence, evaluation, and management of the GI and liver manifestations of COVID-19. It also highlights the role of the interprofessional team in improving care for patients with this illness.

Objectives:

- Review the epidemiology, etiology, and comprehensively explain the pathophysiology of the GI and liver manifestations of COVID-19.
- Describe the GI and liver-related clinical manifestations of COVID-19.
- Describe the laboratory, radiologic, and endoscopic investigations in the management of GI and liver manifestations of COVID-19.
- Describe the management of GI and liver manifestations of COVID-19 and also discuss the importance of patient's education in limiting the transmission of this virus. This review also describes the importance of having a holistic and interprofessional team approach that would enhance delivery of care for patients with GI and liver manifestations in COVID-19 leading to improved outcomes

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Introduction

On March 11, 2020, The World Health Organization (WHO) declared Coronavirus disease 2019 (COVID-19), the illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as a global pandemic after the first cases of an atypical acute respiratory illness initially reported in China in December 2019 spread to more than 100 countries. Since then, the ongoing pandemic has overwhelmed many healthcare systems worldwide, resulting in significant morbidity and mortality emerging as a major global health crisis since the influenza pandemic of 1918. This viral infection readily spreads from person to person via respiratory droplets, mucosal contact, and through contaminated surfaces. SARS-CoV-2 primarily affects the respiratory system; however, it can affect other major organ systems such as the gastrointestinal tract (GI), liver, cardiovascular, central nervous system, and kidneys. Emerging data have shown that patients with COVID-19 infection presented with higher rates of isolated gastrointestinal symptoms in the absence of respiratory symptoms. Patients with any primary GI-related symptoms or concurrent symptoms were at increased risk of hospitalization[1][2][3]. Emerging evidence is notable for the detection of SARS-CoV-2 RNA in fecal samples of asymptomatic COVID-19 patients who tested negative by the nasopharyngeal swab. Continued fecal shedding in symptomatic COVID-19 patients days after clinical recovery for an extended period has been reported which is concerning for possible fecal-oral transmission of this virus[4].COVID-19 is also frequently associated with the elevation of liver biochemistries in patients with or without clinical symptoms. Patients with COVID-19 illness are increasingly being recognized as being at risk of developing prothrombotic complications such as acute mesenteric ischemia and portal vein thrombosis respectively. In this article, we review the latest available data regarding the impact of COVID-19 on the gastrointestinal tract and the liver function in adult patients.

Etiology

Coronaviruses (CoVs) are enveloped positive-sense single-stranded RNA viruses. Based on their genomic structure; they are classified into four different genera: *Alphacoronavirus*(αCoV), *Betacoronavirus*(βCoV), *Gammacoronavirus*(γCoV) and *Deltacoronavirus*(δCoV) [5].SARS-CoV-2 is a beta coronavirus belonging to the same subgenus as the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), which have been previously implicated in epidemics with mortality rates up to 10% and 35%, respectively. Genomic characterization of the 2019 novel coronavirus demonstrated 89% nucleotide identity with bat SARS-like CoV and 82% with human SARS-CoV[6]. The gastrointestinal tract and the liver were frequently involved in both the SARS-CoV and MERS-CoV outbreaks with similar symptoms as reported with SARS-CoV-2.

Epidemiology

Since the first reported cases of COVID-19 from Wuhan, China in December 2019 and the subsequent declaration of COVID-19 as a global pandemic by the WHO after it spread to more than 100 countries, this highly contagious infectious disease has spread to 218 countries so far with more than 90 million cases, and more than 1.93 million deaths reported globally. It is well-known that elderly patients aged >65 years and patients with specific underlying medical comorbidities (severe obesity, hypertension, chronic kidney disease, diabetes, chronic lung disease, being a smoker, post-

transplant patients on chronic immunosuppressants) are at increased risk of developing severe COVID-19 infection. Although there is no data regarding the gender-based difference in COVID-19, published data suggest that male patients are at risk of developing severe illness and increased mortality due to COVID-19 compared to female patients. Similarly, the severity of infection and mortality related to COVID-19 differ between different ethnic groups[7]. Based on the results of a meta-analysis of 50 studies from the US and UK, it was noted that patients of Black and Asian ethnic minority groups were at increased risk of contracting COVID-19 infection than White patients[8]. Recently, two new variant strains of SARS-CoV-2 referred to as SARS-CoV-2 VOC 202012/01 or B.1.1.7 and N501Y, were reported in the United Kingdom and South Africa, respectively. SARS-CoV-2 VOC 202012/01 or B.1.1.7 is presumed to have a series of mutations and is predicted to be highly transmissible. This variant has already been reported in 11 states across the US, and clinical information regarding these variants is currently emerging.

