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ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

ORIGINAL PAPER
ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

Prevalence and clinical significance of gastrointestinal manifestations in COVID-19

ARCHIVES OF HELLENIC MEDICINE 2024, 41(1):62–69
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2024, 41(1):62–69

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Επιπολασμός και κλινική σημασία των γαστρεντερικών εκδηλώσεων στην COVID-19

Περίληψη στο τέλος του άρθρου

OBJECTIVE **The goal of this study was to determine the prevalence of gastrointestinal manifestations in coronavirus disease 2019 (COVID-19) and to show the identification of potential connections between gastrointestinal manifestations and outcomes.** METHOD **This was a retrospective single-centre cohort study, enrolling 205 COVID-19 patients at Saiful Anwar Genera Hospital in Malang, Indonesia, from October 2020 to February 2021. All patients were confirmed by real-time polymerase chain reaction (real-time PCR). Demographics and clinical characteristics, laboratory data, and clinical outcomes were analyzed.** RESULTS **Among 205 patients, 163 patients (79.5%) had gastrointestinal manifestations, including 145 (89.0%) nausea and vomiting, 132 (81.0%) hyporexia/anorexia, 48 (29.4%) abdominal pain, 38 (23.3%) diarrhea, 13 (8.0%) dysphagia, 12 (7.4%) hematemesis/melena, and 4 (2.5%) constipation. In our findings, we revealed that patients with gastrointestinal manifestations were significantly associated with higher body mass index, a longer length of stay, decreased albumin level and increased several parameters, including fibrinogens, D-Dimer, alanine aminotransferase, total bilirubin, random blood glucose, lactate dehydrogenase, ferritin, C-reactive protein, and lactate acid compared to those without gastrointestinal manifestations. Gastrointestinal manifestation in COVID-19 patients was associated with severe/critical degree (odds ratio [OR]: 4.09; 95% confidence interval [CI]: 1.52–10.97; p=0.00) of COVID-19, intensive care unit (ICU) admission (OR: 4.23; 95% CI: 1.24–14.43), and in-hospital mortality (OR: 4.51; 95% CI: 1.41–16.35; p=0.01).** CONCLUSIONS **Gastrointestinal manifestations are frequent in COVID-19 patients and associated with an increased hypercoagulable and inflammatory marker, longer length of stay, severe and critical degree of COVID-19, ICU admission, and in-hospital mortality.**

Key words

Clinical outcome
COVID-19
COVID-19 disease severity
Gastrointestinal manifestation
Mortality

Submitted 27.1.2023
Accepted 11.2.2023

Coronavirus disease 2019 (COVID-19) is a global health issue caused by SARS-CoV-2. The virus was first found in Wuhan, China, in January 2020, and swiftly spread around the world, culminating in a pandemic that infected over two million individuals and impacted global health, economic stability, and social stability.[1] The World Health Organization (WHO) reported 3,930,000 confirmed cases and 122,633 deaths in Indonesia on August 20, 2021, placing it in the top 10 nations with the greatest COVID-19 mortality rates.[2]

COVID-19 commonly manifests as an acute respiratory syndrome, including fever, coughing, and shortness of breath. However, as research on the illness course of COVID-19 progresses, other non-respiratory symptoms have emerged. In COVID-19 individuals, the prevalence of gastrointestinal manifestations such as nausea, vomiting, and diarrhea have been observed to be increasing.[3] According to studies conducted in China, the manifestations in patients infected with SARS-CoV-2 are diverse, with gastrointestinal manifestations accounting for 40–50% of cases.[4,5] A meta-analysis of 47 studies reporting gastrointestinal manifestations revealed that the prevalence of gastrointestinal manifestations (diarrhea, abdominal pain, nausea, and vomiting) was less than 10% in COVID-19 patients.[6]

Although gastrointestinal manifestations are not a characteristic symptom of COVID-19, multiple investigations have established the pathomechanism of SARS-CoV-2 virus infection in the gastrointestinal tract. The interaction of the viral spike protein on the envelope with host receptors, specifically angiotensin-converting enzyme 2 (ACE2), which is abundantly found in glandular cells of the gastrointestinal tract, has been demonstrated to facilitate SARS-CoV-2 virus infiltration into cells.[7] The pathophysiology of COVID-19 in

the gastrointestinal tract is unknown; however, viruses can cause malabsorption, alterations in intestinal permeability, intestinal inflammation due to abnormalities in intestinal microbiota hemostasis, and disturbances in the gut-lung axis balance.[3,8]

