Gastrointestinal Symptoms Associated with Unfavorable Prognosis of Covid-19 Patients

SHAKIR HUSSAIN KEERIO¹, IMRAN ARSHAD², KAMRAN ALMANI³, SHAISTA ZEB⁴, SAQIB ALI⁵

¹Senior Registrar Gastroenterology and Hepatology department, Liaquat Medical University of Health and Science, Hyderabad

^{2,4}Assistant Professor Gastroenterology department, Isra University Hospital, Hyderabad

³Medical Officer Gastroenterology department, Civil hospital, Hyderabad

⁵Assistant Professor, Data Analyst Department of Computer Science, University of Agriculture, Faisalabad

Corresponding author: Dr. Imran Arshad, Email: doctorimranarshad@gmail.com, Contact No: +92 333 4116553

ABSTRACT

Background: COVID-19 pandemic or coronavirus is a systemic disease taken into consideration for vascular system-specific tropism where microcirculation alteration has a significant pathogenic role. The coronavirus affects the gastrointestinal tract, abdominal manifestation, and hepatobiliary system.

Aim: the aim of the present study was to evaluate the association of gastrointestinal symptoms with unfavorable prognosis of coronavirus patients.

Materials and Methods: This single-center cross-sectional study was carried out on 486 patients with or without gastrointestinal symptoms and was conducted for six months duration from January to June 2021 at Gastroenterology department, Isra University Hospital, Hyderabad. All these patients were categorized into two main groups; group-I patients exposed to coronavirus with gastrointestinal symptoms while group-II patients exposed to COVID-19 without gastrointestinal symptoms. Gastrointestinal symptoms were associated with acute respiratory distress syndrome (ARDS), continuous renal replacement therapy (CRRT), non-invasive ventilator treatment, tracheotomy, and tracheal intubation. Multivariable and unilateral regression models were utilized for data analysis.

Results: Of the total 486 patients, 157 (32.3%) were with gastrointestinal symptom patients while 329 (67.7%) were without GI symptoms. Propensity scores were analyzed in both groups. Both groups were equally susceptible to higher mortality risks but COVID-19 patients with gastrointestinal symptoms were at high risk of acute respiratory distress syndrome. Of the 157 patients with GI symptoms, 44 (28.03%) were initially diagnosed and 113 (71.97%) were diagnosed in hospital. The prevalence of vomiting or nausea, diarrhea, abdominal distention, and abdominal pain were 30 (19.1%), 83 (52.9%), 18 (11.5%), and 26 (16.6%) respectively. Dyspnea, fatigue, fever, chest tightness, and cough were common COVID-19 symptomatic patients. The prevalence of GI symptoms patients had dyspnea 23 (14.6%), fatigue 45 (28.7%), fever 128 (81.5%), chest tightness 25 (15.9%), and cough 72 (45.9%) were statistically significant and higher compared to the no symptoms of gastrointestinal disease patients.

Conclusion: Our study found the high prevalence of COVID-19 patients with gastrointestinal symptoms compared to without gastrointestinal symptoms in COVID-19 patients and associated with non-invasive mechanical ventilation and risks of acute respiratory distress syndrome. Hence, COVID-19 patients with gastrointestinal symptoms should be taken care of in healthcare protection.

Keywords: COVID-19, Gastrointestinal symptoms, ARDS or acute respiratory distress syndrome

INTRODUCTION

COVID-19 is a severe acute respiratory syndrome originating from Wuhan City, Province Hubei, China in 2019¹. COVID-19 pandemic or coronavirus is a systemic disease taken into consideration for vascular systemspecific tropism where microcirculation alteration has a significant pathogenic role. The coronavirus affects the gastrointestinal tract, abdominal manifestation, and hepatobiliary system^{2,3}. The World Health Organization (WHO) declared coronavirus disease a pandemic after 10 million infected individuals, approximately half million deaths worldwide⁴. A study conducted on coronavirus at early stages found that COVID-19 pneumonia transmitted from person to person through close touch and contact with infected individuals, respiratory droplets and contaminated objects touching⁵⁻⁷. Hence, patient's isolation and effective control measures for infected individuals could decrease the incidence rate of coronavirus infections⁸. The diagnostic tests, intensive care workload, mitigation strategies such as interpersonal contacts restriction in COVID-19 affected territories have been increased and effectively established⁹.

