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ORIGINAL ARTICLE

Retrospective Study

Comparison of demographic features and laboratory parameters between COVID-19 deceased patients and surviving severe and critically ill cases

Lei Wang, Yang Gao, Zhao-Jin Zhang, Chang-Kun Pan, Ying Wang, Yu-Cheng Zhu, Yan-Peng Qi, Feng-Jie Xie, Xue Du, Na-Na Li, Peng-Fei Chen, Chuang-Shi Yue, Ji-Han Wu, Xin-Tong Wang, Yu-Jia Tang, Qi-Qi Lai, Kai Kang

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Lei Wang, Xue Du, Na-Na Li, Peng-Fei Chen, Chuang-Shi Yue, Ji-Han Wu, Xin-Tong Wang, Yu-Jia Tang, Qi-Qi Lai, Kai Kang, Department of Critical Care Medicine, The First Affiliated Hospital of Harbin Medical University, Harbin 150001, Heilongjiang Province, China

Yang Gao, Department of Critical Care Medicine, The Sixth Affiliated Hospital of Harbin Medical University, Harbin 150028, Heilongjiang Province, China

Zhao-Jin Zhang, Department of Critical Care Medicine, The Yichun Forestry Administration Central Hospital, Yichun 153000, Heilongjiang Province, China

Chang-Kun Pan, Department of Critical Care Medicine, The Jiamusi Cancer Hospital, Jiamusi 154007, Heilongjiang Province, China

Ying Wang, Department of Critical Care Medicine, The First People Hospital of Mudanjiang City, Mudanjiang 157011, Heilongjiang Province, China

Yu-Cheng Zhu, Department of Critical Care Medicine, The Hongxinglong Hospital of Beidahuang Group, Shuangyashan 155811, Heilongjiang Province, China

Yan-Peng Qi, Department of Cardiology, The Hongxinglong Hospital of Beidahuang Group, Shuangyashan 155811, Heilongjiang Province, China

Feng-Jie Xie, Department of Critical Care Medicine, The Hongqi Hospital Affiliated to Mudanjiang Medical University, Mudanjiang 157011, Heilongjiang Province, China

Corresponding author: Kai Kang, MMed, Chief Doctor, Department of Critical Care Medicine, The First Affiliated Hospital of Harbin Medical University, No. 23 Post Street, Harbin 150001, Heilongjiang Province, China. janekk79@126.com

Abstract

BACKGROUND

Coronavirus disease 2019 (COVID-19) has been far more devastating than expected, showing no signs of slowing down at present. Heilongjiang Province is the most northeastern province of China, and has cold weather for nearly half a

year and an annual temperature difference of more than 60°C, which increases the underlying morbidity associated with pulmonary diseases, and thus leads to lung dysfunction. The demographic features and laboratory parameters of COVID-19 deceased patients in Heilongjiang Province, China with such climatic characteristics are still not clearly illustrated.

AIM

To illustrate the demographic features and laboratory parameters of COVID-19 deceased patients in Heilongjiang Province by comparing with those of surviving severe and critically ill cases.

METHODS

COVID-19 deceased patients from different hospitals in Heilongjiang Province were included in this retrospective study and compared their characteristics with those of surviving severe and critically ill cases in the COVID-19 treatment center of the First Affiliated Hospital of Harbin Medical University. The surviving patients were divided into severe group and critically ill group according to the Diagnosis and Treatment of New Coronavirus Pneumonia (the seventh edition). Demographic data were collected and recorded upon admission. Laboratory parameters were obtained from the medical records, and then compared among the groups.

