Correlation between White Blood Cell Count at Admission and Mortality in COVID-19 Patients: A Retrospective Study

Xiaokai Feng
Beijing Chaoyang Hospital
Bin Zhu
Beijing Tiantan Hospital
Chunguo Jiang
Beijing Chaoyang Hospital
Song Mi
Beijing Chaoyang Hospital
Liya Yang
Plastic Surgery Hospital of Peking Union Medical College, Chinese Academy of Medical Sciences
Zhigang Zhao
Beijing Tiantan Hospital
Yong Zhang
Union Hospital, Tongji Medical College, Huazhong University of Science and Technology
Liming Zhang (zhangliming@bjcyh.com)
Beijing Chaoyang Hospital

Research article

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Abstract

Background: Coronavirus disease-19 (COVID-19) has spread rapidly and has become a world health threaten. Its risk factors with death were still unknow. White blood cells (WBC) as a reflection of inflammation had play a vital role in COVID-19, however its level with death were still not know.

Methods: In this retrospective, single-center study, all confirmed patients with COVID-19 on admission at West Branch of Union Hospital from Jan 29 to Feb 28, were collected and analyzed. Demographic and clinical data including laboratory examinations were analyzed and compared between recovery and death patients.

Results: A total of 163 patients including 33 death cases were included in this study. Significant associations were found between WBC level and death (HR = 1.14, 95%CI: 1.09-1.20, p<0.001). The regression analysis results showed there was a significant association between WBC level and death (HR = 5.72, 95%CI: 2.21-14.82, p < 0.001) when use the second quartile as a cutoff value (> 6.16×10^9/L). The difference was still existing after we adjusting for confounding factors (HR = 6.26, 95%CI: 1.72-22.77, p = 0.005). In addition, Kaplan-meier survival analysis showed that there was a significant decline of the cumulative survival rate (p < 0.001) in those with WBC level ≥ 6.16×10^9/L.

Conclusion: WBC at admission is significantly corelated with death in COVID-19 patients. Higher level of WBC should be given more attention in the treatment of COVID-19.

Background

Since December 2019, coronavirus disease 2019 (COVID-19) emerged in Wuhan city and rapidly spread throughout China, and further extended to other countries[1, 2]. As of March 16, 2020, a total of 167,545 cases had been confirmed globally, and 3231 cases were died in China. The pathogen has been identified as a novel enveloped RNA beta coronavirus that has currently been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is sufficiently divergent from SARS-CoV[3, 4]. The most common symptoms are fever, dry cough, and fatigue. Ground-glass opacity (GGO), consolidation lesions, and reticular patterns were the common radiologic findings on chest computed tomography (CT)[5]. No antiviral treatment for coronavirus infection has been proven to be effective[1].

Patients with severe illness may progress to shortness of breath, and might develop acute respiratory distress syndrome (ARDS), septic shock, and require intensive care unit (ICU) admission[6, 7]. At this stage, the mortality rate is high. Older age with comorbidities, higher neutrophil-to-lymphocyte ratio, higher MuLBSTA score, higher Sequential Organ Failure Assessment (SOFA) score, and d-dimer greater than 1 μg/L on admission were associated with worse outcomes[7–9]. However, the data on the clinical characteristics at the early stage and outcomes of patients with SARS-CoV-2 infection remain scarce.

In this study, we investigated the white blood cells (WBC) of patients with confirmed COVID-19 and a definite clinical outcome (death or discharge) who were admitted to the West Branch of Union Hospital in

Wuhan. We aim to explore risk factors of severe disease and in-hospital death for patients, and help clinicians to identify patients on admission with poor prognosis.

