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ORIGINAL RESEARCH

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Epidemiological features and consequences of COVID-19 in patients with and without gastrointestinal symptoms in southwestern Iran. A retrospective observational study

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Abstract

Background and Aims: Some studies have shown that in addition to respiratory symptoms, gastrointestinal (GI) manifestations reported in patients with coronavirus disease 2019 (COVID-19). The aim of this study was to compare the epidemiological features and consequences of COVID-19 in patients with and without GI symptoms.

Methods: This retrospective observational study concluded on 15,323 COVID-19 patients with GI symptoms and 95,724 patients without symptoms. All symptoms and comorbidities of the patients collected. To investigate the differences between qualitative variables in the two groups, χ^2 test was used. Logistic regression analysis also used to identify determinants of mortality in patients with COVID-19.

Results: During the course of the study, 111,047 cases of COVID-19 occurred. Of these, 13.8% of patients had GI symptoms, and 9.9% of deaths due to COVID-19 occurred in these patients. The most common reported GI symptoms among COVID-19 patients were nausea, vomiting, and diarrhea. In addition, comorbidities, such as diabetes, cardiovascular disease, and thyroid disease were significantly higher in patients with GI symptoms. The result of multiple logistic regression showed that the chance of mortality is higher in a patient with COVID-19 who have dyspnea, fever, cough, hypertension, cardiovascular disease, diabetes, immunodeficiency, chronic kidney disease, thyroid disease, chronic pulmonary disease, and male gender. The chance of death was lower in people with GI symptoms.

Conclusion: According to the findings of this study, nausea, vomiting, and diarrhea were the most common GI symptoms. Also, the chance of death is higher in people with co-morbidities such as cardiovascular diseases, diabetes, and high blood pressure. Therefore, it is necessary to follow these people closely.

KEYWORDS

COVID-19, epidemiology, gastrointestinal symptoms, Iran, mortality

1 | BACKGROUND AND AIMS

An outbreak of severe acute respiratory syndrome caused by a virus from the coronavirus family reported in Wuhan, China, in December 2019.[1,2] At the beginning of 2020, the World Health Organization (WHO) introduced coronavirus disease 2019 (COVID-19) as the main cause of this viral outbreak.[3] The disease is extremely contagious,[4] as it has spread around the world In a very short period of time,[5,6] thus the WHO declared it as a global pandemic on March 11, 2020.[7] By June 2023, more than 690 million people were infected, and about 6.9 million died due to COVID-19 worldwide. More than 7.6 million people had been infected in Iran.[8]

The COVID-19 classic symptoms include dry cough, fever, and shortness of breath,[3] and the average incubation period of the disease has been confirmed as 6.4 days.[9] The disease is mainly transmitted through human-to-human contact routes via respiratory droplets.[1] However, some studies demonstrated that, in addition to respiratory symptoms, gastrointestinal (GI) manifestations, reported in these patients.[7,10,11] Early reports from Wuhan, China indicated that 2%–10% of the patients with COVID-19 had GI symptoms, such as abdominal pain, loss of appetite, diarrhea, vomiting, and nausea.[12] In another study, the incidence of GI symptoms was reported as ranging from 1% to 38%,[10] and the virus was detected in fecal samples of 51% of the patients with COVID-19.[13] It indicates possible fecal–oral transmission of the virus.[14] Also, Jin and colleagues and Lin and colleagues showed 28.5%,[14] and 61% [14] of COVID-19 patients had symptoms of GI. Xao and colleagues also showed that 53.4% of people displayed virus excretion in their faces within 1–12 days.[15] The high prevalence of symptoms of GI in patients with Severe Acute Respiratory Syndrome has previously been reported as about 16%–73%.[16,17] The presence of the virus in the GI tract and presentation of GI symptoms can be explained by binding ability of the virus to angiotensin-converting enzyme 2 (ACE2), which is expressed in intestinal cells of epithelial.[18]

Intestinal manifestations pose diagnostic challenges for physicians in the initial treatment of COVID-19 patient's particular in patients with mild to moderate symptoms, because the general believe is based on the respiratory symptoms of this disease and other symptoms of the disease are not taken into account. Therefore, understanding the prevalence and mechanism of GI symptoms can help describe these symptoms better. In addition, improving patient's knowledge about the GI symptoms of COVID-19 can contribute to early identification of these patients and prevent the spread of the disease throughout the community.[19] Therefore, a detailed report on the prevalence of these symptoms and the consequences of COVID-19 patients with GI symptoms, it should be provided by health policymakers for better and more accurate decisions and the public to be aware of the targeted symptoms and modes of disease transmission. Therefore, this study was done to investigate the epidemiological characteristics and clinical consequences in COVID-19 patients with and without GI symptoms in southern Iran.

