

Gastrointestinal Symptoms in Patients with COVID-19: A Single-Center Experience

COVID-19 Hastalarında Gastrointestinal Semptomlar: Tek Merkez Deneyimi

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ABSTRACT

Objective: Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus, the first cases of which were reported in Wuhan, China in December 2019. The disease often presents with major respiratory symptoms. In addition, gastrointestinal (GI) symptoms are observed. They may be the first or even the only symptoms of the disease. The aim of this study is to demonstrate the presentation of GI symptoms and their relationship to other symptoms, the clinical course and prognosis of patients with COVID-19.

Methods: Included in this study were patients over 18 years of age who had been hospitalised for treatment in clinics and intensive care units due to COVID-19 between March and June 2020. The symptoms reported by the patients at the time of admission and the data collected as a result of the clinical follow-up were evaluated.

Results: Out of the 1,045 patients with COVID-19, 140 patients (13.4%) had GI symptoms. The complaints of these 140 patients were nausea (53.6%), vomiting (32.1%), abdominal pain (11.4%), diarrhea (45.7%), anorexia (43.6%) and loss of taste (5.6%). In 3.2% of the patients, only GI symptoms were present, without any respiratory symptoms.

Conclusion: Gastrointestinal symptoms were present at the time of admission in 13.4% of the patients with COVID-19. The most common GI symptom in the patients was nausea. Length of stay in hospital and mortality rate were higher in patients with only GI symptoms. Therefore, GI symptoms should be considered in patients with suspected COVID-19.

ÖZET

Amaç: Coronavirüs hastalığı 2019 (COVID-19); ağır akut solunum sendromu-coronavirus-2 (SARS-CoV-2) virüsün sebep olduğu ve ilk olguların Aralık 2019'da Çin'in Wuhan şehrinde bildirilen hastalıktır. Başlıca solunum sistemi semptomları ile prezente olmaktadır. Ayrıca gastrointestinal (Gİ) sisteme ait semptomlar da görülmektedir. Bu semptomlar hastalığın ilk hatta tek belirtisi olabilir. Çalışmamız ile COVID-19 hastalarında Gİ semptomların prezentasyonu, diğer semptomlarla ilişkisi ve klinik seyir ve prognozunu gösterilmesi amaçlanmaktadır.

Yöntem: Çalışmaya Mart 2020- Haziran 2020 arasında COVID-19 tanısı ile klinik ve yoğun bakım ünitelerinde yatarak tedavi edilen 18 yaşından büyük hastalar dahil edildi. Hastaların başvuru sırasındaki bildirdikleri semptomlar ve klinik takipleri sonucu toplanan verileri değerlendirildi.

Bulgular: COVID-19 olan 1045 hastadan 140 hastada Gİ semptomu saptandı (%13.4). Bu 140 olgunun 75'inde (%53.6) bulantı, 45'inde (%32.1) kusma, 16'sında (%11.4) karın ağrısı, 64'ünde (%45.7) ishal, 61'inde (%43.6) iştahsızlık, tat alamama 3(%5.6) yakınması vardı. Hastaların %3.2'sinde solunum semptomları olmaksızın sadece Gİ semptomları vardı. Hastanede yatış süresi, sadece Gİ semptomları olan COVID-19 hastalarında anlamlı olarak daha yüksekti (p<0.001). Ayrıca dikkat çeken önemli bir nokta olarak mortalite oranları ise sadece Gİ semptomları olanlarda daha yüksek olmasına rağmen istatistiksel olarak anlamlı bulunmadı (p:0.07).

Sonuç: COVID-19 hastalarının %13.4'ünde başvuru esnasında Gİ semptomları mevcuttu. Hastalarda en sık görülen Gİ semptomu bulantı idi. Sadece Gİ semptomu olan hastalarda hastanede yatış süresi ve mortalite oranı yüksekti. Bu nedenle, şüpheli hastalarda COVID-19'un Gİ semptomları akılda tutulmalıdır.