Few studies, particularly in Indonesia, have investigated the clinical outcomes of COVID-19 patients with gastrointestinal manifestations. Several other studies have found that COVID-19 patients with gastrointestinal manifestations have a worse disease course.[9,10] The point of the study is to investigate the prevalence of gastrointestinal manifestations in COVID-19 patients and the connection between all these manifestations and disease severity, length of stay, mechanical ventilation use, intensive care unit (ICU) admission, and mortality in COVID-19 patients at Dr Saiful Anwar Hospital in Malang.

MATERIAL AND METHOD

Study design and participants

This retrospective, single-centre, cohort study was conducted between October 2020 and February 2021. This study was approved by the Ethical Committee of Dr Saiful Anwar Hospital in Malang, Indonesia (400/001/K.3/302/2022). We selected randomly 205 confirmed cases of COVID-19 from general wards and intensive care units at Dr Saiful Anwar Hospital in Malang, East Java Province, Indonesia. Our inclusion criteria for confirmed cases were based on the WHO definition with positive real-time reverse transcription-polymerase chain reaction findings SARS-CoV-2 testing on respiratory specimens obtained through nasooropharyngeal swabs.[11]

Data collection

We collected demographic and clinical data from patients, as well as laboratory and clinical outcomes. Signs and symptoms, body mass index (BMI), comorbidities, laboratory results, length of stay, admission to the intensive care unit (ICU), and in-hospital mortality were all acquired from the patients' medical records. According to the Indonesian Guidelines for COVID-19 Prevention and Control, COVID-19 severity is classed as mild to a critical degree.[16] To fill in any gaps, data was gathered as thoroughly as feasible through a review of medical records and discussions with attending physicians and other health care providers. For first time hospital admissions, laboratory tests, such as a complete blood count, coagulation test, inflammatory markers, random blood glucose, liver, and renal function were performed.

Statistical analysis

Percentages and frequency rates were used to quantify categorical variables. Continuous variables with a normal distribution were represented by the mean, while variables with abnormal distribution were represented by the median and interquartile range (IQR). The t-test was employed to compare normally distributed data; otherwise, the Mann-Whitney test was utilized. When comparing proportions for categorical variables, the Chi-square test was employed, and when data was restricted, the Fisher exact test was utilized. Bivariate analysis was used to discover the factors linked with gastrointestinal manifestations. In the bivariate analysis, variables having a p-value of 0.05 are included in the multivariate analysis. For all statistical studies, the Statistical Package for Social Sciences (SPSS), version 25.0 was utilized.

RESULTS

Baseline characteristics of COVID-19 patients

The goal of this study was to evaluate clinical outcomes in patients confirmed with COVID-19 with and without gastrointestinal manifestations, as well as the severity of COVID-19, length of hospitalization, admission to ICU, usage of mechanical ventilators, and mortality. The research data was taken from October 2020 to February 2021 at Dr Saiful Anwar Hospital, Malang, Indonesia. According to the inclusion and exclusion criteria, the study sample was taken randomly from 205 patients diagnosed with COVID-19 according to the WHO diagnostic criteria, who came to the Emergency Room (ER) to enter the isolation ward.

Data on the baseline characteristics of the study sample from 205 patients are provided in table 1. The median age of the study sample was 57 (44–64) years, where the gender found was 107 patients (51.7%) male and 99 female (48.3%). Comorbidity data showed that 73 patients (35.6%) had hypertension, 73 patients (35.6%) had diabetes mellitus, 52 patients (25.4%) had a history of cardiovascular disease, 37 patients (18.0%) had geriatric problems, 33 patients (16.1%) had dyslipidemia, 25 patients (12.2%) had chronic kidney disease (CKD), 10 patients (4.9%) had malignancy, 11 patients (5.4%) had hepatitis infection, 2 patients (1.0%) had human immunodeficiency virus (HIV) infection, 4 patients (2.0%) had autoimmune disease, and 6 patients (2.9%) had hepatobiliary disease. Laboratory findings of hospitalized patients with COVID-19 with and without gastrointestinal manifestations are provided in table 2.

