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The original pre-print version of this manuscript was first posted online on March 18th, 2020. In that version, the authors reported data collected between January 18th and March 5th, 2020. Some patients in the cohort were still hospitalized at the time of the original submission. Since that time, the authors have collected additional data reflecting the final disposition of their cohort, and the current pre-print reflects those updated results.

The top-line result that digestive symptoms occur in roughly half of COVID-19 patients presenting to hospital remains unchanged. Similarly, patients with digestive symptoms have worse clinical parameters than those without and took longer to seek care. The most meaningful change we note is that the additional data now yield a null result for difference in mortality between group; it was previously reported that patients with digestive symptoms had higher mortality, although the data demonstrate worse biochemical abnormalities in these patients. Refer to the authors' statement, below, for additional information regarding the current pre-print version of their manuscript.

Authors' Statement

At the time of our original submission some patients included in the analysis were still receiving care in the hospital. We reported the data available at that time to expeditiously present our main finding that digestive symptoms are common upon COVID-19 patients presenting to hospital. We now have collected additional outcome data since patients previously hospitalized have either been discharged or died. In this version of the pre-proof, we have updated all the data to reflect full outcome results.

In addition, it was determined that 12 of the original 204 patients were assessed using the fifth edition of the Chinese NHC guidelines rather than the sixth edition. When cases of COVID-19 surged in Wuhan in early February, the NHC released the fifth edition guidelines that allowed diagnosis of suspected cases based on clinical history and characteristic CT imaging features, even in the absence of confirmed RT-PCR positive findings. These clinically diagnosed patients were also admitted to the hospital for systematic treatment, 12 of whom were included in our original report. In late February, the sixth edition guidelines were released, which required a comprehensive epidemiological history, clinical symptoms, and comprehensive of laboratory data to confirm the diagnosis. In retrospect, it was determined that the fifth edition NHC criteria were too loose. Thus, we opted to only apply the more rigorous sixth edition criteria to all patients in this study, which led to replacement of 12 subjects who it was determined had only been diagnosed by the fifth edition criteria. This did not change the main result that half of patients in our cohort reported a digestive symptom (rather than 48.5% it is now 50.5%).

Finally, as this was a multi-center study conducted in short order, it was discovered that some of the lab tests were expressed in different units between sites; these were recalibrated to harmonize units, leading to small differences in values for parameters in Table 3.

Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study

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ABSTRACT

Background: Since the outbreak of coronavirus disease 2019 (COVID-19) in December 2019, various digestive symptoms have been frequently reported in patients infected with the virus. In this study, we aimed to further investigate the prevalence and outcomes of COVID-19 patients with digestive symptoms.

Methods: In this descriptive, cross-sectional, multicenter study, we enrolled confirmed patients with COVID-19 who presented to three hospitals from January 18th to February 28th, 2020. All patients were confirmed by real-time PCR and were analyzed for clinical characteristics, laboratory data, and treatment. Data were followed up until March 18th, 2020.

Results: In the present study, 204 patients with COVID-19 and full laboratory, imaging, and historical data were analyzed. The average age was 52.9 years (SD \pm 16), including 107 men and 97 women. Although most patients presented to the hospital with fever or respiratory symptoms, we found that 103 patients (50.5%) reported a digestive symptom, including lack of appetite (81 [78.6%] cases), diarrhea (35 [34%] cases), vomiting (4 [3.9%] cases), and abdominal pain (2 [1.9%] cases). If lack of appetite is excluded from the analysis (since it is less specific for the gastrointestinal tract), there were 38 total cases (18.6%) where patients presented with a gastrointestinal-specific symptom, including diarrhea, vomiting, or abdominal pain. Patients with digestive symptoms had a significantly longer time from onset to admission than patients without digestive symptoms (9.0 days vs. 7.3 days). In 6 cases there were digestive symptoms but no respiratory symptoms. As the severity of the disease increased, digestive symptoms became more pronounced. Patients with digestive symptoms had higher mean liver enzyme levels, lower monocyte count, longer prothrombin time, and received more antimicrobial treatment than those without digestive symptoms.

Conclusion: We found that digestive symptoms are common in patients with COVID-19. Moreover, these patients have a longer time from onset to admission, evidence of longer coagulation, and higher liver enzyme levels. Clinicians should recognize that digestive symptoms, such as diarrhea, are commonly among the presenting features of COVID-19, and that the index of suspicion may need to be raised earlier in at-risk patients presenting with digestive symptoms. However, further large sample studies are needed to confirm these findings.