2 | METHOD

The present retrospective observational study examined 111,047 patients with COVID-19 which were admitted in hospitals covered by Abadan University of Medical Sciences (AUMS) in the southwest of Khuzestan province, Iran. The population of this region, using national census in 2020 and the databases of health centers, was estimated 627,970, based on the annual growth rate. All infected patients with COVID-19 were recruited in this study from March 1, 2019 to September 27, 2021.

Confirmation of the definite COVID-19 cases was done via RT-PCR targeting using nasal and throat swabs or chest CT scans. People with normal vital signs (e.g., respiration, blood pressure, and pulse rates), the levels of saturated oxygen above 93%, and moderate symptoms were requested to stay home and self-quarantine and were followed by health professionals daily. People with severe symptoms, such as shortness of breath, chest pain, and the levels of saturated oxygen <90% were hospitalized. Patients with saturated oxygen levels between 90% and 93% were either hospitalized or home quarantine.

Duplicate cases were identified and eliminated based on the national identity number of the individuals. The patients were divided into two groups, patients with GI symptoms ($n = 15,323$) and without GI symptoms ($n = 95,724$). First, demographic characteristics, symptoms, and other comorbid diseases were compared between the two study patients groups, then the role of comorbid diseases and symptoms in disease mortality rate and survival rates were comparatively evaluated in all subjects. Finally, the survival of patients with GI symptoms was compared in terms of comorbid diseases and clinical symptoms.

The study variables included age, sex, final outcome (e.g., recovery and death), symptoms (e.g., vomiting, diarrhea, abdominal pain nausea, and GI bleeding, shortness of breath, fever, cough, violation of smell and taste, fatigue, sore throat, muscle pain headache, and dizziness and anorexia), as well as comorbidities, including diabetes, cardiovascular disease (CVD), liver disease, kidney disease, chronic lung disease, immune deficiency, thyroid disease, and a history of contact with hospitalized infected cases in the intensive care unit (ICU).

The protocol of this study reviewed and confirmed by the Ethics Committee of AUMS (code: IR. AUMS. REC.1399.051). All aspects of this study were done concerning AUMS' ethical code.

2.1 | Statistical analyses

Number and percentage were used for qualitative analysis and median for quantitative analysis. χ^2 and Fisher's exact test were used for evaluation the differences between qualitative variables between the two study groups (patients with and without GI symptoms). The Mann–Whitney test also used to evaluate the age difference among patients due to abnormal age of the participants. To evaluate predictors associated with outcome in patients with COVID-19, we

used multivariate logistic regression. At first, we performed univariate analysis and then selected the variables that had significant at the level of 0.2. We used the forward LR and the best model is the variables in Table 3. In addition, the use of multiple logistic regression, Controls possible confounding factors. We used two-sided tests in the statistical analysis. $p < 0.05$ were considered as statistically significant. Data analysis was performed using SPSS, version 25.0 and EXCEL software 2016.

3 | RESULTS

During the course of the study, 111,047 cases of COVID-19 occurred in the cities affiliated to AUMS. The mean age of patients was 36 years (IQR [interquartile range] 28–48). A total of 57.10% of the patients were male, of these 13.79% (n = 15,323) had GI symptoms, 55.85% (n = 8559) had GI symptoms, and 96.57% (n = 14,798) had history of contact with suspected or definite cases of COVID -19. Also, 1.48% of patients (n = 1650) died, of whom 9.87% (163) had GI symptoms (Table 1).

The most common symptoms of GI reported by the study participants were nausea and vomiting (n = 4783, 31.24%) and diarrhea (n = 3864, 25.21%) (Table 1).

