Clinical characteristics of 194 cases of COVID-19 in Huanggang and Taian, China

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Abstract

**Purpose** We aimed to report the clinical characteristics of 194 cases coronavirus disease-19 (COVID-19) in Huanggang, Hubei and Taian, Shandong.

**Methods** We retrospectively investigated the clinical, laboratory characteristics and CT imaging of confirmed cases of COVID-19 from Jan 22 to Feb 28, 2020 in Huanggang Central Hospital and The Second Affiliated Hospital of Shandong First Medical University. Real time PCR was used to detect the new coronavirus in respiratory samples. Immunohistochemical staining was used to detect the expressions of ACE2 in tissues.

**Results** Among the 194 patients infected with COVID-19, 108 patients were male, with a median age of 48.3 years. The average preclinical period was 7.44 day. Except for 37 severe or critically ill patients, the rest of the 157 patients exhibited mild or moderate symptoms. 190 (97.94%) patients were confirmed during the three times nucleic acid test. The main clinical symptom of the patients were fever, sore throat and cough, which accounted for 146 cases (75.26%), 98 (50.52%) and 86 cases (44.33%), respectively. 30 patients (15.46%) showed liver dysfunction. Imaging examination showed that 141 patients (72.68%) showed abnormal, 53 cases (27.32%) had no obvious abnormal density shadow in the parenchyma of both lungs. Up to now, 109 cases were discharged from the hospital, and 9 patients died. The ACE2 expression levels were up-regulated in patients of severe type and critically ill type.

**Conclusion** Clinical symptoms, laboratory tests and CT imaging should be combined for comprehensive analysis to diagnose COVID-19. ACE2 may be the receptor of COVID-19.

**Introduction**

In December 2019, clusters of novel pneumonia caused by COVID–19, the 2019 novel coronavirus, break out in Wuhan, Hubei, China. This novel coronavirus has been recently identified as a type of beta coronavirus, with a diameter of 60–140 nm, which enveloped virions that appear as oval or round and polymorphous following the strong infectivity and general susceptibility to people of all ages and across the globe [1, 2]. Since December 2019, a large number of patients infected with COVID-19 have been reported around the world [3–6].
Up to March 10, 2020, 80,928 cases have been confirmed in China, including 67,760 cases in Hubei Province, 49,965 cases in Wuhan City. Gratifyingly, the outbreak of COVID–19 is well controlled in China now, with the well-healed patients, 60195. Unfortunately, 33,830 cases have been confirmed besides China, including 7,513 cases in South Korea, 9,172 cases in Italy and 8,042 cases in Iran. Although control measures have been applied to prevent further spread in China, including isolation of people suspected to have the disease, the need for better diagnosis and treatment of patients with pneumonia is no longer limited to China now, especially with the increasing numbers of infected patients worldwide, especially in South Korea, Italy and Iran. So far, several studies have described the epidemiological and clinical characteristics of patients infected with COVID–19 [7–10], the clinical characteristics of patients remains indistinct due to the rare samples reported.

In this study, the clinical characteristics and CT imaging features of 194 patients diagnosed with COVID–19 in Huanggang Central Hospital and The Second Affiliated Hospital of Shandong First Medical University were discussed. We believe our findings will give further details to the epidemic situation and clinical characteristics of this novel coronavirus.

Methodology

Patients.

194 patients were consecutively enrolled from January 22th to February 28th, 2020 in Huanggang Central Hospital (178 cases) and The Second Affiliated Hospital of Shandong First Medical University (16 cases). The written informed consent was obtained. All the patients were hospitalized and had laboratory confirmed COVID–19 infection. We collected all the data including demographic data, clinical data, laboratory parameters, chest CT from patients’ medical records and attending doctors.

Laboratory Confirmation.

Epidemiological data, clinical laboratory data and radiological characteristics and treatment and outcomes data were obtained with standardized data collection forms from electronic medical records and checked by both on-site and off-site doctors. The real-time reverse transcriptase polymerase chain-reaction (RT-PCR) test was performed to detect coronavirus according to the manufacturer’s instructions.
Statistical analysis.

Statistical analyses were performed with SPSS (v.19.0; SPSS Inc., Chicago, IL, USA). Categorical data were presented as number (%) and tested with Chi Square test or Fisher’s exact test. Continuous data were presented as mean ± SD (standard deviation) and tested with paired t test.

