JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Improving the early diagnosis of suspected patients with COVID-19: a retrospective study of 106 patients

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Abstract

Introduction: An outbreak of coronavirus disease 2019 (COVID-19) occurred in Wuhan, Hubei Province, China. This study aimed to analyze the clinical and epidemiologic characteristics of patients with COVID-19 to better differentiate the suspected patients in Beijing, China.

Methodology: This was a retrospective, single-center study. Clinical and epidemiologic data were collected from suspected patients with COVID-19 admitted to Beijing Ditan Hospital from January 29 to February 21, 2020.

Results: One hundred and six patients (60 males and 46 females, median age 36 years) were enrolled. Thirty-six patients were ultimately laboratory confirmed. Fifty-three were excluded from the diagnosis of COVID-19. The remaining 17 patients were highly suspected, although their nucleic acid tests were repeatedly negative. The confirmed patients and highly suspected patients had a significantly higher proportion of epidemiologic history than the excluded patients ($P < 0.001$). There was no significant difference in clinical symptoms or the underlying diseases among the three groups. The confirmed patients had a higher frequency of lymphopenia and eosinopenia than the highly suspected and excluded patients. Chest computed tomography scans showed bilateral lung involvement, and ground-glass opacity was more likely observed in the confirmed patients.

Conclusion: The clinical features of the confirmed patients with COVID-19 were insufficient for early diagnosis of COVID-19. The epidemiologic history was of great significance in the early diagnosis of COVID-19. More sensitive diagnostic methods are needed to aid the differential diagnosis of suspected patients with COVID-19.

Key words: COVID-19; SARS-CoV-2; differential diagnosis; epidemiology.

J Infect Dev Ctries 2020; 14(6):547-553. doi:10.3855/jidc.12992

(Received 08 May 2020 – Accepted 19 May 2020)

Introduction

In December 2019, viral pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, Hubei Province, China. It was recently named coronavirus disease 2019 (COVID-19) [1,2]. SARS-Cov-2 belongs to the β-coronavirus genus. Its sequence shares more than 79% homology with the coronavirus responsible for severe acute respiratory syndrome (SARS-CoV) and 50% homology with the coronavirus causing Middle East respiratory syndrome (MERS-CoV) [3]. COVID-19, SARS, and MERS commonly lead to lower respiratory tract disease, presenting with fever and cough. The epidemic of SARS-CoV-2 infection has caused a total of 78961 confirmed cases and 2791 deaths in China and 4691 cases and 67 deaths outside of China as of February 28, 2020 [4].

Currently, the total number of newly confirmed cases of SARS-CoV-2 has gradually decreased across China, showing that the current epidemic has been effectively controlled. Meanwhile, a few clinical investigations of COVID-19 have been performed. Multiple studies have described the clinical and epidemiologic characteristics of COVID-19, but these patients were mainly from Wuhan, Hubei Province. In addition, the subjects were all confirmed patients with

SARS-CoV-2 infection. Currently, sporadic cases outside of Hubei Province have been continuously reported. Because the early clinical features can be similar to those of pneumonia caused by other microorganisms, precise diagnosis of COVID-19 patients is likely to be particularly challenging in the context of other respiratory illnesses. A balanced approach to the early identification of COVID-19 will require clinicians to consider both clinical features and epidemiologic clues that suggest SARS-CoV-2 infection.

To achieve early detection, early report, early quarantine, and early treatment, diagnostic and treatment protocols for COVID-19 pneumonia have been successively updated six times by the National Health Commission of the People's Republic of China so far. According to the present protocol, once the suspected cases are diagnosed, they will be admitted to the suspected ward for single room isolation treatment. At the same time, the CDC will start epidemiologic investigations and conduct isolation observations on their close contacts. After further evaluation, the suspected patients who meet the determined diagnostic criteria will be transferred to the confirmed ward for further treatment, and close contacts can only be released after the exclusion of the diagnosis. Therefore, timely and accurate diagnosis is very important for the next phase of patient treatment and isolation of close contacts. In this study, we aimed to retrospectively analyze the clinical and epidemiologic characteristics of suspected patients with COVID-19 in our hospital to propose the optimal strategy for the early diagnosis of COVID-19.

