Clinical characteristics of moderate and severe cases with COVID-19 in Wuhan, China: a retrospective study

Lingshuang Sheng1 · Xiong Wang2 · Ning Tang2 · Fankai Meng1 · Liang Huang1 · Dengju Li1

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Abstract
With the outbreak of COVID-19 ongoing, this infectious disease has been posing a significant threat to public health. However, we are still relatively inexperienced on recognizing the clinical characteristics of severe COVID-19 and death cases. Therefore, we hereby collected and analyzed a total of 232 cases to illustrate the clinical characteristics of such patients in Wuhan and to find notable marks for early clinical warning. We consider age, comorbidities, platelet count, albumin, D-dimer, LDH, CRP and IL-6 level might be more meaningful marks for COVID-19 prognostic evaluation.

Keywords COVID-19 · SARS-cov-2 · Clinical characteristics

Introduction
Coronavirus disease 2019 (COVID-19) is widely known as a type of severe infectious disease primarily transmitted via respiratory tract and body contact. It has demonstrated a series of clinical characteristics including long incubation period, strong infectivity, high occurrence of multiple organ dysfunction syndrome (MODS) and high mortality rate among severe cases. The infectious disease has been posing a significant threat to public health [1, 2]. On January 31, 2020, World Health Organization (WHO) officially announced COVID-19 as a public health emergency of international concern (PHEIC). As of July 2020, the COVID-19 pandemic has affected more than 200 countries and regions worldwide, with a total of more than 13 million confirmed cases and over 57,000 deaths [3].

The main clinical manifestations of COVID-19 are fever, dry cough and short of breath. Gastrointestinal symptoms and liver damage could also be observed in some cases [4, 5]. Severe patients might progress to dyspnea and even acute respiratory distress syndrome (ARDS), immunological derangement, coagulopathy, septic shock and MODS [6]. As a recent report showed that patients with COVID-19 could also develop the symptoms of anosmia and ageusia [7], we should also be alert for new clinical symptoms caused by the latent mutation of COVID-19 virus.

During this study, we collected and analyzed a total of 232 cases from intensive care unit (ICU) and general wards of Wuhan Tongji Hospital. Our aim was to retrospectively analyze the clinical characteristics of these cases and compare the differences between moderate and severe cases and between survived and death cases, respectively, so as to find some early warning clues for future clinical treatment.

Methods

Data collection
All data were collected from patients diagnosed with COVID-19 according to the diagnostic criteria issued by National Health Commission of the People’s Republic of China [8], who were hospitalized in Wuhan Tongji Hospital.
during the study period. All cases were categorized into two main groups: moderate cases and severe cases (including critical cases). Severe cases met at least one of the following criteria: 1. respiratory distress with respiratory rate over 30 per minute; 2. oxygen saturation ≤ 93% under resting state; 3. arterial blood oxygen partial pressure (PaO₂)/oxygen concentration (FiO₂) ≤ 300 mmHg; 4. chest imaging tests suggesting > 50% progression of lung lesions within 24–48 h. After analyzing our raw data and data from other COVID-19 reports [2, 6, 9–12], we finally picked up markers that were shown as median and interquartile range (IQR) values. 

Viral RNA examination

All patients were confirmed by COVID-19 viral RNA examinations which were conducted by clinical laboratory of Wuhan Tongji hospital. Their nasal and pharyngeal swab specimens were collected for RT-PCR assay. On receipt of the samples, viral RNA extraction was conducted with magnetic viral RNA/DNA extraction kit on PAN9600 Automated Nucleic Acid Extraction System (Tianlong, Xi’an, China), according to the manufacturer’s instructions, followed by polymerase-chain-reaction (PCR) screening for the presence of 2019 novel coronavirus (2019-nCoV) with commercial kits (Tianlong, Xi’an, China), according to the manufacturer’s instructions, followed by polymerase-chain-reaction (PCR) screening for the presence of 2019 novel coronavirus (2019-nCoV) with commercial kits (Tianlong, Xi’an, China) in a volume of 25 µL PCR mixture containing 17.5 µL reaction solution, 1.5 µL probes, 1.5 µL Taq and 5 µL nucleic acid. Conditions for the amplifications include reverse transcription at 50 ºC for 30 min and pre-denaturation at 95 ºC for 10 min, followed by five cycles of 94 ºC for 15 s, 50 ºC for 30 s and 72 ºC for 30 s and 40 cycles of 94 ºC for 10 s and 58 ºC for 30 s for fluoroescence detection. A cycle threshold value (Ct value) ≤ 37 was defined as a positive test, which was based on the recommendation by the National Institute for Viral Disease Control and Prevention (China).