INTRODUCTION

On January 7th, 2020, a novel coronavirus was isolated and named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV) in the wake of an outbreak of pneumonia of unknown cause in Wuhan city, China[1,2]. This pneumonia was called coronavirus disease 2019 (COVID-19) by the World Health Organization on February 11th, 2020. As of this writing, the COVID-19 outbreak has become a pandemic that is threatening global health, undermining the global economy, and destabilizing societies across the world [3-5].

It is well established that most patients with COVID-19 have fever along with respiratory signs and symptoms, such as cough and dyspnea[6-9]. To date, there is some uncertainty about the prevalence of extra-pulmonary symptoms, such as those arising from the gastrointestinal tract. However, with the evolution of the pandemic and the accumulation of case data, we are now able to describe the initial clinical presentations of patients with COVID-19; and our experience is revealing that digestive symptoms are very common[10]. In particular, our initial observations with COVID-19 indicate that many patients present initially with diarrhea, anorexia, and vomiting, not necessarily with respiratory symptoms at first. In this study, we enrolled patients confirmed to have COVID-19 from 3 hospitals in Hubei province, and investigated the prevalence, clinical characteristics, and outcomes of COVID-19 patients with vs. without digestive symptoms.

METHODS

Study design and participants

This descriptive, cross-sectional, multicenter study was conducted in China, from January 18th to February 28th, 2020. All patients were recruited from 3 hospitals in Hubei province, including Wuhan Hanan Hospital, Wuhan Union Hospital, and Huanggang Central Hospital. This study was approved by the Ethics Committee of the above 3 hospitals. We randomly selected 310 patients with pneumonia of unknown cause from general wards and intensive care units (ICU) in the 3 hospitals as the initial study population.

We applied two inclusion criteria:(1) all adult patients were confirmed by real-time PCR and were diagnosed as having COVID-19 according to WHO interim guidance; (2) all patients underwent chest computerized tomography (CT) and complete panel of routine laboratory tests, including complete blood count, urinalysis, blood biochemistry, and blood coagulation function. Patients who did not meet the above inclusion criteria were excluded from the study.

Procedures

The epidemiological history, demographics data, clinical characteristics, laboratory data, treatment programs, and outcome measures were obtained from patients' medical records. Clinical outcomes were followed up to March 18th, 2020. Data were collected as comprehensively as possible through a combination of chart review and, when necessary, through communication with attending doctors and other medical workers to fill-in missing data. All data were separately extracted by two authors (Lei Tu and Mi Mu). Throat swab specimens from the upper respiratory tract obtained from all patients at admission were immediately maintained in viral-transport medium and were tested to confirm COVID-19 by real-time PCR [13]. Additionally, other respiratory viruses including influenza A virus, influenza B virus, and respiratory syncytial virus were also examined. All patients underwent chest CT.

Outcome data

We extracted the epidemiological history (i.e., clear contact history and unclear contact

history), demographic data, clinical characteristics including respiratory symptoms and digestive symptoms on admission, comorbidities, laboratory data, treatment programs, and clinical outcomes (discharged and died).

Statistical analysis

Descriptive data were presented as means (\pm standard deviation [SD]) for normally distributed continuous variables and as medians with interquartile range (IQR) for non-normally distributed data. Categorical variables were presented as percentages. For laboratory results, we also assessed whether the measurements were outside the normal range. All statistical analyses were performed using SPSS version 20 (SPSS, Chicago, IL, USA). Two independent samples were tested by T-test; the analysis of variance or Kruskal-Wallis rank sum test was used for comparison between multiple groups. The Chi-square test was performed to compare count data, and a two-tailed $P < 0.05$ was considered statistically significant.

RESULTS

Patients' flow and baseline characteristics

To build our final study sample, we began by randomly selecting 310 patients with pneumonia of unknown cause admitted to the general wards and ICU in the partner hospitals during the study period (January 18th to February 28th, 2020), which coincided with the initial outbreak of COVID-19 in the region. We excluded 96 patients who lacked complete data, such as no chest CT, missing nucleic acid of SARS-CoV-2 test, a negative SARS-CoV-2 test, or lacked a full set of laboratory data. This resulted in an analyzable population of 204 COVID-19 positive patients, of whom 70(34%) were critically ill. The last follow-up at the time of writing this study was March 18th, 2020. A detailed flowchart of participants is presented in **Figure 1**.