Methodology

Study design and patients

This was a retrospective, single-center study. We recruited hospitalized suspected patients in Beijing Ditan Hospital from January 29 to February21st, 2020. A subgroup analysis was performed according to the final diagnosis. Diagnostic criteria were in accordance with Protocol on Prevention and Control of COVID-19 (Edition 6) [5]. The suspected patients were defined either by the presence of one of four epidemiologic criteria and two of three clinical criteria or the presence of three clinical criteria. The epidemiologic criteria include 1) a history of travel or residence in Wuhan and surrounding areas, or other communities with documented COVID-19 cases within 14 days before the onset of illness, 2) contact with patients infected with SARS-CoV-2 (positive for nucleic acid detection) within 14 days before the onset of illness, 3) history of contact with patients with fever or respiratory symptoms, who travel to or reside in Wuhan and surrounding areas, or in other communities with documented COVID-19 cases within 14 days before the onset of illness, and 4) clustered cases (2 or more cases of fever and/or respiratory symptoms within 14 days in small areas such as home, office, school class, *etc.*). The clinical features include 1) fever and/or respiratory symptoms, 2) typical characteristics of COVID-19 pneumonia on chest computerized tomography (CT), and 3) normal or reduced white blood cell count or reduced lymphocyte count in the early stages following disease onset. Suspected patients who have one of the following etiological factors can be diagnosed as confirmed patients: 1) a positive result of the nucleic acid of SARS-CoV-2 by RT-PCR and 2) high homology with SARS-CoV-2 by viral gene sequencing. Highly suspected patients were defined as suspected patients who had a contact history with a confirmed patient and typical CT pulmonary manifestations.

The study was approved by the Beijing Ditan Hospital Ethics Committee (2020-011-01), and written informed consent was waived.

Data collection

The epidemiological data and clinical symptoms, physical findings, underlying comorbidities, laboratory tests, and CT findings were collected from medical records and the patients. Clinical outcomes were followed up until February 28, 2020.

Laboratory tests

Blood counts, blood biochemistry, coagulation function, procalcitonin (PCT), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum amyloid A (SAA), myocardial enzyme spectrum, influenza A virus RNA, influenza B virus RNA, and H1N1 influenza virus RNA were performed at the laboratory in Beijing Ditan Hospital. All tests for SARS-CoV-2 were performed at the laboratory in Beijing Ditan Hospital and confirmed at the Beijing Centers for Disease Control and Prevention (CDC).

Statistical analysis

Categorical variables were presented as numbers and percentages and compared by the chi-square analysis (Fisher's exact test if needed). Nonparametric tests (Kruskal-Wallis rank sum) were used for pairwise comparisons between two groups. Normally distributed continuous variables were expressed as the mean ± standard deviation (SD) and compared using independent group t tests when the data were normally

distributed; otherwise, the Mann-Whitney test was used. $P < 0.05$ was considered statistically significant. All data were analyzed using SPSS (version 25.0; IBM Corp Ltd., Armonk, NY).

Results

Demographic, clinical and epidemiologic characteristics of patients

A total of 106 suspected patients were included in this study. Patients were divided into a confirmed group, a highly suspected group and an excluded group according to the final diagnoses. The demographic, clinical and epidemiologic characteristics of the patients are shown in Table 1. The confirmed and highly suspected patients were older than the excluded patients ($P = 0.001$). The proportions of males among the confirmed (47.2%) and highly suspected (47.1%) patients were lower than that among the excluded patients (66.0%), but the difference was not significant ($P = 0.147$). Significantly higher rates of a close contact history and disease clustering were observed among the confirmed patients ($P < 0.001$) or highly suspected patients ($P < 0.001$) than among the excluded patients. Thirty-six patients were finally laboratory confirmed with SARS-CoV-2 infection, among whom 24 patients were positive for the first test of SARS-CoV-2 RT-PCR after admission, 6 patients were revealed to be positive in the second test after the first negative result, 3 patients were positive at the third test, and 3 patients were finally positive at the fourth test.

Fever and dry cough were the most common symptoms. The symptoms of the confirmed patients were very similar to those of the suspected and excluded patients, except the rate of fever in the suspected patients ($P < 0.001$). Shortness of breath and dyspnea were uncommon in all patients. The underlying comorbidities were not significantly different among the three groups.

Laboratory tests and radiologic findings

The blood counts showed significant differences in white blood cells ($P = 0.020$), lymphocytes ($P = 0.018$) and eosinophils ($P = 0.001$) among the three groups of patients (Table 2). Further pairwise comparisons showed a significant difference between confirmed and excluded patients ($P = 0.016$). However, the rates of

Table 1. Demographic, clinical and epidemiologic characteristics of patients.