Pathophysiology

Effect of SARS-CoV-2 on the Gastrointestinal (GI) Tract

The pathogenesis of gastrointestinal tract involvement in SARS-CoV-2 is unknown and is likely multifactorial. Several hypotheses have been described so far, including the direct ACE 2 mediated viral cytotoxicity of the intestinal mucosa, cytokine-induced inflammation, gut dysbiosis, and vascular abnormalities. SARS-CoV-2 gains entry into the hosts' cells by binding of the SARS-CoV-2 spike protein to the angiotensin-converting enzyme 2 (ACE2) receptors present on the respiratory epithelium followed by priming of the spike protein by the host transmembrane serine protease 2 (TMPRSS2) that facilitates cell entry and subsequent viral replication[9]. ACE2, a protein receptor is abundantly expressed in the enterocytes of the GI tract as well, mainly in the epithelial cells of the ileum and the colon suggesting a similar mechanism of viral replication in the gastrointestinal tract as evidenced by organoid models[10][11]. In fact, SARS-CoV-2 was detected in endoscopic biopsy specimens of the esophagus, stomach, duodenum, and rectum from several patients[12]. Given the reported propensity of SARS-CoV-2 to spread via the fecal-oral route, many studies have reported evidence of cytokine-induced inflammatory response of the intestinal mucosa in patients with COVID-19, characterized by elevation of fecal calprotectin, which is a specific protein biomarker for intestinal inflammation [13][14]. Several studies have also hypothesized that intestinal infection with SARS-CoV-2 causes alteration of the fecal microbiota that can damage the enterocytes resulting in clinical symptoms of diarrhea[15].

Effect of SARS-CoV-2 on the Liver and Pancreatobiliary System

Elevation in liver biochemistries is frequently noted in 14% to 53% of patients with COVID-19 infection[16]. The severity of the liver injury depends on the severity of the illness, with hepatic dysfunction occurring more frequently in patients with severe COVID-19 illness. Viral hepatitis classically manifests with a hepatocellular injury that is ALT predominant; however, hepatocellular injury in patients with COVID-19 infection appears to be AST predominant[17]. The pathogenesis of liver injury in COVID-19 patients is unknown. Liver injury is likely multifactorial and is explained by various hypotheses that include ACE-2 mediated viral replication in the liver and its resulting cytotoxicity, hypoxic or ischemic damage, immune-mediated inflammatory response, drug-induced liver injury (DILI), or worsening of pre-existing liver disease[18].

Although there is an abundant expression of ACE2 receptors in the enterocytes, there is a limited expression of ACE2 receptors in the hepatocytes [11]. A recent study demonstrated significantly higher ACE2 expression in cholangiocytes (59.7%) than hepatocytes (2.6 %), resulting in increased binding of SARS-CoV-2 to ACE2 receptors in the cholangiocytes but not hepatocytes, which explains why the liver injury in COVID-19 is primarily hepatocellular as opposed to a cholestatic pattern[17]. Severe cytokine-induced systemic inflammation and associated hemodynamic compromise could also contribute to the abnormal liver functions noted in patients with severe COVID-19 infection. Liver enzyme abnormalities can also be attributed to DILI secondary to newer antiviral agents such as remdesivir or concurrent medication use with hepatoxic potential. The role of pre-existing liver disease in the pathogenesis of COVID-19 associated liver injury is not well examined. Based on data of two international registries involving 745 patients with chronic liver disease (with and without cirrhosis) and COVID-19 infection, the mortality rate was significantly higher in patients with cirrhosis at 32 % compared to 8% in patients without cirrhosis. Moreover, the mortality rate was higher depending on their underlying Child-Pugh Class (CPC) score with 19% in CPC A, 25% and CPC B, and 51% in CPC C [19].

