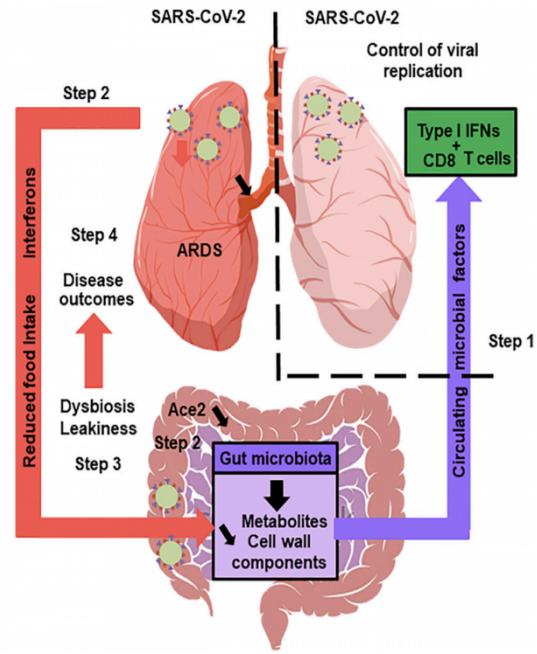

GIT PROBLEMS IN PATIENTS WITH COVID 2019 :

Done By :

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INTRODUCTION :

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is a pandemic and several vaccines have been developed to control the pandemic.
Human coronaviruses were discovered in the 1960s and presently seven strains cause disease. Human coronavirus OC43 (HCoV-OC43), human coronavirus HKU1 (HCoV-HKU1), human coronavirus 229E (HCoV-229E) and human coronavirus NL63 (HCoV-NL63) cause mild disease, while the severe acute respiratory syndrome coronavirus (SARS-CoV-1), Middle East respiratory syndrome–related coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may potentially cause severe disease. Outbreaks of SARS-CoV-1 and MERS-CoV infections occurred in 2002 and 2012, respectively.
SARS-CoV-2 has 70% and 40% genetic sequence similarity with SARS-CoV-1 and MERS-CoV.Although fever and respiratory symptoms predominate in coronavirus infections, gastrointestinal (GI) manifestations were seen in SARS-CoV-1, MERS-CoV and SARS-CoV-2 patients.

Mechanisms for GIT involvement in COVID-19 :

- SARS-CoV-2 enters host cells through ACE2 receptors.

High cell entry efficacy is achieved in three ways: high binding affinity of the receptor-binding domain (RBD) of the spike protein, evasion of the host immune system by reduced exposure of the RBD to the outside and Furin protease activation of the virus before entry into host cells, thus reducing its dependence on target cell proteases such as transmembrane protease, serine 2 (TMPRSS2).
Upon viral binding, the ACE2 receptor and virus are endocytosed, leading to a reduction in cell surface ACE2 levels.

- ACE2 receptor expression :

The ACE2 receptor is expressed in both hollow and solid intestinal organs. ACE2 messenger RNA (mRNA) is highly expressed in the GI tract and is stabilized by the neutral amino acid transporter B0AT1 (SLC6A19), found in the intestinal epithelium. In gut epithelial cells, ACE2 is needed for maintaining amino acid homeostasis, antimicrobial peptide expression and the ecology of the gut microbiome. Thus a reduction of ACE2 may interrupt these processes and increase inflammation.

A study using single-cell transcriptomics found elevated ACE2 expression in the upper oesophagus. However, in a different case–control study, decreased expression of ACE2 and nucleocapsid proteins were found in the oesophagus by immunohistochemistry. Such discrepant results may be due to patient or assay-related variations and ACE2 mRNA expression patterns may differ from its protein expression due to post-translational modification. Oesophageal bleeding with erosions is noted in some severe COVID-19 patients and may be due to high expression of ACE2 in stratified epithelial cells.
SARS-CoV-2 is usually not found in the stomach and this may be because of the highly acidic environment. ACE2 expression has been noted in the lamina propria and enterocytes of the stomach. Thus, although the virus is able to infect cells in the stomach, the low pH may be preventing this. There is high ACE2 expression in proximal and distal enterocytes of the small intestine, with the highest expression seen at the brush border of intestinal enterocytes.
Interestingly, ACE2 and TMPRSS2 are more highly expressed on absorptive enterocytes of the ileum and colon than in the lung.

