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Covid-19 and GIT Manifestations

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ABSTRACT

A severe coronavirus infection is currently producing a worldwide pandemic. The initial method for restricting the virus's transmission has been to advise people to practice vaccination, which entails limiting social gatherings, minimizing public appearances, instituting social distance, & wearing masks as much as possible. Despite this, COVID-19 positive people who are asymptomatic can spread the virus. It has varied effects on different people. The majority of patients have a fever & a respiratory infection, but some may have diarrhoea, vomiting, & stomach pain. The incubation period, on the other hand, might last anywhere from 2 to 14 days without causing any symptoms. It's especially true in the case of GI symptoms, where the patient can continually shed the virus even after the lung symptoms have gone away. Given the high number of patients infected with COVID-19 who report with gastrointestinal symptoms, patients should be screened for GI symptoms. Every organ must be identified since it has the ability to contribute to community health problems & plays significant role in illness monitoring & management. This quick overview's purpose is to keep you informed about the consequences of SARS-CoV-2 infection on Gastroenterology and Hepatology departments, along with our new working techniques.

The goal of this study is to provide current information on covid 19 symptoms in liver & gastrointestinal illnesses, as well as the pandemic's impact on prevention & treatment measures, with an emphasis on how existing procedures have been modified and what modifications may remain in the long term. This review provides gastroenterologists with new clinically relevant information.

Key words: Covid 19 and GIT symptomatology, ACEII receptor and covid 19, Covid 19 on chronic liver disease, Liver injury

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INTRODUCTION

SARS-CoV-2 is a single-stranded RNA virus that causes severe acute respiratory syndrome and belongs to the Beta coronavirus genus [1]. The SARS-COV-2 pandemic has resulted in the disease known as COVID-19 by the World Health Organization [2]. It was thought to be a respiratory disease at first, but because the virus can affect other organs, including the gastrointestinal tract (the most frequent symptoms are anorexia and diarrhea), feco-oral transmission is a possibility in a number of contexts. The virus's effect on the liver is unknown, although it can imperil survival & cause decompensation in chronic liver disease patients, especially those in advanced stages. This page discusses the condition's major gastrointestinal components.

As of May 1, 2020, worldwide more than 3.3 million people had been suffered with Coronavirus Disease 2019 (COVID-19), a respiratory ailment caused by a new coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]). Despite the fact that most occurrences of COVID-19 are moderate, the condition can be serious, leading to admissions to hospitals, respiratory failure, or death. Previous study from Wuhan suggested that 2% to 10% of COVID-19 patients experienced gastrointestinal (GI) manifestations like diarrhoea, but a latest meta-analysis showed that roughly about 20% of COVID-19 infected persons had GI manifestations. Studies have found SARS-CoV-2 virus in anal & faeces specimen in over half of corona patients, giving the impression of multiplication of virus in gastrointestinal tract & its impression outside of the lungs. Furthermore, fecal calprotectin, an indication of inflammatory responses in the gut, was observed to be higher in patients of COVID-19 having diarrhoea. SARS-

CoV-2 gets into the host via angiotensin-converting enzyme 2 (ACE2) receptor, which is abundantly present in both the GI & respiratory systems. ACE2 has a crucial role in gut inflammation & microbial ecology. The gene regulation, metabolism & immune response is influenced by the gut flora which consists of massive amount of bacteria. Intruding viruses can modify the gut's commensal microbiota by either stimulating or suppressing the immune system. According to research, respiratory viral infections are correlated with alterations in the gut microbiota, which may make a person more susceptible patients to bacterial infections in the future. According to a latest meta - analytic review of bronchoalveolar lavage fluid, microbes or upper respiratory commensal bacteria monopolized the microbiota in SARS-CoV-2–infected persons.. Moreover, variations in bacteria species pertaining to the phyla Bacteroidetes & Firmicutes, which have also been shown to affect ACE2 representation in rats, have been related to comorbid conditions frequently diagnosed with serious COVID-19. Understanding the host microbial perturbations which underpin SARS-CoV2 infection is critical, as they may alter infection response & the efficiency of future immunological treatments such as vaccinations [3].