Keywords: SARS-CoV-2, COVID-19, gastrointestinal, symptom, prognosis

Anahtar sözcükler: SARS-CoV-2, COVID-19, gastrointestinal, semptom, prognoz

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INTRODUCTION

The latest coronavirus outbreak, which started in the city of Wuhan, China in December 2019, is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and has caused a pandemic. This outbreak is also commonly known as coronavirus disease 2019 (COVID-19) (1).

SARS-CoV-2 infection is not limited to the respiratory system, and other organs may also be affected (2). In addition to respiratory symptoms, thrombotic complications; myocardial dysfunction and arrhythmia; acute coronary syndrome; acute kidney injury; gastrointestinal (GI) symptoms; hepatocellular damage; hyperglycaemia and ketosis; neurological diseases; ocular symptoms; and dermatological complications can also develop. These clinical courses are the result of the expression of ACE2, the cell entry receptor for SARS-CoV-2 in multiple extrapulmonary tissues (3).

In addition to respiratory transmission, SARS-CoV-2 has the potential for fecal-oral transmission. Long-term presence of SARS-CoV-2's viral RNA has been demonstrated in fecal samples (4). SARS-CoV-2 may present with nausea, vomiting, diarrhea and/or abdominal pain related to the GI system. Other GI symptoms include epigastric pain, belching and anorexia (5-7). Some studies have reported that GI symptoms may appear before the typical respiratory symptoms. Patients with only GI symptoms and without any respiratory symptoms of COVID-19 have been reported (5,8). A recent study demonstrated the possibility of fecal transmission for up to five weeks after the respiratory samples of the patient had tested negative for SARS-CoV-2 RNA (4). While the most mortal complications of COVID-19 include acute respiratory distress syndrome (ARDS), heart failure, kidney failure, liver damage and multi-organ dysfunction syndrome, GI symptoms can contribute significantly to morbidity in infected patients (9).

Complications, such as transaminitis (the most common), acalculous cholecystitis, acute pancreatitis, diffuse hepatic necrosis, hypomotility, ileus, intestinal ischaemia requiring emergency surgery and bowel resection, have been reported in critically ill patients with COVID-19. Despite the fact that these GI complications are caused by rare adverse pharmacological events and metabolic or electrolyte disorders, small vessel thrombosis or viral enteric neuropathy induced by SARS-CoV-2 are the two potential hypotheses that require further investigation (10-12).

In our study, we examined the GI symptoms in patients who were hospitalised due to a diagnosis of COVID-19 in order to investigate the effect of SARS-CoV-2 on the GI system. We investigated the prevalence of the GI symptoms associated with SARS-CoV-2 infection and its relationship with respiratory symptoms. We evaluated the effect of GI symptoms on the clinical course and prognosis.

METHODS

Study design and participants

This retrospective, single-center study included 1,045 patients confirmed to have COVID-19, who were over 18 years of age and hospitalised for treatment and follow-up at Gulhane Training and Research Hospital between 1 March and 30 June 2020. Ethical approval for the study was obtained from the local ethics committee (ethics committee number: 2020/13/274).

SARS-CoV-2 infection was confirmed by a reverse transcription-polymerase chain reaction (RT-PCR) test and/or a computed tomography (CT) scan of the chest in all patients. The patients who did not meet the inclusion criteria were excluded from the study. Demographic data; results of the RT-PCR test; respiratory and digestive symptoms at the time of admission; laboratory data; and clinical results (discharge and death) were obtained from the patients' medical records (patient files) and the hospital's health information system records. Clinical data were collected in a table. Combined throat/nasal smear samples, which were obtained from the upper respiratory tract mucosa in all patients at the time of admission, were submitted to the COVID-19 diagnostic laboratory under the appropriate conditions for virus transport. The diagnosis of COVID-19 was confirmed by the RT-PCR method.

Statistical analysis

SPSS (V22.0) software was used for all statistical analyses. The overall prevalence of GI and respiratory symptoms was presented with a 95% confidence interval. Normal distribution of the variables was evaluated by visual methods and the Kolmogorov-Smirnov test. Continuous variables were

expressed as medians, and categorical variables were expressed as numbers and percentages. Quantitative variables were compared using the Mann-Whitney U and Kruskal-Wallis tests. Pearson's chi-squared or Fisher's exact tests were used for comparing the qualitative variables. A p-value of <0.05 was considered statistically significant.

