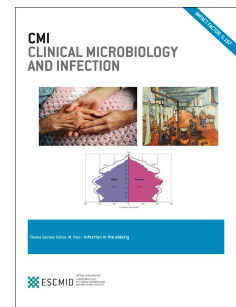


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Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang Hospital

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Abstract

Objectives: Describe the clinical characteristics of patients in Fangcang Hospital.

Methods: Non-critically ill patients with positive SARS-CoV-2 RT-PCR tests admitted to Dongxihu 'Fangcang' Hospital between February 7th and 12th were included, which was promptly constructed because of the rapid, exponential increase in COVID-19 patients in Wuhan, China; clinical course through February 22nd was recorded.

Results: 1012 non-critically ill patients with positive SARS-CoV-2 RT-PCR tests were included in the study. 30 (of 1012, 3.0%) patients were asymptomatic on admission. During hospitalization, 16 of 30 (53.3%) asymptomatic patients suffered from different symptoms. Fourteen of 1012 patients (1.4%) remained asymptomatic from exposure to the end of follow-up, with a median duration of 24 days (IQR 22-27). Fever (761 of 1012, 75.2%) and cough (531 of 1012, 52.4%) were the most common symptoms. Small patchy opacities (355 of 917, 38.7%) and ground-glass opacities (508 of 917, 55.4%) were common imaging manifestations in chest CT scan. One hundred patients (9.9%) were transferred to designated hospitals due to aggravation of illness. Diarrhea emerged in 152 of 1012 patients (15.0%). Male, elder age, diabetes cardiovascular diseases, chills, dyspnea, SO_2 value of $\leq 93\%$, WBC counts of $>10 \times 10^9/L$ and large consolidated opacity on CT images were all risk factors for aggravation of illness.

Conclusions: Non-critically ill patients had different clinical characteristics than critically ill patients. Asymptomatic infections only accounted for a small proportion of COVID-19. Although with a low incidence, diarrhea was observed in patients with COVID-19, indicating the possibility of faecal-oral transmission.

Introduction

The COVID-19 epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had spread all over China and more than 150 other countries [1-5]. As of March 21, China had 81054 confirmed cases in total, 50005 cases of which were identified in Wuhan. Of all the confirmed cases, about 20% were seriously and critically ill, and 3261 cases died (2508 deaths in Wuhan).

As of Feb 22, the final date of our follow-up, although 19927 beds in Wuhan were

prepared to treat COVID-19 patients, with the rapid increase of new cases, there were still many confirmed cases unattended. From the perspective of treating patients and controlling the source of infection, a completely novel model, Fangcang Hospital, emerged, which mainly received non-seriously ill patients with positive SARS-CoV-2 RT-PCR tests.

In this study, we did an exploration of clinical features of 1012 non-critically ill patients with a positive SARS-CoV-2 RT-PCR, admitted to Dongxihu Fangcang Hospital, Wuhan, which was the largest one of the same kind, to date, and simply introduced the operation mode of the hospital.

Methods

Study design and participants

In the absence of proven antiviral therapy for COVID-19, effective infection control measures, including patient isolation, are critical. Given the rapid, exponential increase in COVID-19 patients, the prompt construction of temporary “Fangcang” hospitals was required. Medical personnel at “Fangcang” hospitals came from all over the country to work shifts lasting between six and eight hours. “Fangcang Hospitals” were usually reconstructed by large-scale spaces such as exhibition halls, gymnasiums and workshops to have the basic functions of medical treatment, logistic support, patient beds and living area. Patients from Feb 7 to Feb 12, 2020, at Dongxihu Fangcang Hospital in Wuhan, were enrolled in the retrospective study. Dongxihu Fangcang Hospital was managed by Zhongnan Hospital of Wuhan University. All patients with COVID-19 recruited in this study were diagnosed according to WHO interim guidance. This study was approved by the institutional ethics board of Zhongnan Hospital of Wuhan University (NO.2020011). Written informed consent was waived by the institutional ethics board of the hospital for emerging infectious diseases, but oral consent was obtained from all the patients. Clinical courses were followed until Feb. 22nd.

Patients were admitted to the Fangcang Hospital according to the following criteria:

1. A positive result confirmed by standard SARS-CoV-2 RT-PCR test.
2. Age ≥ 16 with self-care ability.

3. Respiratory rate < 30 with blood oxygen saturation > 93%, at rest.
4. A negative result for influenza virus RT-PCR test.