In addition to the luminal GI tract cells, ACE2 is expressed in the pancreatic islet cells and pancreas microvasculature pericytes as well. Literature describing the effect of SARS-CoV-2 on the pancreas manifesting as acute pancreatitis is uncommon. Hyperlipasemia has been reported in a minority of COVID-19 patients and is not specific to pancreatitis and was not reflective of severe infection or poor clinical outcome[20][21]. However, a single-center prospective clinicopathologic case series study reported focal pancreatitis with necrosis of the pancreatic parenchyma and adjacent adipose tissue and calcifications in 4 patients [22]. Due to the expression of ACE2 receptors in the cholangiocytes, mild elevation of alkaline phosphatase and gamma-glutamyl transferase (GGT) is not uncommon to see in patients with COVID-19[23].

Histopathology

Histopathology Examination of the GI Tract

Histopathological examination of the endoscopic specimens demonstrated positive staining of the viral nucleocapsid protein in the gastric, duodenal, and rectal epithelium cytoplasm. Numerous infiltrating plasma cells and lymphocytes with interstitial edema were seen in the lamina propria of the stomach, duodenum, and rectum. Histopathological examination of small bowel in a patient admitted with mesenteric ischemia was suggestive of prominent endothelitis of the submucosal vessels and apoptotic bodies[24].

Histopathology Examination of the Liver

Postmortem histopathological examination of liver tissue in a deceased patient with COVID-19 infection demonstrated nonspecific findings of moderate macrovesicular steatosis without any intracytoplasmic or intranuclear inclusions that can be seen in underlying nonalcoholic fatty liver disease, sepsis, or secondary to drug-induced liver injury (DILI)[25]. A prospective single-center clinicopathologic case series study involving the post mortem histopathological exam of major organs of 11 deceased patients with COVID-19 reported findings of hepatic steatosis in all patients. The liver specimens of 73 % of patients demonstrated chronic congestion. Different forms of hepatocyte necrosis were noted in 4 patients. 70 % of patients demonstrated nodular proliferation[22].

History and Physical

COVID-19, the illness caused by SARS-CoV-2, has been primarily considered a viral respiratory illness. Patients with SARS-CoV-2 infection can experience a multitude of clinical manifestations ranging from no symptoms to critical illness associated with respiratory failure, septic shock, and/or multiple organ failure. The vast majority of the patients present with clinical symptoms such as fever, cough, sore throat, shortness of breath, anosmia, dysgeusia, malaise, and myalgias. However, COVID-19 can present with GI manifestations alone or in concurrence with the other symptoms as described earlier. Based on a meta-analysis by Elmunzer *et.al* that involved 1992 patients across 36 centers,1052 patients (53%, 95%CI 51-55%) experienced GI symptoms with the most common reported symptoms being diarrhea (34%, 95%CI 32-36%), nausea (27%, 95%CI 25-29%) vomiting (16%, 95%CI 14-17%),abdominal pain (11%, 95% CI 10-13%)[26]. Loss of appetite is also a commonly reported symptom in patients with COVID-19. A case report described the incidence of hemorrhagic colitis demonstrated endoscopically and was attributed to SARS-CoV-2 after all other etiologies, including ischemic injury, were ruled out [27]. Patients with COVID-19 illness are also increasingly being recognized as being at risk of developing prothrombotic complications of the mesenteric and portal vein vasculature manifesting as acute mesenteric ischemia, portal vein thrombosis.[28].This has likely been attributed to an unexplained hypercoagulable state associated with this viral illness.

Viral RNA has also been isolated from stool specimens of COVID-19 patients as evidenced by results of a meta-analysis of 23 published and 6 preprint studies involving 4805 patients, fecal tests were positive for SARS-CoV-2 in 8 studies, and viral RNA shedding was detected in 40.5% (95%CI, 27.4%-55.1%) of patients implying transmission of SARS-CoV-2 via the possible fecal-oral route in addition to respiratory droplet transmission[29].

COVID-19 is also frequently associated with elevation of liver biochemistries in 14% to 53% of patients[16] Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are generally elevated 1-2 times the upper limit of normal (ULN), with normal to mildly elevated total bilirubin. Hepatic dysfunction occurs more frequently in severe COVID-19 illness compared to patients with mild illness, and patients with the presence of liver injury at presentation were at a considerably higher risk of ICU admission and death[23][26]. Due to the expression of ACE2 receptors in the cholangiocytes, it is not uncommon to see a mild elevation of alkaline phosphatase and gamma-glutamyl transferase (GGT) in patients with COVID-19[23].