RESULTS

The study included 1,045 patients with COVID-19, confirmed by an RT-PCR test and/or a CT scan of the chest. Among the 1,045 patients with COVID-19 included in the study, 585 (56%) were male and the median age was 53 (range: 18-98) years. The median age was found to be 53 (18-93) in male patients and was 54 (18-98) in female patients (p:0.07). Of the cases, 58.5% (611) were RT-PCR positive, and in 78.4%, the CT scan of the chest was found to be compatible with COVID-19 pneumonia. Follow-up of 926 patients (88.6%) was performed in the clinical wards for COVID-19, and 119 patients (11.4%) were followed up in the intensive care unit. The mortality rate was found to be 7% (73). The most common symptoms at the time of admission were fever (40.9%), dyspnoea (32.9%) and coughing (26.4%). The (median) length of hospital stay was 7.0 days (range: 0-43). Asymptomatic cases constituted 32.3% (338) of all cases. Asymptomatic patients with COVID-19 were hospitalised for isolation and also for monitoring of symptoms, since the healthcare infrastructure in Turkey was suitable at the beginning of the pandemic, between March and June 2020.

GI symptoms were identified in a total of 140 (13.4%) patients, 77 (13.2%) of whom were male and 63 (13.7%) of whom were female. The median age of the patients with GI symptoms was 49.5 (range: 19-90). The median ages of the male and female patients were 49 (range: 20-90) and 51 (range: 19-88), respectively (p:0.89). At least one GI symptom was reported in 13.4% (140) (95% CI: 11.39-15.61) of the cases. Only GI symptoms were identified in 3.2% of patients (33) (95% CI: 2.18-4.41), and in 10.2% (107) (95% CI: 8.47-12.24) of all patients, GI symptoms were accompanied by other symptoms. When all cases (n= 1,045) were evaluated, the most common GI symptoms were reported as nausea (7.2%), diarrhea (6.1%) and anorexia (5.8%) (Figure 1). Nausea was the most common GI symptom in both male and female patients (Table 1). A single GI symptom was identified in 6.6% (69) of the patients with COVID-19, and multiple GI symptoms were identified in 6.8% (71) of cases. The symptoms in these 140 patients were nausea in 75 (53.6%), vomiting in 45 (32.1%), abdominal pain in 16 (11.4%), diarrhea in 64 (45.7%), anorexia in 61 (43.6%) and loss of taste in three (5.6%). Among all cases, only 33 patients had GI symptoms, and the most common symptoms in these cases were nausea (51.5%), diarrhea (48.5%) and anorexia (42.4%). The differences in GI symptoms according to age are presented in Table 2. Diarrhea was not reported in any of the patients over 80 years of age, and anorexia was not reported in any of the patients over 60 years of age (p:0.01, p:0.04, respectively).

Length of stay in the hospital was significantly higher for patients with COVID-19 who only had GI symptoms (p<0.001). The mortality rate was higher for patients with only GI symptoms; however, there was no statistical significance (p:0.07). The demographic and clinical characteristics of the patients with COVID-19 are presented in Table 3.

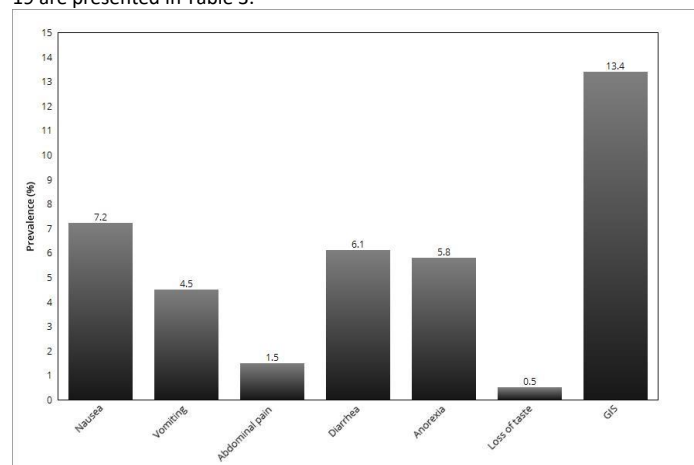


Figure 1. The prevalence of the gastrointestinal (GI) symptoms in patients with COVID-19