Statistical analysis

Collected data were analyzed with Statistical Package for the Social Sciences (SPSS) version 20.0 software. Results were shown as median and interquartile range (IQR) values. Independent group t tests were used for the comparison of means for continuous variables that were normally distributed; conversely, the Mann–Whitney U test was used for continuous variables not normally distributed. Proportions for categorical variables were compared using the χ² test. Two-sided P values of less than 0.05 were considered statistically significant.

Results

Age and comorbidities

The 232 COVID-19 patients ranged in age from 20 to 88 years old, with a median age of 68 years old. The median age was 65 years old in the moderate group (102 cases), and the median age was 71 years old in severe group (130 cases). 88 patients died in the severe group, with the median age of 75 years old, which was significantly higher than that of survivors with the median age of 67 years old (P<0.05). Meanwhile, the age of the severe group was significantly higher than that of the moderate group (P<0.001) (Table 1). Of the 232 patients with COVID-19, 133 (57.3%) patients had comorbidities (i.e., hypertension, diabetes, chronic pulmonary disease), and patients with comorbidities were more likely to become severe cases. However, we did not find any specific comorbidities that could contribute to disease progression (Table 1).

Blood cell count

Blood count analysis showed that the levels of leukocytes and neutrophils in the severe group were significantly higher than those in the moderate group (all P<0.001). Lymphocyte count and platelet decrease were also more significant in the severe group (all P<0.001). However, there were no significant differences in white blood cells, neutrophils and lymphocytes between the death group and the survivors (all P>0.05). Besides, the platelet count in the death group was significantly lower (P<0.05). In terms of hemoglobin level, there was no significant difference between the severe group and the moderate group and between the survivors and the death group (all P>0.05). Analysis of fibrinolysis indicators showed that D-dimer (P<0.001) and fibrinogen (P<0.05) in the severe group were significantly higher than those in the moderate group (P<0.001 and P<0.05). The difference of D-dimer between the survival group and the death group was significant (P<0.001) instead of the difference in fibrinogen level (P>0.05) (Table 1).

Blood biochemical profiles, coagulation function and inflammatory factors

Analysis of blood biochemical indicators found that severe group had significantly lower albumin (P<0.001), higher globulin (P<0.05) and higher LDH level (P<0.001) than those of moderate group. Between the survival group and the death group, only albumin (median P<0.05) and LDH
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(P < 0.001) were significantly different. Besides, there was no difference at the total protein level between the severe group and the moderate group, nor between the survivors and the dead group (all P > 0.05). Analysis of the included four inflammatory indicators (CRP, PCT, IL-6 and IL-2R) found that there were significant differences in all four indicators between the moderate group and the severe group (P < 0.05). Only CRP (P < 0.001) and IL-6 (P < 0.05) were different between the survival group and the death group (Table 1).

