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Article

The Gastrointestinal Manifestations in Patients with COVID-19 and their Clinical Correlates in An Adult Iraqi Population Sample

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Abstract: The gastrointestinal system is one of the many organs in the body that have been affected by the new viral illness known as coronavirus disease 2019 (COVID-19). To find out the GIT symptoms are into patients with Covid-19 and how they correspond with the severity of the illness. At the Al-Shifaa facility, 172 patients infected with COVID-19 participated in our study. A clinical examination, laboratory tests (CRP, D.Dimer, and serum ferritin), a chest CT scan, and a medical history were performed on each patient. The severity of the illness and other factors were taken into consideration while evaluating the gastrointestinal symptoms. Data collection from 172 patients, 91 patients infected with COVID-19 infection, 91 patients (52.9%) had GIT manifestation, while 81 patients (47.1%) had without GIT manifestation. According to the severity 117 patients had severe infection of them 60 patients (51.3%) had GIT manifestation and 57 patients (48.7%) without GIT manifestation; 31 patients had moderate infection 20 patients (64.5%) of them had GIT manifestation, and 11 patients (35.5%) without, 24 patients had mild infection 11 patients (45.8%) had GIT manifestation, and 13 patients(54.2%) without. According to gender, 82 patients(47.7%) were female (50 patients (61.0%) had GIT manifestation and 32 patients (39.9%) without), 90 patients (52.3%) were male (41 patients (45.65%) had GIT manifestation and 49 patients (54.4%) without). By comparison of inflammatory markers (in the form of CRP titer, D.Dimer, and sr. ferritin) which were 99.21 ± 13.71, 2.13 ±0.28, and 642.66±49.95 respectively, in those with SARS-CoV-2 infection and 83.37±8.69, 2.19±0.34 and 606±58.57, respectively, for those with no GIT symptoms (p-value =0.34, 0.89, and 0.62, respectively). GIT manifestations are common symptoms in patients with COVID-19. The incidence of GIT manifestations is not affected by the disease severity in SARS-CoV-2 infection. Inflammatory markers (in the form of CRP titer, ferritin, and D-dimer) are not related to the incidence of GIT manifestations in COVID–19 infection.

Keywords: Gastrointestinal, COVID-19, Inflammation

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1. Introduction

1.1 Background

It is the cause of the coronavirus disease 19 (COVID-19) pandemic [1,2]. The range of mortality rates was 4.3% to 15%. SARS-CoV-2 can produce respiratory symptoms, including cough, SOB, and chest pain with or without hypoxia, as well as general symptoms including fever, fatigue, and headache. It can also cause asymptomatic infections or serious, life-threatening illnesses. COVID-19 can also cause a wide range of extra-pulmonary symptoms. [3]. Among the gastrointestinal symptoms being mentioned

are anorexia, vomiting, nausea, diarrhea, abdominal pain, and discomfort [4]. The most common clear gastrointestinal symptom is diarrhea, although anorexia is reported far more often and is challenging to assess objectively [5]. The median length of diarrhea had been three days (range 1-4 days), and the median number of evacuations each day was four (range 2-6 days) [6]. Most patients had loose, non-dehydrated feces, and no cases of severe diarrhea were seen [7].

Patients with digestive symptoms experienced a substantially longer duration between the start of symptoms and hospital admission (9 versus 7.3 days) compared to those without GI manifestations [7].

1.2 Pathophysiological bases:

The disorders of the GIT in SARS-CoV-2 appear multifactorial, which can be explained by the following disorders:

1.2.1 Stimulation of ACE receptors:-

When the viral spike protein attaches to the receptors on the cell's surface, Angiotensin Converting Enzyme 2 (ACE 2), SARS-CoV-2 can infect a host cell [8].

Both the proximal as well as distal intestines had significant levels of ACE 2 expression [9]. Therefore, its gastrointestinal manifestation may be explained by the virus's highest level of invasiveness and the large number of its attachment receptors along the GIT [5].

1.2.2 Gut-lung axis disturbances:-

The term "gut microbiota" refers to the more than 1014 cells that make up the human GIT and are composed of 500–1000 different kinds of bacteria [10].

The immune system and microbiota have a well-balanced two-way relationship in which the immune system influences the microbiota's composition and activities, while the microbiota is essential to the immune system's growth and maturation. Human illness may result from a disturbance of this equilibrium [10].

Evidence of the significant connection between the gut microbiota and other organs is growing greater these days [11]. The gut-lung axis refers to the connection between the immunological and respiratory systems in the distal GI tract [12].

Recent research has connected alterations in immune function to dysbiosis, or changes in the makeup and activity of microorganisms in the gastrointestinal and respiratory systems, which can cause lung injury [13].