Characteristic	Total (n = 106)	Confirmed patients (n = 36)	Highly suspected patients (n = 17)	Excluded patients (n = 53)	P value
Age, median (IQR), year	36 (26.8-50.0)	43.5 (33.0-55.8)	41.0 (36.0-57.5)	30 (21.5-40.5)	0.001
Male, n, (%)	60 (56.6)	17 (47.2)	8 (47.1)	35 (66.0)	0.147
Hometown of patient, n, (%)					
Hubei Province	8 (7.5)	5 (13.9)	0	3 (5.7)	0.208
Beijing	86 (81.1)	29 (80.6)	15 (88.2)	42 (79.2)	0.708
Other Provinces	12 (11.1)	2 (5.6)	2 (11.8)	8 (14.5)	0.448
Close contact with people from Hubei Province, n (%)	31 (29.2)	12 (33.3)	10 (58.8)	9 (17.0)	0.003
Disease clustering, n (%)	54 (50.9)	28 (77.8)	15 (88.2)	11 (20.8)	< 0.001
Symptoms					
Fever	88 (83.0)	33 (91.7)	10 (58.8)	45 (84.9)	0.011
Dry cough	60 (56.5)	19 (52.8)	10 (58.8)	31 (58.5)	0.850
Sputum production	31 (29.2)	11 (30.6)	2 (11.8)	18 (34.0)	0.211
Headache	12 (11.3)	3 (8.3)	3 (17.6)	6 (11.3)	0.592
Shortness of breath	5 (4.7)	3 (8.3)	0	2 (3.8)	0.463
Dyspnea	3 (2.8)	2 (5.6)	0	1 (1.9)	0.743
Diarrhea	6 (5.7)	2 (5.6)	1 (5.9)	3 (5.7)	1.000
Myalgia	16 (15.1)	8 (22.2)	2 (11.8)	6 (11.3)	0.339
Fatigue	23 (21.7)	10 (27.8)	3 (17.6)	10 (18.9)	0.550
Underlying diseases					
Chronic obstructive pulmonary disease	4 (3.8)	2 (5.6)	1 (5.9)	1 (1.9)	0.486
Hypertension	19 (17.9)	5 (13.9)	6 (35.3)	8 (15.1)	0.124
Diabetes	8 (7.5)	1 (2.8)	2 (11.8)	5 (9.4)	0.371
Coronary heart disease	1 (0.9)	0	0	1 (1.9)	1.000
Cirrhosis	2 (1.9)	0	0	2 (3.8)	0.657
Cancer	3 (2.8)	0	0	3 (5.7)	0.402

IQR: interquartile range.

leukopenia were similar among the three groups (P = 0.842). The proportions of lymphopenia and eosinopenia were highest in confirmed patients among the three groups (P = 0.011). Further pairwise comparisons showed significantly reduced lymphocytes (P = 0.031) and eosinophils (P = 0.003) between confirmed and excluded patients. Creatine kinase (P = 0.003) and creatine kinase MB (P = 0.009) were lower in confirmed patients than in excluded patients by pairwise comparisons. Prolonged thrombin time was found in confirmed patients compared to excluded patients (P = 0.035).

Radiological findings of COVID-19 are varied. Twenty-one (58.3%) patients showed bilateral pneumonia in the confirmed group, compared to 35.3% of the highly suspected patients and 35.8% of the excluded patients (P = 0.028) (Table 3). Most of the confirmed patients (83.3%) presented with ground-

Table 2. Laboratory findings of patients.