**Table 1 Clinical characteristics of patients with COVID-19**

|                         | Normal range | Median (IQR) | All cases (n = 232) | Moderate cases (n = 102) | Severe cases (n = 130) | Survivors (n = 42) | Deaths (n = 88) |
|-------------------------|--------------|--------------|---------------------|-------------------------|-----------------------|-------------------|----------------|
| **Age (median, IQR, range, years)** | 68 (58–90), 20–88 | 65 (52–70), 20–87 | 67 (55–81), 35–88 | 75 (68–81), 47–86     |                       |                   |                |
| **Comorbidities**       |              |              |                     |                         |                       |                   |                |
| Yes                     | 133 (57.3%) | 36 (35.3%)   | 29 (69.0%)          | 68 (77.3%)              |                       |                   |                |
| Chronic pulmonary diseases | 8 (3.4%)   | 1 (1.0%)     | 2 (4.8%)            | 5 (5.7%)                |                       |                   |                |
| Hypertension            | 77 (33.2%)  | 32 (31.4%)   | 17 (40.5%)          | 28 (31.8%)              |                       |                   |                |
| Diabetes                | 25 (10.8%)  | 8 (7.8%)     | 5 (11.9%)           | 12 (13.6%)              |                       |                   |                |
| Cardiovascular diseases  | 25 (10.8%)  | 9 (8.8%)     | 6 (14.3%)           | 10 (11.4%)              |                       |                   |                |
| Chronic liver diseases   | 12 (5.2%)   | 5 (4.9%)     | 3 (7.1%)            | 4 (4.5%)                |                       |                   |                |
| Chronic kidney diseases  | 10 (4.3%)   | 4 (3.9%)     | 2 (4.8%)            | 4 (4.5%)                |                       |                   |                |
| Malignant tumor          | 6 (2.6%)    | 2 (2.0%)     | 1 (2.4%)            | 3 (3.4%)                |                       |                   |                |
| **Laboratory findings** |              |              |                     |                         |                       |                   |                |
| Leucocytes (× 10^9/L)    | 3.5–9.5     | 6.74 (4.82–8.91) | 5.40 (4.40–7.34) | 7.30 (5.72–9.99) | 8.06 (6.05–13.44) |
| Neutrophils (× 10^9/L)   | 1.8–6.3     | 4.53 (2.96–7.29) | 3.55 (2.63–4.78) | 5.47 (3.95–8.72) | 7.19 (4.66–11.85) |
| Lymphocytes (× 10^9/L)   | 1.1–3.2     | 0.98 (0.62–1.46) | 1.34 (0.95–1.74) | 0.82 (0.55–1.12) | 0.62 (0.47–0.95) |
| Hemoglobin (g/L)         | 130–175     | 127 (117–138) | 126 (120–133)       | 131 (116–141)          | 132 (116–141)        |
| Platelet (× 10^9/L)      | 125–350     | 214 (149–297) | 246 (194–337)       | 215 (172–300)          | 137 (103–214)        |
| Total protein (g/L)      | 64–83       | 68.2 (64.7–71.6) | 68.7 (65.4–71.7) | 68.5 (64.4–74.5) | 66.2 (63.5–70.7) |
| Albumin (g/L)            | 35–52       | 34.9 (31.4–40) | 39.1 (34.9–42.3) | 33.7 (31.6–37.5) | 31.2 (28.8–33.2) |
| Globulin (g/L)           | 20–35       | 32.4 (28.4–36.8) | 29.5 (26.5–33) | 35.7 (31.8–37.5) | 36.4 (32.8–40) |
| Lactate dehydrogenase (U/L) | 135–225     | 262 (200–460) | 209 (171–265)       | 310 (207–465)          | 554 (370–808)        |
| C-reactive protein (mg/L) | < 1.0       | 19.1 (2.7–103.7) | 3.9 (0.7–13.4) | 19.9 (12.4–117.4) | 114.9 (64.4–147.7) |
| Procalcitonin (ng/mL)   | < 0.05      | 0.10 (0.05–0.21) | 0.06 (0.05–0.08) | 0.10 (0.08–0.35) | 0.28 (0.15–0.62) |
| D-dimer (µg/mL FEU)     | < 0.5       | 1.30 (0.33–4.64) | 0.38 (0.22–1.34) | 2.21 (1.16–4.59) | 5.38 (1.59–21)     |
| Fibrinogen (g/L)        | 2–4         | 4.54 (3.39–5.75) | 3.85 (2.94–6.28) | 5.09 (4.55–6.28) | 5.14 (3.95–6.55) |
| Interleukin-6 (pg/mL)   | < 7         | 10.75 (1.80–30.49) | 2.64 (1.50–6.30) | 16.71 (10.75–28.71) | 63.54 (23.27–157.40) |
| Interleukin-2 receptor (U/mL) | 223–710 | 644 (323–993) | 388 (259–557) | 821 (624–1506) | 1057 (717–1450) |

*aStatistically significant index when comparing moderate cases with severe cases

*bStatistically significant index when comparing survivors with deaths. P value < 0.05 is considered to be statistically significant

Discussion

With the outbreak of COVID-19 and its continued spread, a rudimentary understanding of the disease has been gained. However, we are still relatively inexperienced on recognizing the clinical characteristics of severe COVID-19 and death cases. Therefore, we summarized the clinical characteristics of 232 COVID-19 patients and analyzed the differences between moderate and severe cases, survivors and deaths. These comparative analyses are useful for early warning and subsequent treatment decisions, with the ultimate goal of improving survival rate in existing critically ill patients.