The 2 different forms of human coronaviruses are

Beta (SARS-CoV-2, HCoV-HKU1, SARS-CoV-1, HCoV-OC43, & MERS-CoV) & Alpha (HCoV-NL63 & HCoV-229E). SARS-CoV-2 & SARS-CoV-1 are genetically related & exploit the same entry receptor, angiotensin-converting enzyme 2 (ACE2) [4]. SARS-CoV-1 & MERS-CoV have a lot more literature on their GI effects than the other coronaviruses. This could be owing to the fact that these coronaviruses have varying amounts of GI involvement. As per previous studies, intestinal lesions & faeces of newborns with necrotizing enterocolitis contain coronavirus-like particles.

HCoV-NL63 & HCoV-HKU1 are two types of HCoV

In stool specimen of children & adults with gastrointestinal problems, HCoV-HKU1 was discovered. There were no samples of stool that were found to be positive for HCoV-OC43, HCoV-NL63, or HCoV-229E. HCoV-HKU1 was found in two of the three stool specimens of HCoV-HKU1-infected people who were hospitalized for acute enteric disease. In up to 57 percent & 38 percent of infected persons, GI symptoms (nausea, vomiting, diarrhoea, & abdominal discomfort) are caused by HCoV-HKU1. HCoV-HKU1-related Gastrointestinal symptoms commonly appear on the fourth day of illness in otherwise healthy adolescents & adults [5,6].

While respiratory symptoms are common in Covid-19 infected individuals, some individuals also reported gastrointestinal manifestations such as diarrhoea, vomiting, & abdominal discomfort as the illness progresses. Nausea, a loss of appetite and other symptoms are also common. The basic manifestations of COVID-19, which include olfactory and gustatory disturbances, have recently been expanded to include anosmia and dysgeusia [2]. In the United States, a 35-year-old man (the first case of Covid-19) who went to the hospital with two days of nausea & vomiting, followed by stomach pain & diarrhoea on the next day [7]. On the seventh day of illness, SARS-CoV-2 RNA was discovered in the patient's faeces using a reverse transcription polymerase chain reaction. During the early outbreak, two adults were found to have diarrhea (ages 36 & 37) out of six patients in a familial group of Covid-19 infections, with bowel habits as frequent as 8 times a day [1]. In following cohorts, Covid-19 individuals have had gastrointestinal problems on a frequent basis. Anal/rectal swabs were found to have viral RNA in over half of the cases, suggesting that this could be additional method of transmission & detection. Endoscopies of the digestive tract can create aerosols, which puts these procedures at risk of infection.

Patients may presents with GI problems earlier than normal in the phase of the illness, as evidenced by their ability to approach with them. The very 1st Covid-19 patient in the United States, for example, had nausea and vomiting two days before admission, followed by diarrhea the next day [7]. The two young patients in the initial Covid-19 group, on the other hand, experienced diarrhea when they arrived [8]. Diarrhea is a common early symptom, & it can even appear before pyrexia or respiratory problems in few cases [9,10].

Symptoms of the gastrointestinal tract

MERS-CoV

MERS-CoV patients exhibited a significant rate of gastrointestinal involvement. In MERS-CoV patients, diarrhoea (26%–33%), nausea (21%) & vomiting (21%–33%) observed. In eastern Saudi Arabia, they investigated GI symptoms in 35% of the patients [11].

Other GI signs and symptoms

In patients with severe illness, major Gastrointestinal manifestation such as bloody diarrhoea are often likely. Other GI signs include constipation & hemorrhagic colitis. Several round herpetic erosions & ulcers are found during an endoscopic examination of a patient of COVID-19 with gastrointestinal bleeding. In individuals with significant symptoms, ulcerative & ischemic alterations seen in rectosigmoidoscopy [12].