Evaluation

A detailed clinical history regarding the onset and duration of symptoms, travel history, exposure to people with COVID-19, underlying medical comorbidities, medication history must be obtained by treating providers. Patients with typical clinical signs suspicious of COVID-19 such as fever, cough, sore throat, loss of taste or smell, malaise, and myalgias should be tested for SARS-CoV-2.

Patients presenting with isolated GI symptoms such as diarrhea, nausea, vomiting, and abdominal pain or incidental findings of elevated serum transaminases should be tested for virologic testing for SARS-CoV-2 in a high COVID-19 prevalence setting[30].

Infectious etiology, especially C. difficile and other viral and bacterial enteric infections, should be ruled out in patients presenting with isolated symptoms of acute diarrhea and abdominal pain.

Patients with underlying chronic liver disease, on chronic immunosuppressive medications, and post-transplant patients presenting with atypical symptoms should also be considered for testing for SARS-CoV-2[31].

Initial laboratory assessment with complete blood count (CBC), a comprehensive metabolic panel(CMP) that includes testing for renal and liver function, coagulation panel, serum lipase should be considered at presentation.

Consider checking troponin and EKG to rule out cardiac injury, especially in patients presenting with liver abnormalities with AST>ALT.

Measuring inflammatory markers such as C-reactive protein (CRP), fecal calprotectin-dimer, and ferritin measurement can be considered.

Initial imaging may include chest x-ray, ultrasound, computerized tomography, magnetic resonance imaging/magnetic resonance cholangiopancreatography if clinically indicated.

Endoscopic evaluation should be considered if clinically indicated with appropriate personal protective equipment (PPE) as recommended by The American Society of Gastrointestinal Endoscopy (ASGE), considering that endoscopy procedures are associated with a high risk of virus transmission.

Patient's with COVID-19 and elevated liver biochemistries should be checked for etiologies unrelated to COVID-19, which must include checking a comprehensive hepatitis panel to rule out other viruses such as hepatitis A, B, and C [32]

In patients with Autoimmune Hepatitis(AIH) and Orthotopic Liver Transplant (OLT) recipients with active COVID-19, It is not recommended to presume disease flare or acute cellular rejection without a biopsy confirmation indicating the same [31].

Treatment / Management

Management of COVID-19 depends on the severity of illness at presentation, and patients should be appropriately triaged based on clinical symptoms. Asymptomatic patients or patients with mild illness can be managed in the ambulatory setting with supportive management and recommendation to self-quarantine. However, patients with moderate to severe illness and patients at risk of developing severe illness should be clinically monitored in the hospital setting and managed as outlined in the updated National Institute of Health (NIH) guidelines. As with other viral enteric infections, the gastrointestinal symptoms such as nausea and vomiting should be conservative with IV fluids, antiemetic medications, and close monitoring of serum electrolytes.

Remdesivir is the first FDA approved drug that has been indicated for use in adults and pediatric patients (over age 12 years and weighing at least 40 kgs) for treatment of hospitalized patients with COVID-19. Liver biochemistries must be performed at baseline and regularly monitored when initiating the patient on remdesivir and during the course of treatment. Potential hepatotoxic agents must be identified early and, if possible, avoided in patients with elevated liver biochemistries. Patients with COVID-19 are associated with an unexplained hypercoagulable state, due to which they are at risk of developing prothrombotic complications such as arterial and venous thrombosis. Clinicians should maintain a high index for these complications and should consider initiating appropriate systemic anticoagulation, provided they are no other contraindications to starting the same.

During the initial stages of the pandemic, all ambulatory endoscopy centers across the country were informed by the Center for Medicare and Medicaid Services (CMS) to temporarily postpone elective procedures and other non-essential ambulatory clinical activities. However, in mid-April 2020, CMS allowed the reopening of endoscopy centers in a phased approach in accordance with COVID-19 protocols as outlined by the CDC, state, and local authorities. Given that SARS-CoV-2 is an airborne pathogen, the nature of endoscopy being an aerosol-generating procedure, and the potential of possible fecal-oral transmission of SARS-CoV-2, gastroenterologists, medical workers, and endoscopy staff are at increased risk of contracting this virus or transmitting it. Following certain precautions, as described below, that can prevent or reduce the transmission of the virus [33].