Patients were not admitted to the Fangcang Hospital if they showed:

1. A negative result of standard SARS-CoV-2 RT-PCR test.
2. Age < 16.
3. Without selfcare ability and ability of daily life activities.
4. Respiratory rate ≥ 30 or blood oxygen saturation $\leq 93\%$, at rest.
5. A positive result for influenza virus RT-PCR test.
6. With serious underlying comorbidities such as acute myocardial infarction, acute intracerebral hemorrhage, acute cerebral infarction, heart failure, renal failure, patients with malignancies in need of comprehensive treatment.
7. With mental disorder such as schizophrenia.
8. With serious psychological disorder such as suicidal tendencies.
9. With other infectious diseases such as active tuberculosis.
10. Excluded by two independent doctors on duty because of conditions that were not mentioned above.

All patients admitted to Dongxihu "Fangcang" from Feb 7 to Feb 12, 2020, were included in this study.

Definitions

Severity of COVID-19

Serious illness was defined if satisfying at least one of the following items: (i) breathing rate ≥ 30 /min; (ii) pulse oximeter oxygen saturation (SpO₂) $\leq 93\%$ at rest; (iii) ratio of partial pressure of arterial oxygen (PaO₂) to fraction of inspired oxygen (FiO₂) ≤ 300 mmHg (1mmHg=0.133kPa).

Critical illness was defined if satisfying at least one of the following items: (i) respiratory failure occurred and received mechanical ventilation; (ii) shock; (iii) failure of other organs and received care in the intensive care unit (ICU).

Epidemiological history

Epidemiological history in this study was defined as follows:

- 1) Residence in an epidemic area (Wuhan city) in the last month, especially in the last 2 weeks.
- 2) A history of contact with a SARS-CoV-2-positive patient in the last month,

especially in the last 2 weeks.

3) A history of exposure to a live poultry market or wild animals.

Clinical outcome

Deterioration of COVID-19

Patients with any one of the following conditions were defined as deterioration of covid-19: (i) Symptoms persisted or worsened for more than 7 days; (ii) Respiratory rate ≥ 30 or blood oxygen saturation $\leq 93\%$, at rest; (iii) Pulmonary imaging showed that the lesions progressed more than 50% within 48 hours.

Deterioration of comorbidities or complications

Deteriorated clinical status caused by conditions mentioned from item 6 to item 9 in exclusion criteria during hospitalization were defined as deterioration of comorbidities or complications.

Discharge

Patients meeting the following criteria could be discharged: Temperature returned to normal for more than three days; respiratory symptoms improved significantly; pulmonary imaging showed that acute exudative lesions were significantly improved; with two consecutive negative results for RT-PCR tests for sputum or nasopharynx swabs samples (with an interval of 24 hours at least).

Data collection

Basic information (gender, age and comorbidities), symptoms (fever, chills, runny nose, nasal congestion, sore throat, cough, expectoration, dyspnea, headache, myalgia, vomiting, diarrhea and abdominal pain), WBC counts and results of chest computed tomography (CT) scan and epidemiological data were collected for each patient from electronic medical records. It should be noted that all of the patients' laboratory and radiological examinations were performed before their admission, thus, not all the patients had related data. All data were checked by two researchers (WX and ZY).

Working procedures of "Fangcang Hospital"

The flowchart of confirmed patients admitted into Fangcang Hospital is shown in Figure 1. The triage flow based on RT-PCR and CT results for outpatients was described in Supplementary materials 1.

Statistical analysis

Categorical data were presented as counts and percentages, and continuous

data were expressed as Mean $\pm$ SD, if the data were normally distributed, or expressed as median with Interquartile Range (IQR) values. Proportions for categorical variables were compared using the χ^2 test, and Fisher exact test was used if the data were limited. Comparisons for medians of non-normal distribution data were performed using Mann-Whitney test. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) Statistics version 24.0 software.

Results

General characteristics of patients with COVID-19

1012 patients with non-critically ill patients COVID-19 were included in the retrospective analysis. The basic information is shown in Table 1.