- Involvement of the GI tract during COVID-19 may be due to direct viral injury and/or an inflammatory immune response and may lead to malabsorption, an imbalance in intestinal secretions and activation of the enteric nervous system. Entry of SARS-CoV-2 into host cells may trigger an inflammatory response. This leads to recruitment of T-helper cells, a cytokine storm and organ damage. Individuals with diabetes are more susceptible to cytokine storm effects of COVID-19. Virus-induced diarrhoea may be due to an alteration of intestinal permeability leading to enterocyte malabsorption.
Anal swabs have been reported to be persistently RT-PCR positive for SARS-CoV-2, even after throat swabs become negative. Positivity rates are higher among asymptomatic children, and this would have implications for its transmission potential.

Gastrointestinal manifestations in COVID-19 :

- PREVALENCE :

Although initial data found the prevalence of GI symptoms to be 2% to 10% among patients with COVID-19, subsequent studies have reported higher rates, could be as high as 50%, but most studies show ranges from 16% to 33%. Presenting with GI symptoms increases the risk of testing positive for COVID-19 . Approximately 50% of patients with COVID-19 have detectable virus in their stool.

Such patients with COVID-19 may present with GI symptoms without respiratory symptoms.
Recent study reported that 14.2% of patients with COVID-19 had digestive symptoms as their main presenting complaint, regardless of age or underlying comorbidities.

- CHARACTERISTICS :

Patients who having GI symptoms has been associated with more severe disease.
The majority of GI symptoms are mild and self-limiting and include anorexia, diarrhoea, nausea, vomiting and abdominal pain/discomfort.
In some studies, anorexia and diarrhoea were the most common GI symptoms, while in others nausea and vomiting were more prominent.

- ANOREXIA

loss of appetite is the most commonly reported symptom in most of studies .
Although rates vary across studies, a meta-analysis of 60 studies found a pooled prevalence of 26.8% in patients with COVID-19. Furthermore, individuals who later developed refractory pneumonia had a higher incidence of anorexia on admission.

- DIARRHEA

was the second most common symptom with a pooled prevalence of 12.5%. A pooled analysis of clinical studies that reported diarrhea found a prevalence of 10.4% (range 2% to 50%) in patients with COVID-19. However, recent US data found higher rates ranging from 23.7% to 33.7%.
Although some studies have described mild diarrhea(non-dehydrating, low-volume , lasting on average 4-5 days and showing improvement by day 13 of illness.) other studies have reported severe diarrhea and acute hemorrhagic colitis associated with COVID-19. The etiology of colitis is not known, but given the thrombotic complications associated with COVID-19, this likely represents ischemia.
About 15% of patients experienced diarrhoea as a first symptom, while in the rest it occurred up to 10 days after the onset of respiratory symptoms.

- NAUSEA AND VOMITING,ABDOMINAL PAIN

According to US data, nausea or vomiting were found in 10.3% to 26.4% of patients with COVID-19, whereas abdominal pain was found in 8.8% to 14.5% of patients.
Abdominal pain is found at a lower rate than other GI symptoms but was common among patients receiving intensive care unit (ICU) care.
A minority of patients presenting with abdominal pain had an important abdominal cause such as acute pancreatitis, acute appendicitis, intestinal

obstruction, small bowel ischaemia, sigmoid ischaemia, and abdominal compartment syndrome.

- OTHER GI MANIFESTATIONS

1-bloody diarrhoea are more common in those with severe disease .
2-Constipation.
3-Endoscopic evaluation showed multiple round herpetic erosions and ulcers in a patient presenting with GI bleeding.
4- Ulcerative and ischaemic changes in rectosigmoidoscopy in patients with severe symptoms.

