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BRIEF COMMUNICATIONS

Effect of Gastrointestinal Symptoms in Patients With COVID-19

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Because of accumulating evidence pointing to continuous person-to-person transmission of coronavirus disease 2019 (COVID-19) in hospital and family settings,[1,2] the World Health Organization has recently declared COVID-19 a public health emergency of international concern. Fever and respiratory symptoms tend to be initial and major, whereas gastrointestinal (GI) symptoms were also observed in a significant portion of patients.[3] Positive findings of reverse transcription polymerase chain reaction further showed that COVID-19 may spread by fecal-oral transmission.[4] In addition, recent studies have shown that the receptor of ACE2, which is essential for cells infected by COVID-19, is highly expressed not only in lung AT2 cells but also in absorptive enterocytes in the ileum and colon.[5,6] These results further confirmed that the digestive system may be a potential route for COVID-19 infection. Therefore, a study exploring the correlation between GI symptoms and patients' symptoms, diagnosis, treatment, and outcomes is of great importance to improve the diagnosis and treatment plan of novel coronavirus–infected pneumonia (NCIP).

Materials and Methods

Study Design

According to the clinical diagnostic standards in the "Diagnosis and Treatment of NCIP"[7] issued by the National Health Commission of the People's Republic of China, suspected infected patients with clinical features of pneumonia could be regarded as clinically confirmed patients. The central hospital of Wuhan is one of the first major hospitals designated by the government to treat patients with NCIP. We enrolled 254 patients clinically confirmed with NCIP from December 20, 2019, through February 9, 2020. Medical staff and nonmedical staff are counted separately. Based on whether they had GI symptoms, patients were divided into GI symptom and non–GI symptom groups. The clinical characteristics, laboratory findings, complications, treatment process, and clinical outcomes were compared between the patients with or without GI symptoms.

Data Collection

The epidemiologic, clinical, laboratory, and radiologic characteristics and treatment outcome data were obtained from medical records. All these data were reviewed by a group of experienced doctors. The recorded information includes medical history, symptoms, signs, potential comorbidities, laboratory findings, and treatment measures.

Statistical Analysis

Categorical variables are described by frequency and percentages, and continuous variables are described by the mean, median, and interquartile range. Patient characteristics were compared by using t tests for continuous variables and chi-squared or Fisher exact tests for categorical variables. All statistical analyses were performed using SPSS, version 23.0, software (SPSS, Chicago, IL). $P \leq .05$ was considered statistically significant.

Results

As outlined in Table 1, this study recruited 254 clinically confirmed patients with NCIP (115 males and 139 females; mean age, 50.6 years; range, 15–87 years), including 93 medical staff and 161 nonmedical staff. Among all patients, 211 (83%), 98 (38.6%), and 66 (26%) complained of fever, cough, and GI symptoms, respectively. The most common complication was pneumonia (209; 82.3%), followed by arrhythmia (16; 0.06%) and shock (7; 0.03%). Patients receiving mechanical ventilation, antibiotics, antivirals, immunoglobulins, hormones, and extracorporeal membrane oxygenation (ECMO) treatment accounted for 7.09%, 97.6%, 75.6%, 59.8%, 88.2%, and 0.008% of the total patients, respectively. At of the end of observation, 46 patients were discharged, 16 died, and 192 continued treatment.

Among nonmedical staff, the proportion of GI symptoms in female patients was significantly higher than in male patients (62.8% vs 37.2%; $P = .033$). Clinical manifestations such as sore throat ($P = .023$), dizziness ($P = .032$), and fatigue ($P = .012$) were also more frequent in patients with GI symptoms. In addition, hemoglobin level in the GI symptom group was significantly lower than in the non–GI symptom group (116.7 [range, 106–127]g/L vs 133 [114–

*Authors share co-first authorship.

Abbreviations used in this paper: COVID-19, coronavirus disease 2019; GI, gastrointestinal; NCIP, novel coronavirus–infected pneumonia.