The baseline characteristics of 204 patients with COVID-19 are provided in **Table 1**. The average age was 52.9 years (SD \pm 16.0), including 107 men and 97 women. The average time from symptom onset to hospital admission was 8.1 days (SD \pm 5.0). Based on epidemiological history, we found that most patients could not recall a clear history of a known exposure. There were 44 (21.6%) patients with cardiovascular diseases, 24 (11.8%) patients with endocrine system diseases, and others with respiratory diseases (9 [4.4%]), malignant tumors (13 [6.3%]) and other disorders as shown in Table 1. After admission, there were 184 (90.2%) patients receiving antiviral treatment (e.g., lopinavir-ritonavir), 141(69.1%) on antibiotics, 80 (39.2%) on glucocorticoids, 96 (47.1%) on nebulized α -interferon, 56 (27.5%) on intravenous immunoglobulin, and 10 (4.9%) on antifungal treatment. Additionally, 16 patients were transferred to the ICU (7.8%), 168 were discharged (82.4%), and 37(17.7%) died. Among the patients, the average hospital stay was 17 days (SD \pm 9.0), and the average length of stay in the ICU was 8.9 days (SD \pm 6.9).

Prevalence and Outcomes of Patients with Digestive Symptoms

The clinical features and medical treatment of COVID-19 patients with digestive symptoms are shown in **Table 1**. One hundred and three patients (50.5%) admitted to the

hospital were found to present with one or more digestive symptoms. Of these 103 patients, 97 had developed respiratory symptoms along with digestive symptoms, and 6 presented with only digestive symptoms in the absence of respiratory symptoms. Among the 101 patients without digestive symptoms, 84 presented only with respiratory symptoms, and 20 neither had respiratory nor digestive symptoms as their chief complaint or as an accompanying symptom.

Figure 2 shows a breakdown of these categories.

Patients with digestive symptoms had a significantly longer time from onset to hospital admission vs. patients without digestive symptoms (9.0 days vs. 7.3 days, $p=0.013$). In **Table 2**, we found that patients with digestive symptoms had a variety of digestive manifestations including lack of appetite (81 [78.64%] cases), diarrhea (35 [34.0%] cases), vomiting (4 [3.9%] cases), and abdominal pain (2 [2.0%] cases). If the non-specific symptom of low appetite is excluded from the analysis, there were 38 total cases (18.6% of full sample) where patients presented with a gastrointestinal-specific symptom, including diarrhea, vomiting, or abdominal pain. Focusing only on diarrhea, there were 35 cases (17% of full sample) presenting with loose stools. Cases of diarrhea were usually not high volume or clinically severe, but more commonly presented as non-dehydrating loose stools, typically up to thrice daily. We found that 69.2% and 100% of moderate and severe patients, respectively, had lack of appetite upon presentation. As the severity of the disease increased, digestive symptoms become more pronounced. However, there was no significant difference in discharge time, days of intensive care, or mortality between the two groups.

In addition, we found that the number of patients with elevated ALT and AST (> 50 U/L) were significantly higher in patients with digestive symptoms (ALT: 21 [20.4%], AST: 17 [16.5%]) than those without the digestive symptoms (ALT: 6 [5.9%], AST: 5 [5.0%]) ($P_{ALT}=0.002$, $P_{AST}=0.008$). Therefore, those patients with digestive symptoms were more likely to suffer liver injury although the mean alanine aminotransferase and aspartate aminotransferase were in the normal range (Table 3). Monocyte counts were lower in patients with digestive symptoms. No significant differences were found in complete blood count, electrolytes, and

kidney function when comparing patients with vs. those without digestive symptoms. However, we did find that prothrombin time prolongation was more significant in patients with vs. without digestive symptoms (13.1s vs.12.5s), while other indicators of coagulation function were not significantly different. Compared to those with digestive symptoms, patients without digestive symptoms were less likely to receive antibiotic treatment 62 (61.4%) vs. 79 (76.7%), interferon 39 (38.6%) vs. 57 (55.3%), and immunoglobulin 17 (16.8%) vs. 39 (37.9%).

DISCUSSION

The present study was conducted by reviewing the medical records of patients with COVID-19 from January 18th to February 28th, 2020, in three heavily affected hospitals during the initial outbreak in Hubei province, where 83% of cases in China were reported. We found that digestive symptoms are a common complaint in patients with COVID-19. By the policy of the local government, Wuhan Union Hospital was deployed as key medical center to treat severe patients. Given the proximity of this hospital to the epicenter of the outbreak and the designation of this hospital to receive severe illness, patients in this sample were more critically ill than in other COVID-19 studies. The other two hospitals were designated to hospitalize mild-to-moderate COVID-19 patients: Wuhan Hannan Hospital, a secondary hospital 50 km from Union Hospital, and Huanggang Central Hospital, a newly-built hospital specifically constructed for COVID-19 patients, about 80km away from Wuhan. Our initial purpose in this study was to investigate the prevalence and characteristics of extra-pulmonary digestive symptoms that might otherwise be under-recognized, thus helping to bring attention to these symptoms, to facilitate earlier recognition of COVID-19, and thus to offer earlier treatment before mild disease progresses to severe illness.