Precautions Against COVID-19 in the GI Office

- Individuals should always maintain a distance of 6 feet or more between other individuals as much as possible, and chairs in the waiting room should be redistributed to reflect the same.
- Patients and staff members patient should be screened using a standard clinical questionnaire, which should include the typical manifestations of COVID-19. Patients and staff should also be screened for travel history within the last 14 days and exposure to people with COVID-19. Positive responses should be appropriately triaged, tested for SARS-CoV-2 if indicated, and followed up
- Temperature checks using non-contact infrared thermometers must be employed.
- It is recommended that patients and staff should be wearing a facemask covering the mouth and nose at all times.
- Telehealth services, if applicable, should be employed as much as possible to limit transmission.
- All patient contact surfaces and examination rooms must be adequately sanitized before rooming the next patient.
- Before and after examination, frequent handwashing must be performed for a minimum of 20 seconds with soap and water.
- Accompanying family members should be limited and advised to remain in the vehicle until the culmination of patients' office visits.

Precautions Against COVID-19 in the GI Endoscopy Suite

- Individuals should always maintain a distance of 6 feet or more between other individuals as much as possible, and chairs in the waiting room should be redistributed to reflect the same.

- Patients and staff members patient should be screened using a standard clinical questionnaire, which should include the typical manifestations of COVID-19. Patients and staff should also be screened for travel history within the last 14 days and exposure to people with COVID-19. Positive responses should be appropriately triaged, tested for SARS-CoV-2 if indicated, and followed up.
- Temperature checks using non-contact infrared thermometers must be employed.
- It is recommended that patient and staff should be wearing a facemask covering the mouth and nose at all times
- Endoscopic procedures must be appropriately triaged based on urgency, and procedures of patients with positive responses must be rescheduled based on clinical severity.
- Accompanying family members of patients undergoing endoscopic procedures should be advised to remain in the vehicle until the procedure is completed, and the patient is ready to be discharged.
- Considering endoscopy is an aerosol-generating procedure, all endoscopists, endoscopy staff, and anesthesia providers must wear full personal protective equipment (PPE): gowns, NIOSH-Approved N95 masks, and face shields for all endoscopies and preferably PAPR for positive COVID-19 cases.
- All endoscopies must be performed in negative pressure rooms if available.
- All endoscopy unit staff must be trained regarding PPE donning/doffing and correct storage of PPE equipment.
- If applicable detailed pictures regarding PPE donning/doffing must be placed in endoscopy suites
- Placement of NIOSH-Approved Air filters in endoscopy rooms should be considered if possible.
- Before and after examination, frequent handwashing must be performed for a minimum of 20 seconds with soap and water.

Differential Diagnosis

Although the GI symptoms are well been defined in patients with active COVID-19 infection, clinicians evaluating the patient must rule out other common etiologies of GI tract and liver disorders as described below

GI Tract

- Non-COVID-19 infectious diarrhea (e.g.; *Difficile*)
- Ischemic colitis
- Inflammatory bowel disease (IBD)
- Irritable Bowel Syndrome (IBS)
- Small Bowel Intestinal Overgrowth (SIBO)
- Delayed presentation of acute pancreatitis
- Acute on Chronic Pancreatitis
- Acute Cholecystitis
- Choledocholithiasis
- Peptic Ulcer Disease (PUD)

Hepatic

- Acetaminophen toxicity
- Viral Hepatitis (A, B, and C)
- Drug-Induced Liver Injury (DILI)
- Ischemic Hepatitis
- Primary Biliary Cholangitis (PBC)
- Budd-Chiari syndrome
- Sepsis
- Autoimmune Hepatitis
- CMV, EBV or HSV infection
- Muscle related disorders such as polymyositis, rhabdomyolysis

Prognosis

The prognosis of COVID-19 is largely dependent on various factors that include the severity of illness at presentation, associated underlying co-morbid conditions, and response to treatment. Based on a large cohort study from China involving 44415 patients, a vast majority (81%) were diagnosed with mild illness and had a favorable clinical course. The other 19 % were diagnosed with severe to critical illness requiring hospitalization, of which 5% developed critical illness characterized by respiratory failure and multiorgan dysfunction[34]. Many studies have reported that patients

with COVID-19 infection who presented with primary GI-related symptoms or concurrent symptoms were at increased risk of hospitalization[1][2][3]. However, this has not been comprehensively assessed, and more studies are needed to elaborate on the same. Acute liver failure is uncommon in patients with COVID-19. However, COVID-19 patients with liver injury on presentation are at significantly higher risk of admission to the intensive care unit (ICU) and death[23][26][23].