1.2.3 Direct and indirect damage to the intestinal epithelium by inflammatory response :

Inflammation or intestinal injury accompany the symptoms of the digestive system. Systemic inflammation results from a loss in intestinal integrity and the presence of gut bacteria that can trigger the production of pro-inflammatory cytokines by both adaptive and innate immune cells [14].

1.2.4 Antibiotic and antiviral use:

The use of antibiotics may be another factor contributing to changes in gut flora. Antibiotics cause dysbiosis and make people more vulnerable to inflammatory diseases and new infections. They may also result in diarrhea linked to antibiotics [10].

2. Materials and Methods

2.1 Design and settings:

172 SARS-CoV-2-infected patients who were hospitalized for treatment at AL-Shifaa Hospital - Baghdad Teaching Hospital between February 15, 2021, and November 30, 2021, are included in this cross-sectional investigation.

2.2 Exclusion group:

An excluded group of patients were pregnant women, patients age younger than 18 years, and patients who is known cases of chronic GI diseases.

2.3 Ethical consideration:

After outlining the purpose of the study, each participant gave their verbal agreement before any data was collected. Every patient has the full, unconditional right to discontinue treatment at any moment. Patients were reassured that their data would only be used for research reasons and that the study would guarantee data confidentiality.

2.4 Data collection:

Demographic and clinical characteristics of patients at the time of admission were collected. These data included : age, gender, smoking habits, and comorbidities (Hypertension, diabetes mellitus, chronic kidney disease, chronic lung disease, ischemic heart disease, heart failure, chronic liver disease, malignancy).

Clinical data, which included gastrointestinal symptoms at the time of admission, were also recorded and include diarrhea, vomiting, and abdominal pain.

Laboratory investigations was send for each patient in plain tubes, and send for the following investigations: CRP titer, D. dimer, Serum ferritin, CBC, renal and liver function , in addition to radiological investigation in the form of a CT scan of the chest.

2.5 Patient categorization:

The patients were categorized according to the WHO guideline into three groups:

Severe cases are characterized as those that meet any or all of the following criteria: respiratory distress and saturation less than 90%, arterial partial pressure of oxygen (PaO2) / percentage of inspired oxygen (FiO2) below 300 mmHg, or cases with chest imaging that clearly showed lesion progression within 24 to 48 hours of more than 50%. Mild cases: imaging shows no signs of infection. In moderate instances (less than 50%), radiological evidence of pneumonia includes fever as well as respiratory symptoms.

2.6 Data analysis:

All of the data will be examined using fundamental descriptive statistics in SPSS. Continuous variables are described as mean +/- standard deviation (SD), whereas binomial variables will be expressed as frequency and percentage. Categorical variables, that were expressed as percentages and numbers, were examined using chi-square analysis. A statistically significant p-value was defined as one that was higher than 0.05.

3. Results and Discussion

Result

3.1 Demographic and clinical characteristics of the patients:

The current study included 172 COVID-19 patients; 82 patients (47.7%) of them were female, and 90 patients (52.3%) were male, see Table 1.

Table 1. The clinical and demographic data of patients (n = 172)

		N (%), mean ± SE
Gender	Female	82 (47.7%)
	Male	90 (52.3%)
co-morbidities	No co-morbidities	39 (22.7%)
	Have co-morbidities	133 (77.3%)
Age group	less than 30 yrs.	13 (7.55%)
	Between 30 and 50 years.	50 (29.06%)
	More than 50 years.	109 (63.3%)
Presence of the GIT sump.	Without GIT sym.	81 (47.1%)
	GIT sym.	91 (52.9%)
Type of GIT symptom	Diarrhea	50 (29%)
	Vomiting	43 (25%)
	Abdominal pain	32 (18%)
Severity	Severe	117 (68.0%)
	Moderate	31 (18.0%)
	Mild	24 (14.0%)
CRP		91.75 ± 8.33
D-dimer		2.17 ± 0.22
S. ferritin		625.74 ± 38.11

3.2 Categorization of patients

Patients were categorized into three groups: mild, moderate, and severe based on the WHO guideline. Accordingly, 24 patients (14%) were found to have mild infection, 31 patients (18%) had moderate infection, and 117 patients (68%) had severe infection, see Figure 1.