At the time of this writing in March 2020, the COVID-19 pandemic remains severe and expanding. In clinical practice, COVID-19 patients are still mainly affected by the respiratory system, but evidence of damage to other system organs has been reported[14,15], and especially critical patients are susceptible to multiple organ dysfunction[16]. Our results indicate that nearly one-half of COVID-19 patients admitted to the hospital reported digestive symptoms, most commonly anorexia and diarrhea. This is important because if clinicians solely monitor for respiratory symptoms to establish case definitions for COVID-19, they may miss cases initially presenting with extra-pulmonary symptoms, or the disease may not be diagnosed later until respiratory symptoms emerge. This theory is supported by our finding that patients with digestive symptoms had a significantly longer time from onset to admission than those without digestive symptoms, possibly because they did not initially exhibit typical respiratory

symptoms and thus did not receive timely diagnoses and treatment for COVID-19. Of note, it was reported that many medical staff in China were infected at the beginning of the epidemic. Although this was related to improper protection of medical personnel early on, it may also have resulted from failing to consider COVID-19 in the face of atypical extra-pulmonary symptoms, especially those with digestive symptoms at the beginning of the outbreak. Less attention of digestive system symptoms by the public might also contribute to the transmission inside the family or in the community.

There are many reasons why COVID-19 appears to cause digestive symptoms. Firstly, SARS-CoV-2 is similar to SARS-CoV and can invade the human body by binding to the human angiotensin converting enzyme 2 (ACE-2) receptor, which causes liver tissue injury by up-regulation of ACE-2 expression in liver tissue caused by compensatory proliferation of hepatocytes derived from bile duct epithelial cells [17]. Secondly, SARS-CoV-2 indirectly or directly damages the digestive system through an inflammatory response. The chain reaction of inflammatory factors and viremia may injure the digestive system. Studies reveal that viral nucleic acid is detected in stool samples in up to 53.4% of patients [18-20]. Enteropathic viruses may directly damage the intestinal mucosa and cause digestive symptoms, but further research is needed to confirm this possibility. Thirdly, the intestinal flora is colonized in the human intestine, and their numbers are astonishing and diverse. The intestinal flora plays a variety of important physiological roles in the body, such as affecting the body's nutritional metabolism, regulating the development and maturation of the body's immune system, and antibacterial effects [21]. The virus itself may cause disorders of the intestinal flora, which could result in digestive symptoms. We are currently in the process of collecting stool samples for testing of intestinal flora diversity to explore the role of intestinal flora in this disease. Finally, the intestine is the largest immune organ in the body. Changes in the composition and function of the digestive tract flora affect the respiratory tract through the common mucosal immune system, and respiratory tract flora disorders also affect the digestive tract through immune regulation. The effect is called the “gut-lung axis” [22,23], which may further explain why patients with COVID-19 pneumonia often have digestive symptoms.

Curiously, our data indicate that patients with digestive symptoms in our case series rarely had underlying digestive diseases. Unlike other studies [14,15], we did not find significant liver injury, which was similar to Wu *et al*'s findings [24]. It is difficult to speculate why there are variations in liver test abnormalities among studies, but these variations should be further investigated to better understand how and when COVID-19 affects hepatic function. Nevertheless, we found that patients with digestive symptoms were more likely to exhibit elevated liver tests, such as AST and ALT, compared to patients without digestive symptoms. This is a topic worthy of attention.

We have noted that as the severity of the disease increases, digestive symptoms become more pronounced. One possibility is that digestive symptoms indicate viral load and replication within the gastrointestinal tract, which leads to more severe disease. Another possibility is that patients with extra-pulmonary symptoms reported later for care because they did not initially have typical respiratory symptoms, and thus presented at a later and less curable stage of disease. These hypotheses deserve close examination in future research.

The present study has several limitations. Firstly, our analysis was based on a retrospective study with a relatively small sample, which might cause bias and limit the reliability or generalizability of our results. Second, we did not test for RNA of SARS-CoV-2 in the stool of patients with COVID-19, so we cannot correlate digestive symptom prevalence and severity with presence of viral RNA in stool specimens. Future research needs to focus on this relationship in order to further explore the prognostic value of stool testing as both a diagnostic and prognostic indicator in COVID-19. Thirdly, blood biochemical examinations are based on a comparison of means in our study that not being subdivided to patients with individual abnormalities. Further more detailed analysis would be useful to mark some differences. Finally, given the dynamic nature of the current COVID-19 pandemic, the relationship between these patients' prognosis and digestive symptoms remains to be investigated with more data worldwide.