The median age of included patients was 50 years (y) old, with IQR 39-58 y, ranging from 16-89 y. 114 of 1012 patients (11.3%) had coexisting illness such as hypertension, diabetes, cardiovascular diseases, respiratory system disease and other diseases. All of 1012 (100%) patients included were at increased risk for COVID-19 with potential or probable exposure and local residents of Wuhan City or had ever lived in Wuhan city in the last month.

311 of 1012 patients (30.7%) were exposed to a SARS-CoV-2-positive patient, . No patients had visited a live poultry market or been exposed to wild animals in the last month.

On admission, the most common symptoms was fever(761 of 1012, 75.2%), and 424 of 1012(41.9%) patients suffered a moderate fever, 37.3 to 38.0°C. Cough was also a common symptom occurred in these patients(531 of 1012, 52.4%). The other symptoms included dyspnea (231 of 1012, 22.8%), expectoration(220 of 1012, 21.7%), chills(182 of 1012, 18.0%), myalgia(170 of 1012, 16.8%), headache(152 of 1012, 15.0%), diarrhea(152 of 1012, 15.0%), sore throat(144 of 1012, 14.2%), nasal congestion (69 of 1012, 6.9%), runny nose(57 of 1012, 5.6%), abdominal pain(37 of 1012, 3.7%), vomiting(36 of 1012, 3.6%).

30 of 1012 (3.0%) patients were asymptomatic from exposure to admission, with a median duration of 10.5 days (IQR 7-13). However, during follow-up from admission to the end, 16 of 30 (53.3%) asymptomatic ones suffered from different symptoms. Fever occurred in 6 of 30 ones (20%), with cough in 8 of 30 (26.7%), myalgia in 3 of 30 (10%), dyspnea in 2 of 30(6.7%), runny nose in 1 of

30(3.3%), nasal congestion in 1 of 30 (3.3%) and abdominal pain in 3.3%. 14 of 1012 patients(1.4%) remained asymptomatic during the whole follow up from exposure to the end, with a median duration of 24 days (IQR 22-27).

Duration for all of the 1012 patients from onset of symptoms for symptomatic patients and first positive SARS-CoV-2 RT-PCR test for asymptomatic ones to admission ranged from 1 to 30 day(s), with a median of 10 days (IQR 10-14).

During hospitalization, 46 of 1012 patients(4.5%) had a low SO_2 value of 89%-93%.

WBC counts were performed in 586 of 1012 patients(57.9%) before admission. The majority of patients (441 of 586, 75.3%) had normal values of WBC counts, 139 of 586patients (23.7%) had WBC counts values below normal, and 6 of 586 patients (1.0%) had WBC counts values above normal.

Before admission, the pulmonary imaging manifestations of COVID-19 patients were roughly divided into three categories including small patchy opacities, large ground-glass opacity and large consolidated opacity [6-8](Figure 2). The proportions of each group were 38.7%(355 of 917), 55.4%(508 of 917) and 5.9%(54 of 917), respectively.

At final follow-up, 100 of 1012 patients (9.9%) had been transferred to designated hospitals due to aggravation of illness, and 93 of 1012 patients (9.2%) had been discharged, with 819 of 1012 patients (80.9%) remaining in hospital. No patients died during the follow-up.(Table 2)

In order to understand the factors that might be associated with the aggravation of illness and transfer of patients from “Fangcang” to designated hospitals, comparisons between patients with (Group 1) and without (Group 2) aggravation of illness during follow up were shown in Table 1 and Table 2. The details of comparisons were described in Supplementary materials 2.

Discussion

Up to March 10th, a total of 16 “Fangcang” hospitals had ever been put into use, receiving more than 12000 non-critically ill patients with COVID-19.

In order to describe the clinical characteristics and outcomes of patients with COVID-19 in a Fangcang Hopspital, this study included 1012 non-critically ill patients infected with SARS-CoV-2 admitted into the “Dongxihu Fangcang

Hospital". Compared with hospitalized patients in some published studies [9-12], similar to those studies, fever(75.2%) and cough (52.4%) were most common symptoms, but there were some noteworthy points.

