COVID-19 and the Gastrointestinal Tract

Subjects: Pathology

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In patients with gastrointestinal comorbidities, a careful monitoring of baseline pathologies and drug-related toxicities and interactions must be closely surveilled, given that the exact expected prognostic significance of the intersectionality of COVID-19 disease and different gastrointestinal pathologies remains to be fully understood.

Keywords: gastrointestinal tract ; COVID-19

1. Introduction

The clinical spectrum of COVID-19 disease varies widely, from asymptomatic infection to multiple organ failure, with lethality rates depending on the characteristics of the studied population. It is estimated that at least one-third of SARS-CoV-2 infections are asymptomatic, and nearly three-quarters of the patients with a positive PCR test but no symptoms at the time of diagnosis remain asymptomatic. However, the definition of “asymptomatic” varies across studies, depending on which specific symptoms were assessed [1].

Among symptomatic cases, the spectrum of disease ranges from mild to critical illness; most cases not been severe. In a report from the Chinese Center for Disease Control and Prevention (CDC) including about 44,500 confirmed infections, mild disease was reported in 81% of patients. Severe disease (e.g., dyspnea, hypoxia, or >50 percent lung involvement) was reported in 14%. Critical disease was reported in 5%, and the overall case fatality rate was 2.3%, with no deaths among noncritical patients [2]. Out of 1.3 million cases reported to the United States Centers for Disease Control and Prevention (CDC) through the end of May 2020, 14% of patients were hospitalized, 2% were admitted to the intensive care unit, and 5% died [3].

Nonspecific symptoms (such as cough, myalgias and headache) are the most commonly reported clinical presentation for mild disease, and pneumonia the most common presentation for moderate and severe disease [4]. However, gastrointestinal symptoms and complications may be found all along the clinical spectrum of COVID-19 disease [3].

In a Chinese retrospective study including 651 confirmed COVID-19 cases, 11.4% of patients presented with at least one GI tract symptom (nausea, vomiting or diarrhoea). Increased AST, but not ALT, was significantly higher in patients with GI symptoms. Finally, although the most common radiographic presentations were similar between patients with and without GI symptoms, the rate of unilateral pneumonia was 12.16% in patients with GI symptoms [5].

2. Upper Gastrointestinal Tract

Single-cell RNA-seq data analysis of ACE2 expression has revealed the differential risk of human organs regarding vulnerability to SARS-CoV-2 infection; more than 1% of ACE2 positive oesophagus epithelial cells has been found, and the esophagus can thus be regarded as high risk. By contrast, gastric and liver cells showed <1%ACE2 positive cell expression levels [6]. ACE2 expression is elevated in the lung and trachea of diet-induced obese male mice and reduced at the oesophagus of obese female mice when compared to lean controls [7].

Even if oesophageal symptomatologies directly attributable to the SARS-CoV-2 infection have not been reported, heartburn is common, (as in the general population) and requires a standard treatment with proton pump inhibitors (PPIs) or H2 receptor antagonists (H 2RAs). A plausible benefit with famotidine in COVID-19 patients who were taking famotidine for acid-related reflux prompted a small study that reported an improved clinical course in COVID-19 patients [8].

On the other hand, the impact of acid suppression on SARS-CoV-2 is unknown; previous data revealed that pH ≤3 impairs the infectivity of the similarly severe acute respiratory syndrome coronavirus 1. An online survey that included 53,130 participants found evidence of an independent, dose-response relationship between the use of antisecretory medications and COVID-19 positivity [9].

There is scarce information on the prognostic implications of bariatric surgery history in people living with obesity in the current COVID-19 pandemic [10]. In a study that included 738 post-bariatric surgery patients, COVID-19-likely events occurred in 8.4% of patients, with 6.4% of them having severe COVID-19 requiring in-hospital treatment and a 1.6% fatality rate. Persistent type 2 diabetes and higher percent weight loss since bariatric surgery were associated with hospitalization rates [11].

3. Gallbladder and Biliary

Given that ACE2 levels are high in the bile ducts and gallbladder epithelial cells [12], it is feasible that direct cytopathic damage, hypoxia, secondary inflammatory damage and thrombosis are responsible for gall bladder and biliary tract involvement, including late cholestasis and acute acalculus cholecystitis gangrenous cholecystitis [13][14].

4. Vaccine-Related Gastrointestinal Symptoms

Even when the available COVID-19 vaccines offer very good safety profiles, a variety of gastrointestinal adverse events have been described and must be taken into account (**Table 1**): Among patients who received COVID-19 mRNA vaccines, gastrointestinal adverse events were the third most common type of adverse events after immunization, being reported in 25.54% of patients. Among the gastrointestinal symptoms, nausea represented 56.41% of symptoms, followed by vomiting (14.7%) and diarrhea (14.13%) [15]. Regarding the Ad26.COV2.S vaccine, nausea was the third most common systemic adverse effect, being present in 14.2% of patients [16].

Table 1. Gastroenterological consideration for clinical practice in COVID-19 patients.

Epidemiological risk.	**Questions remain regarding fecal-oral transmission.** **SARS-CoV-2 RNA can be detected in the endoscopic specimens from the oesophagus, stomach, duodenum and rectum [17].** **Substantial amounts of SARS-CoV-2 RNA can be detected in stool specimens from COVID-19 patients [18].** **SARS-CoV-2 RNA has been detected in the sewage of hospitals treating patients with SACOVID-19 disease and the virus remained infectious up to 2 weeks in sewage water [19].**
Diagnostic procedures	**COVID-19 could possibly be transmitted by endoscopes; theoretically due to contact with mucous membranes and body fluids.** **GI societies have advocate for rescheduling non-urgent procedures and perform only emergent or urgent ones.** **Pre-endoscopy screening was initially recommended; upgraded guidelines state that, with widespread vaccination of health care workers and the general population, pre-endoscopy screening may not always be necessary, and placed a high value on minimizing additional delays in patient care [19][20].**
Current medication history	**Plausible clinical benefit with famotidine in COVID-19 cases [8].** **Impact of acid suppression on risk for COVID-19 is unknown so far [9].** **Immunosupression schedule in patients with IBD must be reassessed on a personalized basis [21].**
Expected clinical course among patients with known comorbidities.	**Among patients with bariatric surgery history and COVID-19 disease 1.6% fatality rate. Persistent type 2 diabetes and higher percent weight loss since bariatric surgery are associated with severe COVID-19 [11].** **Mortality among patients with COVID-19 and cirrhosis has been reported to be 32%, being older age, higher Child-Pugh and alcohol related liver disease the main factors associated with death [22]/** **Similar hospitalization rates, ICU admission and death between patients with AIH and non-AIH CLD [23].** **Among persons living with chronic HBV infection, it has been reported that there is no statistically significant differences in the median time to SARS-CoV2 clearance or progression to severe COVID-19 disease [24].** **COVID-19-HCV coinfected patients have been reported to have higher hospitalization rates, but ICU admission and mortality are similar between those with and without HCV infection [25].** **No current evidence of increased infection rates or worse disease severity of COVID-19 in IBD patients [26].**

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