When the patient comes to the ER, we assess the severity of the COVID-19 infection. We reported 52 patients (25.4%) with a mild degree, 67 patients (32.7%) with a moderate degree, 23 patients (11.2%) with a severe degree, and as many as 63 patients (30.7%) with a critical degree. The median length of stay for patients was 7 (5–13) days, of which 43 patients (21.0%) were treated in the ICU, and 18 patients (8.8%) were on a mechanical ventilator. During treatment, we reported that 47 patients (22.9%) died.

Table 1. Demographics and clinical outcomes of COVID-19 patients.

	All COVID-19 (n=205)	GI manifestations (n=163)	Without GI manifestations (n=42)	Z/x² values	p
Age (years), median (IQR)	56 (44–64)	57 (44–64)	54 (41.75–65.25)	-0.379	0.70
Sex, n (%)				0.197	0.66
Male	106 (51.7)	83 (50.9)	23 (54.8)		
Female	99 (48.3)	80 (49.1)	19 (45.2)		
*BMI (kg/m²), median (IQR)**	23.3 (22.2–24.6)	23.4 (22.4–24.7)	21.9 (18.94–24.6)	-3.645	0.00
Comorbidities, n (%)					
Hypertension	73 (35.6)	60 (36.8)	13 (31.0)	0.5	0.48
Diabetes mellitus	73 (35.6)	57 (35.0)	16 (38.1)	0.142	0.71
Cardiovascular disease	52 (25.4)	38 (23.3)	14 (33.3)	1.77	0.18
Chronic kidney disease	25 (12.2)	22 (13.5)	3 (7.1)	1.26	0.26
Dyslipidemia	33 (16.1)	29 (17.8)	4 (9.5)	1.69	0.19
Malignancy	10 (4.9)	8 (4.9)	4 (9.5)	1.72	0.20
HIV	2 (1.0)	1 (0.6)	1 (2.4)	1.08	0.29
Hepatitis infection	11 (5.4)	10 (6.1)	1 (2.4)	0.927	0.34
Geriatric problems	37 (18.0)	65 (39.9)	17 (40.5)	0.005	0.94
Autoimmune disease	4 (2.0)	3 (1.8)	1 (2.4)	0.051	0.82
Hepatobiliary disease	6 (2.9)	6 (3.7)	0 (0)	1.59	0.21
COVID-19 severity, n (%)					
Mild	52 (25.4)	27 (16.6)	25 (59.5)	-5.291	0.00
Moderate	67 (32.7)	56 (34.4)	11 (26.2)	1.002	0.32
Severe	23 (11.2)	22 (13.5)	1 (2.4)	1.788	0.04
Critical	63 (30.7)	58 (35.6)	5 (11.9)	2.795	0.00
Admission, n (%)				6.098	0.01
ICU	43 (21.0)	40 (24.5)	3 (7.1)		
Non-ICU	162 (79.0)	123 (75.5)	39 (92.9)		
Mechanical ventilation	18 (8.8)	16 (9.8)	2 (4.8)	1.065	0.30
Length of stay (days), median (IQR)	7 (5–13)	10 (6–14)	6 (4–7)	-5.022	0.00
In-hospital mortality, n (%)				7.447	0.00
Survivor	158 (77.1)	119 (73.0)	39 (92.9)		
Non-survivor	47 (22.9)	44 (27.0)	3 (7.1)		

Data were presented in n (%) or median (IQR)

Chi-square test (x² values) for categorical variables

Mann-Whitney test for nonparametric test marked with *

IQR: Interquartile range, GI: Gastrointestinal, BMI: Body mass index, HIV: Human immunodeficiency virus, COVID-19: Coronavirus disease 2019, ICU: Intensive care unit

COVID-19 patients with gastrointestinal manifestations: Prevalence of disease severity and clinical outcomes

Table 3 summarizes the baseline characteristics, disease severity, and clinical outcomes of COVID-19 patients with and without gastrointestinal manifestations. We have reported that 163 (79.5%) COVID-19 patients had gastrointestinal manifestations. The prevalence of gastrointestinal manifestations we found, were nausea and vomiting [145 (89.0%)], hyporexia/anorexia [132 (81.0%)], abdominal pain [48 (29.4%)], diarrhea [38 (23.3%)], dysphagia [13 (8.0%)], hematemesis/melena [12 (7.4%)], and constipation [4 (2.5%)] (tab. 3).