Table 1. Evaluation of the gastrointestinal symptoms in different genders

Symptoms	Female (n=460)		Male (n=585)		P value
	N	(%)	N	(%)	
Nausea	37	8.0	38	6.5	0.34
Vomiting	19	4.1	28	4.8	0.61
Abdominal pain	6	1.3	10	1.7	0.60
Diarrhea	29	6.3	35	6.0	0.83
Anorexia	30	6.5	31	5.3	0.40
Loss of taste	1	0.2	4	0.7	0.28

Table 2. Examination of age-related differences in gastrointestinal symptoms

Symptoms	Age Groups								p
	18-40 (n=298)		41-60 (n=376)		61-80 (n=277)		>80 (n=94)		
	n	(%)	n	(%)	N	(%)	n	(%)	
Nausea	18	6.0	37	9.8	14	5.1	6	6.4	0.08
Vomiting	11	3.7	21	5.6	9	3.2	6	6.4	0.35
Abdominal pain	4	1.3	10	2.7	1	0.4	1	1.1	0.12
Diarrhea	22	7.4	30	8.0	12	4.3	0	0.0	0.01
Anorexia	11	3.7	32	8.5	14	5.1	4	4.3	0.04
Loss of taste	3	1.0	2	0.5	0	0.0	0	0.0	0.31

Table 3. Demographic and clinical characteristics of COVID-19 patients

Item, No (%)	Only Respiratory No.=567	Only Digestive No. =33	Digestive respiratory No.=107	+ Without symptoms No.=338	any	P value
Age (years)*	55 (18-98)	49 (22-85)	50 (19-90)	51 (18-93)		<0.001
Gender						
Female	234 (41.3)	15 (45.5)	48 (44.9)	163 (48.2)		0.24
Male	333 (58.7)	18 (54.5)	59 (55.1)	175 (51.8)		
Age Groups						
18-40	143 (25.2)	8 (24.2)	34 (31.8)	113 (33.4)		<0.001
41-60	187 (33)	20 (60.6)	43 (40.2)	126 (37.3)		
61-80	172 (30.3)	3 (9.1)	25 (23.4)	77 (22.8)		
>80	65 (11.5)	2 (6.1)	5 (4.7)	22 (6.5)		
RT-PCR						
Negative	234 (41.3)	18 (54.5)	43 (40.2)	139 (41.1)		0.49
Positive	333 (58.7)	15 (45.5)	64 (59.8)	199 (58.9)		
positive CT scan	468 (82.5)	15 (45.5)	85 (79.4)	251 (74.3)		<0.001
Length of stay*	6 (1-28)	14 (3-23)	8 (0-43)	8 (0-18)		<0.001
Admission to ICU	60 (10.6)	4 (12.1)	13 (12.1)	42 (12.4)		0.85
Mortality	29 (5.1)	4 (12.1)	9 (8.4)	31 (9.2)		0.07

No., number of patients * median (range); % column percentage; RT-PCR, Reverse Transcription-Polymerase Chain Reaction; ICU, intensive care unit; CT, Computed Tomography; P<0.05, significant. If P> 0.05, nonsignificant

DISCUSSION

This study was conducted by reviewing the medical records of patients with COVID-19, who were hospitalised between 1 March and 30 June 2020 in a tertiary hospital, which was assigned as a pandemic hospital by the Ministry of Health in Ankara, Turkey.

Fever and respiratory symptoms are the most common and severe symptoms of COVID-19 infection. Studies in China reported the frequency of GI symptoms as 79% in patients with COVID-19 (13-15), supported by studies conducted in the United States (16-17). In a study of 105 patients in Italy, the prevalence of GI symptoms was 8.8% in patients with COVID-19 (18). We found that the prevalence of GI symptoms at the time of admission was comparable to the prevalence reported in other studies. In our study, the prevalence of digestive symptoms was relatively low, found to be 13.4% in patients with COVID-19. The GI symptoms that were most frequently reported in patients with COVID-19 were nausea (7.2%), diarrhea (6.1%) and anorexia (5.8%). There were only GI symptoms in 3.2% of the patients who did not have any respiratory symptoms.

