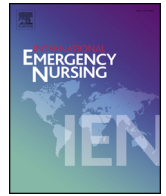




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Clinical characteristics of diarrhea in 90 cases with COVID-19: A descriptive study

Yaru Xiao, Sufang Huang*, Li Yan, Hui Wang, Fang Wang, Ting Zhou, Juan Deng, Mei He

Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, No. 1095 Jiefang Avenue, Qiaokou District, Wuhan, China

ARTICLE INFO

Keywords:

COVID-19
Infection
Diarrhea
Fecal-oral transmission
Gastrointestinal symptoms
Nutrition
Nursing

ABSTRACT

Background: The novel coronavirus disease (COVID-19) has spread worldwide. Herein, we aimed to clarify the epidemiological and clinical characteristics of patients presenting with diarrhea.

Methods: A descriptive design was adopted from Jan 10 to Feb 17, 2020. All the cases included were diagnosed with COVID-19 under the interim guidance of the WHO.

Results: 912 patients with COVID-19 were admitted to hospital, in which, 90 cases (9.87%) presented with diarrhea. Among the 90 cases, 8 cases (9%) presented with diarrhea as the initial symptom, and 24%, 17%, and 24% of the patients complained of nausea, vomiting, and poor appetite, respectively. The most common fecal characteristics on admission were watery stool (64%) and mushy stool (28%). For the defecation frequency, 37% of the cases defecated over three times a day. The median time from illness onset to diarrhea was 3.0 days (IQR 0.0–5.0) and the median duration of diarrhea was 5.0 days (IQR 2.0–9.3).

Conclusion: Clinicians are required to promptly identify the patients with initial diarrhea symptoms and pay adequate attention to the nutrient requirements of the patients with diarrhea during hospitalization. Standardized management is also recommended for the discharge of the patients to avoid potential fecal-oral transmission.

1. Introduction

The novel coronavirus disease (COVID-19) has spread worldwide and the rapidly increasing cases indicate that COVID-19 can be transmitted from person to person [1]. During the current pandemic, droplets and contact are considered the main transmission routes of the novel coronavirus. Although fever and respiratory signs are the common initial and major symptoms, gastrointestinal (GI) symptoms (i.e. diarrhea) have also been observed in 2%–18.1% of the patients [2–7]. It has been reported that some patients showed only gastrointestinal symptoms without other typical manifestations of the COVID-19 infection but were subsequently confirmed to be infected by testing the collected fecal samples [7–9], suggesting the potential occurrence of fecal-oral transmission. Therefore, it is speculated that the digestive system may serve as an alternative infection route. Among the gastrointestinal symptoms in COVID-19 cases including diarrhea, nausea, vomiting, and abdominal pain, diarrhea is the one that possibly increases the chance of potential fecal-oral transmission but could be easily overlooked by health care workers. Herein, we conducted a comprehensive study on the clinical features of ninety COVID-19 patients with diarrhea as the symptom before admission based on our

first-hand experience, aiming to achieve a better understanding of the clinical manifestations of COVID-19 and help the clinicians accurately and promptly identify infected cases.

2. Methods

2.1. Study design and participants

This study was approved by the Medical Ethical Committee of Tongji Hospital (No. TJ-C20200136). We enrolled 90 cases of COVID-19 admitted to our hospital from Jan 10 to Feb 17, 2020, whose diagnosis of COVID-19 was based on the WHO interim guidance. The outcomes of all patients were recorded.

2.2. Data collection

The clinical, laboratory, and treatment outcome data were collected from electronic medical records. The recorded information included demographic data, medical history, underlying comorbidities, symptoms, signs, and laboratory findings. Disease onset was defined as the day when the symptom was noticed. Fecal characteristics during

* Corresponding author.

E-mail address: sfhuang2008@163.com (S. Huang).

<https://doi.org/10.1016/j.ienj.2020.100912>

Received 4 April 2020; Received in revised form 13 July 2020; Accepted 5 August 2020

1755-599X/ © 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Table 1
Demographics and clinical characteristics of patients presenting with diarrhea.