Results

The clinical characteristics of patients infected with COVID-19.

In this study, 194 cases infected with COVID-19 in Huanggang Central Hospital and The Second Affiliated Hospital of Shandong First Medical University. Among them, the average preclinical period was 7.44 day. The longest preclinical period was 18 day and the shortest period was 0.08 day. 96.9 % patients were imported infections (with a history of epidemic in Wuhan) and 3.1% patients had contact with the seafood market in Wuhan, China. 108 patients (55.67 %) were male. 106 patients (54.64%) were aged 31–50 years, 41 patients (21.13%) were aged 51–70 years, 17 patients (8.76%) were aged 18–30 years, 8 patients (4.13%) were under 18 years old, 22 patients (11.34%) were over 71 years old. In term of clinical classification, 116 (59.79%) patients were mild type, 41 (21.13%) patients were moderate type, 25 (12.89%) patients were severe type and 12 patients (6.19%) were critically ill type. During the diagnostic procedure by nucleic acid tests, we found that 112 patients (57.73%) got a positive result in the first test, 45 patients (23.30%) got a positive result in the second test, 33 patients (17.01%) got a positive result in the third test, 3 patients (1.55%) got a positive result in the fourth test. Surprisingly, another 1 patient (0.51%) remained negative until the fifth test (Table 1). The most common symptoms were fever, sore throat and cough, which accounted for 146 cases (75.26%), 98 (50.52%) and 86 cases (44.33%), respectively. 71 cases (36.60%) had shortness of breath. In addition, 44 (22.68%) patients had muscle ache, 33 patients (17.10%) had headache, and 36 patients (18.56%) had diarrhea symptom. Unfortunately, 9 patients (4.64%) were died.

Table 1. Demographics, baseline and clinical characteristics of patients infected with COVID-19.

| Variables     | Patients (n=194) |
|---------------|-----------------|
| Age (Y)       |                 |
| <18           | 8 (4.13%)       |
| 18-30         | 17 (8.76%)      |
| 31-50         | 106 (54.64%)    |
51-70 | 41 (21.13%)  
>71  | 22 (11.34%)  

Sex  
| Female | 86 (44.33%)  
| Male   | 108 (55.67%)  

Clinical classification  
| Mild type | 116 (59.79%)  
| Moderate type | 41 (21.13%)  
| Severe type | 25 (12.89%)  
| Critically ill type | 12 (6.19%)  

Types of infection  
| Huanan Seafood Wholesale | 6 (3.1%)  
| Imported infections | 188 (96.9%)  

Number of nucleic acid tests  
| The first time | 112 (57.73%)  
| The second time | 45 (23.20%)  
| The third time | 33 (17.01%)  
| The fourth time | 3 (1.55%)  
| The fifth time | 1 (0.51%)  

Signs and symptoms at admission  
| Fever | 146 (75.26%)  
| Cough | 86 (44.33%)  
| Shortness of breath | 71 (36.60%)  
| Muscle ache | 44 (22.68%)  
| Headache | 33 (17.01%)  
| Sore throat | 98 (50.52%)  
| Chest pain | 47 (24.22%)  
| Diarrhoea | 36 (18.56%)  
| More than one sign or symptom | 169 (87.11%)  

Chest x-ray and CT findings  
| Bilateral pneumonia | 101 (52.06%)  
| Unilateral pneumonia | 40 (20.62%)  
| No abnormal density shadow | 53 (27.32%)  

Clinical outcome  
| Discharged | 109 (56.19%)  
| Remained in hospital | 76 (39.17%)  
| Died | 9 (4.64%)  

\( n/N \) (%), where \( N \) is the total number of patients with available data.
Laboratory findings of patients infected with COVID-19.

The white blood cell (WBC) count of 75 patients (38.66%) was lower than the normal range (3.5×10^9/L) and 29 patients (14.95%) was higher than the normal range (9.5×10^9/L). 94 patients (48.45%) had lymphocytopenia (the lymphocyte count was less than 1.0×10^9/L). 51 patients (26.29%) had platelets lower than the normal range (100×10^9/L), and no patients had platelets higher than the normal range (300×10^9/L).