Severe acute respiratory syndrome infection and mortality rate were significantly higher among the male population compared to the female¹⁰. The main contributing factors for COVID-19 spreading and transmission by droplets were sneezing, coughing, and indirect contamination¹¹.

Several studies reported an increasing trend of gastrointestinal symptoms and sign during the COVID-19 pandemic^{12,13}. Certainly, gastrointestinal symptoms such as vomiting and nausea besides respiratory symptoms were found in the USA's first known COVID-19 patient¹⁴. Previous literature on COVI-19 patients reported abdominal pain without typical SARS-CoV-2 respiratory symptoms. Hence, the first physician to suggest COVID-19 infection would be an abdominal radiologist because of abdominal tomography (CT) findings in lower lung lobes. Some studies suggested additional CT of the whole chest for abdominal pain in coronavirus infection¹⁵. Patients with severe gastrointestinal symptoms could be declared as coronavirus disease and mild gastrointestinal symptoms were not considered as COVID-19 patients. Loss of appetite followed by vomiting and nausea are the most common gastrointestinal symptoms while abdominal pain and diarrhea is in small percentage GI symptoms¹⁶.

A retrospective study conducted on 141 COVID-19 patients reported abdominal pain was the common gastrointestinal symptom with the positive and negative prevalence of CT abdominal findings 53.8% and 73.8% respectively. Gastrointestinal tract segmented wall thickness was the main CT findings in most cases. Additionally, about 64% of abdominal patient's with negative or no positive findings on CT however lung bases COVID-19 pneumonia were suggestive and shown gastrointestinal symptoms on CT. This concluded thatCOVID-19 must have abdominal symptoms without correlating abdominal CT findings¹⁶. Another study reported abdominal findings incidence in coronavirus patients without or with abdominal symptoms and found that COVID-19 patient's abdomen most common finings was the bowel abnormalities. Fat stranding of the edematous wall, pneumatics of small bowel with portal venous gases, severe colitis, gastritis, and no wall thickening of the fluidfilled colon were the CT abdomen findings¹⁷. The present study was conducted with an aim to assess the gastrointestinal symptoms in the unfavorable prognosis of COVID-19 patients.

METHODS

This single-center cross-sectional study was carried out on 486 patients with or without gastrointestinal symptoms at Gastroenterology department, Isra University Hospital, Hyderabad for six months duration from January to June 2021. All these patients were categorized into two main groups; group-I patients exposed to coronavirus with gastrointestinal symptoms while group-II patients exposed to COVID-19 without gastrointestinal symptoms. Gastrointestinal symptoms were associated with acute respiratory distress syndrome (ARDS), continuous renal replacement therapy (CRRT), non-invasive ventilator treatment, tracheotomy, and tracheal intubation. Multivariable and unilateral regression models were utilized for data analysis. All the individual enrolled in this study was coronavirus diagnosed patients followed the WHO criteria for new coronavirus pneumatic prevention program. Based on clinical symptoms, nasopharyngeal swabs, and real-time reverse transcription PCR (RT-PCR) positive tested COVID-19 patients were diagnosed. All the individuals underwent chest chromatography and were divided into GI symptoms and no GI symptoms.

Demographic, clinical, epidemiological, treatment and outcomes information was extracted from the patient's medical record and were analyzed by the investigator. The data collected includes gender, age, comorbidities, exposure history, chronic heart failure, kidney disease, liver dysfunction, chronic pulmonary disease, cerebrovascular disease, gastrointestinal symptoms such as acid reflux, diarrhea, abdominal distention, and abdominal pain), ordinary symptoms (cough, chest pain, fever, fatigue, headache, and chest tightness), laboratory and radiological findings include corticosteroids, antivirals, high-flow nasal oxygen therapy, antibiotics, and proton pump inhibitors (PPIs). Additionally, complications such as acute liver injury, acute respiratory distress syndromes and acute kidney failure or injury and mortality status. The COVID-19 patients with GI symptoms were correlated with clinical features such as tracheotomy, non-invasive ventilator treatment, ARDS, tracheal intubation, and continuous renal replacement therapy (CRRT) and mortality were examined. Other outcomes involve high-flow nasal oxygen therapy, AKI, non-invasive mechanical ventilation, tracheotomy, CRRT, tracheal intubation, and, acute liver injury were investigated.