	Patients (n = 90)
Age, years	61.0 (48.3–69.0)
Sex	
Male	51 (57%)
Female	39 (43%)
Comorbidity	57 (63%)
Hypertension	35 (39%)
Diabetes	18 (20%)
Coronary heart disease	15 (17%)
Pulmonary disease	7 (8%)
Cholecystectomy	5 (6%)
Subgastrectomy	1 (1%)
Duodenal ulcer	2 (2%)
Initial symptom	
Fever	65 (72%)
Cough	12 (13%)
Diarrhea	8 (9%)
Dyspnea	3 (3%)
Poor appetite	2 (2%)
Symptoms before admission	
Fever	80 (89%)
Cough	62 (69%)
Fatigue	43 (48%)
Dyspnea	28 (31%)
Chest tightness	28 (31%)
Myalgia	19 (21%)
Asthma	17 (19%)
Hemoptysis	2 (2%)
Abdominal pain	6 (7%)
Pharyngalgia	4 (4%)
Chest pain	8 (9%)
Dizziness	16 (18%)
Headache	16 (18%)
Nausea	22 (24%)
Vomiting	15 (17%)
Poor appetite	22 (24%)
Highest temperature, °C	
37.3–38.0	23/79 (29%)
38.1–39.0	36/79 (46%)
> 39.0	20/79 (25%)
Fecal characteristics	
Mushy	14/50 (28%)
Loose	4/50 (8%)
Watery	32/50 (64%)
Frequency of diarrhea, per day	
1–3	40/63 (63%)
4–6	17/63 (27%)
> 6	6/63 (10%)
Time from illness onset to admission, days	10.0 (6.0–14.0)
Hospital length of stay, days	14.0 (9.0–19.0)
Time from illness onset to diarrhea, days, 31cases	3.0 (0.0–5.0)
Diarrhea length of stay, days, 24cases	5.0 (2.0–9.3)
Nutrition patterns during hospitalization	
General diet	89 (99%)
Enteral nutrition	4 (4%)
Parenteral nutrition	2 (2%)
None	1 (1%)

hospitalization were also included.

2.3. Statistical analysis

Categorical variables were represented by frequency and percentages, and continuous variables were described by mean (SD) if they were normally distributed otherwise by median (IQR). For laboratory results, we had assessed whether the measurements were outside the normal range of laboratory standards of Tongji Hospital. SPSS (version 19.0) was used for all analysis.

3. Results

Among the 912 cases with COVID-19 we retrieved, 90 patients

(9.87%) presented with diarrhea, and their demographics, clinical characteristics, and outcomes were summarized, as shown in Table 1. The median age was 61.0 years (IQR 48.3–69.0), ranging from 22 to 82 years, with the number of male cases slightly outnumbering that of female cases. The top two common initial symptoms were fever and cough, followed by diarrhea which occurred in 8 cases (9%). Besides, 24%, 17%, and 24% of the patients complained of nausea, vomiting, and poor appetite, respectively. Comorbidities were presented in over half of the patients, with hypertension being the most common comorbidity, followed by diabetes and coronary heart disease.

The most common fecal characteristics on admission were watery stool (64%) and mushy stool (28%). As for the frequency of diarrhea, 23 (37%) out of 63 cases defecated over three times a day. The number of cases receiving general diet, enteral nutrition, and parenteral nutrition was 89 (99%), 4 (4%), and 2 (2%), respectively (Table 1).

The median time from illness onset to admission was 10.0 days (IQR 6.0–14.0) and the length of stay in hospital was 14.0 days (IQR 9.0–19.0). The median time from illness onset to diarrhea was 3.0 days (IQR 0.0–5.0) and the median duration of diarrhea was 5.0 days (IQR 2.0–9.3). See Table 1 for details.

Laboratory findings are shown in Table 2. Lymphocyte and albumin counts were below normal in 43% and 46% of all the cases, respectively. C-reactive protein levels were elevated in more than two-thirds of all cases. Routine stool examinations showed normal in most of the

Table 2
Laboratory findings of patients presenting with diarrhea.

