Original Research

IJNHS

Levels of Lymphocytes, Neutrophils, Leukocytes, and Outcome of Covid-19 Patients

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Article info

Article history:
Received: October 14th, 2022
Revised: November 14th, 2022
Accepted: December 9th, 2022

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International Journal of Nursing and Health Services (IJNHS)
Volume 5, Issue 6, December 20th, 2022
DOI: 10.35654/ijnhs.v5i6.652
E-ISSN: 2654-6310

Abstract

Introduction: Coronavirus Disease 2019 can cause systemic infections that significantly affect the immune response and hemostatic conditions. A biomarker is needed to predict patients in the severity of the disease or severe complications or when doing triage upon admission to the hospital, providing early intervention to reduce mortality. Changes in levels of lymphocytes, neutrophils, and leukocytes can predict the risk of worsening Covid-19 patients. **Objective:** to determine the effect of lymphocytes, neutrophils, and leukocytes on the outcome of Covid-19 patients. **Method:** This study uses an observational analytic design with a retrospective approach. The population of this research is medical records of Covid-19 confirmed positive by real-time Polymerase chain reaction (rt-PCR) from the Laboratory of H. Adam Malik General Hospital Medan for the period January-December 2021. Sampling using purposive sampling of as many as 175 medical records. The test used to determine the relationship of lymphocytes, neutrophils, and leukocytes to the outcome of Covid-19 patients is the Spearman correlation test. **Result:** The results showed that there was a weak and positive relationship between lymphocytes (p = 0.006; r = 0.208) and the outcome of Covid-19 patients, there was a moderate and positive relationship between neutrophils (p = 0.000; r = 0.276) and the outcome of Covid-19 patients. moderate and positive relationship between leukocytes (p = 0.000; r = 0.350) and the outcome of Covid 19 patients. **Recommendation:** It is recommended to conduct a study in a large group by comparing the severity of the disease and the length of stay.

Keywords: Covid-19, lymphocytes, neutrophils, leukocytes, outcome

INTRODUCTION

Coronavirus disease 2019 (Covid-19) was declared a global pandemic from March 2020 until May 2021. It has infected nearly 163 million people worldwide and caused the death of 3.3 million people by the end of August 2021. This pandemic has infected 217 million people and caused the death of 4.5 million people. WHO (2022) confirmed that on October 3, 2022, there were 615.310.890 confirmed cases of Covid-19 and approximately 6.524.568 deaths (1).

Based on data from the Ministry of Health of the Republic of Indonesia on October 4, 2022, it was found that Indonesia had 6,437,570 confirmed cases (+ 1,851), 6.262.820 cases recovered (97.3%), 158,156 cases died (2.5%) and 16.594 cases of Active (0.3%) (2). The high gravity of this disease requires early detection, prevention, and rapid treatment to reduce the incidence. The WHO standard regarding early detection is the examination of saliva, nasal mucus, or blood specimens for the presence of the nucleic acid of the SARS-CoV-2 virus (3).

Examination of hematological parameters is essential, especially in asymptomatic patients suspected of positive PCR results. In addition to other supporting tests, namely chest X-rays and clinical manifestations that occur in patients. Some evidence suggests that Covid-19 patients with severe symptoms may experience a compromised immune response, which may lead to the development of hyperinflammation of the virus. Therefore, biomarkers (biological markers) in the blood circulation can represent inflammatory and immune status that are useful as potential predictors in the prognosis of Covid-19 patients.

Early and effective predictors based on hemostasis laboratory results are needed because they can assess risk levels, compare therapeutic methods, assess survival, and predict patient prognosis. Changes in laboratory results can occur in Covid-19 patients, including thrombocytopenia, lymphopenia, increased D-dimer, and increased inflammatory markers, such as lactate dehydrogenase (LDH), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and ferritin (4). Elevated biomarkers are associated with bleeding and inflammatory disorders suggesting an increased risk of ICU admission, need for ventilators, and death (5). A study confirmed that most of the Covid-19 patients at the time had lymphocytopenia (83.2%), thrombocytopenia (36.2%), and leukopenia in 33.7% (6). This study aims to determine the effect of laboratory biomarker parameters of lymphocytes, neutrophils, and leukocytes on the outcome of Covid-19 patients.