The propensity scores measures the COVID-19 specific exposure probability with gastrointestinal versus gastrointestinal symptoms without as baseline measurement covariates. COVID-19 patients with GI symptoms covariate were dependent variables, gender, age, comorbidities, and exposure history estimated by propensity scores. Categorical and continuous variables were expressed as frequency, percentage n (%), and median (IQR) respectively. χ^2 -test and Mann Whitney test associate the coronavirus patients with or without gastrointestinal symptoms. Multivariable and univariable regression models explored the association among intubation, CRRT, treatment on a non-invasive ventilator, acute respiratory distress syndrome, and GI symptoms. Statistically p-value <0.05 was considered significant. SPSS version 20 analyzed the data.

RESULTS

Of the total 486 patients, 157 (32.3%) were with gastrointestinal symptom patients while 329 (67.7%) were without GI symptoms. Both groups propensity scores were analyzed in. Both groups were equally susceptible to higher mortality risks but COVID-19 patients with gastrointestinal symptoms were at high risk of acute respiratory distress syndrome. Of the 157 patients with GI symptoms, 44 (28.03%) were initially diagnosed and 113 (71.97%) were diagnosed in hospital in Figure 1. Demographic characteristics such as age distribution and gender distribution is demonstrated in Table-1. Propensity scores was almost same before and after matching.

Table-1 Demographic Characteristics of 486 patients (with or without GI symptoms)

Parameters	Patients with	Patients without	P-value
	GI Symptoms (n=157)	GI Symptoms (n=329)	
Age (years)	59.3±3.4	57.6±2.7	0.059
	<18	0	1
	19-42	28 (17.8%)	77 (23.4%)
	43-63	85 (54.1%)	146 (44.4%)
	>64	44 (28.03%)	105 (31.9 %)
Gender n (%)			0.673
Male	75 (48%)	171 (52%)	
Female	82 (52%)	158 (48%)	
Exposure History n (%)	21 (13.4%)	46 (13.9%)	0.582
Hypertension n (%)	57 (36.3%)	104 (31.6%)	0.395
Comorbidities n (%)	86 (54.8%)	164 (49.8%)	0.354
Chronic heart failure n (%)	8 (5.17%)	7 (2.3%)	0.046
Pulmonary disease n (%)	11 (7%)	14 (4.6%)	0.167
Chronic kidney disease	12 (7.6%)	13 (3.8%)	0.055
Liver dysfunction	12 (7.6%)	27 (8.1%)	0.791



Figure-1 Prevalence of initial and hospitalized diagnosed patients (n=157)



Figure-2. Prevalence of GI manifestations (n=157)

Table-2 Prevalence	of COV/ID-19 r	natients with	GI symptoms
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GI Symptoms	Frequency n	Percentage %
Dyspnea	23	14.6
Fatigue	45	28.7
Fever	128	81.5
Chest tightness	25	15.9
Cough	72	45.9



Figure-3. Prevalence of COVID-19 patients with GI symptoms

The prevalence of GI manifestations such as vomiting or nausea, diarrhea, abdominal distention, and abdominal pain were 30 (19.1%), 83 (52.9%), 18 (11.5%), and 26 (16.6%) respectively as shown in Figure 2. Dyspnea, fatigue, fever, chest tightness, and cough were common COVID-19 symptomatic patients. The prevalence of GI symptoms in COVID-19 patients had dyspnea 23 (14.6%), fatigue 45 (28.7%), fever 128 (81.5%), chest tightness 25 (15.9%), and cough 72 (45.9%) were statistically significant and higher compared to the no symptoms of gastrointestinal disease patients as shown in Table 2/Figure 3.

In COVID-19 patients, various treatment has been prescribed and given to patients with or without gastrointestinal symptoms. Antibodies [125 (79.6%) versus 219 (66.6%)], antiviral [150 (95.5%) versus 297 (90.3%)], and corticosteroids [65 (41.4) versus 112 (34%)] with pvalue < 0.001, =0.04, and =0.02 respectively were the treatment given to with or without GI symptoms patients as shown in Table-3. A therapy of high flow nasal was given to 130 (82.8%) COVID-19 patients with GI symptoms. Other treatments were tracheal intubation 9 (5.7%), non-invasive mechanical ventilation 24 (15.3%), and CRRT 3 (1.9%) in Figure-4. Besides acute kidney and liver injuries, respiratory distress syndrome was the most prevalent COVID-19 complication. The COVID-19 patients with GI symptoms had a higher prevalence of ADRs compared to those without GI symptoms.