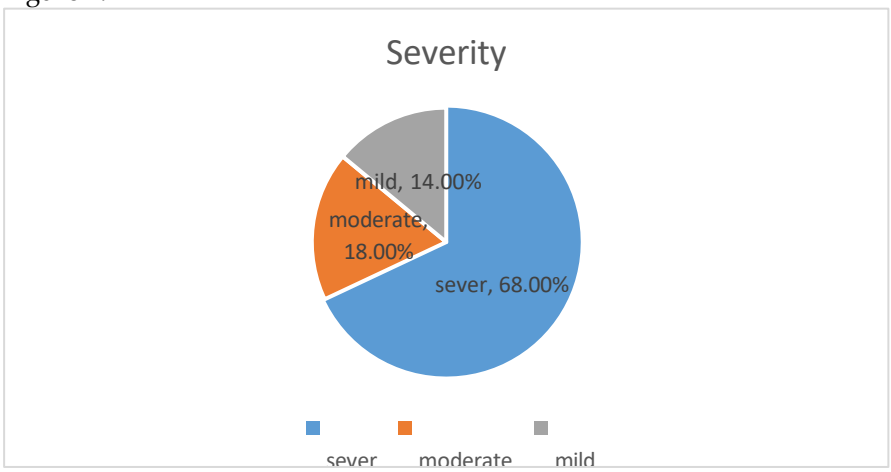

Figure 1. Proportion of mild, moderate, and severe cases of COVID-19

3.3 The association between the severity of COVID-19 infection and the GIT manifestations

From the 117 patients with severe SARS-CoV-2 infection, 60 patients (51.3%) out of them had GIT manifestations, while 20 patients (64.5%) out of 31 patients with moderate infection had GIT manifestations, and 11 patients (45.8%) out of 24 patients with mild infection had GIT manifestations.

No statistically significant association was found between disease severity and type of presenting symptom (p-value 0.31), see Figure 2.

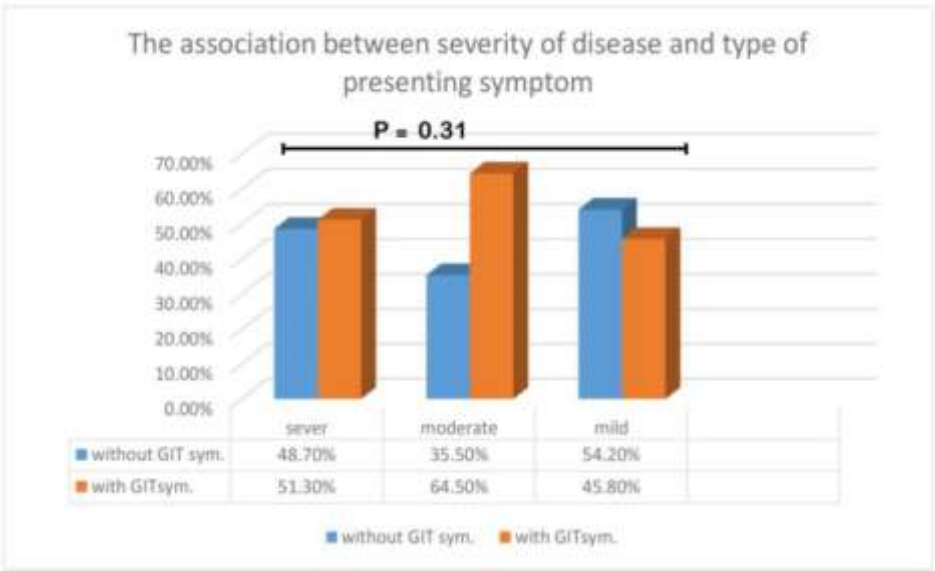

Figure 2. The association between severity of disease and the GIT manifestations in COVID-19 patients.

3.4 The association between gender and age with the GIT manifestations in patients with COVID-19 infection.

Regarding female gender, 32 out of 82 (39%) had no GIT symptoms, and 50 out of 82 (61.0%) had GIT symptoms. While in the male gender, 49 out of 90 (54.4%) had no GIT symptoms, and 41 out of 90 (45.6%) had GIT symptoms, a statistically significant association was found between gender and the GIT manifestations (p-value 0.04), see Table 2.

Regarding the age group of the patients: those patients with an age group of less than 30 years; 7 patients (53.8%) out of 13 had GIT symptoms, while those with an age group of 30 years or older had no GIT symptoms.-50 yrs. 24 patients (48.0%) out of 50 had GIT manifestations, and those with an age group of more than 50 yrs. Fifty-five patients (50.4%) out of 109 had GIT manifestations. No significant statistical association was found between the age group of patients with SARS-CoV-2 and GIT manifestations (p-value = 0.39), see Table 2.

Table 2. The association between the gender and age group of patients with COVID-19 infection and the GIT manifestations.

		Symptom		Total	p-value
		Without GIT sym.	GIT sym.		
Gender	Female	32 (39.0%)	50 (61.0%)	82 (100.0%)	0.04*
	Male	49 (54.4%)	41 (45.6%)	90 (100.0%)	
Age	< 30	7 (53.8 %)	6 (46.1%)	13 (100%)	0.39
	30 – 50	24 (48%)	26 (52%)	50 (100%)	
	> 50	55 (50.4%)	54 (49.5%)	109 (100%)	

3.5 The association between the level of inflammatory markers and the GIT manifestations

The mean level of CRP, D-dimer, and sr. ferritin in patients with no GIT symptoms were 83.37 ± 8.69, 2.19 ± 0.34, and 606.72 ± 58.57, respectively, while the mean level of CRP, D. Dimer, and sr. Ferritin in patients with GIT symptoms were 99.21 ± 13.71, 2.13 ± 0.28, and 642.66 ± 49.95, respectively. No significant statistical association was found (p-value 0.34, 0.89, and 0.62, respectively), see Table 3.