Variable	All Patients (N = 106)	Confirmed patients (N = 36)	Highly suspected patients (N = 17)	Excluded patients (N = 53)	P-Value
White blood cell count, × 10^9/L	6.04 (4.76–8.25)	5.17 (4.27–6.48)	6.25 (4.07–8.99)	7.16 (4.98–8.67)	0.020
< 4, n (%)	16 (15.2)	6 (17.1)	3 (17.6)	7 (13.2)	0.842
Neutrophil count, × 10^9/L	4.16 (2.81–5.83)	3.70 (2.25–4.78)	3.60 (2.21–6.62)	4.97 (3.38–5.99)	0.096
Lymphocyte count, × 10^9/L	1.41 (1.09–1.93)	1.16 (0.89–1.63)	1.54 (1.26–2.05)	1.48 (1.18–2.07)	0.018
< 1, n (%)	22 (21.0)	13 (37.1)	1 (5.9)	8 (15.1)	0.011
Monocyte count, × 10^9/L	0.36 (0.25–0.46)	0.36 (0.24–0.46)	0.30 (0.24–0.44)	0.39 (0.27–0.47)	0.538
Eosinophils, × 10^9/L	0.04 (0.01–0.10)	0.01 (0.00–0.04)	0.09 (0.04–0.14)	0.06 (0.02–0.14)	0.001
< 0.02, n (%)	34 (32.4)	18 (51.4)	3 (17.6)	13 (24.5)	0.011
Hemoglobin, g/d	141 (129–154)	139 (129–154)	141 (133–153)	142 (127–155)	0.915
Platelet count, × 10^9/L	204 (158–257)	200 (155–240)	229 (193–261)	201 (154–254)	0.365
Alanine aminotransferase, U/L	21.1 (13.8–35.2)	21.1 (14.2–31.3)	21.1 (10.4–21.4)	22.0 (14.7–36.8)	0.909
Aspartate aminotransferase, U/L	24.2 (18.9–30.4)	22.8 (17.6–29.8)	21.4 (13.7–30.4)	25.3 (20.2–30.9)	0.464
Total bilirubin, mmol/L	10.5 (7.4–12.9)	10.3 (7.5–13.3)	10.6 (8.8–13.0)	9.9 (6.3–12.8)	0.713
Direct bilirubin, mmol/L	3.3 (2.5–4.8)	3.5 (2.5–4.8)	3.5 (2.7–4.0)	3.2 (2.1–5.5)	0.840
Albumin, g/L	43.6 (39.7–47.0)	41.5 (36.0–44.5)	46.7 (41.4–48.0)	44.7 (40.7–47.4)	0.005
Creatinine, μmol/L	65.6 (53.1–77.3)	65.5 (54.1–78.8)	62.4 (50.0–75.2)	66.8 (53.0–77.4)	0.518
estimated glomerular filtration rate (ml/min/1.73m^2)	109.71 (99.30–122.33)	108.29 (97.21–116.44)	107.97 (93.62–118.48)	114.19 (102.14–129.33)	0.178
Creatine kinase, U/L	85.8 (50.4–129.0)	55.9 (41.5–107.1)	82.1 (57.0–153.6)	98.7 (79.5–154.1)	0.003
Creatine kinase MB	16.8 (13.4–21.0)	14.8 (12.6–16.9)	17.6 (13.7–21.0)	18.3 (14.0–24.1)	0.011
α-hydroxybutyric dehydrogenase (U/L)	185 (161–220)	170 (153–209)	180 (166–221)	193 (171–222)	0.295
Lactate dehydrogenase, U/L	224.3 (191.2–270.5)	206.2 (178.8–267.7)	197.0 (183.1–260.7)	237.6 (205.8–281.2)	0.062
C-reactive protein (mg/L)	6.0 (1.3–25.1)	6.3 (1.8–32.5)	1.2 (0.1–5.2)	8.0 (1.8–38.9)	0.011
Serum amyloid A (mg/L)	22.1 (3.5–177.3)	12.1 (4.4–123.5)	5.0 (1.0–41.9)	57.2 (4.1–304.5)	0.118
T cell	1122 (79–1686)	1165 (823–1530)	1119 (786–1901)	986 (655–1792)	0.862
$CD8^+$T cell	356 (233–629)	396 (231–600)	346 (265–905)	354 (232–1011)	0.886
$CD4^+$T cell	691 (448–901)	726 (496–862)	696 (432–920)	588 (297–888)	0.630
NK cell	176 (136–280)	195 (123–286)	176 (151–210)	149 (96–349)	0.746
B cell	180 (114–280)	203 (117–252)	262 (114–346)	132 (108–180)	0.306
Erythrocyte sedimentation rate (mm/h)	19.5 (7.0–33.8)	21.0 (7.5–36.0)	7.0 (5.0–21.0)	27.5 (12.3–38.3)	0.150
International Normalized Ratio	1.11 (1.04–1.16)	1.11 (1.05–1.17)	1.10 (1.03–1.15)	1.11 (1.04–1.17)	0.928
D-dimer, mg/L	0.34 (0.24–0.63)	0.32 (0.25–0.69)	0.29 (0.23–0.54)	0.41 (0.22–0.63)	0.770
Fibrin degradation product	1.31 (0.89–1.94)	1.09 (0.87–1.80)	0.83 (0.49–1.61)	1.72 (1.14–2.10)	0.044
Thrombin time, s	16.0 (15.0–17.4)	16.5 (15.6–18.0)	16.1 (15.0–18.4)	15.5 (14.3–16.7)	0.028
PO_2	12.05 (10.05–14.24)	10.34 (7.30–12.54)	12.1 (11.6–13.0)	13.2 (10.6–14.3)	0.132
PCO_2	5.19 (4.48–5.61)	5.26 (4.84–5.45)	5.51 (5.11–5.80)	5.07 (4.40–5.57)	0.462
PO2/FiO2	430.5 (358.5–507.5)	376.0 (299.0–471.5)	469.1 (426.7–617.1)	483.0 (379.0–508.0)	0.241

Table 3. Chest CT findings of patients.