RESULTS

Twelve COVID-19 deceased patients, 27 severe cases and 26 critically ill cases were enrolled in this retrospective study. No differences in age, gender, and number of comorbidities between groups were found. Neutrophil percentage (NEUT%), platelet (PLT), C-reactive protein (CRP), creatine kinase isoenzyme (CK-MB), serum troponin I (TNI) and brain natriuretic peptides (BNP) showed significant differences among the groups ($P = 0.020$, $P = 0.001$, $P < 0.001$, $P = 0.001$, $P < 0.001$, $P < 0.001$, respectively). The increase of CRP, D-dimer and NEUT% levels, as well as the decrease of lymphocyte count (LYMPH) and PLT counts, showed significant correlation with death of COVID-19 patients ($P = 0.023$, $P = 0.008$, $P = 0.045$, $P = 0.020$, $P = 0.015$, respectively).

CONCLUSION

Compared with surviving severe and critically ill cases, no special demographic features of COVID-19 deceased patients were observed, while some laboratory parameters including NEUT%, PLT, CRP, CK-MB, TNI and BNP showed significant differences. COVID-19 deceased patients had higher CRP, D-dimer and NEUT% levels and lower LYMPH and PLT counts.

Key Words: COVID-19; SARS-CoV-2; Deceased patients; C-reactive protein; D-dimer; Neutrophil percentage; Lymphocyte count; Platelet

Core Tip: Early detection and intervention of coronavirus disease 2019 (COVID-19) patients with a higher risk of death will contribute to rationally allocate limited medical resources and reduce the case-fatality rate. Our results illustrated that some laboratory parameters, including neutrophil percentage (NEUT%), platelet (PLT), C-reactive protein (CRP), creatine kinase isoenzyme, serum troponin I and brain natriuretic peptides showed significant differences in COVID-19 deceased patients compared with surviving severe and critically ill cases. COVID-19 deceased patients had higher CRP, D-dimer and NEUT% levels and lower lymphocyte count and PLT counts. Our study added evidence to the notion that the pathogenesis of COVID-19 deceased patients was related to the superimposed bacterial or fungal infection, cellular immune deficiency, coagulation disorder, activation of inflammatory cytokine responses, and impaired organ function, which in turn could interact with each other, forming a complicated network.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) has been far more devastating than expected, showing no signs of slowing down at present. COVID-19 has led to more deaths than the sum of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome CoV infection. The case-fatality rate of COVID-19 as reported previously varied from 3.77% to 28% in Wuhan (epicenter area)[1-8], and this percentage was significantly higher than that in other non-epicenter areas of China[7,9]. The two consecutive outbreaks of the epidemic resulted in a total of 559 locally confirmed cases and 13 deceased patients in the Heilongjiang Province, China, with a crude case-fatality rate of about 2.3%, which is lower than the national average of 5.58% (4634/83027). This once again suggested that continuously enriching the management of COVID-19 and gradually alleviating the temporary shortage of public health capacity could effectively reduce the case-fatality rate[9], although its reasons might be manifold[7]. Studies on COVID-19 deceased patients were of great significance as they contribute to better understand the underlying pathogenesis of it, especially in other regions of China with different demographic characteristics, except Hubei Province.

Angiotensin converting enzyme 2 (ACE2) is the functional host receptor for SARS-CoV-2 and route of viral entry. It is mainly distributed in the alveolar epithelial type II cells[10,11], and so a high prevalence of pneumonia is observed in COVID-19 patients clinically rather than upper respiratory symptoms. ACE2 had stronger binding affinity with SARS-CoV-2 than SARS-CoV, and this might account for its greater pathogenicity[12]. Heilongjiang Province is the most northeastern province of China, and has cold weather for nearly half a year and an annual temperature difference of more than 60°C, which increases the underlying morbidity associated with pulmonary diseases, and thus leads to lung dysfunction[13,14]. Chronic pulmonary disease plays an important role in predicting the in-hospital mortality in critically ill patients and even contributes to the case-fatality rate of COVID-19 patients[15,16]. What are the demographic features and laboratory parameters of COVID-19 deceased patients in Heilongjiang Province with such climatic characteristics remains a question.

To better address the above issue, the demographic features and laboratory parameters of COVID-19 deceased patients in Heilongjiang Province were compared with those of surviving severe and critically ill cases. This study was conducted in order to better understand the underlying pathogenesis of COVID-19 deceased patients, identify these patients as early as possible, guide clinical treatment regimens, and thus improve the clinical outcomes.

