



<https://doi.org/10.34883/PI.2023.12.4.021>



Mammadova H.
Azerbaijan Medical University, Baku, Azerbaijan

Assessment of Complications in Patients Diagnosed with COVID-19 According to the Degree of Severity

Conflict of interest: nothing to declare.
The article is published in the author's edition.

Submitted: 13.11.2023
Accepted: 27.11.2023
Contacts: mic_amu@mail.ru

Abstract

The coronavirus infection 2019 (SARS-CoV-2, COVID-19) is mainly classified as mild, moderate and severe and critical. Peripheral blood parameters such as total leukocyte count, lymphocytes, neutrophils, as well as other blood biochemical parameters and coagulation factors were investigated to be associated with the severity of the COVID-19 infection. In our presentation, the identification of biomarkers that predict the severity and outcome of patients with COVID-19 was very helpful. Our results show that severe lymphopenia and elevated C-reactive protein (118.41 mg/L) are associated with hypoxemia severity and predicted hospital mortality. In addition, changes in leukocyte count during the first 4 days after hospitalization were highly associated with complications, $pU < 0.001$.

Keywords: COVID-19, blood parameters, complication rate

Мамедова Х.Г.
Азербайджанский медицинский университет, Баку, Азербайджан

Оценка осложнений у пациентов с диагнозом COVID-19 в зависимости от степени тяжести заболевания

Конфликт интересов: не заявлен.
Статья опубликована в авторской редакции.

Подана: 13.11.2023
Принята: 27.11.2023
Контакты: mic_amu@mail.ru

Резюме

Течение инфекции COVID-19 в основном классифицируется как легкое, среднетяжелое, тяжелое и критическое (крайне тяжелое). Были исследованы параметры периферической крови, такие как общее количество лейкоцитов, лимфоцитов, нейтрофилов, а также другие биохимические параметры крови и факторы свертывания,

которые связаны с тяжестью инфекции COVID-19. Выявлены биомаркеры, предсказывающие тяжесть и исход пациентов с COVID-19. Наши результаты показывают, что тяжелая лимфопения и повышенный уровень С-реактивного белка (118,41 мг/л) связаны с тяжестью гипоксемии и прогнозируемой госпитальной смертностью. Кроме того, изменения количества лейкоцитов в течение первых 4 дней после госпитализации были в высокой степени связаны с осложнениями ($pU < 0,001$).

Ключевые слова: COVID-19, показатели крови, частота осложнений

■ INTRODUCTION

Coronavirus disease 2019 (COVID-19) which emerged in Wuhan, China, has spread to almost all countries and regions of the world, becoming one of the most lethal pandemic after the Spanish flu in 1918–1920. It is caused by an RNA virus (2019 novel coronavirus or 2019-nCoV or SARS-CoV-2). As of July 13, 2020, a total of 12,768,307 confirmed COVID-19 cases and 566,654 related deaths have been reported [1]. Beyond its important morbidity and mortality and the huge burden of health care systems, COVID-19 has a massive societal and economic impact globally.

To date, there is no established curative treatment for COVID-19. Although some drugs such as hydroxychloroquine are integrated in treatment guidelines or under investigation in interventional studies, the management of COVID-19 is mostly supportive [2–4]. Identifying biological abnormalities induced by COVID-19 may contribute to a better understanding of the pathophysiology of the disease and ultimately guide the development of targeted adjuvant therapies besides antiviral drugs. Furthermore, such information on the biological profile of COVID-19 can guide clinicians in the assessment and treatment of these patients.

Clinically, most of COVID-19 cases (80%) are either asymptomatic or have mild forms [4, 5]. However, about 13.8 and 6.1% have severe and critical life-threatening disease that require admission to hospital and sometimes in the intensive care unit [5]. In the context of overstretched health care systems and limited resources, risk stratification is pivotal to identify patients who the most need in-hospital and intensive management. Biomarkers along with some clinical factors might help to predict adverse outcomes among COVID-19 patients. Hence, we conducted this systematic review and meta-analysis to summarize available data on the association between some common hematological, inflammatory, biochemical parameters and the severity of COVID-19.