The urgency of the research is that the impact of Covid-19 varies from asymptomatic or mild symptoms to acute respiratory distress syndrome, multi-organ failure, and death. Recognizing/evaluating the early signs of the emergency of Covid-19 patients through the results of biomarker examinations is very important to predict patients falling into the degree of disease or severe complications and identifying outcomes. Identification of Covid-19 effects is needed to prepare for further management to maintain quality of life. Specific parameters are required to be able to predict the clinical outcome of Covid-19 patients, in addition to providing appropriate treatment and resource efficiency, as well as reducing mortality in Covid-19 sufferers.

OBJECTIVE

The study aimed to determine the effect of lymphocytes, neutrophils, and leukocytes on the outcome of Covid-19 patients at Haji Adam Malik General Hospital Medan.

METHODS

Design

This study is an observational analytical study with a retrospective design. The samples obtained from the medical records of Covid-19 confirmed positive by real-time Polymerase chain reaction (rat-PCR) from the Laboratory of Haji Adam Malik General Hospital Medan. The sampling technique used purposive

sampling met the inclusion and exclusion criteria with a total of 175 medical records respondents. The research instrument used was the observation sheet for the results of blood laboratory examinations. The normal laboratory value is based on Haji Adam Malik General Hospital examination guidelines.

Data collection process

This study uses secondary data sourced from medical records with inclusion criteria of patients aged over 18 years with a confirmed diagnosis of Covid-19 with real-time Polymerase chain reaction (rat-PCR) obtained from the Laboratory of Haji Adam Malik General Hospital Medan, complete medical records, patients treated at Haji Adam Malik General Hospital Medan for the period January 2021 to December 2021.

Data analysis

Data obtained from the medical records of Covid-19 confirmed positive by real-time Polymerase chain reaction (rat-PCR) from the Laboratory of Haji Adam Malik General Hospital Medan for January-December 2021. It was tabulated and analyzed using descriptive statistics such as frequencies, percentage distribution, and weighted item means for the quantitative portion.

The test used to determine the relationship of lymphocytes, neutrophils, and leukocytes to the outcome of Covid-19 patients is the Spearman correlation test.

Ethical consideration

Before the data gathering, ethics clearance was obtained from the research Ethics of the Muhammadiyah University of North Sumatra with letter number 393/KEPK/FKUMSU/2022.

RESULTS

table 1 shows that most Covid 19 patients are early elderly (32.6%), and 92 are female (52.6%). More than half of them have no comorbidities (61.7%). The results of laboratory examinations showed more than half of the respondents have normal lymphocytes (52%). Some of them also have normal neutrophils (51.4%). While most of them also were normal leukocytes (73.1%). Most of the outcomes of Covid 19 patients in 2021 were recovered (88%).

Table 2 shows a weak and positive relationship between lymphocytes ($p = 0.006$; $r = 0.208$). The outcome of Covid 19 patients, there is moderate. Whereas there was a positive relationship between neutrophils ($p = 0.000$; $r = 0.276$) and the outcome of Covid-19 patients. there is a moderate and positive relationship between leukocytes ($p = 0.000$; $r = 0.350$) and the outcome of Covid-19 patients.

Table 1. Frequency distribution based on age, gender, comorbidities, results of laboratory examinations, and Covid-19 patient outcomes in 2021 (n = 175)

Variables	Frequency	Percentage (%)
Age		
Late Teen	11	6.3
Early Adult	17	9.7
Late Adult	23	13.1
Early Elderly	57	32.6
Late Elderly	36	20.6
Seniors	31	17.7
Gender		
Male	83	46.5
Female	92	52.6
Comorbidities		
There aren't any	108	61.7
There is	67	39.3
- Heart disease	1	0.7
- Hypertension	28	16
- Diabetes Mellitus	23	13.1
- Chronic Kidney Failure	3	1.7
- Diabetes Mellitus + hypertension	3	1.7
- Other diseases	9	5.1
Laboratory Results		
Lymphocytes		
Normal	60	46.5
Low	59	45.7
High	10	7.9
Neutrophils		
Normal	61	47.3

Low	12	9.3
High	56	43.4
Leukocytes		
Normal	128	73.1
Low	10	5.7
High	37	21.1
Outcome		
Healed	117	90.7
Die	12	9.3