	Patients (n = 90)
Stool routine	
Color	
Yellow	31/33 (94%)
Brown yellow	2/33 (6%)
RBC in stool sample	
None	32/33 (97%)
WBC in stool sample	
None	33/33 (100%)
White blood cell count, ×10 ⁹ / L	7.4 (4.8–12.1)
< 4	12/89 (13%)
4–10	47/89 (53%)
> 10	30/89 (34%)
Lymphocyte count, ×10 ⁹ /L	1.2 (0.7–1.7)
< 1.1	38/89 (43%)
≥ 1.1	51/89 (57%)
Haemoglobin, g/L, 89 cases	127.0 (115.0–138.0)
Alanine aminotransferase, U/L	29.0 (15.5–43.5)
≤ 41	64/89 (72%)
> 41	25/89 (28%)
Albumin, g/L	35.7 (31.1–38.3)
< 35	41/89 (46%)
≥ 35	48/89 (54%)
Sodium, mmol/L	140.2 (138.3–142.4)
< 136	10/89 (11%)
≥ 136	79/89 (89%)
Potassium, mmol/L	4.5 (4.0–4.7)
< 3.5	7/89 (8%)
3.5–5.1	71/89 (80%)
> 5.1	11/89 (12%)
Hypersensitive C-reactive protein, mg/L	16.2 (1.9–78.3)
< 1	13/88 (15%)
1–3	15/88 (17%)
> 3	60/88 (68%)
D-dimer, ug/mL	0.8 (0.4–1.9)
< 0.5	30/73 (41%)
0.5–1	14/73 (19%)
> 1	29/73 (40%)
High-sensitivity troponin I, pg/mL	8.3 (2.6–34.5)
≤ 34.2	53/70 (76%)
> 34.2	17/70 (24%)
BNP (pg/mL)	125.0 (27.0–601.0)
< 116	32/67 (48%)
≥ 116	35/67 (52%)

cases. Hyponatremia and hypokalemia occurred in 10 (11%) and 7 (8%) cases, respectively.

4. Discussion

In this study, 9% and 2% of the 90 patients showed initial symptoms of diarrhea and poor appetite, respectively. Additionally, the first COVID-19 case in the United States also reported a 2-day history of nausea and vomiting on admission, and both the virus nucleic acid tests of the stool and respiratory samples were subsequently confirmed as positive [10]. Such patients might be overlooked, resulting in potentially serious consequences to the patients and a high risk of infecting more people. Thus, it is vital that clinicians are aware of that COVID-19 patients may present with initial gastrointestinal symptoms such as diarrhea, keep appropriate vigilance, and maintain an index of suspicion for early detections, early diagnoses, early isolations, and early interventions.

It is worth noting that COVID-19 patients with mild to moderate liver injuries, including elevated aminotransferases and hypoproteinemia, have also been reported, and some of the patients had digestive system impairment [11]. In our study, 24% of the patients showed clinical signs of poor nutrition. The reduced susceptibility of albumin to viral infections could be attributed to the loss of nutrients and liver damage. There is a clinical problem in how to meet the nutritional needs of patients, especially severely ill ones. Seriously ill patients who had interrupted oxygen administration when having a meal or going out to the bathroom were found to have repeated drops in oxygen saturation to less than 80%. Severe hypoxia attacks made the condition turn down rapidly since it was difficult to be recovered, resulting in a subsequent multi-organ failure or even sudden death [12]. In fact, these patients generally had difficulty in eating, thus some experts recommend a five-step nutritional therapy [13]. For patients receiving non-invasive ventilator, meals can be offered smaller and more frequently to help increase tolerance. Patients with an intolerance should be given enteral nutrition as soon as possible to help maintain the intestinal mucosal barrier function and supplement the body's needs. In addition, frequent defecation in patients with diarrhea increases the challenges of caring and the risk of occupational exposure for caregivers.

In a recent study, the testing result of 2019-nCoV RNA in respiratory samples remained positive for median 16.7 days and that of the fecal samples remained positive for median 27.9 days from the symptom onset [14]. It was suggested that the duration of viral shedding in fecal samples could be possibly extended up to 5 weeks after the patients' respiratory samples tested back to negative. Therefore, positivity for virus RNA of the fecal samples normally lags behind that of the respiratory tract samples. Even though knowledge about the viability of 2019-nCoV is incomplete [15], the virus might remain viable in the environment for days, resulting in the potential fecal-oral transmission, which could even happen after viral clearance in the respiratory tract. Moreover, the asymptomatic transmission had also been reported [16]. Although experts have not suggested any additional testing of fecal samples in the diagnostic procedures for COVID-19, routine testing of virus RNA in stool samples is highly recommended after the clearance of viral RNA in patients' respiratory samples. Besides, strict precautions to prevent transmission should be taken for patients who are in hospitalization or self-quarantine if their fecal samples have tested positive. A study recently done in China showed that four patients with COVID-19 who met criteria for discharge or discontinuation of quarantine had positive 2019-nCoV RNA test results 5 to 13 days later [17]. This finding suggests that at least a few of discharged patients may still be virus carriers. Therefore, discharge education plays an important role in the management of patients. After discharge, the patients are required to continue undergoing 14 days of medical observation, isolation management, and health monitoring. Finally, patients must take actions to reduce close contact with family

members, such as having separate meals, and receive follow-up visits regularly.