The median age of patients with GI symptoms was 36 years (IQR: 28–48) and in patients without GI symptoms was 36 years (IQR: 28–48). In both study groups, the highest frequency of the disease was reported in age group of 20–34 years (35.40% of patients with GI symptoms vs. 35.10% of patients without symptoms of GI), and the lowest frequency was observed among 5-year-old patients (1% of patients with GI symptoms vs. 1.10% of patients without symptoms of GI) (Table 1).

Overall, the highest frequency of the disease in both male and female patients reported in the age group of 20–34 years, while the

TABLE 1 Demographic and clinical characteristics of patients with and without GI symptoms.

Variable	Total (n = 111,047) Number (%)	Patients with GI manifestations (n = 15323) Number (%)	Patients without GI manifestations (n = 95,724) Number (%)	p Value
Age, median (IQR)	36 (28–48)	36 (28–48)	36 (28–48)	0.20
Sex				
Male	63439 (57.10)	8559 (55.85)	54,880 (57.33)	0.001
Female	47,608 (42.90)	6764 (44.15)	40,844 (42.67)	
Symptoms				
Fever	52,717 (47.47)	7311 (47.71)	45,406 (47.43)	0.53
Cough	42,556 (38.32)	3406 (22.22)	39,150 (40.89)	<0.001
Dyspnea	31,875 (28.70)	6320 (41.24)	25,555 (26.69)	<0.001
Muscular pain	27,897 (25.12)	3996 (26.07)	24,501 (25.59)	<0.001
Sore throat	13,524 (12.17)	1144 (7.46)	12,380 (12.93)	<0.001
Headache	15,400 (13.86)	4169 (27.20)	11,231 (11.73)	<0.001
Decreased sense of smell, taste	8718 (7.85)	712 (4.64)	8006 (8.36)	<0.001
Comorbidities				
CVD	4381 (3.94)	691 (4.50)	3690 (3.85)	<0.001
Diabetes	5983 (5.38)	877 (5.72)	5106 (5.33)	0.04
Hypertension	3396 (3.05)	397 (2.59)	2999 (3.13)	<0.001
Immunodeficiency	204 (0.18)	32 (0.20)	172 (0.17)	0.44
Chronic liver disease	180 (0.16)	20 (0.13)	160 (0.16)	0.29
Thyroid disease	201 (0.18)	40 (0.26)	161 (0.16)	0.01
Chronic kidney disease	915 (0.82)	133 (0.86)	782 (0.81)	0.51
Chronic pulmonary disease	1738 (1.56)	254 (1.65)	1484 (1.55)	0.32
Hospitalization history in ICU	246 (0.22)	24 (0.15)	222 (0.23)	0.04
Exposure to disease	10,1501 (91.40)	14,798 (96.57)	86,703 (90.57)	<0.001
Mortality	1650 (1.48)	163 (1.06)	1487 (1.55)	<0.001

Abbreviations: CVD, cardiovascular disease; GI, gastrointestinal; ICU, intensive care unit; IQR, interquartile range.

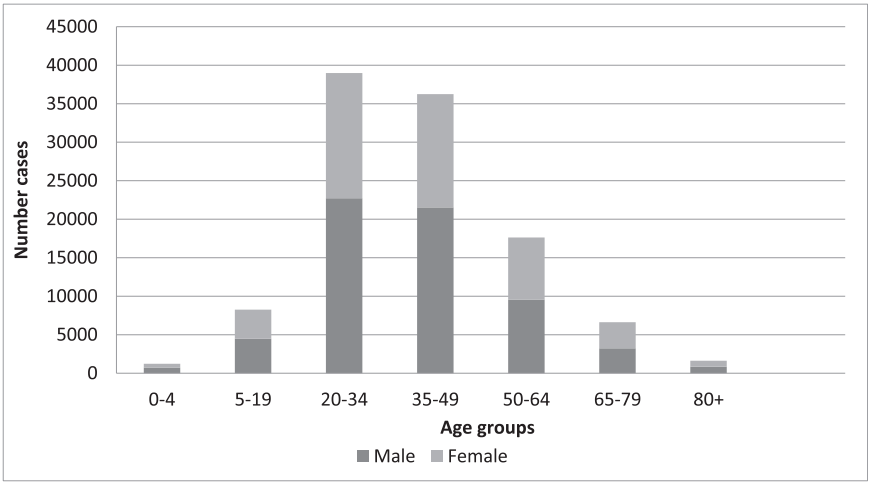

FIGURE 1 The frequency of coronavirus disease 2019 patients by age and sex.