Patients And Methods

Patients

The COVID-19 patients's clinical characteristics were retrospective analysis from Jan 29 to Feb 28. in the West Branch of Union Hospital in Wu Han province. All patients who were diagnosed with COVID-19 pneumonia according to WHO interim guidance (Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance, January 28, 2020). Throat swab specimens were collected at admission and the laboratory nucleic acid tests using real time polymerase chain reaction (RT-PCR) for COVID-19 RNA were conducted immediately in the Laboratory department of West Branch of Union hospital. Meantime, all patients recessive chest x-rays or chest CT to further identify the bilateral ground-glass opacity of infiltrates of lung. The study was approved by the Ethics Committee of West Branch of Union hospital, Tongji Medical College, Huazhong University of Science and Technology and written informed consent was obtained from patients involved before enrolment when data were collected retrospectively.

Laboratory Assays

Fasting blood samples from the elbow veins of each participant were collected at admission. The biochemical parameters comprising WBC, neutrophil, serum lipid profiles and other index were examined in the Laboratory department of West Branch of Union hospital.

Date Collected

Medical records including death time and other clinical diagnosis and therapeutic schedules were carefully extracted using a standardized case report form. If information was not clear, then the doctors or other healthcare providers who were in charge were consulted.

Statistical analysis

Data were presented as Means (SD) or medians (25th percentile-75th percentile) and proportions were calculated for population characteristics. Cox proportional hazard regression analysis was performed to evaluate the relationship between death and WBC level. In addition, we adjusted for age, sex, systolic blood pressure, diastolic blood pressure, body mass index, fasting glucose, total cholesterol, triglycerides and hdl cholesterol in the multivariable model. The relationship of death rate WBC was estimated using the Kaplan-Meier method. Survival differences between groups were compared using the log-rank test. All statistical tests were 2-sided with the significant level set at 0.05. Statistical analyzes were performed

using Empower Stats (http://www.empowerstats.com) and the R software, version 3.3.1 (http://www.R-project.org/).

Results

Clinical characteristics of patients

A total of 163 patients were included in this study and 33 patients were dead at last. There were 68 female in non-death group and 11 in death group. The average age of non-death was 56.4 ± 13.5 and the pneumonia severity index(PSI)was 50.6 ± 36.6. The average age of death was 70.3 ± 9.7 and the PSI was 105.5 ± 22.2. Of the death case, 13 patients with hypertension history, 6 patients with diabetes history, 6 patients with coronary heart disease history. The demographics characteristics were in Table 1.

Table 1
Baseline characteristics of the study participants by death.

Variables	Stratified by Death		
	Non-Death	Death	*P value*
No.	130	33	
Female, n (%)	68 (52.3)	11 (33.3)	0.080
Age, y	56.4 ± 13.5	70.3 ± 9.7	< 0.001
SBP, mmHg	129.7 ± 16.9	132.0 ± 19.8	0.500
DBP, mmHg	81.9 ± 10.6	78.1 ± 16.3	0.110
BMI,kg/m^2	23.9 ± 3.0	24.1 ± 3.8	0.828
PSI	50.6 ± 36.6	105.5 ± 22.2	< 0.001
WBC, × 10^9/L	6.2 ± 3.3	10.3 ± 4.7	< 0.001
APO-A	0.9 ± 0.3	0.7 ± 0.2	< 0.001
APO-B	1.0 ± 0.2	1.0 ± 0.3	0.135
Fasting glucose, mmol/L†	5.8 (5.4, 6.9)	7.2 (6.1, 9.1)	< 0.001
Total cholesterol, mmol/L†	4.2 (3.7, 4.7)	3.9 (3.6, 4.3)	0.163
Triglycerides, mmol/L†	1.4 (1.0, 2.0)	1.3 (1.2, 2.0)	0.704
HDL cholesterol, mmol/L†	0.9 (0.8, 1.2)	0.8 (0.6, 1.0)	0.013
CURB.65			< 0.001
0	67 (51.5)	2 (6.1)	
1	42 (32.3)	4 (12.1)	
2	19 (14.6)	17 (51.5)	
3	2 (1.5)	10 (30.3)	
BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein;			
*For continuous variables, values are presented as mean ± SD.			
†Values are presented as median (IQR)			