There were 119 patients (61.34%) with high C-reactive protein (CRP). The level of D-dimer was increased in 27 patients (13.92%). 19 patients (9.80%) had lower albumin level than the normal range (35 g/L). In terms of liver function, 30 patients (15.46%) showed alanine transaminase (ALT) and aspartate aminotransferase (AST) above the normal range. 65 patients (32.51%) had abnormal myocardial enzyme spectrum, indicating the increase of creatine kinase (CK). The level of creatinine increased in 24 patients (12.37%). The level of lactate dehydrogenase (LDH) increased in 83 patients (42.78%) (Table 2).
| Laboratory results                        | Patients (n=194)     |
|------------------------------------------|----------------------|
| White blood cell count, \( \times 10^9/\text{L} \) | 5.6 (3.6-11.1)       |
| <4                                       | 75 (38.66%)          |
| 4-10                                     | 90 (46.39%)          |
| 10                                       | 29 (14.95%)          |
| Lymphocyte count, \( \times 10^9/\text{L} \) | 1.2 (0.7-2.6)       |
| <1                                       | 94 (48.45%)          |
| 1-3.3                                    | 61 (31.44%)          |
| 3.3                                      | 39 (20.11%)          |
| Platelet count, \( \times 10^9/\text{L} \) | 168 (117-239)       |
| <100                                     | 51 (26.29%)          |
| 100-300                                  | 143 (73.71%)         |
| 300                                      | 0 (0.0%)             |
| C-reactive protein, mg/L                | 15.8 (8.9-21.2)      |
| \( \leq 10 \)                            | 75 (38.66%)          |
| 10                                       | 119 (61.34%)         |
| D-dimers, mg/L                          | 0.3 (0.1-0.4)        |
| \( \leq 0.5 \)                           | 167 (86.08%)         |
| 0.5                                      | 27 (13.92%)          |
| Albumin, g/L                             | 43.5 (36.1-48.3)     |
| \( \leq 35 \)                            | 19 (9.80%)           |
| 35                                       | 175 (91.20%)         |
| Alanine aminotransferase, U/L           | 25.6 (22.1-37.7)     |
| \( \leq 40 \)                            | 164 (84.54%)         |
| 40                                       | 30 (15.46%)          |
| Aspartate aminotransferase, U/L         | 30.1 (15.1-36.9)     |
| \( \leq 40 \)                            | 16484.54%            |
| 40                                       | 30 (15.46%)          |
| Creatinine, \( \mu \text{mol/L} \)      | 79.0 (55.0-99.0)     |
| \( \leq 115 \)                           | 170 (87.63%)         |
| 115                                      | 24 (12.37%)          |
| Creatine kinase, U/L                    | 138.0 (62.2-218.6)   |
| \( \leq 200 \)                           | 129 (66.49%)         |
| 200                                      | 65 (32.51%)          |
| Lactate dehydrogenase, U/L              | 201.0 (127.0-316.0)  |
| \( \leq 250 \)                           | 111 (57.22%)         |
| 250                                      | 83 (42.78%)          |
Data are median (IQR), n/N (%), where N is the total number of patients with available data.

**Imaging features of patients infected with COVID-19.**

Among the 194 patients, 141 (72.68%) showed abnormal chest CT images, consisting 101 cases (52.06%) of bilateral pneumonia and 40 cases (20.62%) of unilateral pneumonia (Table 1). Some lesions might have a mixed pattern of consolidation in the center and ground glass opacity in the peripheral (Figure 1). In severe or critically severe patients, multiple patches or an integrated larger patch of ground glass opacity, consolidation or mixed consolidation and ground glass opacity might present in bilateral lungs (Figure 2).

**Treatment for patients infected with COVID-19.**

All patients were treated empirically with the antibiotic, mainly ribavirin or lopinavir or resochin and IFN-α. The duration of antibiotic treatment was less than 10 day. 5 patients used the invasive ventilator.

**The prognosis of patients infected with COVID-19.**

Up to March 3, 109 patients (56.19%) were discharged from the hospital and 9 (4.64%) patients have died. The average length of stay of discharged patients was 10.2 days. Fitness for discharge was based on temperature returned to normal for more than 3 days, respiratory pathogenic nucleic acid test was negative for two consecutive time and the improvement of chest radiographic evidence.