The first one was clinical outcome. In a recent study, 32 of 52(61.5%)patients admitted into intensive care unit (ICU) in Jinyintan Hospital, had died at 28 days, and the median duration from admission to ICU to death was 7 (IQR, 3–11) days for non-survivors[12]. In our study, no patients died during the follow-up, and only 10% of patients were transferred to designated hospitals due to aggravation of illness, indicating a significant difference between non-critically ill and critically ill patients. Male gender, elder age, diabetes or cardiovascular diseases, chills or dyspnea, SO_2 value of $\leq 93\%$, WBC counts of >10 and large consolidated opacity on chest CT images were all risk factors for aggravation of illness and transfer of patients from "Fangcang" to designated hospitals.

Second, our study revealed that 30 of 1012 (3.0%) patients were asymptomatic on admission, but 14 of 1012 patients (1.4%) remained asymptomatic during the whole follow up, with a median duration of 24 days (IQR 22-27) . Asymptomatic people might easy to be ignored and potentially infectious. It had been reported that asymptomatic patients could spread the disease to family members [13], indicating that timely isolation of asymptomatic infected people was important for epidemic prevention and control.

Third, diarrhea was an atypical symptom of low incidence in COVID-19 patients. In some published studies, incidence of diarrhea in patients with COVID-19 ranged from 2% to 10% [9, 11, 14-15]. Our percentage was higher than in those studies, maybe explained by use of some drugs such as abidol and moxifloxacin before admission to the Fangcang Hospital. Recent studies found positive SARS-CoV-2-RNA in anal swabs and fecal samples and found that positive results of the anal swabs were associated with the severity of the disease [16, 17]. Although it was unclear whether there was a definite link between diarrhea and COVID-19, both the studies raises a question concerning whether the gastrointestinal tract might be another site of viral replication, indicating possibility of faecal-oral transmission.

This study has some limitations. It is a single-center study. However, patients came from different regions of Wuhan, and the sample size is large. The

“Fangcang Hospital” was not a regular hospital, but a temporary one. Routine tests such as biochemical examination and C-reactive protein test could not be carried out during the follow-up.

There might be a possible association between the features of chest CT manifestation and the course of COVID-19. We could not perform this analysis because of loss function of displaying CT images in the temporary electronic medical record system and the limited information of our data.

In conclusion, non-critically ill patients had different clinical characteristics with critically ill patients. Asymptomatic infections only accounted for a small proportion of patients infected with SARS-CoV-2, but might be potential source of infection. Although with a low incidence, diarrhea in patients with COVID-19 should not be ignored, indicating possibility of faecal-oral transmission.

Declaration of interests

Declaration of personal interests: None.

Funding

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Acknowledgments

We thank all the patients included in this study.

Contributors

ZQ and WX designed this study. WX and ZY collected the epidemiological and clinical data. WX and FJ carried out the Patients' satisfaction survey. WX, CL, DF, ZR, GL, WF and ZY took part in the data collection. CQ shot the videos about “Fangcang Hospital”. WX drafted the manuscript, and ZQ revised the final manuscript.

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Table 1. Demographics, baseline characteristics and epidemiological history of 1012 non-critically ill patients with COVID-19 admitted into Dongxihu Fangcang Hospital.

	Patients in total (n=1012)	Patients with aggravation of illness during follow up(n=100)	Patients without aggravation of illness during follow up(n=912)	Comparisons between subgroups (<i>P</i> value)
Gender				
Male	524(51.8%)	62(62.0%)	462(50.7%)	0.03
Female	488(48.2%)	38(38.0%)	450(49.3%)	
Age				
Range	16-89	21-79	16-89	<0.01
Median(IQR)	50 (39-58)	55.5(47-62)	50(38-58)	
<18	3(0.3%)	0	3(0.3%)	<0.01
18-39	257(25.4%)	12(12.0%)	245(26.9%)	
40-59	516(51.0%)	51(51.0%)	465(51.0%)	
≥60	236(23.3%)	37(37.0%)	199(21.8%)	
Chronic medical illness	114(11.3%)	17(17%)	97(10.6%)	0.06
Hypertension	46(4.5%)	6(6.0%)	40(4.4%)	0.63
Diabetes	27(2.7%)	7(7.0%)	20(2.2%)	0.01
Cardiovascular diseases	15(1.5%)	5(5.0%)	10(1.1%)	<0.01
Respiratory system disease	20(2.0%)	2(2.0%)	18(2.0%)	1