Relationship Of Wbc And Death

The relationship of WBC level and death are presented in Table 2. Significant associations were found between WBC level and death (HR = 1.14, 95%CI: 1.09–1.20, p < 0.001). Once adjust for covariables such as age, sex, systolic blood pressure, diastolic blood pressure, body mass index, fasting glucose, total cholesterol, triglycerides and hdl cholesterol, the significance still exists (HR = 1.16, 95%CI: 1.07–1.25, p < 0.001). To further explore the influence of WBC level to death, we use second quartile and the normal range of the WBC level as a cutoff value to evaluate their relationship (Fig. 1). The regression analysis results showed when we use second quartile as a cutoff value (> 6.16 × 10^9/L), there was significant association between WBC level and death (HR = 5.72, 95%CI: 2.21–14.82, p < 0.001),even after we adjusting for confounding factors (HR = 6.26, 95%CI: 1.72–22.77, p = 0.005). Nevertheless, we did not observe any significant association when the WBC use normal range as a cutoff value (HR = 3.76, 95%CI: 1.82–7.77, p = 0.001, adjusting for the confounding factors HR = 2.08, 95%CI: 0.83–5.21, p = 0.118) (Table 2, Fig. 1).

Table 2
The association between fasting blood glucose and death.

White Blood Cell, × 10^9/L	**N**	**Case (%)**	**Crude model**		**Adjusted model***	
			HR (95%CI)	***P value***	**HR (95%CI)**	***P value***
WBC, as continuous	163	33 (20.2)	1.14(1.09,1.20)	< 0.001	1.16(1.07,1.25)	< 0.001
Categories1						
B1(< 6.16)	81	5 (6.2)	*Ref*		*Ref*	
B2(≥ 6.16)	82	28 (34.1)	5.72(2.21,14.82)	< 0.001	6.26(1.72,22.77)	0.005
Categories2						
< 10	141	22 (15.6)	*Ref*		*Ref*	
≥ 10	22	11 (50)	3.76(1.82,7.77)	< 0.001	2.08(0.83,5.21)	0.118
***** Adjusted for age, sex, systolic blood pressure, diastolic blood pressure, body mass index, fasting glucose, total cholesterol, triglycerides, hdl cholesterol						
Figure 1						

In addition, Kaplan-meier survival analysis was also used to compare the variation trend of survival rate between the WBC ≥ 6.16 × 10^9/L and WBC 6.16 × 10^9/L during hospitalization. The results showed that there was a significant decline of the cumulative survival rate (p < 0.001) in those with WBC level ≥ 6.16 × 10^9/L (Fig. 2).

Discussion

Nowadays, newly evolved Coronaviruses have posed a global threat to public health[10, 11]. Although, the epidemiological and clinical characteristics of patients were well documented, understanding of the clinical spectrum of COVID-19 infection is still limited. As a human-to-human transmission disease, middle-aged and elderly patients with underlying comorbidities are susceptible to respiratory failure and may have a poorer prognosis[12, 13]. Explore the risk factors related to the prognosis would be helpful for doctors to take an even more effective treatment. In this study, we systematically investigated the effect of WBC on mortality. Our results showed that the death risk was associated with the WBC level at admission, although the index is at the normal range, those with higher WBC level patients were facing a much higher death possibility. These results were not reported elsewhere.

Although epidemiology and the genome had been well elucidated, much remain unknown. The risk factors which influence death are still not clear and until now. The immune system is essential to control and eliminate CoV infections. Nevertheless, accumulating evidence suggests that patients with severe COVID-19 might have a cytokine storm syndrome[14–16]. Patients of COVID-19 with maladjusted immune responses, may result in immunopathology and dead. Followed a deeper understanding of the interaction between Coronaviruses and the innate immune systems of the hosts may shed light on the development and persistence of inflammation in the lungs

Liu et al. had observed that nearly 80% of the patients had normal or decreased white blood cell counts, and 72.3% (99/137) had lymphocytopenia[17]. Zhang et al. had also reported a result of 9 patients, which their peripheral white blood cell counts were most normal And PCT were all negative[18]. These results were similar with ours. In our study we had found that most of the patients were with a normal range of WBC level. However, those with higher WBC lever patients were at a high risk of death.