The onset of GI symptoms might happen at any time. They appear during the beginning of the disease (before any other clinical symptoms), but in most of the cases, they appear later. Only 11.6 percent of COVID-19 patients had Gastrointestinal manifestation when they were admitted to the hospital, with the rest acquiring symptoms later. Those suffering from gastrointestinal issues were admitted to the hospital far later than those suffering from respiratory problems. As a result, there was a delay in diagnosis & treatment. Patients with gastrointestinal manifestations were expected to arrive late to the hospital & obtain an incorrect diagnosis. When compared to non-GI counterparts, their clinical course was more erratic, with a higher frequency of severe

illness progression (requiring mechanical ventilation & ICU treatment). They had to stay in the hospital longer because their discharge had been delayed until the infection had been cleared. This result might be due to a number of factors. While a delay in treatment may have had a role, studies reveal that persons who experience GI symptoms have greater viral replication & levels. Because they exhibited greater chances of faecal RT-PCR positive than the overall population, patients with gastrointestinal symptoms should have routine reverse transcription polymerase chain reaction (RT-PCR) testing. Moreover, no relationship has been shown in several investigations among both positive PCR findings & the occurrence of GI manifestation and the seriousness of the condition. Ethnic/geographical variances, concurrent comorbidities, or the adoption of differing clinical & diagnostic criteria might all contribute to variations in GI indicators & onset time. It's critical to be conscious of the vast spectrum of Gastrointestinal manifestation related with COVID-19 so that this possibility can be looked into right away. Physicians should be on the lookout for patients with pyrexia & gastrointestinal manifestations, since this might be the only predictor of COVID-19, signifying the onset of a severe illness with life-threatening effects. Beyond the pre-existing liver disease, there were no other known risk factors for the development of GI symptoms, making the prognostic value of developing such clinical signs complicated [13-15].

Injuries to the liver in Covid-19 patients

Patients of Covid-19 can develop liver damage as well as gastrointestinal problems, as evidenced by increased enzymes in blood tests. Aspartate aminotransferase (AST) & alanine aminotransferase (ALT) levels were abnormal in Covid-19 patients, & blood bilirubin levels were typically modestly elevated [16,17]. Though serious liver damage is conceivable, most liver injuries are minor & only last a few days. People with acute Covid-19 disease also had a higher risk of liver damage. Covid-19 had one critical patient with acute hepatitis, having blood ALT levels approaching 7590 U/L, whereas the Wuhan group had 43 patients with elevated ALT or AST values [17].

There have been no reports of acute liver failure. When individuals come with a more severe condition, they are more likely to have liver impairment. It's hard to tell the difference between the independent effect of viral infection & the innumerable forms of treatment used in these patients, such as antibiotics & experimental antiviral medicines. These changes could also be generic anomalies caused by infection, hypoxia or sepsis. Other laboratory disturbances like creatinine kinase, thrombocytopenia, & leukopenia were even more prevalent in individuals who have been worse at the time of diagnosis or died. Except for one case who received an autopsy, which revealed micro vesicular steatosis & mild lobular & portal inflammation on liver histology, there is no data on liver pathology [18].

The etiology of liver damage is unknown; however it might be hepatocyte viral infection, immune-related harm, or medication toxicity. By adhering to cholangiocytes via the ACE2 receptor, the virus may be able to affect liver function. Hepatocytes have less ACEII receptors than cholangiocytes. In the liver of a deceased Covid-19 patient, histological testing revealed microvesicular steatosis and modest lobular activity. SARS-CoV-2 infection or drug-induced liver damage might be the source of these histological alterations. Despite this, there was no sign of viral inclusion in the liver. It's still unknown if SARS-CoV-2 targets the liver in the same way as SARS-CoV does, or if it employs distinct methods to destroy the liver.

Mechanisms involving the gastrointestinal tract

Virus specific RNA & proteins are generated in the cytoplasm after viral entrance in order to construct new virions that may be discharged into the gastrointestinal tract. The existence of viral RNA in stools on regular basis shows that infectious virions are released by gastrointestinal cells infected with virus. Infectious SARS-CoV-2 had been lately found through faeces, indicating that infectious virions were released into the gastrointestinal system. As a result, fecal-oral transmission might be the way for viruses to propagate. To reduce the spread of the virus, avoidance of fecal-oral transmission must be considered [19].