**The expression of ACE2 in patients with COVID-19.**

We used IHC to detect the ACE2 protein levels from two patients who died of COVID-19. The results showed that the ACE2 protein levels were up-regulated in severe type and critically ill type compared with the adjacent normal tissue of lung, especially in critically ill type (Figure 3).

**Discussion**

Coronaviruses infect many species of animals including humans, causing acute and chronic diseases [11], which are a family of viruses within the Nidovirus superfamily, were divided into three groups due to the antigenic reactivity, including alpha, beta and gamma coronaviruses [12].
Recently, the COVID-19 infection occurred and spread in the mainland of China, South Korea, Italy and Iran, and so on. This novel COVID-19 has been recently identified as a type of beta coronavirus, with a diameter of 60–140nm [2]. Researchers revealed that the COVID-19 virus was similar to severe acute respiratory syndrome coronavirus (SARS-CoV). The closest genetic similarity was found in a coronavirus isolated from bats [13, 14]. SARS is a novel infectious disorder that was first diagnosed in November 2002 in China and subsequently spread worldwide [15, 16]. SARS was documented in over 8000 persons with 778 deaths before the outbreak was extinguished [17]. Unfortunately, until to now, COVID-19 was documented in over 94084 persons with 3218 deaths.

In 2003, patients with SARS were via airborne droplets and through fomites [17]. At present, patients with COVID-19 are the main source of infection through respiratory droplets and contact [18, 19]. Clinically, patients with SARS had a triphasic pattern of disease, including fever, a nonproductive cough, sore throat, and myalgia [20]. In present study, patients with COVID-19 were fever (75.26%), cough (44.33%), sore throat (50.52%), and myalgia (22.68%).

Kuba K et al reported that the expression levels of ACE2 on the surface of lung cells were downregulated after infection with SARS-CoV [21]. However, we found that the ACE2 protein levels were up-regulated in severe type and critically ill type compared with the adjacent normal tissue of lung, especially in critically ill type. This result demonstrates that ACE2 maybe the receptor of COVID-19. Recently, Hoffmann M et al reported that SARS-CoV-2 Cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor [22]. They also reveal the important commonalities between SARS-CoV-2 and SARS-CoV infection and identify a potential target for antiviral intervention. Because there is no specific drug for the treatment of patients with COVID-19 now.

In terms of laboratory tests, 38.66% patients had a decreased number of WBC and nearly half (48.45%) of the patients had a decreased number of lymphocytes. The CRP level was increased in 119 patients (61.34%). In some patients, the alanine aminotransferase, aspartate aminotransferase, creatinine, creatine kinase and lactate dehydrogenase may increase. In addition, all cases were confirmed by nucleic acid test. 112 (57.73%) patients got positive results during the 3 tests.
Furthermore, the CT images of 72.68% patients were abnormal. Due to the complexity and non-determinacy, clinical symptoms, laboratory tests and CT should be combined for comprehensive analysis to diagnose COVID-19.

In summary, COVID-19 is dangerous and severe, the mechanism of occurrence and development of COVID-19 is unclear by this time, in-depth study is still needed for patients with COVID-19.

Declarations

Funding.

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Conflicts of interest.

All authors declared that there were no competing interests.

Ethical approval.

The second affiliated hospital of Shandong first medical university approved the study (COVID-19–2020) and this approval was confirmed the first medical university of Shandong. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Informed consent.

Yes, informed consent is obtained.

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Figures
Chest CT of a male patient, 51 years old. (A) He underwent a chest CT examination on February 4th, which showed a piece of peripheral ground glass opacity with consolidation in the lower lobes of the two lungs. (B) 6 days after treatment, the CT images of February 10th showed a decrease in density of the pulmonary lesions with fibrosis formation.
Chest CT of a male patient, 47 years old. (A) He underwent a chest CT examination on February 10th, which showed multiple lesions of peripheral ground glass opacity with consolidation and fibrosis in the two lungs. (B) 18 days after treatment, the CT images of February 10th showed a decrease in density of the pulmonary lesions with fibrosis format.
The expression levels of ACE2 in patients with COVID-119. (A) IHC showed the expression levels of ACE2 in the adjacent tissues of lung. (B) IHC showed the expression levels of ACE2 in Severe type of COVID-19. (C) IHC showed the expression levels of ACE2 in Critically ill type of COVID-19.
in the severe type. (C) IHC showed the expression levels of ACE2 in the critically ill type.