Notable achievements have been made in understanding of COVID-19. As a largest known viral RNA genome, coronaviruses are enveloped, nonsegmented, positive-sense single-stranded RNA virus genomes in the size ranging from 26 to 32 kilobases[19]. However, the relationship of the virus with immune system is still unknow. Gaining a deeper understanding of the interaction between Coronaviruses and the innate immune systems may shed light on the treatment of lung inflammation caused by CoVs. Our study had only observed a phenomenon, the potential mechanism still worth exploring. In addition, some limitations still exist, such as due to the limited number of patients and death cases, the conclusion needs to be verified by larger samples. Meantime, a dynamic WBC level during the treatment were not observed. Thus, the results should be considered as preliminary ones and further research is necessary.

Conclusion

In conclusion, our study suggests that WBC at admission is significantly corelated with death in COVID-19 patients. Higher level of WBC should be given more attention in the treatment of COVID-19.

Abbreviations

COVID-19: Coronavirus disease-19; WBC: White blood cells; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; GGO: Ground-glass opacity; CT: Computed tomography; ARDS: Acute respiratory distress syndrome; ICU: Intensive care unit; SOFA: Sequential Organ Failure Assessment; 2019-nCoV: 2019-novel coronavirus; RT-PCR: Real time polymerase chain reaction; PSI: Pneumonia severity index.

Declarations

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Availability of data and materials

Not applicable.

Authors' Contributions

XKF, BZ and CGJ designed the study. BZ wrote the first draft. XKF and CGJ collected the data. SM and LYY guided the methodology and responsible for statistics. ZGZ, YZ and LMZ critically reviewed, discussed, and modified the manuscript. All authors read and approved the final manuscript for publication.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of West Branch of Union hospital, Tongji Medical College, Huazhong University of Science and Technology and written informed consent was obtained from patients involved before enrolment when data were collected retrospectively.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