Complications

Considering the involvement of major organ systems, COVID-19 can be regarded as a systemic viral illness. The complications of COVID-19 are likely due to progressive or sudden clinical deterioration leading to acute respiratory failure, acute respiratory distress syndrome, and multiorgan failure. Patients with COVID-19 illness are also increasingly being recognized at risk of developing prothrombotic complications. Thrombosis of the mesenteric vasculature and the portal venous system manifesting as acute mesenteric ischemia and portal vein thrombosis respectively is being described specific to the gut. Acute mesenteric ischemia is a life-threatening abdominal emergency and is associated with poor clinical outcomes [28]. These prothrombotic complications are likely attributable to the unexplained hypercoagulable state associated with this viral illness. The other complications such as severe hepatitis, hemorrhagic colitis, pancreatic necrosis could be multifactorial in the setting of hypoxia, cytokine-induced inflammation, and hypoperfusion[27][22].

Deterrence and Patient Education

- Patients must be educated and encouraged to adhere to social distancing guidelines and use of facemasks as per CDC guidelines and social distancing protocols of state and local authorities.
- Patients must be educated about frequent handwashing for a minimum of 20 seconds with soap and water when they come in contact with contaminated surfaces.
- Patients should be educated and encouraged to seeking emergency care when necessary.
- Patients should be educated and given an option for telehealth services in lieu of office visits to especially for pre-screening and routine post-endoscopy evaluations if applicable.
- Given the concern of possible fecal-oral transmission of SARS-CoV-2, Clinical providers must educate and inform the patients and their close contacts about fecal shedding of the virus and advised to maintain contact precautions to prevent the spread of the virus.

Enhancing Healthcare Team Outcomes

COVID-19 has wreaked havoc across the world and has overwhelmed many healthcare systems and economies of many countries. Currently, two vaccines have been authorized for use in the general population by the US FDA under an Emergency Use Authorization(EUA) after clinical trials demonstrated more than 90% efficacy. Until the majority of the world's population gets vaccinated against this illness, COVID-19 will remain a threat to global public health. Prevention and management of this highly contagious viral illness require a holistic and interprofessional approach that includes physicians across specialties, nurses, pharmacists, public health experts, and governmental authorities. Clinical providers managing COVID-19 patients on the frontlines should consider assessing for GI symptoms while evaluating patients suspected of COVID-19. Clinicians should maintain a high index of suspicion in patients from a high risk of exposure area or recent travel to a high exposure area who present with isolated GI symptoms even in the absence of pulmonary symptoms and should be appropriately triaged and tested for COVID-19. Gastroenterology and Hepatology teams must be consulted when clinically indicated. Resources for contact tracing and testing must be enhanced to limit the spread of this virus. Patients must be educated and encouraged to adhere to social distancing guidelines and use of facemasks as per CDC guidelines and COVID-19 protocols of state and local authorities. Given the concern of possible fecal-oral transmission of SARS-CoV-2, the presence of live virus in feces of COVID-19 patients who tested negative by nasopharyngeal swab and had continued fecal shedding in COVID-19 patients days after clinical recovery is detrimental to the containment of this virus[35]. Clinical providers must educate and inform the patients and their close contacts about fecal shedding of the virus and maintain contact precautions to prevent the spread of the virus. Additionally, healthcare systems must adopt national infection control guidelines when managing this group of patients with these atypical symptoms. Such a multi-pronged approach enhances improved patient care and outcomes. It also reduces the burden of hospitalizations that could potentially lead to exhaustion of healthcare resources. Such measures could immensely change the dynamic of healthcare infrastructure and go a long way in eradicating this virus and limiting its devastating effect on socioeconomic and healthcare situation across the entire world.

Review Questions

- Access free multiple choice questions on this topic.
- Comment on this article.

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