Table-3 Comparison of Treatment given to COVID-19 patients with or without GI symptoms

Treatment	COVID-19	COVID-19 Patients	P-value		
	Patients with GI	without GI			
	Symptoms	symptoms n=329,			
	n=157, %	%			
Antibodies	125 (79.6)	219 (66.6%)	<0.001		
Antiviral	150 (95.5)	297 (90.3)	0.04		
Corticosteroids	65 (41.4)	112 (34)	0.02		



Figure.4 Prevalence of Treatment given to COVID-19 patients with GI symptoms n=157

DISCUSSION

COVID-19 pandemic referred to as infectious diseases causing disastrous consequences and extraordinary challenges for human health are increasing day by day globally¹⁸⁻²¹. Coronavirus's significant manifestations are respiratory symptoms spread by humans to humans through physical contact and droplets caused by sneezing and coughing²². The mitigation strategy of COVID-19 spreading is complete isolation by staying home or quarantine at an isolation center²³. Various clinical symptoms were noticed since the outbreak of COVID-19 in Wuhan, China. The present study focused on gastrointestinal symptoms present in COVID-19 patients based on the hypothesis that coronavirus patients had a spectrum of symptoms. Another study found respiratory symptoms such as fever and cough as a majority feature among the coronavirus spectrum of symptoms. It has been reported that GI symptoms are manifested consistently as secondary symptoms in COVID-19 patients²⁴. GI bleeding, vomiting, diarrhea, nausea, hepatic involvement, anorexia, and abdominal pain were the main gastrointestinal symptoms among COVID-19 patients²⁵. In infected patients, the initial and prevalent GI symptom was diarrhea²⁶. Loss of appetite was more common in adults compared to children vomiting²⁷. One study reported 3% diarrhea in infected patients as gastrointestinal symptoms which concluded that unusual GI symptoms can be present in coronavirus infected patients²⁸.

COVID-19 spreading can be effectively controlled by early diagnosis of inestimable importance of GI symptoms and awareness among infected patients. The infectious disease complications increase day by day due to its novel nature. Endoscopy and colonoscopy were performed to distinguish the inflammatory bowel or cancer disease from coronavirus disease. The present study reported that higher risks of acute respiratory distress syndrome, tracheal intubation, and non-invasive mechanical ventilation was associated with gastrointestinal syndrome in COVID-19 patients. Although mortality risks among coronavirus patients were the same for both with or without GI symptoms. Another study conducted on 2,226 COVID-19 patients reported lower mortality rates among patients who had GI symptoms²⁹. In contrast, one study found a high severity rate among coronavirus infected patients with GI symptoms compared to those without any GI symptoms³⁰.

In our study, a high prevalence of GI symptoms such as chest tightness, myalgia, fever, fatigue, cough, and dyspnea were infectious disease clinical characteristics. Also, a higher tendency toward disease severity and acute respiratory distress syndrome complications were noticed in coronavirus patients with GI symptoms compared to those without GI symptoms similar to a previous study³¹. Increased procalcitonin levels, CRP, decreased serum levels, lymphocyte count was the evidence for electrolyte disturbance and bacterial translocation. Additionally, acute liver and kidney injuries increasing incidence were same in both GI symptoms and without GI symptoms coronavirus patients. In COVID-19patients, GI symptoms patients contain above 133 µmol/L of creatinine and AST level at a hiaher rate compared to those without GI symptoms. Previous studies reported higher rate of acute respiratory distress syndrome, tracheal intubation, and noninvasive ventilation (mechanical) were significantly associated with GI symptoms present in COVID-19 patients^{32,33}. However, the present study found no increase in the mortality rate of COVID-19 patients with GI symptoms.

CONCLUSION

Our study found the high prevalence of COVID-19 patients with gastrointestinal symptoms compared to without gastrointestinal symptoms in COVID-19 patients and associated with non-invasive mechanical ventilation and risks of acute respiratory distress syndrome. Hence, COVID-19 patients with gastrointestinal symptoms should be taken care of in healthcare protection.

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