ARE GI SYMPTOMS ASSOCIATED WITH WORSE OUTCOMES?

Early data showed GI symptoms were associated with a worse disease course and prognosis. In one study, patients with diarrhea, nausea, or vomiting were found to have a more severe disease course, including higher rates of mechanical ventilation, than patients without GI symptoms.
In one of the first case series of inpatients with COVID-19, patients admitted to the intensive care unit (ICU) were more likely to have digestive symptoms, including abdominal pain and anorexia, than non-ICU patients.
Recent US retrospective study found that patients with digestive symptoms had a 4-fold increased risk of hospitalization compared with patients without GI symptoms.
Other studies, however, including those with US data, have not found an association between GI symptoms and worse outcomes.
Although the reason for these differences is unclear, possible explanations may include variations in reporting, distinct patient populations, and different viral strains.
In addition, viral clearance among patients with digestive symptoms appears to be significantly longer compared with patients with respiratory symptoms only. Interestingly, patients with COVID-19 and GI symptoms also appear to have a longer illness duration and present later for medical care than patients without GI symptoms.

DIAGNOSIS RELATED GI MANIFESTATIONS :

there are no accepted protocols for investigation of GI manifestations in COVID-19, the decision should be made based on individual circumstances considering the therapeutic benefit of the intervention and the potential risk of exposure to healthcare workers. In such patients, no further investigations specific to the GI system are needed.

1- Endoscopy

Routine endoscopy is not useful in the diagnosis of mild disease and should be performed cautiously due to the risk of exposure of healthcare workers.
is useful in selected patients with GI bleeding for both diagnostic and therapeutic purposes

2- Stool RT-PCR, peritoneal biopsies and peritoneal fluid RNA tests have been performed, their usefulness in management is limited.

3- abdominal computed tomography scan and angiogram:
used in patients with acute abdomen and peritonitis. The reported positive findings include small bowel volvulus, acute enterocolitis, splenic flexure contrast extravasation, acute appendicitis, haemoperitoneum and haemopneumoperitoneum .

TREATMENT :

- Supportive :

As most virus-induced GI manifestations are mild and self-limiting, supportive care and symptomatic treatment are usually sufficient.
Supportive treatment with oxygen, optimal hydration, analgesics and anti-emetics may be necessary.
Although studies are limited, endoscopy in selected patients has shown ulceration and bleeding. Avoidance of non-steroidal anti-inflammatory drugs (NSAIDs) and gastric acid prophylaxis should be considered in patients with GI manifestations.
Those with paralytic ileus or excessive vomiting may require nasogastric tube decompression and nothing by mouth.
Patients with diarrhoea need appropriate rehydration therapy and anti-diarrheal medications. Those with GI manifestations have increased rates of electrolyte disturbance and thus regular monitoring and correction of electrolytes is needed and medications that may induce electrolyte imbalance should be administered with caution.
Those with severe GI manifestations or acute abdomen should be managed by a specialized multidisciplinary team including a physician, critical care specialist, nutritionist, gastroenterologist and surgeon.

- Medications :

To date, no specific antiviral medications have been shown to reduce mortality in COVID-19 patients. The antiviral drugs used for treatment of COVID-19 include remdesivir and lopinavir–ritonavir. Remdesivir was shown to reduce hospital stays in patients with severe disease.

Immunomodulatory agents including glucocorticoids, convalescent plasma and anti-cytokine therapy have been used to reduce the negative effects of the overwhelming systemic inflammatory response.However, except for dexamethasone, the other agents have not shown definite therapeutic benefits, although they may be beneficial in selected subgroups.
The loss of gut mucosal integrity and dysfunction of intestinal flora are important complications in severe viral illnesses, including COVID-19. The use of probiotics has been suggested to improve GI symptoms of SARS-CoV-2 infection. *Irrational use of broad-spectrum antibiotics should be avoided, as they cause the loss of commensal intestinal flora and alteration of gut mucosal integrity.*

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