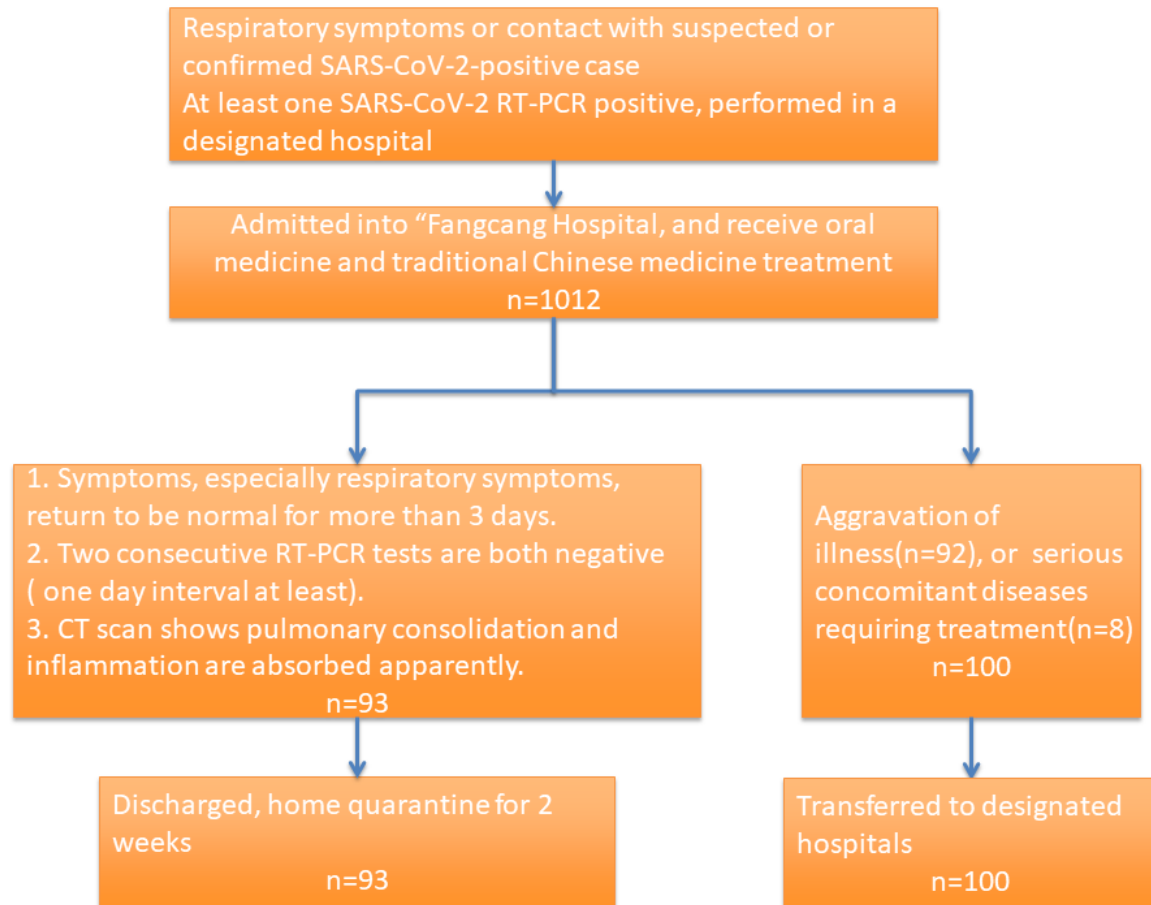
Other diseases	34(3.3%)	3(3.0%)	31(3.4%)	1
Epidemiological history				
A history of live in an epidemic area(Wuhan city) in the last month, especially in 2 weeks.	1012(100%)	100(100%)	912(100%)	1
A history of contact with a SARS-CoV-2-positive patient in the last month, especially in 2 weeks	311(30.7%)	25(25%)	286(31.4%)	0.19
A history of exposure to a live poultry market or wild animals	0	0	0	N/A