MATERIALS AND METHODS

Study design

The COVID-19 deceased patients from different hospitals in Heilongjiang Province, China were included in this retrospective study and compared with the severe and critically ill cases who survived from the COVID-19 treatment center of the First Affiliated Hospital of Harbin Medical University. The surviving patients were identified as severe group and critically ill group according to the Diagnosis and Treatment of New Coronavirus Pneumonia (the seventh edition). Demographic data were collected and recorded upon admission. Laboratory parameters, including white blood cell count (WBC), neutrophil percentage (NEUT%), lymphocyte count (LYMPH), platelet (PLT) count, fibrinogen (FIB), D-Dimer, C-reaction protein (CRP), albumin (ALB), creatinine (CRE), creatine kinase isoenzyme (CK-MB), serum troponin I (TNI) and brain natriuretic peptides (BNP) levels were obtained from the medical records, and then were compared among the groups. This study was approved by the Ethics Committee of the First Affiliated Hospital of Harbin Medical University (IRB number: IRB-AF/SC-04).

Study population

Twelve COVID-19 deceased patients, 27 severe cases and 26 critically ill cases were enrolled in this retrospective study. The respiratory samples of all enrolled COVID-19 patients were confirmed by SARS-CoV-2 nucleic acid detection. COVID-19 patients with incomplete medical records were excluded from the study.

Data collection

Demographic data, including age, gender and number of comorbidities, and laboratory parameters, including WBC, NEUT%, LYMPH, PLT, FIB, D-dimer, CRP, ALB, CRE, CK-MB, TNI and BNP were collected and recorded from the medical records through dedicated personnel. The members of our research group were unaware of the patient's private information other than the data acquired for this study.

Statistical analysis

SPSS 22.0 (SPSS Inc., Chicago, IL, United States) was adopted for statistical analyses. Analysis of variance (ANOVA), χ^2 test and Kruskal-Wallis rank sum test were employed for performing intergroup

comparison of age, gender and number of comorbidities. Kruskal-Wallis rank sum test was used for intergroup comparison of CRP due to non-normal distribution, while one-way ANOVA was employed for intergroup comparison of other laboratory parameters with normal distribution. Pair-wise comparison was completed by least significance difference. Pearson correlation analysis was used to analyze the correlation between dynamic profile of laboratory parameters and death of COVID-19 patients. *P* values of < 0.05 were considered as statistically significant.

RESULTS

Intergroup comparison of age, gender, and number of comorbidities

The ratio of COVID-19 deceased patients in men and women was 1:1, with a median age of 71.50 years. A quarter of these deceased patients demonstrated no comorbidities. COVID-19 deceased patients with 1, 2, 3, and 4 types of comorbidities accounted for 25.0%, 25.0%, 8.3% and 16.7% respectively. As shown in Table 1, there were no differences in age, gender, and number of comorbidities among the groups.

Intergroup comparison of laboratory parameters

As shown in Table 2, laboratory parameters, including NEUT%, PLT, CRP, CK-MB, TNI and BNP showed significant differences among the groups ($P = 0.020$, $P = 0.001$, $P < 0.001$, $P = 0.001$, $P < 0.001$, $P < 0.001$, respectively), except for WBC, LYMPH, FIB, D-dimer, ALB and CRE ($P = 0.131$, $P = 0.220$, $P = 0.809$, $P = 0.766$, $P = 0.306$, $P = 0.923$, respectively).

The correlation between dynamic profile of laboratory parameters and death of COVID-19 patients

The increase in CRP, D-dimer and NEUT% levels, as well as the decrease of LYMPH and PLT counts showed significant correlation with the death of COVID-19 patients ($P = 0.023$, $P = 0.008$, $P = 0.045$, $P = 0.020$, $P = 0.015$, respectively) (Table 3).