The National Early Warning Score (NEWS), first introduced in 2012 and updated in 2017 (NEWS2), has received a formal endorsement from the National Health Service to become the early warning system for deterioration of acutely ill patients in the United Kingdom (UK) [6, 7]. The NEWS/NEWS2 is a scoring system based on routine physiological parameters, which can be obtained easily and rapidly at the bedside. Each indicator is given a score, where 0 is considered normal, and simple addition allows a total score from 0 to 23. A score of 5 or more represents the key threshold for urgent response, and patients with a score of 7 or more would be deemed to have a high clinical risk and trigger a high-level clinical alert [6, 7]. Since some components (e.g., temperature, oxygen saturation, and supplemental oxygen dependency) were proved to be associated with

the progression of COVID-19 [8, 9], guidelines from the Royal College of Physicians [10] and the Swiss Society of Intensive Care Medicine [11] advocate the use of the NEWS2 for initial assessment in patients with COVID-19. However, these recommendations were only based on expert opinions, and there have been no published meta-analyses to evaluate the predictive performance of the NEWS2.

■ PURPOSE

The purpose of this study is to describe the current state of complete blood count changes during COVID-19 infection and to summarize the crucial role of some hematological parameters during the course of the disease.

■ MATERIALS AND METHODS

Our study included 212 patients with a confirmed diagnosis of COVID-19, 110 (51.9%) without complications and 102 with complications (48.1%). 95 patients (44.8%) were male, 117 patients (55.2%) were female. Also, patients were divided into age groups older than 65 years and younger than 65 years old, so that the average age was 55.4 ± 1.3 years in the group without complications, and 59.6 ± 1.4 years in the group with complications.

When comparing the blood groups and rhesus factors of the patients included in the study according to the degree of complications, it was determined that 1st blood group and rhesus factor positive(+) patients are more prone to complications, respectively 35.4% and 92.9%.

Among the patients under observation, concomitant diseases were also studied, which is one of the factors leading to a high risk of complications in infected patients. In our study, comorbidities were observed in 94 patients (42.9%), and among them, the most prevalent endocrine pathology was type 2 diabetes (28.3%).

Microsoft Excel was used to analyze the clinical symptoms and Laboratory results. Single-arm meta-analysis was performed using Stata 15.0 software. Heterogeneity among studies was tested using the Cochran Chi-square test and I^2 , when $I^2 < 50\%$, a fixed-effects model was used, while when $I^2 > 50\%$, a random-effects model was selected. If there was statistical heterogeneity among the results, a further sensitivity analysis was conducted to determine the source of heterogeneity. After the significant clinical heterogeneity was excluded, the randomized effects model was used for meta-analysis. Student's t-test, Mann-Whitney test were used to detect the publication bias. $P < 0.05$ was considered as statistically significant.

■ RESULTS AND DISCUSSION

It was clarified that the length of hospital stay in the group of patients with complications was longer compared to other patients. So, this period was 13.6 ± 0.5 days on average in the group of 102 patients with complications. A statistical significance was achieved between the length of hospital stay between the two groups $P < 0.001$.

X-ray examination of chest organs is used as a radiological method in the dynamic assessment of the prognosis of patients diagnosed with COVID-19. Although 102 complicated patients under our observation – 100.0% bilateral pneumonia was detected, including 94 patients without complications (85.5%) pneumonia was accompanied (Table 1).

Table 1**The rate of complication depends on X-ray examination of chest organs**

X-Ray	Complication		χ^2
	No Abs (%)	Yes Abs (%)	
Normal	16 (14.5)	0 (0.0)	0,130
Pneumonia	94 (85.5)	100.0 (100.0)	0.003

Peripheral blood parameters were also analyzed between groups. As we know, the processes taking place in the etiopathogenesis of the infection are directly manifested in the morphological structure of the blood. White blood cells (leukocyte, lymphocyte neutrophil count), inflammatory parameters (C-reactive protein, procalcitonin, ferritin, erythrocyte sedimentation rate), coagulation (prothrombin time, D-dimer) and biochemical level (Alat, Asat) are found in the blood with the highest frequencies, creatinine, sugar are the changes.