5. Conclusion

Clinicians are required to promptly identify the patients with initial diarrhea symptoms and pay adequate attention to the nutrient requirements of the patients with diarrhea during hospitalization. Standardized management is also recommended for the discharge of the patients to avoid potential fecal-oral transmission.

There are also several limitations in this study. Firstly, there were no nucleic acid tests carried out in the fecal samples of all the 90 cases. Secondly, in view of a retrospective study, specific diarrhea conditions in some patients were unknown from the electronic medical records. Further studies need to be conducted on the viability and infectivity of 2019-nCoV in feces.

Ethical statement

This study was approved by the Medical Ethical Committee of Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology (No. TJ-C20200136).

Funding

This work was supported by the special fund for novel coronavirus pneumonia from Huazhong University of Science and Technology (Grant No. 2020kfyXGYJ023).

CRedit authorship contribution statement

Yaru Xiao: Data curation, Writing - original draft. **Sufang Huang:** Conceptualization, Supervision, Writing - review & editing. **Li Yan:** Funding acquisition, Methodology. **Hui Wang:** Conceptualization, Methodology. **Fang Wang:** Visualization. **Ting Zhou:** Investigation. **Juan Deng:** Software. **Mei He:** Investigation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020;382(13):1199–207.
- [2] Fei Z, Ting Y, Ronghui D, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020. [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3). published online March 12.
- [3] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020;323(11):1061. <https://doi.org/10.1001/jama.2020.1585>.
- [4] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2020;395(10223):497–506.
- [5] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet* 2020;395(10223):507–13.
- [6] Guan W-J, Ni Z-y, Hu Yu, Liang W-H, Ou C-Q, He J-X, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382(18):1708–20.
- [7] Zhou Z, Zhao N, Shu Y, Han S, Chen B, Shu X. Effect of gastrointestinal symptoms on patients infected with COVID-19. *Gastroenterology* 2020. <https://doi.org/10.1053/j.gastro.2020.03.020>.
- [8] Luo S, Zhang X, Xu H. Don't overlook digestive symptoms in patients with 2019 novel coronavirus disease (COVID-19). *Clin Gastroenterol Hepatol* 2020;18(7):1636–7.
- [9] Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential fecal-oral transmission. *Gastroenterology* 2020;158(6):1518–9.

- [10] Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med* 2020;382(10):929–36.
- [11] National Health Commission of China. New coronavirus pneumonia prevention and control program (seventh edn). Mar 4, 2020. <http://www.nhc.gov.cn/xcs/zhengcwj/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml> (in Chinese).
- [12] Chinese society of parenteral nutrition. Covid-19 enteral parenteral nutrition therapy for critically ill patients. *Chinese J Med* 2020;100(00):E009-E009, doi: 10.3760/cma.j.cn112137-20200212-00261 (in Chinese).
- [13] Shi HP, Xu HX, Li SY, et al. Committee of tumor nutrition and supportive therapy, Chinese association against cancer. Five-step therapy for malnutrition. *J Tumor Metabolism Nutrition*, 2015;2(1):29–33(in Chinese).
- [14] Wu Y, Guo C, Tang L, Hong Z, Zhou J, Dong X, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. *Lancet Gastroenterol Hepatol* 2020;5(5):434–5.
- [15] Goh GK-M, Dunker AK, Foster JA, Uversky VN. Rigidity of the outer shell predicted by a protein intrinsic disorder model sheds light on the COVID-19 (Wuhan-2019-nCoV) infectivity. *Biomolecules* 2020;10:e331.
- [16] Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, Wang M. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 2020;323(14):1406. <https://doi.org/10.1001/jama.2020.2565>.
- [17] Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, Xu H. Positive RT-PCR test results in patients recovered from COVID-19. *JAMA* 2020;323(15):1502. <https://doi.org/10.1001/jama.2020.2783>.