The prevalence of mild COVID-19 degree with gastroin-

Table 2. Laboratory findings of hospitalized patients with COVID-19 with and without gastrointestinal manifestations.

Laboratories parameters	Normal value	All COVID-19 (n=205)	GI manifestations (n=163)	No GI manifestations (n=42)	Z values	p
		Median (IQR)				
Hemoglobin, g/dL	13.4–17.7	13.50 (11.1–14.7)	13.50 (11.2–16.0)	13.40 (10.00–14.63)	-0.8333	0.41
WBC, $\times10^3$/L	4.3–10.3	8.37 (6.16–11.32)	8.34 (6.11–11.64)	8.54 (6.71–10.41)	-0.051	0.96
PLT, $\times10^3$/L	142–424	228 (179–347)	224 (181–337)	256 (171–366)	-0.831	0.41
PPT, sec	9.4–11.3	10.96 (10.5–11.25)	10.96 (10.50–11.50)	11.59 (10.65–11.74)	-0.830	0.43
INR	<1.5	1.05 (1.01–1.06)	1.05 (1.02–1.10)	1.10 (1.02–1.14)	-0.052	0.82
aPTT, sec	24.6–30.6	29.04 (27.0–29.24)	29.04 (26.60–29.04)	29.24 (27.78–29.36)	-0.812	0.15
Fibrinogen, mg/dL	154.3–397.9	418.36 (353.20–445.60)	418.36 (409.72–418.47)	353.20 (341.16–360.20)	-11.392	0.00
D-Dimer, mg/L	≤0.5	47.88 (3.38–52.60)	47.88 (24.52–54.32)	1.73 (1.55–2.33)	-10.550	0.00
ALT, U/L	0–41	53.97 (31.5–58.45)	58.45 (37.00–94.60)	42.50 (25.00–53.97)	-2.801	0.00
AST, U/L	0–40	41.00 (21.50–46.00)	42.00 (23.00–45.61)	31.00 (16.75–52.71)	-0.044	0.965
Albumin, g/dL	3.5–5.5	3.46 (3.31–3.67)	3.46 (3.39–3.55)	3.67 (3.46–4.14)	-5.209	0.00
Total bilirubin, mg/dL	<1.0	1.06 (0.54–1.54)	1.54 (1.29–3.29)	1.06 (0.56–1.91)	-6.113	0.00
Potassium, mmoL/L	3.5–5.0	4.01 (3.55–4.11)	3.95 (3.08–4.11)	4.01 (3.83–4.79)	-0.400	0.69
RBS, mg/dL	<200	178.62 (122.00–192.60)	189.49 (133.00–277.80)	157.08 (71.00–216.00)	-2.692	0.00
Urea, mg/dL	16.6–48.5	36.2 (27.35–52.16)	44.20 (22.20–52.16)	36.20 (17.70–44.53)	-1.318	0.19
Creatinine, mg/dL	<1.2	1.13 (0.86–2.41)	1.32 (0.80–2.41)	1.13 (0.63–1.16)	-1.556	0.12
LDH, U/L	240–480	748.0 (638.33–1,017.19)	1,017.19 (748.00–1,235.00)	638.33 (542.30–670.35)	-11.392	0.00
Ferritin, ng/mL	30–400	1,296.39 (963.32–1,496.12)	1,496.12 (1,296.39–1,735.60)	1,296.39 (370.80–1,447.12)	-5.285	0.00
CRP, mg/dL	<0.3	8.74 (2.55–13.41)	10.57 (3.46–26.2)	6.04 (0.40–9.14)	-3.980	0.00
Procalcitonin, ng/mL	<2	0.43 (0.12–2.39)	0.42 (0.12–2.39)	0.48 (0.11–1.21)	-1.702	0.09
Lactate acid, mmol/L	<2	3.57 (2.45–4.02)	3.57 (2.20–4.00)	1.42 (0.66–1.76)	-10.509	0.00

Data were presented in median (IQR)