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Table 1. Clinical Features, Treatment and Prognosis of Patients Infected With 2019-nCoV

		Medical staff				Nonmedical staff			
	Total (N = 254)	Total (n = 93)	GI symptoms (n = 23)	Non-GI symptoms (n = 70)	*P* value	Total (n = 161)	GI symptoms (n = 43)	Non-GI symptoms (n = 118)	*P* value
GI symptoms, n (%)	66 (26.0)	23	23 (100)	0 (0)	—	43	43 (100)	0 (0)	—
Abdominal pain	3 (1.2)	0	0 (0)	0 (0)	—	3	3 (7.0)	0 (0)	—
Vomiting	15 (5.9)	1	1 (4.3)	0 (0)	—	14	14 (32.6)	0 (0)	—
Diarrhea	46 (18.1)	19	19 (82.6)	0 (0)	—	27	27 (62.8)	0 (0)	—
Nausea	21 (8.3)	5	5 (21.7)	0 (0)	—	16	16 (37.2)	0 (0)	—
Age, *y*, median (IQR)	50 (36–65)	36 (31–41)	35 (30–40)	36 (31–42)	.614	62 (49–69)	61 (49–67)	62 (49–70)	.615
Sex, n (%)					.45				.033
Male	115 (45.3)	32	6 (26)	26 (37)		83	16 (37)	67 (57)	
Female	139 (54.7)	61	17 (74)	44 (63)		78	27 (63)	51 (43)	
Symptom, n (%)									
Fever	213 (83.9)	80	19 (83)	61 (87)	.729	133	39 (91)	94 (80)	.157
Sore throat	16 (6.3)	6	0 (0)	6 (9)	.33	10	6 (14)	4 (3)	.023
Dry cough	98 (38.6)	41	7 (30)	34 (49)	.152	57	14 (33)	43 (36)	.712
Expectoration	107 (42.1)	31	6 (26)	25 (36)	.454	76	17 (40)	59 (50)	.286
Chest tightness	67 (26.4)	21	3 (13)	18 (26)	.261	46	8 (19)	38 (32)	.115
Dyspnea	10 (3.9)	2	1 (4)	1 (1)	.435	8	2 (5)	6 (5)	> .99
Dizziness	18 (7.1)	10	4 (17)	6 (9)	.256	8	5 (12)	3 (3)	.032
Headache	28 (11.0)	17	3 (13)	14 (20)	.549	11	3 (7)	8 (7)	> .99
Fatigue	133 (52.4)	52	12 (52)	40 (57)	.809	81	29 (67)	52 (44)	.012
Myalgia	86 (33.9)	41	10 (44)	31 (44)	> .99	45	17 (40)	28 (24)	.073
Sign, median (IQR)									
MAP, *mm Hg*	92 (85–96)	90 (85–96)	88 (83–98)	92 (87–96)	.252	93 (85–98)	90 (85–98)	93 (86–97)	.075
HR, *beats/min*	85 (79–98)	84 (80–100)	82 (76–103)	87 (80–100)	.302	85 (78–98)	86 (78–98)	85 (78–98)	.902
Comorbidities, n (%)									
Hypertension	63 (24.8)	6	0 (0)	6 (9)	.33	57	14 (33)	43 (36)	.712
DM	26 (10.2)	3	0 (0)	3 (4)	.572	23	4 (9)	19 (16)	.321
CHD	17 (6.7)	2	0 (0)	2 (3)	> .99	15	6 (14)	9 (8)	.231
Malignancy	2 (0.8)	1	0 (0)	1 (1)	> .99	1	0 (0)	1 (1)	> .99
CKD	0 (0)	0	0 (0)	0 (0)	—	0	0 (0)	0 (0)	—
CVD	13 (5.1)	1	0 (0)	1 (1)	> .99	12	3 (7)	9 (8)	> .99
CLD	3 (1.2)	1	0 (0)	1 (1)	> .99	2	0 (0)	2 (2)	> .99
COPD	6 (2.4)	1	0 (0)	1 (1)	> .99	5	2 (5)	3 (3)	.61
HIV infection	1 (0.4)	0	0 (0)	0 (0)	—	1	1 (2)	0 (0)	.267
Laboratory findings									
HB, g/L	—	—	112 (109.5–111)	120.2 (112.5–127)	.104	—	116.7 (106–127)	133 (114–141)	.028
WBC, ×10^9/L	—	—	5.5 (2.6–9.2)	5.6 (3.2–6.5)	.962	—	5.9 (3.5–6.3)	5.5 (3.3–6.7)	.708
Neutrophil, ×10^9/L	—	—	5.1 (1.3–7.2)	5 (1.5–8)	.968	—	5.9 (1.7–9.9)	7.6 (2.3–7.7)	.604
LYM, ×10^9/L	—	—	1.1 (0.7–1.2)	1 (0.8–1.1)	.524	—	1 (0.7–1.1)	0.8 (0.7–0.9)	.108
PLT, ×10^9/L	—	—	223 (86–408)	184 (88–237)	.653	—	192 (111–248)	176 (112–186)	.842
CRP, mg/dL	—	—	2.2 (0.7–2.6)	3 (1–2.5)	.491	—	7.3 (2.9–6.6)	3.8 (1.8–5.8)	.021
ALT, U/L	—	—	65.9 (23.3–103.3)	75.6 (44.5–114.8)	.698	—	64.1 (51.2–64.4)	46.6 (31.9–61.2)	.049