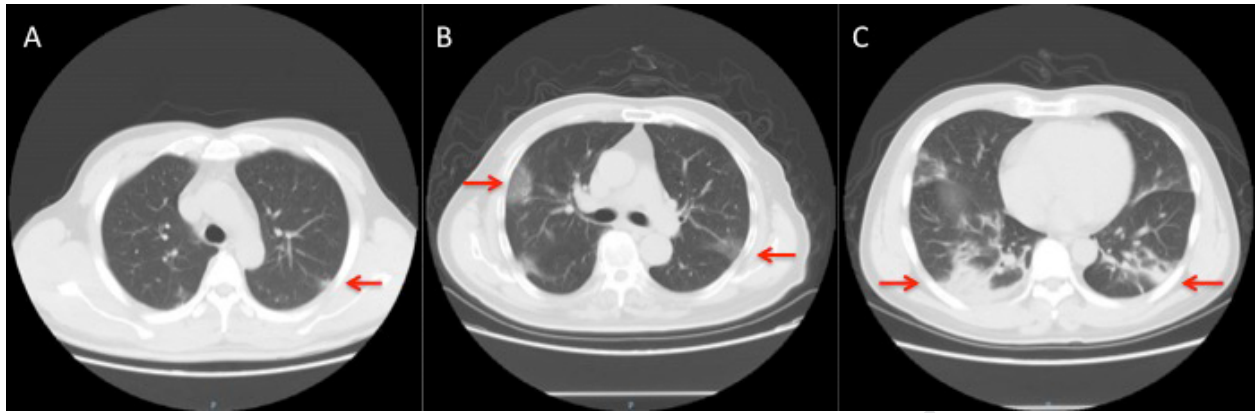
Table2. Clinical characteristics and outcome of 1012 non-critically ill patients with COVID-19 admitted into Dongxihu Fangcang Hospital.

	Patients in total (n=1012)	Patients with aggravation of illness during follow up(n=100)	Patients without aggravation of illness during follow up(n=912)	Comparisons between subgroups (<i>P</i> value)
Signs and Symptoms on admission				
Asymptomatic condition	30(3.0%)	2(2.0%)	28(3.1%)	0.77
Fever	761(75.2%)	76(76.0%)	685(75.1%)	0.85
Highest temperature, °C				
37.3-38.0	182(18.0%)	25(25.0%)	157(17.2%)	
38.1-39	424(41.9%)	42(42.0%)	382(41.9%)	0.05
>39	155(of 1012,15.3%)	9(9.0%)	146(16.0%)	
Chills	182(18.0%)	28(28.0%)	154(16.9%)	<0.01
Runny nose	57(5.6%)	8(8.0%)	49(5.4%)	0.29
Nasal congestion	69(6.9%)	10(10.0%)	59(6.5%)	0.20
Sore throat	144(14.2%)	16(16.0%)	128(14.0%)	0.59
Cough	531(52.4%)	55(55%)	476(52.2%)	0.59
Expectoration	220(21.7%)	27(27.0%)	193(21.2%)	0.18
Dyspnea	231(22.8%)	36(36.0%)	195(21.4%)	<0.01
Headache	152(15.0%)	19(19.0%)	133(14.6%)	0.24
Myalgia	170(16.8%)	17(17.0%)	153(16.8%)	0.96
Vomiting	36(3.6%)	6(6.0%)	30(3.3%)	0.27
Diarrhea	152(15.0%)	17(17.0%)	135(14.8%)	0.56
Abdominal pain	37(3.7%)	6(6.0%)	31(3.4%)	0.30
Duration from onset of symptoms to admission (days)				
Range	1-30	2-21	1-30	N/A
Median(IQR)	10(7-14)	10(7.5-14)	10(7-14)	0.02
<7	152(15.0%)	4(4%)	148(16.2%)	
7-14	641(63.3%)	74(74%)	567(62.2%)	<0.01
>14	219(21.6%)	22(22%)	197(21.6%)	
Blood oxygen saturation during hospitalization, (%)				
Range	89-100	89-99	89-100	N/A