Coronavirus has a propensity for the gastrointestinal tract, according to previous studies. In stool samples from SARS patients, SARS-CoV RNA was discovered, & in both the small & large intestines, electron microscopy of biopsy & autopsy materials revealed active viral multiplication. ACE2 is expressed in abundance throughout the gastrointestinal tract, particularly in the small & large intestines, & type II alveolar cells (AT2) in the lungs [20,21]. SARS-CoV 2 infects git through its viral receptor ACEII, which is found on enterocytes in the colon & ileum. In humans, the ACEII receptor is involved in amino acid homeostasis, the gut microbiome, & innate immunity. SARSCOV2 binding to ACEII in the GI tract may generate GIT symptoms as a result. ACEII are significantly expressed in patients with pre-existing colorectal cancer or adenomas as compared to healthy controls, but whether they have a higher risk of infection is unknown.

Because human intestinal epithelial cells are particularly sensitive for the virus & may undergo vigorous viral multiplication, MERS-CoV could cause enteric illness. This gastrointestinal tropism could explain why coronavirus infections are so common. Fomite transmission can be aided by this fecal source, particularly when infective aerosols are produced by the toilet plume [22].

Consequences for patient care & infection prevention

The SARS-gastrointestinal CoV-2 tropism, positive stool detection, & the GI symptoms it causes have serious consequences for patient safety & infection control.

Physicians should be aware of Covid-19's GI effects, which might manifest before pyrexia & respiratory issues. Furthermore, viral RNA has been found in the feces or anal/rectal swabs of Covid-19 patients in several studies [19,23].

SARS-CoV-2 RNA was discovered in the feces of 39 (53.4%) of 73 Covid-19 patients in a study, with positive stool lasting one to twelve days. Despite the fact that lung samples were negative, 17 (23.3%) people had high quantities of stool virus RNA in their systems [20]. In a separate trial that followed 10 children & analyzed both nasopharyngeal & rectal swabs, 8 children screened positive on colorectal swabs even after nasopharyngeal eradication of the virus [24]. Furthermore, following clearing with two positive rectal swabs, two children had two consecutive negative rectal swabs separated by at least 24 hours. In contrast to the cycle threshold (Ct) value of 36–38 on having an illness, the longitudinal Ct values in youngsters were frequently less than 35 [24]. Stool samples from the first US taken on day 7 revealed that viral transmission through the GI system can be widespread & continue long after clinical symptoms have disappeared. In fact, a prior research of SARS-CoV identified viral RNA in the feces of SARS patients 30 days after infection. The dynamics of SARS-viral CoV-2 in the GI system, on the other hand, are unknown & may differ from those in the respiratory tract. Our findings will very certainly have an immediate effect on disease infectivity. According to a recent environmental experiment, SARS-CoV-2 might live for hours in aerosols & at least 72 hours on plastic & stainless steel. While additional study is needed to determine its replication potential, the presence of SARS-abundant CoV-2 in feces & the environmental stability would favor its dissemination among human hosts. The virus remained longer & achieved peak viral load later in contrast to respiratory samples; the virus load peaked between the third & fourth weeks after the sickness began. The evolution of GI symptoms is crucial to be aware of because they could be one of the earliest signs of COVID 19 infection. COVID19 diagnosis may be problematic due to the presence of early GI symptoms, which may deceive clinicians.

CONCLUSION

SARS-CoV-2 is a global epidemic that has killed a lot of people. The prognosis of patients with comorbidities is poor. As the disease's natural history & range of clinical manifestations have developed, extra pulmonary signs of covid 19 have surfaced. Because of Covid-19's gastrointestinal involvement, a variety of clinical interventions would need to be explored, including rectal swab testing before patients were discharged & our readiness for personal protective equipment in the endoscopic situation. As a result, doctors should be aware of gut symptomatology, which can occur before pyrexia or respiratory symptoms appear. Even if no respiratory symptoms are evident, COVID 19 infection is connected to a variety of gastrointestinal symptoms. As a result, people who have a lot of gastrointestinal problems might look into covid 19. Because viral RNA can be found in feces, a fecal test may be positive even if respiratory samples are negative.. These factors will be crucial in our fight against Covid-19.

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