Characteristic	Total (n = 106)	Confirmed Patients (n = 36)	Highly suspected patients (n = 17)	Excluded patients (n = 53)	P Value
Bilateral lung involvement	46 (43.4)	21 (58.3)	19 (35.8)	6 (35.3)	0.028
Ground-glass opacity	63 (59.4)	30 (83.3)	24 (45.3)	9 (52.9)	0.001
Consolidation	30 (28.3)	15 (41.7)	13 (24.5)	2 (11.8)	0.054
Pleural effusion	3 (2.8)	3 (8.3)	0	0	0.066
Local patchy shadowing	15 (14.2)	5 (13.9)	7 (13.2)	3 (17.6)	0.899
Stripe sign	25 (24.3)	10 (30.3)	12 (22.6)	3 (17.6)	0.567
Pulmonary nodule	25 (24.3)	4 (12.1)	18 (34.0)	3 (17.6)	0.056
Tree-in-bud pattern	5 (4.7)	1 (2.8)	4 (7.5)	0	0.567
Lung cavitation	1 (0.9)	0	0	1 (5.9)	0.160

Data are shown: n (%).

glass opacity (P = 0.001) compared to the highly suspected and excluded patients. According to chest CT, consolidation was also common in the confirmed group (41.7%), and pleural effusion occurred in three (8.3%) confirmed patients; however, these findings were not found to be significantly different among the groups (P = 0.054).

Diagnostic mode and final diagnosis

According to the diagnosis and treatment protocol (the sixth edition), the diagnostic criteria of suspected cases were divided into two modes: mode 1, the presence of either one of three epidemiologic criteria and two of three clinical criteria or mode 2, no epidemiologic history, and the presence of all three clinical criteria. The rates of patients with epidemiologic history were significantly different among the three groups (P < 0.001). More confirmed patients had an epidemiologic history than excluded patients (P < 0.001) (Table 4). Among the 53 patients excluded from the diagnosis of COVID-19, there were 4 cases of influenza A, 2 cases of influenza B, 3 cases of AIDS complicated with infection, 1 case of tuberculosis and 1 case of chicken pox. Although the highly suspected patients underwent repeated negative nucleic acid tests for SARS-CoV-2, four patients were diagnosed with positive IgM and IgG at the follow-up visit after discharge for 2 weeks when the serum antibody test was available. The remaining patients did not have a definite diagnosis due to lack of etiological evidence.

Discussion

Our study presented the epidemiologic and clinical characteristics and final diagnosis of 106 suspected patients with COVID-19 in Beijing. Since the beginning of our department in January 2020, we have mainly been responsible for the differential diagnosis of suspected patients with COVID-19. The inadequate ability to make a rapid differential diagnosis between confirmed and suspected cases counted partly for a rapidly growing number of infected patients during the early phase of the epidemic. Therefore, improving diagnostic efficiency is urgent and essential to further contain COVID-19.

In our study, we enrolled 106 suspected cases, including 36 cases that were ultimately laboratory-confirmed and 53 cases for which a diagnosis of COVID-19 was ruled out. A definitive diagnosis was not established before discharge in any of the remaining 17 highly suspected patients. Our results suggested that the patients with COVID-19 were middle-aged, and the highly suspected and excluded patients were younger, which was in line with the previous literature [6]. However, COVID-19 may occur in patients of all age groups and does not have a typical age of onset [7]. The most common symptoms of COVID-19 were fever and dry cough, and fewer patients had gastrointestinal symptoms, which was also consistent with published articles [8 – 10]. No obvious differences were found in the clinical symptoms of patients among the confirmed, highly suspected and excluded patients. However, the clinical manifestations are nonspecific. It is unclear whether the viral load affects the clinical presentation. The viral load that was found in asymptomatic patients

Table 4. Diagnostic mode of highly suspected patients with COVID-19.

