Covid-19: A review of its clinical features, effects on gastrointestinal system and possibility of faecal transmission

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ABSTRACT

In China, Wuhan in the province of China, COVID-19 a patient suffering from pneumonia was tested and to identify the cause, the throat swab of the patient was tested. On 7th January 2020 WHO declared the identification as COVID-19. And then it was proclaimed as a pandemic. It classically causes a respiratory illness presenting as a mild cough, fever and dyspnoea. However, several investigators have advocated the involvement of the gastrointestinal tract and liver in COVID-19 infection similar to other coronavirus infections. Further research studies have shown results that are expanding the possibility of faecal transmission because RT-PCR assessment has shown significant evidence for the presence of virus not only in oropharyngeal samples but also in stool samples. Studies have shown that virus in stool samples have got positive results even after the illness has resolved, and two respiratory tests were done 24 hours after COVID-19 being tested negative. The review article summarises the different findings of the clinical presentation of COVID-19. It sheds light on the effects of COVID-19 in the gastrointestinal system along with the reasons for the high possibility of transmission of COVID-19 through the faecal-oral route.

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ISSN: 0975-7538
DOI: https://doi.org/10.26452/ijrps.v11iSPL1.2881

INTRODUCTION

At the end of 2019 as we were all gearing up for the welcoming of the new year of 2020 who would have believed that a viral disease of this magnitude was brewing silently in the form of another coronavirus after the damages caused by SARS and MERS a few decades ago. Coronavirus is an RNA virus belonging to Nidovirales order and belongs to the family Coronaviridae, Anteroviridae and Roniviridae. COVID-19 is a disease caused by SARS-CoV-2 virus which is a member of the genus Betacoronavirus (Chan et al., 2020). On genome sequencing, the scientists were able to learn that there was 82 per cent resemblance between SARS-CoV and SARS-CoV-2 (Wan et al., 2020).

Novel coronavirus was studied extensively from the period between December 2019 and March 2020, and it was declared as a global pandemic on 11th March 2020 by the WHO. By that time the virus had spread from Wuhan to many other parts of the world and had affected lacs already. A disease is said to be called as a pandemic if the spread of the disease is not contained to a particular region, and instead, it affects every nook and corner of the world. There is no drug or vaccine up until now to stop the spread of COVID-19. Many of the recently published articles related to established COVID -19 report that patients present with subtle gastrointestinal symptoms in the initial stages such as anorexia, nausea, diarrhoea, vomiting and abdominal pain with diarrhoea and anorexia being the most common symptom (Chen et al., 2020).
As of 19th April 2020, more than 23 hundred thousand cases and about 1,62,018 deaths due to COVID-19 has been reported across the globe, the United States of America being the most affected country followed by Spain and Italy. The starting point of this disease was mainly from the Wuhan wet market, which is known to be an animal wholesale market. It is expected that the spread of the disease must have started from this market only because of its unhygienic handling of animals as there was no proper regulating body.

In the last few decades, we have witnessed many dangerous endemics caused by different forms of coronavirus itself, such as SARS and MERS. In the SARS outbreak that occurred in 2003, an average of around 45 per cent of people suffered from diarrhoea in the first week of the illness itself. The substantial similarity in the genomic structure of SARS-CoV AND SARS-CoV-2 is also a significant reason that many scientists believe that the occurrence of symptoms also might be similar. Furthermore, RNA of SARS-CoV was detected in stools of the patients starting from the 5th day of illness, peaked around the 11th day. In a small group study done on the effects of SARS-CoV, scientists were able to find out that viral RNA of the patient occurred in faeces even after 30 days of illness (Chan et al., 2004).

The infection and surveillance of COVID-19 - to control the same; this current focus is on the respiratory system. When compared to SARS (27%), gastrointestinal symptoms are uncommon (Huang et al., 2020). These symptoms should, however, not to be ignored because many COVID confirmed cases have diarrhoea. One study has shown out of 138 cases 14 presented with diarrhoea (Wang et al., 2020). As the SARS and SARS-CoV-2 have an almost identical genome and share Angiotensin-converting enzyme two receptor gastrointestinal symptoms can be higher in COVID-19 patients (Donnelly et al., 2020).

Basic Virology
Coronaviruses are usually found in mammals and many other vertebrates. It mainly causes respiratory and enteric diseases. The first occurrence of it in the past was in the form of severe acute respiratory syndrome coronavirus (SARS) and Middle East respiratory syndrome coronavirus (MERS) which had led to a dangerous endemic at the respective timelines when they had occurred.