Table 1. Continued

		Medical staff				Nonmedical staff			
	Total (N = 254)	Total (n = 93)	GI symptoms (n = 23)	Non-GI symptoms (n = 70)	*P* value	Total (n = 161)	GI symptoms (n = 43)	Non-GI symptoms (n = 118)	*P* value
AST, U/L	—	—	26.4 (12.7–45.5)	40.4 (12.9–65.3)	.271	—	47.8 (18.2–50.6)	53.8 (35.7–58.5)	.44
Albumin, g/L	—	—	35.2 (34.5–38.1)	36.7 (34.7–38.7)	.327	—	35.4 (33.9–36.4)	35 (32.8–37.8)	.648
Globulin, g/L	—	—	39.7 (37.6–42)	38.7 (30.7–43.8)	.766	—	26.1 (22.7–29.4)	28.9 (25.3–31.6)	.185
LDH, U/L	—	—	156.2 (103–194.8)	289 (229–370.3)	.069	—	358.9 (256–425)	312.5 (251.5–335)	.322
CK, U/L	—	—	29.8 (15.8–35)	398.5 (28.1–587.3)	.143	—	316.3 (86–276.5)	201.3 (77.8–294.5)	.359
Creatinine, μmol/L	—	—	68 (64.2–75.5)	67.6 (73.2–79.3)	.981	—	56.9 (43.9–72.1)	70.1 (43.8–95.9)	.217
FBG, mmol/L	—	—	8 (6.2–8.7)	7.7 (6.5–8.1)	.787	—	7.3 (6.3–8.2)	8.3 (6.3–9.5)	.106
Na^+, mmol/L	—	—	142.6 (139.3–145.8)	134.2 (131–136.4)	.05	—	138.9 (134.8–141.9)	139.3 (135–145.4)	.88
K^+, mmol/L	—	—	3.9 (3.3–4)	4 (3.2–4.5)	.934	—	3.3 (3.1–3.5)	9.1 (3.2–4)	.052
PH	—	—	7.4 (7.4–7.5)	7.5 (7.4–7.5)	.485	—	7.4 (7.5–7.5)	7.4 (7.4–7.5)	.9
Sao_2, mmHg	—	—	91 (97–99)	92 (91–99)	.962	—	93 (92–94)	92 (91–97)	.796
Pao_2, mmHg	—	—	74 (62–85)	109 (52–151)	.256	—	84 (65–105)	86 (62–113)	.809
$Paco_2$, mmHg	—	—	42 (33–51)	35 (31–39)	.263	—	35 (31–36)	35 (31–35)	.777
Complications, n (%)									
Pneumonia	209 (82.3)	70	18 (78.3)	52 (74.3)	.787	139	38 (88.4)	101 (85.6)	.798
Shock	7 (2.8)	2	0 (0)	2 (2.9)	> .99	5	1 (2.3)	4 (3.4)	> .99
AHF	6 (2.4)	1	1 (4.3)	0 (0)	.247	5	0 (0)	5 (4.2)	.326
Arrhythmia	16 (6.3)	12	2 (8.7)	10 (14.3)	.724	4	1 (2.3)	3 (2.5)	> .99
ARDS	5 (2)	2	1 (4.3)	1 (1.4)	.435	3	1 (2.3)	2 (1.7)	> .99
Treatment									
MV	18 (7)	5	1 (4.3)	4 (5.7)	> .99	13	2 (4.7)	11 (9.3)	.516
Antibiotics	248 (97.6)	91	23 (100)	68 (97.1)	> .99	157	42 (97.7)	115 (97.5)	> .99
Antivirals	192 (75.6)	63	16 (69.6)	47 (67.1)	> .99	129	31 (72.1)	98 (83.1)	.179
Immunoglobulins	152 (59.8)	62	19 (82.6)	43 (61.4)	.07	90	28 (65.1)	62 (52.5)	.209
Hormones	224 (88.2)	77	20 (86.9)	57 (81.4)	.75	147	37 (86)	110 (93.2)	.204
ECMO	2 (0.8)	2	1 (4.3)	1 (1.4)	.435	0	0 (0)	0 (0)	—
Clinical outcome									
Discharge from hospital	46 (18.1)	32	4 (17.4)	28 (40)	.075	14	4 (9.3)	10 (8.5)	> .99
Staying in hospital	192 (75.6)	59	18 (78.3)	41 (58.6)	.134	133	36 (83.7)	97 (82.2)	> .99
Death	16 (6.3)	2	1 (4.3)	1 (1.43)	.435	14	3 (7)	11 (9.3)	.457