Conclusions

In summary, we have found that patients with COVID-19 are prone to digestive symptoms and nearly half report a digestive symptom in addition to fever and/or respiratory symptoms upon presentation to hospital. In rare instances, patient can even present with digestive symptoms in the absence of respiratory symptoms. Compared to COVID-19 patients without digestive symptoms, those with digestive symptoms have a longer time from onset to admission and evidence of more laboratory derangements, including prolonged coagulation and higher liver enzymes tests. These results obligate additional research evaluating the prevalence, incidence, predictors, and outcomes of digestive symptoms in this still emerging pandemic. In the meantime, clinicians must bear in mind that digestive symptoms, such as diarrhea, may among the presenting features of COVID-19, in some cases may arise before respiratory symptoms, and on rare occasions is the only presenting symptom of COVID-19. Clinicians should raise their index of suspicion when at-risk patients, such as those exposed to COVID-19, present with fever and digestive symptoms, even in the absence of respiratory symptoms. This knowledge may help with earlier identification of COVID-19, faster time to treatment, earlier quarantine, and lower exposure to bystanders.

Conflict of interest

Guarantor of the article: Lei Pan, Guogang Xu, and Lei Tu accept full responsibility for the conduct of the study.

Specific author contributions: Conceiving and designing the experiments: Lei Pan, Guogang Xu, Lei Tu. Case collection: Mi Mu, Chao Hu, Yuan Jin, Rongyu Ping, Yingzhen Du, Tianzhi Li, Junhong Yan. Data Extraction: Xun Niu, Pengcheng Yang, Yu Sun, Jing Wang, Runsheng Wang. Statistical Analysis: Lei Pan, Hong Gang Ren, Mi Mu. Interpretation of results: Pibao Li, Baoguang Hu, Guogang Xu, Qinyong Hu, Lei Tu. Writing and revising paper: Lei Pan, Guogang Xu, Mi Mu, Pengcheng Yang, Yu Sun. We thank Wuhan Medical Treatment Expert Group for COVID-19, Dr Hong Gang Ren and Prof Chengxia Liu for preparations of the manuscript.

Financial support: Beijing Municipal Natural Science Foundation (CN, 7192197), National Natural Science Foundation of China (CN, 81700490), Health and Family Planning Commission of Shandong Province (CN, 2017WS366), Traditional Chinese Medicine Administration Plan Project of Shandong Province (CN, 2019-0503) and Technology Plan Project of Binzhou Medical University (CN, BY2017KJ30).

Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ COVID-19 is currently a pandemic that threatens global health.
- ✓ Most patients with COVID-19 present with typical respiratory symptoms and signs.
- ✓ However, early experience with the outbreak in Wuhan, China, revealed that many people experienced extra-pulmonary digestive symptoms upon presentation.

WHAT IS NEW HERE

- ✓ Digestive symptoms are common in COVID-19 in addition to fever and respiratory symptoms, and are reported in nearly half of patients presenting to hospital; In rare cases digestive symptoms may occur in the absence of any respiratory symptoms
- ✓ When focusing only on diarrhea, in contrast to other digestive symptoms, 17% of COVID-19 patients in this series reported loose stools upon initial presentation.
- ✓ COVID-19 patients with digestive symptoms have a longer time from symptom onset to admission than that of patients without digestive symptoms; this may reflect diagnostic delay since typical respiratory symptoms were not initially predominant
- ✓ COVID-19 patients with digestive symptoms have laboratory evidence of prolonged coagulation and higher liver tests compared to those without digestive symptoms, emphasizing the importance of including symptoms like diarrhea to diagnose COVID-19 early

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Figure Legends

Figure 1. Patients flowchart.

Figure 2. Frequency of COVID-19 patients with or without digestive symptoms.

Table 1: Baseline characteristics and clinical outcomes of patients with COVID-19