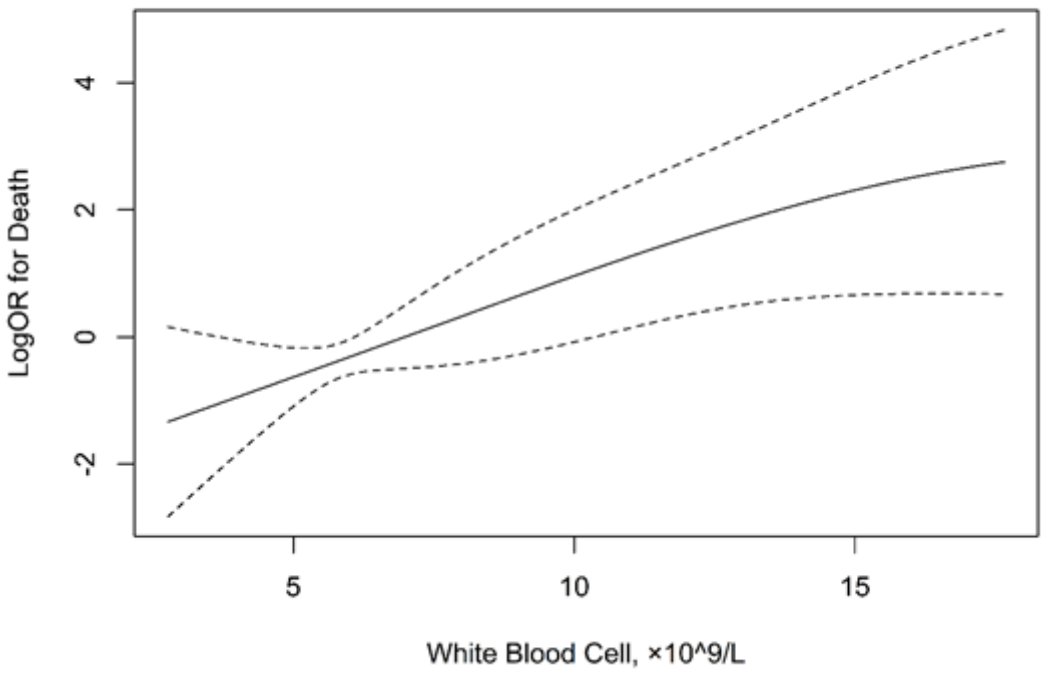

Figure 1

Smooth curves between WBC level and death.

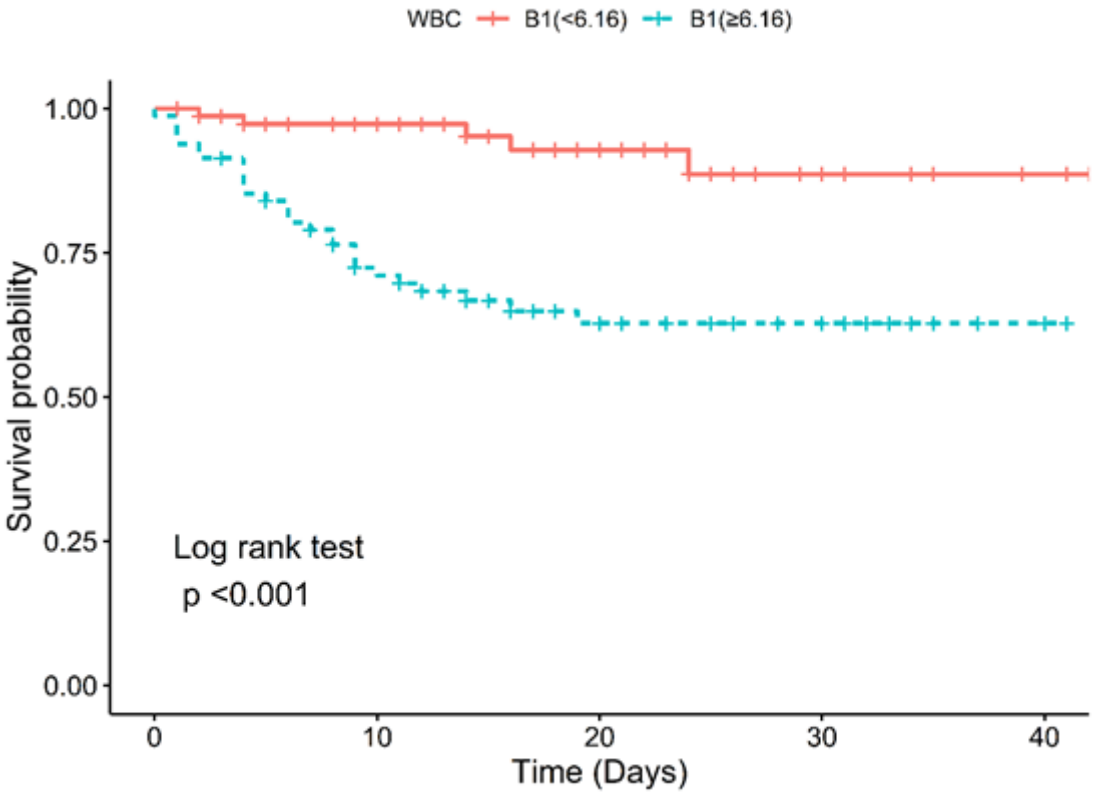

Figure 2

The survival rate of patients with COVID-19 which use second quartile of WBC during hospitalization.