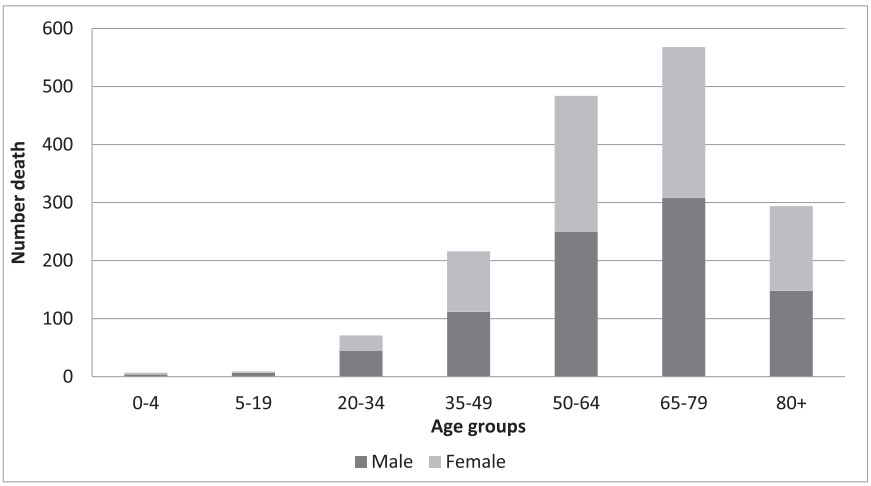

FIGURE 2 The frequency of the coronavirus disease 2019 patient's death by age and sex.

lowest frequency in both genders seen in patients under 5 years of age (Figure 1).

The highest frequency of deaths in both genders was reported in the age group of 65–79 years, while the lowest frequency was in male patients under 5 years of age and female patients aged 5–19 years old (Figure 2).

Besides, comorbidities such as diabetes (877 (5.72%) vs. 5106 (5.33%)) ($p = 0.04$), CVDs (691 (4.50%) vs. 3690 (3.85%)) ($p < 0.001$), thyroid disease (40 (0.26%) vs. 161 (0.16%)) ($p = 0.01$) were higher in patients with symptoms of GI than in patients without symptoms of GI. Moreover, hypertension was higher in patients without GI symptoms (2999 (3.13%) vs. 397 (2.59%)) ($p < 0.001$) (Table 1).

Cough, loss of taste and smell, and sore throat were significantly higher in patients without GI symptoms ($p < 0.001$) than in patients with GI symptoms. In addition, muscle pain, shortness of breath, and headache were significantly higher in patients with GI symptoms ($p < 0.001$) than in patients without GI symptoms. Patients without GI symptoms displayed higher mortality rate (1.55% in patients without GI symptoms vs. 1.06% in patients with GI symptoms). ($p < 0.001$). A history of contact with suspected or definite cases of COVID-19 was more common in patients with GI symptoms compared to those without GI symptoms (96.57% vs. 90.57%) ($p < 0.001$) (Table 1).

Among the 15,323 COVID-19 patients with GI symptoms, no survivors were significantly older than those who survived (Middle age 65 years (IQR 56–75) vs. 36 (IQR 28–48)) ($p < 0.001$). The chance of comorbidities, such as heart disease, hypertension, diabetes, immunodeficiency, liver and chronic lung diseases, ICU stay were significantly higher in COVID-19 no survivors than in survivors ($p < 0.05$) (Table 2).

Multiple logistic regression analysis showed that predictors of COVID-19 deaths included dyspnea (odds ratio [OR] = 1.722, 95% confidence interval [CI]: 1.531–1.937), fever (OR = 1.409, 95% CI: 1.256–1.580), cough (OR = 1.213, 95% CI: 1.075–1.368), hypertension (OR = 2.633, 95% CI: 2.296–3.019), CVD (OR = 1.335, 95% CI: 1.160–1.537).