Characteristics	All patients (n= 204)	Patients without digestive symptoms (n= 101)	Patients with digestive symptoms (n= 103)	<i>P</i> value	Classification of patients with digestive symptoms*			
					Mild (n= 1)	Moderate (n= 65)	Severe (n= 14)	Critical (n= 23)
Age, years [Mean (SD)]	52.91±15.98	53.61±16.10	52.21±15.92	0.533	24	47.91±14.85	60.00±9.63	60.87± 16.44
Sex (M/F)	107/97	52/49	55/48	0.784	1/0	31/34	7/7	16/7
Respiratory rate	21.57±4.02	21.02±3.08	22.11±4.72	0.053	23	20.62 ± 2.04	21.79±5.00	26.48±7.06
Days from illness onset to admission	8.11 ± 4.91	7.26 ± 4.20	8.95± 5.40	0.013	1	8.35±4.02	7.64±4.29	11.78±8.00
Epidemiological history								
Clear contact history	41(20.10%)	18(17.82%)	23 (22.33%)	0.422	1(100%)	18(27.69%)	3(21.43%)	1 (4.35%)
Unclear contact history	163(79.90%)	83(82.18%)	80 (77.67%)	0.422	0 (0.00%)	47 (72.31%)	11 (78.57%)	22(95.65%)
Chronic medical illness								
Respiratory system disease	9(4.41%)	2(1.98%)	7(6.80%)	0.182	1(100%)	1(1.54%)	2(14.29%)	3(13.04%)
Digestive system disease	7(3.43%)	3(2.97%)	4(3.88%)	1.000	0 (0.00%)	4(6.15%)	0(0.00%)	0(0.00%)
Cardiovascular system disease	44(21.57%)	21(20.79%)	23(22.3%)	0.789	0 (0.00%)	10(15.38%)	3(21.43%)	10(43.48%)
Nervous system disease	5(2.45%)	4(3.96%)	1(0.97%)	0.353	0 (0.00%)	1(1.54%)	0(0.00%)	0(0.00%)
Endocrine system disease	24(11.76%)	14(13.86%)	10(9.71%)	0.357	0 (0.00%)	5(7.69%)	1(7.14%)	4(17.39%)
Malignant tumor	13(6.37%)	5(4.95%)	8(7.77%)	0.410	0 (0.00%)	4(6.15%)	0(0%)	4(17.39%)
Medical treatment after admission								
Antibiotic treatment	141(69.12%)	62(61.39%)	79(76.70%)	0.018	0 (0.00%)	44(67.69%)	14(100%)	21(91.30%)
Antifungal treatment	10(4.90%)	3(2.97%)	7(6.80%)	0.347	0 (0.00%)	2(3.08%)	1(7.14%)	4(17.39%)
Antiviral treatment	184(90.20%)	90(89.11%)	94(91.26%)	0.605	0 (0.00%)	59(90.77%)	12(85.71%)	22(95.65%)
Glucocorticoids	80 (39.22%)	36(35.64%)	44(42.72%)	0.301	0 (0.00%)	17(26.15%)	12(85.71%)	15(65.22%)

Nebulized α -interferon	96(47.06%)	39(38.61%)	57(55.34%)	0.017	1 (100.0%)	40(61.54%)	7(50.00%)	9(39.13%)
Intravenous immunoglobulin	56(27.45%)	17(16.83%)	39(37.86%)	0.001	0 (0.00%)	18(27.69%)	7(50.00%)	14(60.87%)
Number of cases transferred to intensive care unit	16 (7.84%)	10 (9.90%)	6(5.94%)	0.279	0 (0.00%)	0 (0.00%)	2 (14.29%)	4 (17.39%)
Clinical outcome								
Discharged	168(82.35%)	84(83.16%)	84(81.55%)	0.762	1(100%)	65(100%)	14(100%)	4 (17.39%)
Died	36(17.65%)	17(16.83%)	19(18.45%)	0.762	0 (0.00%)	0 (0.00%)	0 (0.00%)	19 (82.61%)
Discharged								
Total days in hospital	17.06 \pm 9.02	16.84 \pm 7.90	17.28 \pm 10.03	0.728	10.00	18.40 \pm 6.80	23.86 \pm 12.01	10.43 \pm 12.79
Days of intensive care	8.94 \pm 6.92	10.00 \pm 7.90	7.17 \pm 5.04	0.448	\	\	8.50 \pm 3.54	6.50 \pm 6.03

Note: *The classification of COVID-19 severity was mainly determined according to the COVID-19 prevention and control program issued by China's National Health Commission (<http://www.nhc.gov.cn/>). Mild patients were those without lesions in the chest computerized tomography (CT). Moderate patients were those with lesions in the chest CT.