AHF, acute heart failure; ALT, alanine aminotransferase; ARDS, acute respiratory distress syndrome; AST, aspartate transaminase; CHD, coronary heart disease; CK, creatine kinase; CKD, chronic kidney disease; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; CRP, C-reaction protein; CVD, cerebrovascular disease; DM, diabetes mellitus; ECMO, extracorporeal membrane oxygenation; FBG, fasting blood glucose; HB, hemoglobin; HR, heart rate; LDH, lactate dehydrogenase; LYM, lymphocyte count; MAP, mean arterial pressure; MV, mechanical ventilation; nCoV, novel coronavirus; PLT, platelet count; WBC, blood leukocyte count.

141]g/L, respectively; $P = .028$), whereas C-reactive protein (7.3 [range, 2.9–6.6]mg/dL vs 3.8 [range, 1.8–5.8]mg/dL, respectively; $P = .021$) and alanine aminotransferase (64.1 [51.2-64.4]U/L vs 46.6 [31.9-61.2]U/L, respectively; $P = 0.049$) levels were significantly higher than in the GI symptoms group.

However, GI symptoms among medical staff were not significantly correlated with symptoms and laboratory findings. Finally, the GI symptom group appeared to have a similar rate of complications, treatment, and clinical prognosis as the non–GI symptom group among medical and nonmedical staff.

Discussion

The study suggests that GI symptoms are common clinical symptoms in patients with NCIP. Among nonmedical staff, women are more likely to have GI symptoms, accompanied by higher inflammatory levels and poorer liver function. However, no significant correlation between GI symptoms and clinical features was observed among medical staff. In addition, the clinical outcome and treatment of patients with NCIP were not associated with GI symptoms in either medical or nonmedical staff.

A possible explanation for nonmedical staff with GI symptoms being more likely to have more symptoms and poorer liver function is the changes in the intestinal microecology under the dysfunction of the central nervous system. The infection of COVID-19 in intestinal tissues may lead to GI symptoms, such as diarrhea and abdominal pain. Metabolic disorders increase the absorption of harmful metabolites, which will affect the function of the central nervous system through the gut-brain axis and then lead to dizziness and fatigue. Disorders of intestinal metabolism further lead to more harmful metabolites that are harmful to liver tissue.

The reason why medical staff are less susceptible to GI symptoms may be that most of the infected medical staff were younger nurses without comorbidities. In addition, there is less delay from the onset of symptoms to hospital admission. Taking these factors into consideration, we can hypothesize that most of the medical staff infected by COVID-19 had mild symptoms on the day of hospital admission.

There are also some deficiencies in this study. First, the standard diagnosis of patients with NCIP is based on nucleic acid testing, but most cases in our study are clinically confirmed patients, which will inevitably lead to several patients without NCIP being included. Second, most patients were still hospitalized at the time of submission. Therefore, it is difficult to further assess the correlation between GI symptoms and clinical outcomes.

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Conflicts of interest
The authors disclose no conflicts.

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