Mann-Whitney test for the nonparametric test

IQR: Interquartile range, WBC: White blood cell, PLT: Platelet, PPT: Plasma prothrombin time, aPTT: Activated partial thromboplastin time, INR: International normalizing ratio, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, RBS: Random blood sugar, LDH: Lactate dehydrogenase, CRP: C-reactive protein

testinal manifestations was found to be lower than those without gastrointestinal manifestations [27 (16.6%) versus 25 (59.5%); p=0.00). In COVID-19 individuals with gastrointestinal manifestations and those without, there was no significant difference in moderate severity [56 (34.4%) versus 11 (26.2%); p=0.32]). In comparison to COVID-19 patients without gastrointestinal manifestations, we found a considerably greater proportion of severe [22 (13.5%) versus 1 (2.54%); p=0.04] and critical [58 (35.6%) versus 5 (11.9%); p=0.00]) COVID-19 patients with gastrointestinal manifestations.

Our findings show that patients with gastrointestinal manifestations in COVID-19 had a longer median length of hospital stay compared to COVID-19 patients without gastrointestinal manifestations [16 (6–14) versus 6 (4–7) days; p=0.00]. There was no significant difference in the use of mechanical ventilators [16 (9.8%) versus 2 (4.8%); p=0.30]. A higher prevalence of ICU admission was found [40 (24.5%) versus 3 (7.1%); p=0.01] and significantly higher mortality rate in COVID-19 patients with gastrointestinal manifestations compared to those without gastrointestinal manifestations [44 (27.0%) versus 3 (7.1%); p=0.00].

COVID-19 patients with gastrointestinal manifestations: Clinical outcomes

During hospitalization, we observed gastrointestinal manifestations that appeared in patients with COVID-19. Gastrointestinal manifestations included nausea, vomiting, abdominal pain, diarrhea, constipation, hematemesis/melena, hyporexia/anorexia, and dysphagia. The clinical outcomes studied were the length of hospital stay, ICU admission, mechanical ventilator use, and mortality. The

Table 3. Prevalence of gastrointestinal manifestations and its associations with clinical outcomes.

Laboratories parameters	Normal value	All COVID-19 (n=205)	GI manifestations (n=163)	No GI manifestations (n=42)	Z values	p
		Median (IQR)				
Hemoglobin, g/dL	13.4–17.7	13.50 (11.1–14.70)	13.50 (11.2–16.00)	13.40 (10.0–14.63)	-0.8333	0.41
WBC, $\times 10^3$/L	4.3–10.3	8.37 (6.16–11.32)	8.34 (6.11–11.64)	8.54 (6.71–10.41)	-0.051	0.96
PLT, $\times 10^3$/L	142–424	228.00 (179.00–347.00)	224.00 (181.00–337.00)	256.00 (171.00–366.00)	-0.831	0.41
PPT, sec	9.4–11.3	10.96 (10.5–11.25)	10.96 (10.50–11.50)	11.59 (10.65–11.74)	-0.830	0.43
INR	<1.5	1.05 (1.01–1.06)	1.05 (1.02–1.10)	1.10 (1.02–1.14)	-0.052	0.82
aPTT, sec	24.6–30.6	29.04 (27.0–29.24)	29.04 (26.60–29.04)	29.24 (27.78–29.36)	-0.812	0.15
Fibrinogen, mg/dL	154.3–397.9	418.36 (353.20–445.60)	418.36 (409.72–418.47)	353.20 (341.16–360.20)	-11.392	0.00
D-Dimer, mg/L	≤0.5	47.88 (3.38–52.60)	47.88 (24.52–54.32)	1.73 (1.55–2.33)	-10.550	0.00
ALT, U/L	0–41	53.97 (31.5–58.45)	58.45 (37.00–94.60)	42.50 (25.00–53.97)	-2.801	0.00
AST, U/L	0–40	41.00 (21.5–46.00)	42.00 (23.00–45.61)	31.00 (16.75–52.71)	-0.044	0.965
Albumin, g/dL	3.5–5.5	3.46 (3.31–3.67)	3.46 (3.39–3.55)	3.67 (3.46–4.14)	-5.209	0.00
Total bilirubin, mg/dL	<1.0	1.06 (0.54–1.54)	1.54 (1.29–3.29)	1.06 (0.56–1.91)	-6.113	0.00
Potassium, mmoL/L	3.5–5.0	4.01 (3.55–4.11)	3.95 (3.08–4.11)	4.01 (3.83–4.79)	-0.400	0.69
RBS, mg/dL	<200	178.62 (122.00–192.60)	189.49 (133.00–277.80)	157.08 (71.00–216.00)	-2.692	0.00
Urea, mg/dL	16.6–48.5	36.20 (27.35–52.16)	44.20 (22.20–52.16)	36.20 (17.7–44.53)	-1.318	0.19
Creatinine, mg/dL	<1.2	1.13 (0.86–2.41)	1.32 (0.80–2.41)	1.13 (0.63–1.16)	-1.556	0.12
LDH, U/L	240–480	748.00 (638.33–1,017.19)	1,017.19 (748.00–1,235.00)	638.33 (542.30–670.35)	-11.392	0.00
Ferritin, ng/mL	30–400	1,296.39 (963.32–1,496.12)	1,496.12 (1,296.39–1,735.60)	1,296.39 (370.80–1,447.12)	-5.285	0.00
CRP, mg/dL	<0.3	8.74 (2.55–13.41)	10.57 (3.46–26.20)	6.04 (0.40–9.14)	-3.980	0.00
Procalcitonin, ng/mL	<2	0.43 (0.12–2.39)	0.42 (0.12–2.39)	0.48 (0.11–1.21)	-1.702	0.09
Lactate acid, mmol/L	<2	3.57 (2.45–4.02)	3.57 (2.20–4.00)	1.42 (0.66–1.76)	-10.509	0.00