Diabetes (OR = 1.704, 95% CI: 1.497–1.939), immunodeficiency (OR = 2.043, 95% CI: 1.153–3.620), chronic kidney disease (OR = 2.122, 95% CI: 1.656–2.721), thyroid disease (OR = 4.588, 95% CI: 2.199–9.575), chronic pulmonary disease (OR = 1.581, 95% CI: 1.225–2.041), digestive symptoms (OR = 0.543, 95% CI: 0.431–0.685).

TABLE 2 The baseline characteristics of survivors and nonsurvivors in COVID-19 patients with GI Symptoms.

Variable	Total (*n* = 15,323) Number (%)	Survivors (*n* = 15,160) Number (%)	Nonsurvivors (*n* = 163) Number (%)	*p* Value
Age, median (IQR)	36.00 (28–48)	36.00 (28–48)	65 (56–75)	<0.001
Sex				
Male	8559 (55.85)	8473 (55.89)	86 (52.76)	0.42
Female	6764 (44.15)	6687 (44.11)	77 (47.24)	
Symptoms				
Fever	7311 (47.71)	7228 (47.67)	83 (50.92)	0.40
Cough	3406 (22.22)	3363 (22.00)	43 (26.38)	0.19
Dyspnea	6320 (41.24)	6249 (41.22)	71 (43.55)	0.55
Muscular pain	3996 (26.07)	3966 (26.16)	30 (18.40)	0.23
Sore throat	1144 (7.46)	1137 (7.50)	7 (4.29)	0.11
Headache	4169 (27.20)	4130 (27.24)	39 (23.92)	0.35
Comorbidities				
CVD	691 (4.50)	668 (4.40)	23 (14.11)	<0.001
Diabetes	877 (5.72)	835 (5.50)	42 (25.76)	<0.001
Hypertension	397 (2.59)	353 (2.32)	44 (26.99)	<0.001
Immunodeficiency	32 (0.20)	29 (0.19)	3 (1.84)	<0.001
Chronic pulmonary disease	254 (1.65)	248 (1.63)	6 (3.68)	0.04
Chronic kidney disease	133 (0.86)	122 (0.80)	11 (6.74)	<0.001
Exposure to disease	14,798 (96.57)	14,649 (96.62)	149 (91.41)	0.03
Hospitalization history in ICU	24 (0.15)	22 (0.14)	2 (1.22)	0.001

Abbreviations: COVID-19, coronavirus disease 2019; CVD, cardiovascular disease; GI, gastrointestinal; ICU, intensive care unit; IQR, interquartile range.

In addition, the role of age was (OR = 1.075, 95% CI: 1.071–1.078), and male gender was 1.1 (OR = 1.122, 95% CI: 1.011–1.245) (Table 3).

4 | DISCUSSION

In this retrospective observational study that recruited 111,047 COVID-19 patients in southern Iran to evaluate and compare the clinical features and mortality of COVID-19 patients with and without GI symptoms. Of these, 15,323 (13.79%) had GI symptoms, and 1.48% of patients (1650) died, of which 9.87% (163) had GI symptoms.

In our study, of 111,047 patients, 15,323 cases (13.79%) had GI symptoms. GI symptoms reported in different studies are very different. A meta-analysis on 60 studies and 4243 patients showed that 17.6% of patients had symptoms of GI. Accordingly, Grassia (17.6%),[1,20] Guan (5%),[21] Cheng (3.5%),[22] Fang (22.4%),[23] Zhou (4.7%),[24] Zhang (39.6%),[2] Wang (10.1%),[25] Liu (8%),[26] Peng (13.4),[27] Zhao (3%),[28] Chen (2%),[29] Xu (5.6%).[30] This difference is due to the different sample size of the studies as well as the difference in the age of the patients, the cultural, and economic and health status of different regions, the access to health and treatment facilities, and the time of the study, which caused the GI symptoms to be different in them. In addition, colleagues showed the presence of GI symptoms in COVID-19 patients. It seems that due to prolonged hypoxemia, the cell necrosis caused by tissue hypoxia may damage mucosal cells and the GI tract, resulting in scarring and bleeding.[18] Regarding the mechanism of the occurrence of GI symptoms, the ACE2 receptor is thought to be involved in the pathogenesis of COVID-19, this receptor is present plentifully in the GI tract. The novel coronavirus can bind to these receptors through prominent protein appendages on its surface and causes GI symptoms. GI problems can also be caused by irritation of the stomach and intestines following a lung infection and appear as the first sign of the disease, or in the absence of the disease, the disease may be more difficult for the person to tolerate due to other causes, such as specific behaviors or eating habits.[7,11,31,32]