Table 2: Summary of clinical features of COVID-19 patients with digestive symptoms

Characteristics	Patients (n= 103)	Mild patients (n= 1)	Moderate patients (n= 65)	Severe patients (n= 14)	Critical patients (n=23)
Symptoms					
Lack of appetite	81 (78.64%)	0 (0.00%)	45 (69.23%)	14 (100%)	22 (95.65%)
Diarrhea	35 (33.98%)	1 (100%)	24 (36.92%)	3 (21.43%)	7 (30.43%)
Vomiting	4 (3.88%)	0 (0.00%)	2 (3.08%)	1 (7.14%)	1 (4.35%)
Abdominal pain	2 (1.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (8.70%)
Digestive diseases					
Hepatitis B	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatitis C	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
fatty liver	1 (0.97%)	0 (0.00%)	1 (1.54%)	0 (0.00%)	0 (0.00%)
Cirrhosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic					
insufficiency	1 (0.97%)	0 (0.0%)	1 (1.54%)	0 (0.00%)	0 (0.00%)
Gastritis	1 (0.97%)	0 (0.0%)	1 (1.54%)	0 (0.00%)	0 (0.00%)
Gastroesophageal					
reflux disease	1 (0.97%)	0 (0.00%)	1 (1.54%)	0 (0.00%)	0 (0.00%)
Ulcerative colitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peptic ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Intestinal polyps	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Crohn's disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Colitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Irritable bowel					
syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholelithiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholecystitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholangitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pancreatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Accompanying symptoms					
Fever	95 (92.23%)	1 (100%)	57 (87.69%)	14 (100%)	23 (100%)
Weakness	54 (52.42%)	0 (0.00%)	28 (43.08%)	10 (71.43%)	16 (69.57%)
Muscle pain	15 (14.56%)	0 (0.00%)	8 (12.31%)	2 (14.29%)	5 (21.74%)

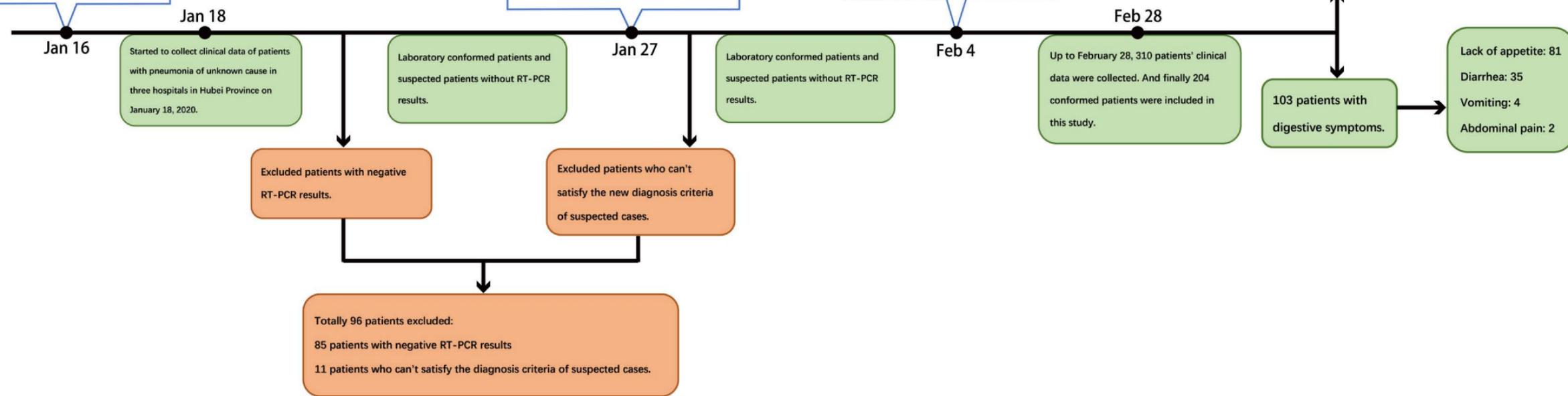
Table 3: Laboratory findings of patients with COVID-19 on admission