Data were presented in median (IQR)

Mann-Whitney test for the nonparametric test

IQR: Interquartile range, WBC: White blood cell, PLT: Platelet, PPT: Plasma prothrombin time, aPTT: Activated partial thromboplastin time, INR: International normalizing ratio, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, RBS: Random blood sugar, LDH: Lactate dehydrogenase, CRP: C-reactive protein

relationship of each gastrointestinal manifestation to the severity of the disease and clinical outcome is summarised in table 3.

We reported that the manifestations of nausea and vomiting were associated with severe and moderate disease severity (odds ratio [OR]: 3.77; 95% confidence interval [CI]: 1.39–10.22; p=0.00), ICU admission (OR: 4.14; 95% CI: 1.20–14.21; p=0.02), and the incidence of mortality during hospitalization (OR: 4.95; 95% CI: 1.45–16.93; p=0.01). We found no association with nausea, vomiting, and mechanical ventilation (OR: 2.14; 95% CI: 0.47–9.81; p=0.33). The presence of abdominal pain was linked to the severity of the disease at the severe and moderate levels (OR: 6.26; 95% CI: 2.09–18.68; p=0.00), ICU admission (OR: 5.91; 95% CI: 1.57–22.19; p=0.00), and the incidence of mortality during hospitalization (OR: 7.13; 95% CI: 1.91–26.55; p=0.00). Abdominal pain and mechanical ventilation had no association (OR: 2.86; 95% CI: 0.54–14.99; p=0.22). Diarrhea was linked to the severity of the disease in both severe and moderate cases (OR: 3.42; 95% CI: 1.07–10.87; p=0.03). There was no association between diarrhea and mechanical ventilation (OR: 2.86; 95% CI: 0.54–14.99; p=0.22), ICU admission (OR: 4.03; 95% CI: 1.00–16.23; p=0.05), and the incidence of mortality during hospitalisation (OR: 3.47; 95% CI: 0.85–14.19; p=0.08).

Severe and moderate disease severity were related to hematemesis/melena (OR: 13.67; 95% CI: 1.27–146.99; p=0.00), ICU admission (OR: 13.00; 95% CI: 2.55–66.40; p=0.00), and the incidence of mortality during hospitalisation (OR: 18.20; 95% CI: 3.52–94.01; p=0.00). There was no association between hematemesis/melena and mechanical ventilation (OR: 4.00; 95% CI: 0.50–31.98; p=0.19). Hyporexia/anorexia was associated with severe and moderate disease severity (OR: 4.09; 95% CI: 1.51–11.12; p=0.00), ICU admission (OR: 4.69; 95% CI: 1.36–16.15; p=0.01), and the

