



GASTROINTESTINAL MANIFESTATIONS OF COVID 19: A BRIEF REVIEW

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ABSTRACT

Background: In Dec 2019, a series of pneumonia cases were identified in Wuhan, China with presentations similar to viral pneumonia which later spread worldwide and was declared as COVID 19 Pandemic. Most common presentation were fever and respiratory symptoms and less common symptoms include GI symptoms like nausea, vomiting, abdominal pain and diarrhea. **Objectives:** The objective of this article is to review the gastrointestinal manifestations of COVID 19 patients and to understand its importance while diagnosing patients with COVID 19. **Methodology:** Pubmed database and Google scholar database were searched between Dec 2019 to June 2020 for studies including COVID 19 confirmed patients with GI symptoms. **Findings:** Many of these studies observed gastrointestinal symptoms like decreased appetite, diarrhea, nausea, vomiting and abdominal pain to be present in a substantial no of COVID 19 confirmed patients. **Conclusions:** Failure to recognize COVID 19 patients with predominant digestive symptoms may lead to undue spread of virus for a much longer period and may lead to uncontrollable dissemination of the virus. **Recommendation:** All COVID 19 confirmed patients should be evaluated for GI symptoms also apart from respiratory symptoms. Patients with predominantly GI symptoms should also be suspected as COVID 19 patients during the current COVID 19 pandemic phase.

KEYWORDS : COVID 19, Gastrointestinal symptoms, GI Manifestations

INTRODUCTION

Coronaviruses are enveloped non segmented positive sense RNA viruses which belong to the family Coronaviridae. They have been broadly distributed among humans and other mammals and are responsible for various illnesses involving the respiratory, gastrointestinal and nervous systems. (Douglas D. et al., 2016; Weiss & Leibowitz, 2011)

In Dec 2019, a series of pneumonia cases were identified in Wuhan, China with presentations similar to viral pneumonia. However, initially no distinct cause could be identified. With the use of molecular techniques and unbiased DNA sequencing it was found that novel betacoronavirus (n-CoV) was the likely cause of severe pneumonia in these patients. On Full-genome sequencing and phylogenetic analysis 2019-nCoV showed feature typical of the coronavirus family and thus was classified in the beta coronavirus 2 b lineage. The betacoronavirus were also associated with SARS and MERS. —(Chen et al., 2020; WHO | Novel Coronavirus China, 2020; Zhu et al., 2020)

SARS (Severe Acute respiratory syndrome) was first identified as a global threat when it caused major outbreaks in 2002 and 2003 in Guangdong, China. Later MERS CoV was found to be responsible for severe respiratory disease outbreaks in Middle East. (Drosten et al., 2003; Ksiazek et al., 2003; Zaki et al., 2012; Zhong NS et al., 2003)

The most common symptoms of SARS nCoV include fever, dry cough, myalgia and dyspnoea and the less common symptoms are headache, nausea, vomiting, abdominal pain and diarrhea. The incidence of non-respiratory symptoms may vary across different population. —(Wang et al., 2020) Recent studies have suggested the transmission of SARS CoV via faeco-oral route (Hui & Zumla, 2019) and SARS CoV nucleic acid has also been found in patient feces. (Holshue et al., 2020)

In the past it was known that coronaviruses affect respiratory and intestinal system in animals. However, Leung et al for the first time reported the presence of active viral replication in the small and large intestine of patients with SARS. (Leung et al., 2003)

In some cases of COVID 19, gastrointestinal symptoms could be the initial presentation and may thus be neglected leading

to delayed or no diagnosis at all. (Han et al., 2020)

The objective of this article is to review the gastrointestinal manifestations of COVID 19 and to understand its importance while diagnosing patients with COVID 19.

METHODOLOGY:

Pubmed database and Google scholar database were searched between Dec 2019 to June 2020 for English language studies-case reports, case series and reviews, related to recent pandemic of SARS COVID 19. Studies in which COVID 19 patients presented with at least one symptom of gastrointestinal manifestation of SARS COVID 19 were selected. However studies where no GI symptoms were recorded were excluded. Database was also searched through June 2020 for past knowledge about Coronaviruses-Severe Acute Respiratory Virus (SARS) and its gastrointestinal association.