Characteristics	All patients (n= 204)		Patients without digestive symptoms (n=101)		Patients with digestive symptoms (n= 103)		<i>P</i> value
	Mean	Std	Mean	Std	Mean	Std	
White blood cell count, $\times 10^9/L$	6.09	3.70	6.59	3.87	5.60	3.48	0.056
Neutrophil count, $\times 10^9/L$	4.48	3.70	4.90	3.92	4.06	3.44	0.105
Hemoglobin, g/L	128.08	18.52	128.77	18.40	127.41	18.70	0.601
Neutrophil ratio, %	67.85	16.21	68.36	15.26	67.35	17.16	0.658
Lymphocyte count, $\times 10^9/L$	1.13	0.55	1.18	0.52	1.08	0.58	0.197
Monocyte count, $\times 10^9/L$	0.42	0.22	0.46	0.23	0.39	0.20	0.021
Platelet count, $\times 10^9/L$	201.14	88.38	195.73	84.09	206.44	92.49	0.388
Prothrombin time, s	12.83	1.91	12.53	1.89	13.13	1.88	0.024
Activated partial Thromboplastin time, s	34.19	6.22	33.47	5.20	34.89	7.05	0.103
Fibrinogen, g/L	4.40	1.57	4.27	1.41	4.54	1.71	0.220
Alanine aminotransferase, U/L	35.98	35.82	29.53	23.58	42.24	43.83	0.011
Aspartate aminotransferase, U/L	31.36	25.55	27.48	23.98	35.12	26.58	0.032
Glutamate/alanine aminotransferase	1.10	0.56	1.09	0.53	1.10	0.59	0.899
Total bilirubin, mmol/L	13.65	10.26	13.46	8.11	13.83	12.03	0.797
Albumin, g/L	36.00	6.07	35.84	5.63	36.16	6.49	0.707
Blood nitrogen, mmol/L	5.11	2.76	5.14	2.92	5.08	2.62	0.877
Creatinine, $\mu\text{mol/L}$	75.54	26.87	76.21	26.51	74.88	27.33	0.725
Serum sodium, mmol/L	138.42	4.26	138.26	4.70	138.56	3.81	0.617
Serum potassium, mmol/L	4.17	0.64	4.20	0.61	4.14	0.68	0.508

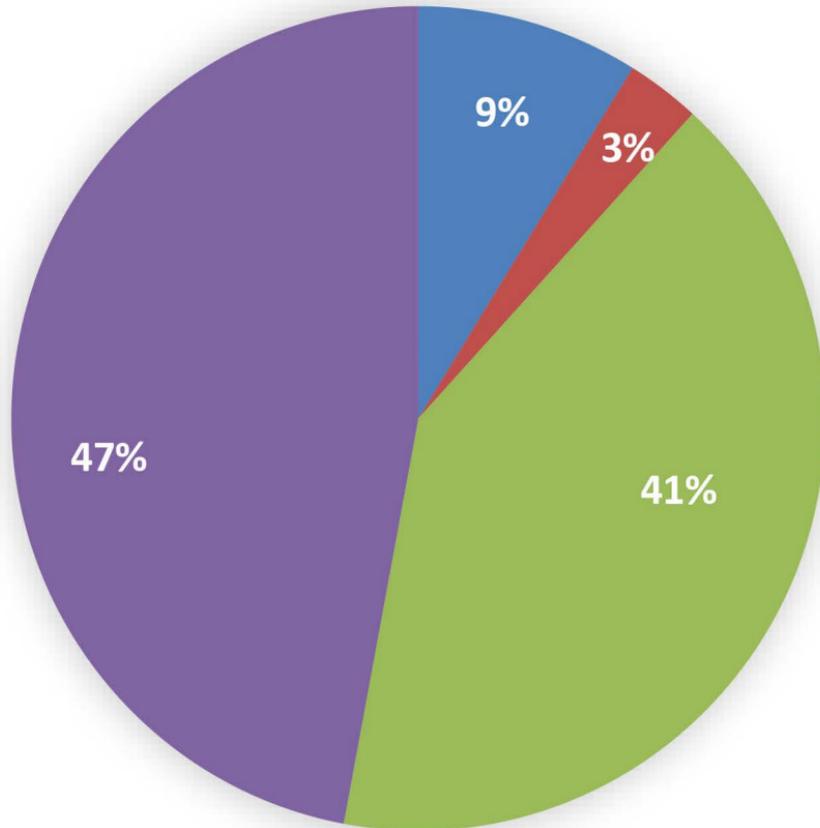
The diagnosis criteria of suspected and confirmed cases with COVID-2019 (version 1) published by NHC:
Patients who satisfies any of the epidemiological history and any of the clinical manifestations can be diagnosed as a suspected case.
The suspected cases whose RT-PCR results are positive can be identified as conformed cases.

The diagnosis criteria of suspected and confirmed cases with COVID-2019 (version 4) published by NHC:
Patients with a positive epidemiological history and any two of the clinical manifestations are considered as a suspected case.

The diagnosis criteria of suspected and confirmed cases with COVID-2019 (version 5) published by NHC:
Patients who with a positive epidemiological history and any two of the clinical manifestations or patients without definite epidemiological history but with all the clinical manifestations is considered as a suspected case.
The suspected cases with the imaging characteristics of pneumonia can be diagnosed as clinical diagnosis cases (without RT-PCR results) in Hubei Province.



Frequency of COVID-19 patients with or without digestive symptoms



- Without digestive, nor respiratory symptoms (n=17)
- With digestive symptoms, without respiratory (n=6, most patients have fever, except 1)
- With respiratory symptoms, without digestive symptoms (n=84)
- With digestive and respiratory symptoms (n=97)