In the present study, diarrhea reported in 3.5% of all patients. Compared to other studies, diarrhea has been reported less. As such, Guan (3.8%),[21] Fang (22.4%),[26] Zhou (4.7%),[24] Yang (7.4%),[33] Zhang (12.9%),[2] Wang (10.1%),[25] Liu (8%),[26] Tian (2–49.5,[18] a meta-analysis study (13%),[34] Ha and colleagues (12.5%),[35] Jin (18.2%),[14] Lin (24.2%),[36] Jin and colleagues (8.1%),[14] and Lin and colleagues (24.2%)[36] Showed diarrhea in patients. The results of a review study

TABLE 3 Predictor variables of mortality in COVID-19 patients based on the results of multiple logistic regression.

Predictors	Odds ratio (95% CI)	*p* Value
Age	1.075 (1.071–1.078)	<0.001
Sex		
Female	Reference	
Male	1.122 (1.011–1.245	0.03
CVD		
No	Reference	
Yes	1.335 (1.160–1.537)	<0.001
Diabetes		
No	Reference	
Yes	1.704 (1.497–1.939)	<0.001
Hypertension		
No	Reference	
Yes	2.633 (2.296–3.019)	<0.001
Immunodeficiency		
No	Reference	
Yes	2.043 (1.153–3.620)	0.01
Chronic kidney disease		
No	Reference	
Yes	2.122 (1.656–2.721)	<0.001
Thyroid disease		
No	Reference	
Yes	4.588 (2.199–9.575)	<0.001
Chronic pulmonary disease		
No	Reference	
Yes	1.581 (1.225–2.041)	<0.001
Dyspnea		
No	Reference	
Yes	1.722 (1.531–1.937)	<0.001
Cough		
No	Reference	
Yes	1.213 (1.075–1.368)	0.002
Fever		
No	Reference	
Yes	1.409 (1.256–1.580)	<0.001
Digestive symptoms		
No	Reference	
Yes	0.543 (0.431–0.685)	<0.001

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; CVD, cardiovascular disease.

also showed that the most common GI symptom was diarrhea in both children and adults (2%–49.5%).[31] There might be several causes for diarrhea, including infection, medication, or may occur during treatment procedure. Viral infection has been shown to change the intestinal permeability, which may disrupt the function of enterocytes. The results showed that intestinal problems were associated with elevated severity of the infection.[37]

In the present study, the most common GI symptoms reported by the patients were vomiting and nausea (n = 4783, 31.24%), which was more than other studies. Accordingly, China (5%), Fang (29.4% nausea) (15.9% vomiting), Zhou (3.7%), Yang (1.3%), Zhang (17.3% nausea), and (5% vomiting), Wang (nausea (10.1%)/vomiting (3.6%), Zhao (2%), Chen (2%), Han (11.7%), Lin (nausea (17.9%)/vomiting (4.2%), Redd (nausea (8.7%)/vomiting) (4.5%), Luo (nausea (11.7%)/vomiting (10.4%), and Hajifathalian (nausea (15.9%)/vomiting (8.6%)), reported the occurrence of GI symptoms, nausea, and vomiting in COVID-19 patients.[2,21,23–25,28,29,33,36,38–41] According to the results of a review study, vomiting in children was more common compared to adults (3.6% vs. 15.9%).[18] These contradictions may be due to different sample sizes of various studies as well as differences in the cultural, economic, and health status of the affected areas, which has led to a wide variation in the prevalence of chronic diseases across different regions.