RESULTS:

A total 10 studies were found where gastrointestinal manifestations of COVID 19 were described. Majority of these studies were from Wuhan city, China, where the COVID 19 outbreak first started.

Many of these studies observed gastrointestinal symptoms to be present in a substantial no of COVID 19 confirmed patients. In a study in Wuhan, among the 138 SARS-COV confirmed patients majority of them presented with the usual symptoms of nCov i.e. fever (98.6%), cough (59.4%), fatigue (69.6%). However, among the lesser common symptoms, a substantial no of persons (10%) presented with nausea and diarrhea. Diarrhea was mostly observed during the first week and was mostly self limited. Intestinal biopsy showed very minimal disruption of small and large intestinal architecture. However active viral multiplication was observed in both small and large intestine. —(Wang et al., 2020)

In another study in Wuhan, a unique subgroup of 206 n Cov confirmed patients with low severity and with one or more gastrointestinal symptoms (nausea, vomiting or diarrhea) were identified and studied in follow up. Among these patients, 48 presented with GI symptom alone, 69 with both digestive and respiratory symptoms and 89 with respiratory symptom alone. Fever was present among 62.4% of patients who presented with one or more digestive symptom. Among the patients who presented with diarrhea, 19.4 % of them

experienced it as the first symptom. The diarrhea lasted from 1-14 days and the average duration was 5.4±3.1 days. nCoV patients with digestive symptoms were less likely to seek early care early as compared to those who presented with respiratory symptoms (16.067.7 vs 11.665.1 days, P < 0.001) which led to delayed diagnosis among nCov patients with digestive symptoms compared to nCoV patients with respiratory symptoms alone. (Han et al., 2020)

In a case series Luo et al did a retrospective study among 1141 COVID 19 patients and found that some patients of COVID 19 may present with gastrointestinal symptom without presence of other common manifestations of COVID 19. Among the 1141 patients studied, 183(16%) presented with gastrointestinal symptoms. Among these, 37% and 25% patients presented with diarrhea and abdominal pain respectively. Most common GI symptom was loss of appetite and about two third patients presented with nausea and vomiting. (Luo et al., 2020)

Some other studies reported digestive symptoms among COVID 19 confirmed patients, however it was found to be present in only very few patients. Like in a study in Wuhan, 99 nCoV confirmed patients were analyzed retrospectively and was found that majority of the patients presented with fever and cough. However, few patients (2%) also presented with gastrointestinal complaints like nausea, vomiting and diarrhea. Among them 11(11%) of patients died with multiple organ failure. (Chen et al., 2020)

Table 1 summarizes the various GI symptoms across COVID 19 case studies.

Sample Size	Place of study	At least one GI symptom	Anorexia	Diarrhoea	Vomiting	Abdominal Pain	Nausea
		No (%)	No (%)	No (%)	No (%)	No (%)	No (%)
N =204	Hubei, China		83 (83.8)	29 (29.3)	8 (0.8)	4(0.4)	
N = 41	Wuhan			1(3)			
N = 651	Zhejiang	74 (11.4)					
N = 1141	Wuhan	183 (16)	180(16)	68(6)	119(10.5)	45(3.9)	134(11.7)
N =206	Wuhan			69(33.5)			
N = 138	Wuhan			14 (10)	5(3.6)	3(2.2)	14(10)
N = 99	Wuhan			2(2)	1(1)		1(1)

Mechanism of GI manifestations in COVID 19 patients:
SARS CoV-2 can enter cells which express Angiotensin Converting Enzyme-2 (ACEII). It is well know that ACE II is widely distributed in lungs which explains the predominant respiratory manifestations of SARS COVID 19. However, evidence has shown that ACE II can also be expressed in the upper esophagus and in the stratified epithelial cells and absorptive enterocytes present in ileum and colon. This explains the mechanism behind GI manifestations of COVID 19 patients. (Gui et al., 2017; Luo et al., 2020; Zhu et al., 2020)