Median(IQR)	97(96-98)	96(94.5-97)	97(96-98)	<0.01
89-93	46(4.5%)	15(15%)	31(3.4%)	
>93	966(95.5%)	85(85%)	881(96.7%)	<0.01
WBC counts($\times 10^9/L$)	586(of 1012, 57.9%)	58(of 100, 58%)	528(of 912, 57.9%)	0.98
Range	0.67-20.0	0.78-20.0	0.67-11.1	N/A
Median(IQR)	4.7(4.0-6.0)	4.8(4.1-6.0)	4.7(4.0-6.0)	0.74
<4	139(of 586, 23.7%)	14(of 58, 24.1%)	125(of 528, 23.7%)	
4-10	441(of 586, 75.3%)	40(of 58, 69.0%)	401(of 528, 75.9%)	<0.01
>10	6(of 586, 1.0%)	4(of 58, 6.9%)	2(of 528, 0.4%)	
Chest CT scan*	917(of 1012, 90.5%)	86(of 100, 86%)	831(of 912, 91.1%)	0.09
Small patchy opacities	355(of 917, 38.7%)	37(of 86, 43.0%)	318(of 831, 38.3%)	
Large ground-glass opacity	508(of 917, 55.4%)	39(of 86, 45.3%)	469(of 831, 56.4%)	0.02
Large consolidated opacity	54(of 917, 5.9%)	10(of 86, 11.6%)	44(of 831, 5.3%)	
Clinical outcome				
Transferred to designated hospitals due to aggravation of illness	100(9.9%)	100(100%)	N/A	
Discharge	93(9.2%)	N/A	93(10.2%)	N/A
Remained in hospital	819(80.9%)	N/A	819(89.8%)	
Died	0	0	0	

“*” indicated that only one dominant manifestation on chest CT scan for each patient was recorded by the doctors on duty.





The triage flow based on RT-PCR and CT results for outpatients

For outpatients with at least two negative results of RT-PCR but with a positive result of chest CT scan in some designated hospitals, they would be admitted to the designated hospitals to be treated or designated location to be quarantined. If they had at least two negative results of RT-PCR, with a negative result of chest CT scan but fever, they were also admitted to designated location to be quarantined. Designated location generally referred to hotels listed by the government, but there were also some places, such as university dormitories, which were temporarily transformed into isolation points. For those that had exposure to confirmed or suspected patients, if they had no symptoms and at least two negative results of RT-PCR, they would be asked to be quarantined at home for 2 weeks.

For outpatients with a positive result of RT-PCR, they were admitted into “Fangcang Hospitals” or designated hospitals (real hospitals), due to their clinical status.

Comparisons for clinical characteristics of patients with (Group 1) and without (Group 2)

aggravation of illness during follow up.

62 of 100 (62%) patients in Group 1 were male, which is more than the proportion (462 of 912, 50.7%) of Group 2 ($P<0.05$). Patients in Group 1 had an elder age (Median 55.5, IQR 47-62) than that of Group 2 (Median 50, IQR 38-58, $P<0.01$), and the proportion of patients aged ≥ 60 years in Group 1 was bigger than that of Group 2 (37 of 100, 37.0% vs 199 of 912, 21.8%, $P<0.01$). The proportions of patients accompanied with diabetes (7 of 100, 7%) and cardiovascular diseases (5 of 100, 5%) in Groups 1 were both greater than those in Group 2 (20 of 912, 2.2%, $P<0.05$, for diabetes; 10 of 912, 1.1%, $P<0.01$, for cardiovascular diseases, respectively). Patients in Group 1 had a bigger proportion of cases with highest temperature 37.3-38.0 °C than patients in Group 2 (25 of 100, 25% vs 157 of 912, 17.2%, but only a boundary value was found ($P=0.05$)). There were also statistical difference when comparisons were performed for chills (28 of 100, 28.0% in Group 1 vs 154 of 912, 16.9% in Group 2, $P<0.01$), and for dyspnea (36 of 100, 36% in Group 1 vs 195 of 912, 21.4% in Group 2, $P<0.01$). Although with similar medians with IQR for duration from onset of symptoms to admission in both the groups, a significant difference was still observed ($P<0.05$), further subgroup analysis found different data distribution between groups ($P<0.01$). Patients in group 1 had a smaller median of SO_2 value (96, IQR 94.5-97) than that in Group 2 (97, IQR 96-98, $P<0.01$), and higher proportion of cases with SO_2 value ranging from 89-93 in Group 1 than that in Group 2 (15 of 100, 15% vs 31 of 912, 3.4%, $P<0.01$). The proportion of patients with WBC counts of >10 in Group 1 was greater than that in Group 2 (4 of 58, 6.9% vs 2 of 528, 0.4%, $P<0.01$). The proportion of patients with large consolidated opacity on chest CT images in Group 1 was higher than that in group 2 (10 of 86, 11.6% vs 44 of 831, 5.3%, $P<0.05$).