Fortunately, and because of our improved resources in viral sequencing, we were able to sequence the new coronavirus in possible record time. Through further studies, scientists were able to connect the origin of the novel coronavirus primarily to bats. Bats have previously shown to be an aggressive transmitter of many viral diseases to human beings because of its higher relations with humans. Scientists were able to find out that there was the alarming similarity between SARS-CoV-2 and SARS-CoV which had occurred in February 2003, which had primarily given them strong evidence that it had the possibility of turning into a dangerous pandemic. The spike protein of SARS-CoV has a strong binding affinity to human ACE2 receptors in the human body (Zhang et al., 2020a). Both SARS-CoV and SARS-CoV-2 enter the cell through the ACE2 receptor (Wan et al., 2020). The SARS-CoV-2 primarily affects lower airways and binds to ACE2 receptors on alveolar epithelial cells. ACE2 receptor was also found in intestinal epithelial cells. This evidence suggests that the SARS-CoV-2 can grow, infect and replicate even in the GIT, which provides the increased possibility of faecal-oral transmission this will have serious implication to disease management and communication.

DATA AND METHODS
It is primarily based on a systematic literature search using PubMed, Web of Science and many other certified online databases from December 2019 to March 2020. The leading search words were: COVID-19; SARS-CoV, faecal-oral route in covid-19, gastrointestinal symptoms, clinical features, virology, at least one result that reported gastrointestinal symptoms and the presence of viruses in the stool.

DESCRIPTION
The main content of this article can be broadly divided into 3 subheadings.

1. Clinical presentation of COVID-19
2. Effects of SARS-CoV-2 in the gastrointestinal system
3. Reasons for the possibility of faecal-oral transmission of COVID-19

Clinical features of COVID-19
COVID-19 has a broad range of clinical symptoms ranging from asymptomatic patients on one side to multi-organ failure and septic shocking the worst-case scenario. COVID-19 can be categorised into 3 levels based on the severity of the infection and symptoms:

Mild level
COVID-19 in the mild form presents typically in the way of upper respiratory tract infection such as dry
cough, nasal congestion and a mild form of fever. Most of the COVID-19 cases have mild symptoms with the possibility of escalating into severe disease.

Moderate level
This patient presents with dyspnea and tachypnea, dyspnea being the most critical bridge between mild cases and the moderate and severe cases and is the significant symptoms to determine whether the patient needs exclusive health care through hospitals or whether it is manageable in their respective homes through self-care and rest.

Severe level
COVID-19, in its severe forms, appears in the form of acute respiratory distress syndrome-ARDS, severe pneumonia and these conditions might further worsen leading into sepsis and septic shock. Clinical presentations include severe symptoms such as.

1. Dyspnea
2. Tachypnea
3. Respiratory distress syndrome

People with comorbidities have a severe form of illness. And through many studies, scientists were able to connect the increased mortality rate with increased number and severity of comorbidities that occurred in patients.

Transmission and Protective measures
One person affected with COVID-19 is expected to transmit the disease to a global average of 2.2 people (Li et al., 2020). Main source of infectious particles are fomites. Some studies suggest that the RNA of novel coronavirus was found in stool samples due to persistent viral shedding in the gastrointestinal tract (Holshue et al., 2020). Handwashing is the most important and essential practice to be followed for viral control as we are not entirely sure about the sources of transmission because the topic of COVID-19 is still in beginning stages in terms of scientific research. Contact isolation gear, such as masks, gowns, and gloves, have also been proved useful. Transmission via the ocular surface is possible, so eye protection should also be used (Lu et al., 2020). There are some studies which suggest transmission through the faecal-oral route (Cipriano et al., 2020) about which we would further learn about as we go towards the end of the article.

Effects of COVID-19 in the Alimentary system
Gastrointestinal symptoms
Gastrointestinal symptoms play a significant role in diagnosing the coronavirus because many studies now suggest that many patients with mild COVID surprisingly often shows only gastro symptoms. Compared to patients with respiratory symptoms, those having digestive symptoms were more likely COVID-19 positive. Though gastrointestinal symptoms are mostly very mild and aren't critical, it plays a crucial role to find and isolate COVID-19 patients and thereby prevent the spread of disease. So now many doctors are advising patients with mild new-onset GI symptoms and possible contact with COVID-19 patient to undergo testing despite having no travel history. The main symptoms of GIT are

1. Diarrhoea
2. Vomiting
3. Abdominal pain
4. Anorexia
5. Nausea
6. Gastrointestinal bleeding

In a scientific study was done based on patients in the United States of America, 278 COVID-19 positive patients and 238 COVID-19 negative patients were tested. The scientists were able to conclude that patients who showed gastrointestinal symptoms such as diarrhoea and vomiting were more likely to test positive than to test negative. Sixty-one per cent of patients having gastrointestinal symptoms tested positive, while only 39 per cent tested negative. This being more than 50 makes it an important point to be noted (Nobel et al., 2020).