Table 3. Mean ± SE of CRP, D-dimer, and s. Ferritin according to GIT manifestations in COVID-19 patients.

	Symptom	Mean ± SE	p-value
CRP	no-GIT sym.	83.37 ± 8.69	0.34
	GIT sym.	99.21 ± 13.71	
D-dimer	no-GIT sym.	2.19 ± 0.34	0.89
	GIT sym.	2.13 ± 0.28	
s. ferritin	no-GIT sym.	606.72 ± 58.57	0.62
	GIT sym.	642.66 ± 49.95	

Discussion

Although the COVID-10 infection mostly affects the lungs, it may also impact other organs such as the kidneys, gastrointestinal tract, or heart muscle.

GIT symptoms occurred in 52.9% of the 91 participants in this research. The incidence of gastrointestinal symptoms was 47%, which was comparable to the current results, according to a retrospective research conducted by Alexandra et al. that included 634 American patients with a COVID-19 diagnosis [15]. In addition, a study showed a higher incidence of gastrointestinal problems: 61% of patients hospitalized to the Massachusetts hospital had GI symptoms overall [11].

Some studies found that people infected with COVID-19 had a lower risk of gastrointestinal complaints. They all demonstrate that GI symptoms were present in 30% of patients at the time of presentation [1]. However, 10% to 12% of patients experienced

GI issues, according to pooled data collected by an early meta-analysis conducted by a study till March 2020 [16].

This discrepancy in the results could be explained by the following: GI symptoms were not identified during the early stages of the pandemic outbreak until the first case was reported in the United States, when a patient's stool tested positive for COVID-19. As medical attention increased quickly, the available medical staff was trained to concentrate primarily on severe and evident respiratory symptoms and life-threatening complications and to provide prompt isolation.

Of the GI symptoms recorded in this study, diarrhea accounted for 29%, vomiting for 25%, and stomach pain for 18%. An Italian study of 292 COVID-19-infected individuals found that 27% for the participants experienced diarrhea, which is consistent with our results [17]. Although the study. A report that as many as 39% of patients in this American study had diarrhea [15], an Egyptian survey found that the prevalence of diarrhea of COVID-19 patients is only 10% [18]. With a P value of 0.04, female patients in the current research were more inclined than male participants to come up with gastrointestinal symptoms (61% vs. 45%).

An Italian study similarly discovered in China that patients with and without GI signs did not significantly vary in their clinical outcomes [19]. This outcome was comparable to the conclusion reached from the meta-analysis of 6064 COVID-19 patients [20]. While an Indian study revealed a higher severity of COVID-19 infection in patients with GI manifestations compared to those without GI symptoms, Alexandra et al. demonstrated that patients with GI manifestations had a lesser degree of illness than those without GI manifestations [15]. The authors explained this discrepancy by suggesting that either dietary differences or different (less virulent) genotypes of SARS-CoV-2 in different countries could be to blame [4]. Further research is necessary to determine the best explanation for this, though.

We found no difference between individuals without GI symptoms and those with GI symptoms in terms of the levels of inflammatory indicators for COVID-19 infection, such as serum ferritin, D-dimer, and CRP titer [11]. According to other research, patients with SARS-CoV-2 who experienced gastrointestinal symptoms, which were linked to less severe disease, had lower levels of inflammatory markers [17,15], whereas patients with GI symptoms, which were linked to more severe disease, had higher levels of inflammatory markers [18, 4].

4. Conclusion

4.1 Conclusions:

1. Gastrointestinal manifestations are common symptoms in patients with SARS-CoV-2, and diarrhea was the most common symptom.
2. The incidence of GIT manifestations does not affected by the disease severity in SARS-CoV-2 infection.
3. Inflammatory markers (in the form of CRP titer, sr. ferritin, and D-dimer) does not related to the incidence of GIT manifestations in SARS-CoV-2 infection.
4. The incidence of GIT manifestations occurs more in female patients in SARS-CoV-2 infection.

4.2 Recommendations:

1. Recognition of GIT manifestations as a part of SARS-CoV-2 acute infection can limit unnecessary GI investigations during active disease.
2. Further studies are need to be performed to explain the role of feco-oral transmission in patients with SARS-CoV-2 infection, and the protection measures should be considered regarding this issue.

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