DISCUSSION

As a highly pathogenic human CoV, SARS-CoV-2 had unprecedented pathogenicity and complex clinical manifestations that range from asymptomatic infection to fatal pneumonia. In China, about 15%-30% confirmed COVID-19 patients developed into severe and critically ill cases, usually presenting with acute respiratory distress syndrome and requiring some form of ventilatory support[1,2,17,18]. The case-fatality rate of critically ill patients with COVID-19 even exceeded 60%[19]. At present, the number of COVID-19 deceased patients worldwide has exceeded six million without any sign of slowing down. Moreover, the absence of available specific medications for treating COVID-19 was a clinical reality. Therefore, there is an urgent need to understand the demographic features and laboratory parameters of COVID-19 deceased patients in clinical practice so as to identify and intervene in the early stage and thus improve the clinical outcomes, and explore the underlying pathogenesis by comparing with those of surviving severe and critically ill cases.

At present, most of the studies on COVID-19 deceased patients in China were concentrated in Wuhan but lacked in other regions. Different generations of SARS-CoV-2 infection in patients with different demographic characteristics have inevitably led to different clinical characteristics[20]. Heilongjiang Province has unique climatic characteristics that affect lung function and the morbidity associated with respiratory diseases. The two consecutive outbreaks of COVID-19 in Heilongjiang Province were related to secondary or tertiary transmission of imported cases from Wuhan and the United States[21]. The question is that whether COVID-19 deceased patients caused by secondary or tertiary transmission of imported cases in Heilongjiang Province have special demographic features and laboratory parameters?

In our study, COVID-19 deceased patients in Heilongjiang Province included men and women in 1:1 ratio with a median age of 71.50 years. Contrary to the results of other studies, no differences were observed in age, gender, and number of comorbidities in COVID-19 deceased patients when compared to surviving severe and critically ill cases. The primary reason for this is that only COVID-19 deceased patients, and surviving severe and critically ill cases were collected in our study, lacking asymptomatic, mild, and moderate cases. We believed that comparing asymptomatic, mild, and moderate cases with COVID-19 deceased patients would expand the clinical characteristics that were associated with poor outcomes and confuse the true facts. COVID-19 patients included in our study were significantly older than those reported in other studies[3,22-24], and this might be a reason partly.

It has been widely accepted that SARS-CoV-2 infection causes a decrease in the absolute number of lymphocyte count, especially in severe and critically ill cases, and deceased patients[1,6,16,24,25]. The inhibited and delayed interferon (IFN) response signaling induced by SARS-CoV infection sensitized T cells to apoptosis *via* tumor necrosis factor-mediated pathway[26]. Furthermore, IFN weakens the T cell responses by up-regulating the expression of negative immune regulatory molecules[27]. It is speculated that due to high degree of homology, the mechanism on destruction of lymphocytes by

Table 1 Intergroup comparison of age, gender, and number of comorbidities

	COVID-19 deceased patients	Critically ill group	Severe group	F/χ^2	*P* value
Age	71.50 ± 10.41	63.78 ± 11.58	65.59 ± 11.75	1.978	0.147
Gender				0.053	0.974
Female	6	12	13		
Male	6	14	14		
Number of comorbidities				4.251	0.119
0	3	12	8		
1	3	9	6		
2	3	2	8		
3	1	2	5		
4	2	1	0		

COVID-19: Coronavirus disease 2019.