Injury to the liver in COVID-19 patients
Apart from gastrointestinal symptoms, many patients also had a severe liver injury due to increased levels of the enzyme in the blood. In a study, it was found out that about 14 to 53 per cent of the patients had increased levels of ALT and AST (Zhao et al., 2020). GGT elevation was also seen in 54 per cent of patients (Zhang et al., 2020b). In most of the cases, liver injury was mostly of the mild form with severe damage of liver-only seen in severe cases associated with other comorbidities in COVID-19. Though the study behind the reason for liver damage though not complete many scientists still believe that it might be due to infection of the liver cells (Xu et al., 2020). Some studies also suggest that the virus can bind to cholangiocytes and affects the liver function through ACE 2 receptors (Zhang et al., 2020c). Apart from these immune responses such as cytokine storm and pneumonia-related hypoxia, other causes also might lead to
injury to the liver. Cytokine storm is expected to be the primary feature of COVID-19 that might lead to severe damages to the liver. Other possible liver disorders that can occur due to COVID-19 are viral hepatitis and fatty acid disease either due to alcoholic or non-alcoholic reasons. Further studies must be done to find out exactly how COVID-19 affects the liver so that certain medications can be provided to prevent the adverse effects of COVID-19 in the liver.

**Reasons for the possibility of faecal-oral transmission of COVID-19**

Based on an article published in Nature Medicine, during the clinical characterisation of 10 pediatric patients in China, out of which most of them did not require intensive care as they had very mild symptoms. Out of these ten patients, 8 of them tested positive on RT-PCR through rectal swab even after throat swab test testing negative. On further testing, researchers were able to find out that out of those eight patients who tested positive in the rectal swab, four patients got negative rectal swabs for two consecutive times. Interestingly out of these four patients, a rectal swab of 2 of these patients became positive again after some time though the nasopharyngeal tests remain negative. This strongly suggests that the viral shedding from the gastrointestinal tract may occur even long after the absence of clinical symptoms and negative nasopharyngeal test. A study based on SARS-CoV found out that viral RNA was detected even after 30 days in the stool of the patient. With all these studies, a person named Mary Estes from Baylor College of Medicine concluded that "Asymptomatic children and adults may be shedding infectious virus and they could transmit it". In one such research published we could understand that from among 73 patients who were hospitalised infected with SARS-CoV-2, 39 that is 53.42% of total patients tested including 25 male and 14 female patients, showed positive results for SARS-CoV-2 RNA in the stool. The duration of positive stool results being ranged from a minimum of 1 to a maximum of 12 days. Out of all patients in the study, 17 patients who account to 23.29 per cent of tested patients continued to show positive results in stool even after their nasopharyngeal test showing negative effect in the nasopharyngeal test (Xiao et al., 2020). Existing studies made during previous SARS and MERS outbreak shows that that viral RNA was found to be present in conditions that facilitate faecal-oral transmission such as sewage water (Wang et al., 2005). SARS-CoV being genetically similar to novel coronavirus raises some serious questions on whether COVID-19 is capable of faecal-oral transmission or not. Further studies must be done in this topic to come to a proper conclusion on the viability of SARS-CoV-2 in different environmental conditions and whether gastrointestinal symptoms are in any way related with increased shedding of viral RNA through the GIT.

**CONCLUSION**

From all the research that is done till now on the effects of COVID-19 in the gastrointestinal system, we can conclude that though the impact of COVID-19 in the GIT is mostly mild and doesn't lead to any significant symptoms other than diarrhoea and anorexia, the interesting finding through many studies is that that in many cases digestive symptoms tend to appear first in an individual suffering from COVID-19 even if they may not show any signs of fever or respiratory problems. At the same time, the virus shedding also takes a longer time in the intestine, making it very difficult to rule out the absence of COVID-19 by only using the nasopharyngeal test. Suppose these patients who have been tested based solely on nasopharyngeal swab test are discharged from the hospital. In that case, they can still be carriers of the infection and thereby spread the virus without their knowledge. So before releasing a patient who recently recovered from COVID-19, both nasopharyngeal and rectal swabs should be tested negative. Based on some studies done till now, which suggest that some patients, especially of pediatric age group, show gastric symptoms as a primary symptom even if fever and other respiratory symptoms, are absent. So doctors can be advised to use COVID-19 as a differential diagnosis for all patients complaining of gastrointestinal symptoms and check if they have had any contact with COVID-19 positive individual.

**ACKNOWLEDGEMENT**

Nil.

**Conflict of Interest**

Nil.

**Source(s) of support**

Nil.

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