In the present study, the prevalence of anorexia was 2.9%, which was less than other studies. According to the findings of a review study, anorexia was the most common GI symptom among adults (39.9%–52.2%).[18] Lin and colleagues (17.9%),[36] Zhang (12.2%),[2] Wang and colleagues (39.9%),[25] Pan and colleagues (39.9%),[42] Wang (10.1%),[43] Han (49.5%),[38] Nobel and colleagues (22.7%),[11] Redd (34.8%),[39] luo (15.8%),[40] and Hajifathalian (22.7%),[41] found that anorexia or decreased food intake were common symptoms during infectious diseases, inflammation, and malignant diseases. Anorexia is induced by the cytokines activity in the brain. Key cytokines involved in illness-induced anorexia and weight loss include tumor necrosis factor-alpha and interleukin-1β.[44]

In this study, the results of logistic regression showed a significant relationship between diabetes and COVID-19 mortality rate, that is, the mortality rate in patients with diabetes was 70.4% higher than nondiabetic patients. There is a two-way relationship between diabetes and COVID- 19.[45] The results of our study were consistent with the results of other studies.[46–49] The higher mortality rate in diabetics can be attributed to a weakened immune system in these patients.[50] Pulmonary dysfunction in diabetic patients and also their lung capacity is reduced and they have respiratory problems.[51] COVID-19 can also affect the pathogenicity of diabetes as well as blood glucose control,[48] all of which together can increase death rate in these individuals.

In this study, a significant relationship observed between thyroid disease and COVID-19 mortality rate. There is evidence that COVID-19 patients have lower Thyroid Stimulating Hormone and T3 (triiodothyronine) levels which is positively associated with the severity of COVID-19 disease.[52]

In our study, regression results showed a statistically significant relationship between COVID-19 mortality and CVD, that is, the risk of COVID-19-related death was 33.5% higher in patients with CVD than in patients without CVD. The reason for higher rate of COVID-19 -related mortality among CVD patients is still unknown.[53] However, some studies have shown that COVID-19 patients with CVDs displayed reduced cardiac function and accelerated myocardial infarction, as well as increased metabolic and myocardial demand, which in turn increase the risk of death. It should be noted that many antiviral drugs can cause heart failure, arrhythmias, or other cardiovascular disorders.[45]

The results of logistic regression in this study showed that mortality rate was 45% lower in patients with symptoms of GI than in patients without symptoms of GI for example, Farnoosh and colleagues found that the frequency of anorexia was 9.1% among recovered patients, 4% among no survivors. They also found that nausea rate was 7.2% in recovered patients and 9.4% in no survivors, while the prevalence of diarrhea was 4.6% in survived patients and 4% in no survivors, and vomiting rate was 2.6% in recovered patients and 8% in no survivors.[54] Grassia and colleagues showed that 11.8% of COVID-19 patients with mild to moderate symptoms and 17.1% of patients with severe symptoms reported GI symptoms.[20] In a meta-analysis, 11.8% of the patients with mild to moderate symptoms and 17.1% of patients with severe symptoms reported GI symptoms.[7] Tabata and colleagues, revealed that diarrhea was prevalent in 11% of all patients, 12% in patients with moderate symptoms, and 11% in patients with severe symptoms.[55] This variation can be attributed to several different sample sizes across the studies.

4.1 | Strengths and limitations

One of the limitations of our study, radiological and laboratory results were not available for further analysis. Although, we included possible confounding variables such as age, gender, and comorbidities, but there may also be uncontrolled confounding variables. This paper benefited from having a large sample size and examined all cases of the disease, both mild and severe, while most of the previous studies have examined exclusively patients with severe forms of COVID-19.

5 | CONCLUSION

According to the findings of this study, nausea, vomiting, and diarrhea were the most common GI symptoms. Also, the chance of death is higher in people with co-morbidities such as CVDs, diabetes, and high blood pressure. Therefore, it is necessary to follow these people closely.

AUTHOR CONTRIBUTIONS

Habibollah Azarbakhsh: Conceptualization; formal analysis; methodology; writing—original draft; writing—review and editing. **Leila Moftakhar**: Conceptualization; investigation; writing—original draft; writing—review and editing. **Aliasghar Valipour**: Project administration; software; supervision; writing—review and editing. **Alireza Mirahmadizadeh**: Data curation; validation; writing—review and editing. **Hekmat Allah Moradi**: Visualization; writing—original draft; writing—review and editing. **Elahe Piraee**: Conceptualization; methodology; software; visualization; writing—original draft; writing—review and editing. All authors have read and approved the final version of the manuscript. Elahe Piraee had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data will be available upon request.

TRANSPARENCY STATEMENT

The lead author Elahe Piraee affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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