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LETTER TO THE EDITOR

Analysis of hematological indexes of COVID-19 patients from fever clinics in Suzhou, China

Dear Editors,

The 2019 novel coronavirus, formally denominated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused the pandemic of coronavirus disease 2019 (COVID-19). Early identification, diagnosis, quarantine, and centralized treatment are key factors in the Chinese experience of epidemic prevention and control. Fever clinics have been used for early identification of suspected COVID-19 patients in China, which proved to be an effective paradigm in several prior public health incidents, such as SARS in 2003. Patients with fever, respiratory symptoms, or related epidemiological history were guided to the fever clinics. Studies have reported that complete blood count (CBC) in COVID-19 patients and most of the leukocyte changes were not specific. A decrease in absolute lymphocyte count was frequently observed,[1] and an elevation in D-dimer level was more common in severe COVID-19 cases.[2] The present study aimed to explore practical biomarkers derived from a conventional hematological examination for COVID-19 management in fever clinics.

According to the Chinese guideline for diagnosis and treatment of novel coronavirusinfected pnemomia, COVID-19 patients from six hospital fever clinics in Suzhou, whose diagnosis was confirmed by reverse transcription-polymerase chain reaction (RT-PCR), were enrolled between January 10 and March 1, 2020. All of these COVID-19 patients were transferred to the Affiliated Infectious Disease Hospital of Soochow University. Severe COVID-19 cases met one of the following criteria: (a) respiratory distress, respiratory rate ≥30 bpm; (b) oxygen saturation ≤93%; (c) arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) <300 mm Hg; (d) respiratory failure requires mechanical ventilation and shock, or other organ failure requires ICU treatment. The study was approved by the Institutional Review Board of the First Affiliated Hospital of Soochow University, and written consent was obtained from all the patients and healthy donors.

The epidemiological and clinical history was collected at the fever clinics, and every patient underwent vital sign measurements. Pharyngeal swabs were sampled and sent to Suzhou Center for Disease Control for RT-PCR detection. Basic laboratory examinations in the fever clinics included complete blood count, coagulation panel, and optional test for inflammatory factors.

A standard case questionnaire was used for data collection. The statistical software SPSS 22.0 for Windows (IBM, Armonk, NY, USA) was used for data analysis. Continuous variables were described as mean ± standard deviation or median (range), while categorical variables were expressed as frequencies (%). Mann-Whitney tests were used to compare the differences between the two COVID-19 groups.

A total of 40 COVID-19 patients were enrolled with an average age of 47.7 ± 13.4 years, including 26 males and 14 females. The patients were classified into 31 mild/moderate cases and nine severe cases. Among them, 30 cases had travel or residence history in epidemic areas (mainly Hubei Province) within 14 days before the onset of illness and three cases had contact history with COVID-19 patients. Sixteen COVID-19 cases presented with family clustering. The median time from symptom onset to diagnosis was 5.2 ± 3.2 days. The underlying chronic diseases included three hypertension cases, three diabetes cases, one chronic obstructive pulmonary disease case, and one stroke case. Most of the COVID-19 patients had a fever (36 cases, 90%) and cough (27 cases, 67.5%), which was in agreement with early reports from Wuhan.[3] The average values for respiratory rate, peripheral oxygen saturation, heart rate, and mean blood pressure were 19.10 ± 1.66 bpm, 98.28 ± 1.63%, 90.60 ± 12.45 bpm, and 95.37 ± 8.37 mm Hg, respectively.

All 40 patients received a complete blood count test. The average leukocyte, neutrophil, lymphocyte, monocyte, platelet, and hemoglobin numbers were 4.63 ± 1.63 × 10^9/L, 2.85 ± 1.37 × 10^9/L, 1.20 ± 0.42 × 10^9/L, 0.52 ± 0.24 × 10^9/L, 170.1 ± 61.2 × 10^9/L, and 139.3 ± 13.9 g/L, respectively (Table 1). A total of 18 cases of lymphopenia, nine cases of neutropenia, eight cases of thrombocytopenia, and seven cases of anemia were observed. Lymphopenia was the most common. In the present study, white blood cell differential count results indicated that only neutrophil numbers showed statistical differences between the mild/moderate and severe groups ($P = .047$). A recent report on pathological autopsy cases confirmed the presence of hematological changes in COVID-19 patients.[4] Clinical application of neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and lymphocyte-monocyte ratio (LMR) has been receiving increased attention. One meta-analysis suggested that peripheral blood leukocyte ratios were useful biomarkers for the diagnosis of bacteremia and influenza virus infection.[5] Qin et al found that monitoring of NLR and lymphocyte subsets may be helpful for early warning, diagnosis, and treatment of COVID-19.[6] However, normal reference ranges for NLR, PLR, and LMR remain elusive.