Table 2 Intergroup comparison of laboratory parameters

Laboratory parameters	COVID-19 deceased patients	Critically ill group	Severe group	F/χ^2	*P* value
WBC	7.65 ± 6.62	7.58 ± 2.32	5.77 ± 2.32	2.103	0.131
NEUT%	75.35 ± 11.41	82.19 ± 10.25	72.62 ± 14.13[1]	4.151	0.020
LYMPH	1.08 ± 0.98	0.72 ± 0.48	0.89 ± 0.48	1.554	0.220
PLT	141.62 ± 59.88	261.69 ± 110.42[1]	238.04 ± 119.17[1]	5.301	0.001
FIB	4.28 ± 2.01	4.68 ± 2.23	4.78 ± 1.96	0.212	0.809
D-Dimer	3.22 ± 5.98	6.43 ± 8.18	6.25 ± 16.49	0.268	0.766
CRP	107.20(147.11)	31.15(44.10)[1]	24.37(32.65)[1]	15.846	< 0.001
ALB	31.10 ± 4.49	29.07 ± 3.95	30.44 ± 3.99	1.208	0.306
CRE	61.44 ± 23.04	63.26 ± 47.38	66.26 ± 28.08	0.081	0.923
CK-MB	45.74 ± 67.48	7.77 ± 8.65[1]	8.07 ± 6.44[1]	7.941	0.001
TNI	1.32 ± 1.97	0.03 ± 0.03[1]	0.01 ± 0.01[1]	13.504	< 0.001
BNP	575.50 ± 484.94	164.80 ± 225.64[1]	63.04 ± 66.25[1]	10.614	< 0.001

[1]Represent significant differences compared with coronavirus disease 2019 deceased patients.
COVID-19: Coronavirus disease 2019; WBC: White blood cell count; NEUT%: Neutrophil percentage; LYMPH: Lymphocyte count; PLT: Platelet; FIB: Fibrinogen; CRP: C-reaction protein; ALB: Albumin; CRE: Creatinine; CK-MB: Creatine kinase isoenzyme; TNI: Serum troponin I; BNP: Brain natriuretic peptides.

SARS-CoV-2, as a similarly enveloped RNA virus, is known to be involved, but further studies are needed to confirm these. Therefore, a dynamic decrease in lymphocyte count is considered as an important sign of cellular immune deficiency and an indicator for disease progression[28]. As a prototypical acute phase serum protein, CRP is rapidly elevated in excessive host inflammatory response to virus invasion, becoming a useful marker for the severity of inflammatory response[29]. Complications from hypercoagulability induced by COVID-19 have been reported recently[30,31]. Due to wide distribution of ACE2 receptors in multiple organs[11], SARS-CoV-2 infection could cause multiple organ dysfunction[19,24,28,32], including heart damage in our results.

The abnormalities in the levels of NEUT%, LYMPH, D-dimer, PLT, CRP, CK-MB, TNI and BNP usually indicated superimposed bacterial or fungal infection, cellular immune deficiency, coagulation disorder, activation of inflammatory cytokine responses, and impaired cardiac function. Close monitoring of the dynamic profile of the above laboratory parameters is considered essential for identifying COVID-19 patients who are at risk of poor outcomes in time. Our study added evidence to

Table 3 The correlation between dynamic profile of laboratory parameters and death of coronavirus disease 2019 patients

	CK-MB	CRE	CRP	D-dimer	FIB	LYMPH	NEUT%	PLT	TNI	WBC
Correlation coefficient	-0.122	0.364	0.675[1]	0.746[1]	-0.533	-0.684[1]	0.613[1]	-0.709[1]	0.464	0.238
Significance	0.721	0.271	0.023	0.008	0.091	0.020	0.045	0.015	0.177	0.481

[1]Significant correlation with the death of coronavirus disease 2019 patients.

CK-MB: Creatine kinase isoenzyme; CRE: Creatinine; CRP: C-reaction protein; FIB: Fibrinogen; LYMPH: Lymphocyte count; NEUT%: Neutrophil percentage; PLT: Platelet; TNI: Serum troponin I; WBC: White blood cell count.

the notion that the pathogenesis of COVID-19 deceased patients was related to the superimposed bacterial or fungal infection, cellular immune deficiency, coagulation disorder, activation of inflammatory cytokine responses, and impaired organ function[33], which in turn could interact with each other, forming a complicated network.