First of all, when examining WBC (leukocytes) from peripheral blood indicators, we see that significant statistical differences were obtained between both groups. Leukocytosis (elevation of leukocytes) was observed in the blood when comparing patients with exacerbations to the other group. The average indicator of WBC was $10.0 \pm 1.0 \times 10^9/l$, and the highest level was $12.0 \times 10^9/l$ in patients with complications. During dynamic observation, 32 patients with complications had a decrease in WBC count, but 49 patients had an increase $P < 0.001$.

In addition, the level of NEU (neutrophil) in the blood was also examined, and the average indicator of this parameter was $6.7 \pm 0.5 \times 10^9/l$ in 102 patients without complications. When we analyzed the level of NEU in both groups in blood samples taken from patients both on the day of admission to the hospital and on the following days during consecutive measurements, we see that neutrophilia (an increase in neutrophils) was observed in the blood and an honest difference was obtained during each statistical analysis $P < 0.001$.

LYM (lymphocyte) in peripheral blood examination is of particular importance in predicting the course of infection. Thus, as with other viral infections, lymphopenia (decrease of lymphocytes) is characteristic of COVID-19 infection. During our study, significant changes in the absolute number and percentage of LYM in the blood were obtained (Table 2).

Table 2**Analysis of general indicators of blood in patients between groups**

Parametrs	Aggravating patients (n=102)	Non-aggravating patients (n=110)	pF	pU
LEU $10^9/l$	10.0 ± 1.0 (7.9–12.0)	6.7 ± 0.3 (6.0–7.3)	$<0.001^*$	$<0.001^*$
LYM $10^9/l$	1.23 ± 0.10 (1.04–1.43)	1.33 ± 0.07 (1.20–1.47)	0.393	$<0.001^*$
NEU $10^9/l$	6.7 ± 0.5 (5.8–7.6)	4.5 ± 0.3 (3.9–5.1)	$<0.001^*$	$<0.001^*$

Note: * «0» hypothesis is rejected.



Table 3
Analysis of blood coagulation parameters in patients between groups

Parametrs	Aggravating patients (n=102)	Non-aggravating patients (n=106)	pW	pU
PT sec.	13.0±0.2 (12.1–13.4)	12.5±0.2 (12.1–12.8)	<0.001*	<0.001*
INR sec.	1.09±0.116 (0.86–1.32)	0.93±0.013 (0.94–0.95)	<0.001*	<0.001*

Note: * – «0» hypothesis is rejected.

An important role is played by the comparative study of coagulation parameters in blood samples of patients with and without complications diagnosed with COVID-19. It was clarified that PT (prothrombin time) tended to be prolonged in groups of patients with aggravated blood levels, the average indicator during the initial examination in aggravated patients was 13.0±0.2 seconds, and in the following days it was 13.6±0.3 seconds $p=0.017$. During the dynamic observation of blood samples taken from patients 3 times, the INR indicator in blood resulted in an increase in 54 patients in the group of complications, and in 16 patients without complications, $p<0.05$. In turn, D-dimer showed a high result (4.93 mg/L) in the aggravated patient groups and showed a statistical difference ($P<0.001$) (Table 3).

In our study, the level of CRP (C-reactive protein) as an inflammatory parameter was calculated as 101.19±8.68 mg/L in the group of 101 aggravated patients, and the highest result was 118.41 mg/L, the differences were honest ($pU<0.005$). In blood samples taken for the 3rd time, the level of erythrocyte sedimentation rate (erythrocyte sedimentation rate) increased 1.5 times in the group of patients with complications compared to patients diagnosed with COVID-19 without complications .1 mm/hour, $pU<0.001$). Another inflammatory parameter PCT (procalcitonin) and ferritin were analyzed, which showed honesty between groups when calculated by Mann – Utney method, $p=0.010$, $p=0.043$, respectively.

When biochemical indicators were differentiated between both groups, statistically different results were obtained only at the level of creatinine. Anova analysis showed that the mean level of creatinine was 2.08±0.35 mg/L in patients with complications ($p<0.05$).

■ CONCLUSION

Thus, the presence of both clinical indicators ($SpO_2 < 90\%$) and changes in peripheral blood (lymphopenia, leukocytosis, elevated CRP, prolongation of prothrombin time, etc.) in patients with complications as a final result are important and important biomarkers to consider, which Timely detection of indicators can prevent the reduction of deaths.

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