The mean values for NLR, PLR, and LMR in 80 healthy donors who underwent a pretransplant health examination were 2.05 ± 0.75,

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TABLE 1 Hematological indexes of COVID-19 patients from Suzhou fever clinics

Hematological indexes	Reference	Mild/moderate cases	Severe cases		Total cases
Complete blood count		n = 31	n = 9	*P*	n = 40
Leukocyte (10^9/L)	3.50-9.50	4.42 ± 1.54	5.39 ± 1.78	.114	4.63 ± 1.63
Neutrophil (10^9/L)	1.80-6.30	2.61 ± 1.20	3.70 ± 1.63	.047*	2.85 ± 1.37
Lymphocyte (10^9/L)	1.10-3.20	1.25 ± 0.45	1.05 ± 0.24	.147	1.20 ± 0.42
Monocyte (10^9/L)	0.10-0.60	0.50 ± 0.23	0.61 ± 0.30	.306	0.52 ± 0.24
Platelets (10^9/L)	125-350	169.87 ± 65.25	171.00 ± 48.14	.354	170.1 ± 61.2
Hemoglobin (g/L)	130-175	138.26 ± 13.93	142.89 ± 14.11	.61	139.3 ± 13.9
NLR		2.27 ± 1.12	3.71 ± 1.78	.018*	2.59 ± 1.41
PLR		147.03 ± 61.21	170.16 ± 63.41	.235	152.2 ± 61.7
LMR		2.76 ± 0.98	2.13 ± 1.36	.037*	2.62 ± 1.09
Coagulation Panel		n = 22	n = 5		n = 27
PT (s)	10.0-14.0	11.91 ± 0.93	11.54 ± 0.44	.38	11.8 ± 0.90
APTT (s)	20.0-40.0	30.90 ± 5.32	28.64 ± 6.88	.49	30.5 ± 5.6
Fibrinogen (g/L)	2.00-4.00	3.57 ± 0.78	4.08 ± 1.32	.74	3.66 ± 0.90
increased		8	1		9
D-dimer (μg/L)	0-550	235 (110-990)	450 (150-1180)	.69	250 (110-1180)
increased		2	2		4

Abbreviations: APTT, activated partial thromboplastin time; CRP, C-reactive protein; LMR, lymphocyte-monocyte ratio; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; PT, prothrombin time.

* $P < .05$.

140.8 ± 44.3, and 5.03 ± 1.64, respectively. The reference range was determined according to the one-sided 90% range as follows: NLR < 3.21, PLR < 191.7, and LMR > 2.93. The mean for LMR was significantly lower than donor reference control (5.03 ± 1.64). Based on the calculated reference range, 11 patients had elevated NLR (including five severe cases), 12 had elevated PLR (five severe cases), and 26 had reduced LMR (eight severe cases). By comparing the two groups of COVID-19 patients, it was determined that NLR and LMR differences were statistically significant between mild/moderate and severe cases. NLR was higher, while LMR was lower in severe cases. Compared with single neutrophil, lymphocyte, and monocyte counting, NLR and LMR seemed to have a better performance in prediction and severity stratification of COVID-19.

Twenty-seven patients were tested for a coagulation panel, of which prothrombin time (PT) and activated partial thromboplastin time (APTT) were normal, while nine patients had elevated fibrinogen levels with the mean value of 3.66 ± 0.90 g/L, and four patients (two severe cases) had elevated D-dimer levels. However, no statistical difference in fibrinogen and D-dimer levels was found between the two groups. Studies have confirmed that D-dimer levels were significantly increased in severe COVID-19 patients admitted to the ICU.[7,8] Specifically, D-dimer levels greater than 1000 μg/L could help clinicians to identify patients with poor prognosis at an early stage.[9] Only 11 patients were tested for inflammatory factors and all patients had a negative procalcitonin level (0.05 ± 0.03 ng/mL), while eight patients had elevated C-reactive protein levels, with the mean (range) of 14.67 (2.95-60.83) mg/L. C-reactive protein can be routinely tested in most fever clinics, and procalcitonin might be helpful in excluding complicated bacterial pneumonia.

In summary, COVID-19 patients diagnosed in the fever clinics were mainly exported cases. For COVID-19 patients in the fever clinics, abnormal changes in hematological index were common. Lymphopenia and elevated levels of fibrinogen, D-dimer, and C-reactive protein were observed. Compared with mild/moderate COVID-19 cases, severe cases had a higher NLR and absolute neutrophil count and a lower LMR. Clinical application for conventional hematological indexes should be fully explored in the fever clinic in the future.

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CONFLICT OF INTEREST

The authors declare no conflict of interests.

AUTHOR CONTRIBUTION

J. Kong and J. Fu designed the work and performed patient data collection, analyzed the data, and wrote the manuscript. T. Wang, D. Zou, B. Shi, X. Yu, C. Huang, Y. Yang, H. Sun, and D. Yuan performed patient data collection in this retrospective clinical study. D. Wu revised the manuscript. All the authors approved the submission.

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