However, there are several limitations in our study. Firstly, retrospective study with small sample size decreases the credibility of our conclusion, and should be further verified in larger sample size in the near future. Secondly, interventions to COVID-19 deceased patients from different hospitals in Heilongjiang Province are uneven, which might have impact on the results of our study. Thirdly, no further analysis of specific comorbidities was performed because of small sample size. Finally, the observational indicators included in our study are limited to demographic features and laboratory parameters, and lacked more comprehensive and in-depth indexes that reveal the pathogenesis of COVID-19 deceased patients.

CONCLUSION

In summary, the crude case-fatality rate of COVID-19 in Heilongjiang Province, which is the most northeastern province in China, was 2.3%. Our study added evidence to the notion that the pathogenesis of COVID-19 deceased patients was related to the superimposed bacterial or fungal infection, cellular immune deficiency, coagulation disorder, activation of inflammatory cytokine responses, and impaired organ function, which in turn could interact with each other, forming a complicated network. Further clinical or animal trials should focus on identification of specific pathogenesis after SARS-CoV-2 invasion.

ARTICLE HIGHLIGHTS

Research background

The coronavirus disease 2019 (COVID-19) has been far more devastating than expected, however, the demographic features and laboratory parameters of COVID-19 deceased patients in Heilongjiang Province, China are still not clearly illustrated.

Research motivation

This study was conducted in order to better understand the underlying pathogenesis of COVID-19 deceased patients, identify these patients as early as possible, guide clinical treatment regimens, and thus improve the clinical outcomes.

Research objectives

In this study, we aimed to illustrate the demographic features and laboratory parameters of COVID-19 deceased patients in Heilongjiang Province by comparing with those of surviving severe and critically ill cases.

Research methods

COVID-19 deceased patients from different hospitals in Heilongjiang Province were included in this retrospective study and compared their characteristics with those of surviving severe and critically ill cases in the COVID-19 treatment center of the First Affiliated Hospital of Harbin Medical University. The surviving patients were divided into severe group and critically ill group according to the Diagnosis and Treatment of New Coronavirus Pneumonia (the seventh edition). Demographic data were collected and recorded upon admission. Laboratory parameters were obtained from the medical records, and then compared among the groups.

Research results

Twelve COVID-19 deceased patients, 27 severe cases and 26 critically ill cases were enrolled in this retrospective study. No differences in age, gender, and number of comorbidities between groups were found. Some laboratory parameters showed significant differences among the groups. The increase of C-reactive protein (CRP), D-dimer and neutrophil percentage (NEUT%) levels, as well as the decrease of lymphocyte count (LYMPH) and platelet (PLT) counts, showed significant correlation with death of COVID-19 patients.

Research conclusions

Compared with surviving severe and critically ill cases, no special demographic features of COVID-19 deceased patients were observed, while some laboratory parameters showed significant differences. COVID-19 deceased patients had higher CRP, D-dimer and NEUT% levels and lower LYMPH and PLT counts.

Research perspectives

COVID-19 deceased patients had higher CRP, D-dimer and NEUT% levels and lower LYMPH and PLT counts.

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FOOTNOTES

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Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

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ORCID number: Lei Wang 0000-0001-8464-6703; Yang Gao 0000-0002-0612-0818; Zhao-Jin Zhang 0000-0002-0655-3197; Chang-Kun Pan 0000-0001-9878-4461; Ying Wang 0000-0002-1716-5974; Yu-Cheng Zhu 0000-0002-0447-9894; Yan-Peng Qi 0000-0003-2987-242X; Feng-Jie Xie 0000-0001-6229-7039; Xue Du 0000-0003-3563-7389; Na-Na Li 0000-0002-0683-3439; Peng-Fei Chen 0000-0003-1963-1171; Chuang-Shi Yue 0000-0002-3688-3357; Ji-Han Wu 0000-0003-1332-0639; Xin-Tong Wang 0000-0001-7895-0178; Yu-Jia Tang 0000-0003-4113-0779; Qi-Qi Lai 0000-0003-0411-5158; Kai Kang 0000-0001-9694-4505.

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