Our results showed that the mean age of critically ill patients was older, which was consistent with the findings of other scholars [9, 10]. The elderly patients have limited organ compensatory function, more basic diseases before infection and more complications during infection. These may be the reasons for the high proportion of severe patients in elderly COVID-19 patients, so more attention should be paid to elderly patients. It has been reported that the COVID-19 was more likely to occur in older men with
comorbidities [2, 9, 21], which was consistent with our conclusion. However, we did not find any specific comorbidities that could directly contribute to disease progression, indicating that elder patients with chronic comorbidities who have weaker immune functions are more susceptible to COVID-19 infection.

Comparison analysis of blood cell count showed that severe cases had higher neutrophils count, lower lymphocytes and platelet count than moderate cases. Besides, death cases had lower platelet count than survival cases. This conclusion largely matches that of previous studies [11, 12], except that decreasing platelet count in death cases should be highlighted, which is possibly related to sepsis complication. Studies on intensive care medicine revealed that platelet count is related to the prognosis of sepsis patients [13, 14], but it is still unclear whether thrombocytopenia is a cause or consequence of sepsis severity and how platelets contribute to sepsis progression. Therefore, we should keep an eye on COVID-19 patients combined with thrombocytopenia and take measures including blood transfusion or anti-inflammatory therapy if necessary. This phenomenon reflects that severe patients experience more intense inflammatory responses which lead to heavier damage of immune cells. Thrombocytopenia might be primarily attributed to consumption, which may be further linked to widespread thrombosis or disseminated intravascular coagulation (DIC). Another reason could be inflammatory response which inhibits the development and maturation of human megakaryocytes in bone marrow.

Fibrinolysis index analysis showed that severe cases had higher fibrinogen and D-dimer level than moderate cases. Besides, death cases had higher D-dimer level than survival cases. This difference suggests that fibrinolysis was inhibited in severe cases of COVID-19. Extensive thrombus formation was also found at autopsy in patients who died from COVID-19 [15]. Published COVID-19-related coagulation studies have also confirmed the prevalence of hypercoagulation [16–18]. All of these phenomena support the necessity of prophylactic anticoagulation in patients without anticoagulant contraindications.

There were also differences in peripheral blood biochemical and inflammatory indicators between severe cases and moderate cases, which are similar to previous recognition about COVID-19 [19, 20]. This is probably related to the degree of difference on liver injury and inflammatory response between them. It is more necessary to actively improve organ function, fight infection and inflammation to severe patients.

With the rapid control of the outbreak in Wuhan, it is not easy to collect more cases for analysis, which limits our research. But given all the above, we consider age, platelet count, albumin, D-dimer, LDH, CRP and IL-6 level might be more meaningful marks for early prognostic evaluation of COVID-19. Our analysis of COVID-19 patients’ clinical data showed that age, fibrinolytic factors, degree of inflammation, and degree of liver function damage all significantly affected the prognosis of patients and provided data from the early stage of this pandemic for further systematic research, which is the strength of our study. Through the clinical observation of large number of cases and the autopsy of more dead patients, we will surely obtain more abundant clinical information and formulate more reasonable plans or measures for the control and prevention of the global ravages of COVID-19.

Conclusions

In summary, we consider age, comorbidities, platelet count, albumin, D-dimer, LDH, CRP and IL-6 level might be more meaningful marks for COVID-19 prognostic evaluation.

Acknowledgments

No other authors have disclosures to declare.

Compliance with ethical standards

Conflict of interest

The authors declare that there is no conflict of interest regarding this article.

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