incidence of mortality during hospitalisation (OR: 5.06; 95% CI: 1.47–17.39; p=0.01). Mechanical ventilation had no correlation with hyporexia/anorexia (OR: 2.37; 95% CI: 0.52–10.89; p=0.27). Dysphagia was associated with severe and moderate disease severity (OR: 12.30; 95% CI: 1.15–131.10; p=0.04), ICU admission (OR: 5.78; 95% CI: 1.09–30.48; p=0.04), and the incidence of mortality during hospitalisation (OR: 5.78; 95% CI: 1.09–30.48; p=0.04). Dysphagia and mechanical ventilation did not appear to be associated (OR: 0.60; 95% CI: 0.03–13.29; p=0.75).

DISCUSSION

The COVID-19 epidemic is still a significant public health concern in Indonesia. Patients with COVID-19 in clinical practice often have typical respiratory symptoms, but as COVID-19 reporting develops, evidence of organ system dysfunction other than respiratory is emerging.[12–14] In this study, more than two-thirds of patients had gastrointestinal manifestations, and the most common were nausea and vomiting (89.0%), hyporexia/anorexia (81.0%), followed by abdominal pain, diarrhea, dysphagia, hematemesis/melena, and constipation (2.5–29.4%) (tab. 3). Another study in Italy showed that hyporexia/anorexia and diarrhea were the most common gastrointestinal manifestations in that study, accounting for 51% and 37.9%, respectively.[3] Several studies have described the manifestations of hyporexia/anorexia associated with elevated levels of C-reactive protein (CRP), leukocytes, and fibrinogen.[15] Other studies have also described hyporexia/anorexia reflecting a cytokine-induced systemic inflammatory state, leading to a cytokine storm syndrome that can worsen the COVID-19 disease course.[16]

COVID-19 patients with gastrointestinal manifestations were reported to have a higher severity in previous investigations.[17] COVID-19 patients with gastrointestinal manifestations showed a greater incidence of critical severity than COVID-19 patients without gastrointestinal manifestations, according to this study. COVID-19 individuals with substantial gastrointestinal manifestations had a higher mortality rate. When comparing COVID-19 patients with to without gastrointestinal manifestations, there were no significant differences in length of stay, ICU admission, or usage of a mechanical ventilator. Another study found that an increase in viral load and viral replication in the gastrointestinal component was linked to an increased prevalence of severe and critical severity in COVID-19 patients with gastrointestinal manifestations. Some of these studies have also illustrated that COVID-19 patients with gastrointestinal manifestations often have no or mild respiratory complaints that cause delays in the initiation of more intensive therapy.[5]

Several hypotheses explaining the involvement of COVID-19 with gastrointestinal manifestations are the presence of SARS-CoV-2 viral invasion of extrapulmonary organs mediated by viral binding to ACE2 receptors expressed in the gastrointestinal tract. In addition, there is direct or indirect damage due to infection with the SARS-CoV-2 virus, which triggers an inflammatory reaction in the gastrointestinal tract. Several studies have described the finding of SARS-CoV-2 nuclei in stool samples in 53.4% of the patients studied. Enteropathic viruses can cause direct damage to the intestinal mucosa and cause gastrointestinal manifestations.[18–20] Intestinal flora plays a vital role in the body's physiology, including its involvement in nutrient metabolism, regulation of the immune system, and antibacterial effects. Another study has described the association with the finding of SARS-CoV-2 protein with dysbiosis of normal flora in the gastrointestinal tract, which affects the effect of the "gut-lung axis", which plays a vital role in the regulation of the immune system.[20–23]

In conclusion, the COVID-19 pandemic is a new worldwide health concern in which the epidemiology, pathogenesis, management and therapy, as well as prognosis are still evolving. We investigated the prevalence and clinical significance of gastrointestinal manifestations in COVID-19. The findings of the present study illustrate that COVID-19 patients with gastrointestinal manifestations have an increased risk of higher severity and higher mortality rates than COVID-19 patients without gastrointestinal symptoms. Our findings are consistent with several studies in other countries. Manifestations that often appear in this study are hyporexia/anorexia, nausea, abdominal pain, vomiting, and diarrhea. Those gastrointestinal manifestations have also been reported in several other studies related to the risk of worsening conditions and mortality. Based on these findings, COVID-19 patients with gastrointestinal manifestations should receive more attention and intensive treatment management considerations related to the risk of increasing severity and mortality rates.