In a meta-analysis study by Zarifian et al., the prevalence of anorexia was the most common GI symptom at 16.2%. It increased to 20% after the correction of pre-existing comorbidities and continued to be the most common GI symptom in patients with COVID-19 (19). In meta-analysis by Mao et al., the most common symptoms in patients were diarrhea (9%), nausea or vomiting (6%) and abdominal pain (3%) (20). In their meta-analysis study, Cheung et al. demonstrated a higher prevalence of anorexia (26.8%) as the most common GI symptom in cases of COVID-19. Nonetheless, after comorbid chronic conditions were eliminated, diarrhea outpaced anorexia, which was the most common symptom (21).

Although rare, the patient may present GI symptoms in the absence of respiratory symptoms. When only respiratory symptoms are monitored as the case definition for COVID-19, patients may be overlooked or delayed in terms of diagnosis. This may contribute to widespread transmission within families or communities. In addition, GI symptoms may be associated with an underlying comorbid disease and are mostly not due to COVID-19; however, it is still necessary to pay attention to them and consider the possibility of COVID-19 as a cause (22-23). Nonetheless, COVID-19 can also present with constipation or other uncommon GI symptoms (24).

The role of COVID-19 in the pathological mechanisms related to the GI system has not yet been clarified. Nonetheless, since the virus targets ACE2 in human cells, it infects the cells expressing ACE2 cell receptors in the bowel in the same way. In addition, viral particles have been detected for longer periods of time in fecal samples of patients with COVID-19, usually accompanied by diarrhea.²¹ The diagnostic kit used in the COVID-19 diagnostic laboratory was not validated for fecal samples; therefore, the presence of viral particles in fecal samples from the patients in our study could not be investigated. We report this as a limitation of our study.

In the present study, the length of stay in the hospital was significantly higher in patients with only GI symptoms. We observed that the mortality rate was slightly higher in patients with only GI symptoms. This can be explained by comorbidities. Contrary to our study, Papa et al. found that the length of stay in hospital and mortality rates were lower in patients with GI symptoms (18). In the present study, patients who initially presented GI symptoms had longer stays in the intensive care unit. The mortality rate was slightly higher in the group of patients with GI symptoms. However, this difference was not statistically significant. Different results have been reported regarding the severity of the disease in the presence of GI symptoms. In a symptom analysis study based on the severity of COVID-19 by Guan et al. (according to the community-acquired pneumonia guidelines published by the American Thoracic Society), the presence of diarrhea was higher in patients with severe illness compared to the patients with non-severe illness (5.8% and 3.5%, respectively). This suggested a relationship between the presence of diarrhea and the severity of the disease (25). Similarly, there was an increased necessity for mechanical ventilation in patients with COVID-19 who had symptoms of diarrhea, nausea and vomiting, and ARDS was detected at a significant level compared to patients without GI symptoms (26). In a case series of 138 patients, Wang et al. found that 14 patients (10.1%) had diarrhea present at the onset of the disease, and it was not associated with the need for further intensive care (5).

There are some limitations of this study. This is retrospective study. Also we were not able to perform a detailed review of the patients' medical histories regarding GI symptoms and comorbidity. The presence of SARS-CoV-2 was not investigated in fecal samples from the patients with the aim of demonstrating the tropism of SARS-CoV-2 in patients with GI symptoms.

As a result, 13.4% of the patients with COVID-19 reported GI at the time of admission. This rate is significantly low considering the high rates reported in literature on the subject. The most common digestive symptom in patients was nausea. In 3.2% of the patients, there were only GI symptoms, without any respiratory symptoms. The length of stay in the hospital was prolonged in patients who only had digestive symptoms. However, the mortality rate did not differ significantly between patients with only respiratory symptoms and those with combined respiratory and GI symptoms. In conclusion, fever and respiratory symptoms are commonly reported symptoms; however, patients may present only with GI symptoms. Therefore, every clinician should be particularly attentive when encountering a patient with these symptoms.

Conflict of interest

No conflict of interest was declared by the authors.

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