Mode	Confirmed patients (n = 36)	Highly suspected patients (n = 17)	Excluded patients (n = 53)	P value
1	35 (97.2)	17 (100)	20 (37.7)	< 0.001
2	1 (2.8)	0	33 (62.3)	

Data are shown: n (%).

was similar to that in patients with symptoms [11]. Ai *et al*. observed that clinical severity was not associated with viral load [12]. However, Liu *et al*. found that the viral load was associated with disease severity and was especially strongly correlated with the lung injury Murray score [13]. Hence, the diagnosis of COVID-19 could not be made merely on diverse clinical manifestations.

Our research suggested that only 34.0% (36/106) of patients were ultimately diagnosed with COVID-19 and that for 50% of the patients, a diagnosis of COVID-19 was eventually ruled out. The rate of confirmation of diagnosis in all suspected patients was low. There were no significant differences in clinical symptoms between the confirmed and excluded patients. More confirmed patients had a decreased lymphocyte count, eosinophil count and thrombin time. A high frequency of bilateral lung involvement and ground-glass opacity was also observed in the chest CT of the confirmed patients. The results were consistent with previous studies [14 – 16]. However, the difference in symptoms, blood count and chest CT of suspected patients was not enough to confirm the diagnosis. In fact, many suspected patients who had similar symptoms, blood count and images of chest CT to those of the confirmed patients were ultimately excluded. It was suggested that the diagnostic criteria of suspected cases were not reliable based on three clinical features.

Our study also included 17 highly suspected patients whose nucleic acid detection had been repeatedly negative. According to the existing diagnosis and treatment protocol, these patients should be excluded. However, all of the highly suspected patients had a clear epidemiologic history. Combined with nonspecific clinical manifestations, lymphopenia and ground-glass opacity in chest CT, they were difficult to rule out from the diagnosis of COVID-19. In fact, four of the highly suspected patients in our study were indeed diagnosed with positive IgM and IgG. The current sixth version of the diagnosis and treatment protocol has not given clear recommendations for their treatment, isolation and next follow-up management. Currently, the definitive diagnosis is made mainly on the basis of nucleic acid tests. In our confirmed cases, 33.3% (12/36) of the nasopharyngeal swab specimens were negative for RT-PCR the first time and were then positive on the second or even third or fourth time. A recent study reported that 3 of 17 patients tested negative for SARS-CoV-2 by RT-PCR and were ultimately diagnosed through metagenomics sequencing. It was estimated that at least 15% of the false negative rate of RT-PCR was due to low viral loads in the upper respiratory tract [12]. Due to the different locations of the samples collected (upper or lower respiratory tract), severity of the disease (severe or mild), and sampling time (time from onset), the total positive rate of RT-PCR was reported to be approximately 29.6-88.9% at initial presentation [17]. The results suggested that the current RT-PCR for SARS-CoV-2 also had the possibility of a false negative rate. Although serum antibody detection for SARS-CoV-2 was recommended as one of the diagnostic criteria in the released 7th edition of the diagnostic and treatment protocol for COVID-19 pneumonia, its sensitivity and specificity need to be further evaluated [18,19].

Our study has several limitations. First, this was a single-center study with a small number of patients. It could not fully reflect the characteristics of all suspected patients. Second, during the epidemic period, some pathogenic tests were not carried out due to biosafety. Some highly suspected and excluded patients could not be diagnosed clearly because there was no etiological evidence. Last, our results were based on the second or third generation of cases from Wuhan city or Hubei Province, which might not be appliable to cases from a large-scale community-based transmission.

Conclusion

According to the current diagnostic criteria, the proportion of suspected patients with clinical manifestations but no epidemiological history who were ultimately diagnosed with COVID-19 was low. The differences in clinical features were not sufficient for the early clinical diagnosis of COVID-19. The most significant difference was the epidemiologic history between the confirmed and excluded patients, which was of great significance in the early diagnosis of COVID-19. The highly suspected patients could not completely exclude a diagnosis of COVID-19, as more sensitive diagnostic methods were needed to aid the diagnosis of the disease.

Acknowledgements

This work was supported by the Construction of high-level health technical personnel in the Beijing health system (No. 2014-3-093); and the China's National Science and Technology Major Project (No. 2018ZX10715-005).

Authors' contributions

Study conception and design: Xuefei Duan, Guiju Gao and Xuesong Gao. Data acquisition: Zheng Yuan, Xiaomin Liu, Wenshan Zhao, Te Xiao, and Yanlin Guan. Data analysis and interpretation: Di Yang, Yijin Zhang, Hongjie Li, and Ping

Gao. Draft revision: Xuefei Duan and Guiju Gao. All the authors approved the final version for submission.

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Conflict of interests: No conflict of interests is declared.