AUTHORS' CONTRIBUTIONS

S., S.M., and B.P.W. designed, directed and supervised the project. T.W.I.D., A.L.H,. and R.B.W. collected the research data, performed the statistic analysis, and wrote the manuscript in consultation with S.

ΠΕΡΙΛΗΨΗ

Επιπολασμός και κλινική σημασία των γαστρεντερικών εκδηλώσεων στην COVID-19

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Αρχεία Ελληνικής Ιατρικής 2024, 41(1):62–69

ΣΚΟΠΟΣ Ο προσδιορισμός του επιπολασμού των γαστρεντερικών εκδηλώσεων στη νόσο COVID-19 και ο εντοπισμός πιθανών συνδέσεων μεταξύ γαστρεντερικών εκδηλώσεων και έκβασης. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Είναι μια αναδρομική μελέτη κοόρτης ενός κέντρου, στην οποία συμμετείχαν 205 ασθενείς με COVID-19 στο Γενικό Νοσοκομείο Saiful Anwar στο Malang της Ινδονησίας, από τον Οκτώβριο του 2020 έως τον Φεβρουάριο του 2021. Όλοι οι ασθενείς επιβεβαιώθηκαν με αλυσιδωτή αντίδραση πολυμεράσης (PCR) σε πραγματικό χρόνο. Αναλύθηκαν δημογραφικά και κλινικά χαρακτηριστικά, εργαστηριακά δεδομένα και κλινικά αποτελέσματα. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Από τους 205 ασθενείς, 163 (79,5%) εμφάνισαν γαστρεντερικές εκδηλώσεις, από τους οποίους 145 (89%) ναυτία και έμετο, 132 (81%) υπορεξία/ανορεξία, 48 (29,4%) κοιλιακό άλγος, 38 (23,3%) διάρροια, 13 (8%) δυσφαγία, 12 (7,4%) αιματέμεση/μέλαινα και 4 (2,5%) δυσκοιλιότητα. Παρατηρήθηκε ότι οι γαστρεντερικές εκδηλώσεις συσχετίστηκαν σημαντικά με υψηλότερο δείκτη μάζας σώματος, μεγαλύτερη διάρκεια παραμονής στο νοσοκομείο, μειωμένο επίπεδο λευκωματίνης και αυξημένες άλλες παραμέτρους, όπως ινωδογόνο, D-Dimer, αμινοτρανσφεράση αλανίνης, ολική χολερυθρίνη, γλυκόζη αίματος τυχαίου δείγματος, γαλακτική αφυδρογονάση, φεριτίνη, C-αντιδρώσα πρωτεΐνη (CRP) και γαλακτικό οξύ, σε σύγκριση με εκείνους χωρίς γαστρεντερικές εκδηλώσεις. Η γαστρεντερική εκδήλωση σε ασθενείς με COVID-19 συσχετίστηκε με σοβαρή νόσηση COVID-19 (σχετικός λόγος [OR]: 4,09, 95% διάστημα εμπισοσύνης [CI]: 1,52–10,97, p=0,00), εισαγωγή στη μονάδα εντατικής θεραπείας (ΜΕΘ) (OR: 4,23, 95% CI: 1,24–14,43) και αυξημένη ενδονοσοκομειακή θνητότητα (OR: 4,51, 95% CI: 1,41–16,35, p=0,01). **ΣΥΜΠΕΡΑΣΜΑΤΑ** Οι γαστρεντερικές εκδηλώσεις είναι συχνές σε ασθενείς με COVID-19 και σχετίζονται με αυξημένους υπερπηκτικούς και φλεγμονώδεις δείκτες, μεγαλύτερη διάρκεια παραμονής στο νοσοκομείο, σοβαρού και κρίσιμου βαθμού COVID-19, εισαγωγή στη ΜΕΘ και αυξημένη ενδονοσοκομειακή θνητότητα.

Λέξεις ευρετηρίου: Γαστρεντερικές εκδηλώσεις, Θνησιμότητα, Κλινική έκβαση COVID-19, Σοβαρότητα νόσου COVID-19

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