DISCUSSION:

The new coronavirus (SARS-CoV-2) pandemic which originated from Wuhan, China in December 2019, has posed a serious threat to global health. Patients with COVID-19 typically present with fever or a respiratory syndrome. However many case series and case reports have analysed that COVID 19 may present with some GI symptoms like loss of appetite, nausea, vomiting, diarrhea, abdominal pain etc. In a study in Wuhan, among 206 COVID 19 confirmed patients, a substantial number (46 out 206) of patients presented with GI symptom alone. (Han et al., 2020)

Another study in Zhejiang among 651 COVID 19 confirmed patients, it was reported that 74 (10.4%) patients presented with at least one GI symptom. Moreover, the severity of illness was higher in these patients with higher rates of fever, fatigue and shortness of breath as compared to patients without GI symptoms. These findings have more clinical significance since these patients may otherwise remain undetected. (Jin et al., 2020)

On 2 Jan 2020, a cluster of 41 laboratory confirmed nCoV patients were admitted in a hospital in Wuhan. Most of them were men and median age was 49 years. 27(66%) patients were exposed to Huanan sea food market. Common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were sputum production (11 [28%] of 39), headache (three [8%] of 38), haemoptysis (two [5%] of 39), and diarrhoea (one [3%] of 38). (Huang et al., 2020)

In a cross sectional multicentre study, 204 COVID 19 confirmed patients were enrolled between January 18th to February 28th 2010. Most of these patients presented with fever and respiratory symptoms However a significant no i.e. 103 patients (50.5%) reported a digestive symptom, including lack of appetite (81 [78.6%]), diarrhea (35 [34%]), vomiting (4 [3.9%]), and abdominal pain (2 [1.9%]). Patients with digestive symptoms had higher liver enzyme levels and longer coagulation. (Pan et al., 2020)

In a study outside Wuhan in Zhejiang province, Jin et al reported the largest cohort of 651 COVID 19 confirmed patients with GI symptoms. These patients were enrolled from 17 Jan to 8th Feb 2020. Among the patients enrolled, 74 (11.4%) presented with at least one GI symptom (nausea, vomiting or diarrhea). Significantly higher rates of fever, fatigue, shortness of breath and headache was found among COVID 19 patients with GI symptoms compared to COVID 19 patients without GI symptoms. (Jin, 2020)

SARS-CoV-2 can enter cells which express angiotensin converting enzyme II. Since apart from lungs, cells of upper esophagus and the enterocytes of ileum and colon also express ACE II, this is the probable mechanism described for the GI manifestations of COVID 19. (Gui et al., 2017; Luo et al., 2020; Zhu et al., 2020)

Evidence has shown feco-oral transmission of SARS CoV 2. These findings are consistent with the findings of past studies which showed that 30% and 10.6% of patients with MERS and SARS respectively presented with diarrhea. (Chan et al., 2020; Hui & Zumla, 2019)

In a study among 73 SARS CoV 2 infected hospitalised patients, Xiao et al found that 53.42 % of these patients tested positive in stool.(Xiao et al., 2020) This finding establishes earlier finding by Hui and Zumla who reported feco-oral transmission of coronaviruses. (Hui & Zumla, 2019)

Failure to recognize COVID 19 patients with predominant digestive symptoms may lead to undue spread of virus for a much longer period and may lead uncontrollable dissemination of the virus.

CONCLUSION AND RECOMMENDATIONS:

Failure to recognize COVID 19 patients with predominant digestive symptoms may lead to undue spread of virus for a much longer period and may lead to uncontrollable dissemination of the virus. All COVID 19 confirmed patients should be evaluated for GI symptoms also apart from respiratory symptoms. Patients with predominantly GI symptoms should also be suspected as COVID 19 patients

during the current COVID 19 pandemic phase.

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