Table 2. The Relationship between Biomarker Examination Results and Outcome in Covid-19 Patients in 2021 (n = 175)

Variables	p	r
Lymphocytes	0.006	0. 208
Neutrophils	0.000	0. 276
Leukocytes	0.000	0.350

DISCUSSION

The relationship between lymphocytes and the outcome of Covid-19 patients

The results of this study showed that laboratory examination results for Covid-19 patients were normal lymphocytes (46.5%), low lymphocytes (45.7%), and high lymphocytes (7.8%). Several studies in various countries found biomarkers often found in laboratory results of Covid-19 patients, a decrease in lymphocytes in 83.2% of patients, a decrease in platelet levels in 36.2%, and a decrease in leukocyte levels in 33.7% of patients. Most patients have elevated levels of C-reactive protein, and increased levels of D-dimer were found.

According to Liu et al., lymphocyte count decreased in most patients, and the absolute value of lymphocytes was correlated with the severity of Covid-19. This can be caused because Covid-19 mainly attacks lymphocytes (4). SARSCoV-2 is also more likely to infect people with chronic comorbidities such as heart disease, cerebral hemorrhage, and diabetes. 1%) had DM. The previous study (7) also found that 35 people had comorbidities at Fuyang Second People's Hospital. Seven of them (16.28%) had DM, whereas 13 people (30.23%) had hypertension, and three people (0.69%) had diabetes.

This study's respondents were early elderly (46-55 years). A previous study also confirmed that some of the COVID-19 patients at Mekar Sari Hospital were 46–59-year (37.3%). Along with increasing age, the ability of the body's immune system to fight infection will decrease, including the speed of the immune response. Therefore, the risk of illness will increase. The reaction of lymphocytes in the immune system is also reduced, where the immune system of the elderly group reacts more slowly than the adult group. According to Liu et al., lymphocyte count decreased in most patients, and the absolute value of lymphocytes was correlated with the severity of Covid-19 (9). This can be caused because Covid-19 mainly attacks lymphocytes.

Lymphopenia is associated with increased mortality, the incidence of acute respiratory distress syndrome (ARDS), the need for treatment in the intensive care unit (ICU), and the incidence of severe Covid-19 symptoms (4). This study's results indicate a positive and weak relationship between lymphocytes and the outcome of Covid-19 patients. Several previous studies have shown significant differences in lymphocyte counts between Covid-19 patients with severe and non-severe cases, ICU and non-ICU patients, and survivors and Non-survivor patients.

The relationship between neutrophils and the outcome of Covid-19 patients

The results of this study showed normal neutrophils (47.3%). Some of them were high neutrophils (43.4%). In contrast to the study of Tandjungbulu et al. (2021), neutrophils decreased by four samples (3.7%), and some of them showed normal neutrophils (40.2%). However, more than half of them was a high level of neutrophils (56.1%) (10). Study literature reported an increased number of neutrophils and a decrease of lymphocytes among High NLR in severe patients (11).

Neutrophils are the main component of leukocytes that actively migrate to the immune system or organ. An increase in the number of neutrophils indicates the intensity of the inflammatory response, while a decrease in the number of lymphocytes indicates a damaged immune system.

Dysregulation in immune cell responses results in immunological abnormalities that are essential to the degree of inflammation caused by viruses. This increase in the neutrophil count agrees with the study (12), showing that a high neutrophil count independently predicts the occurrence of critical illness. The results showed a positive and moderate relationship between neutrophils (p = 0.001; r = 0.292) and the outcome of Covid-19 patients. In contrast, the study's results found that the number of leukocytes, neutrophils, and lymphocytes had no relationship to mortality or shock. However, leukocytes can predict shock in septic patients (13).

Relationship between Leukocytes and Outcomes of Covid-19 patients

This study showed that the most normal leukocytes were 128 people (73.1%). In line with the research of Huang et al., most patients with Covid-19 had normal leukocyte levels, and only 25% of patients with Covid-19 experienced a decrease in leukocyte levels (14). Research by Tandjungbulu et al. (2020) found that leukocytes were normal (53.3%), decreased (9.3%), and increased (37.4%) (10).

Wang et al. in 2020 in China found that there were changes and differences in the leukocyte component in mild to severe Covid-19 patients in the form of monocyte activation, a decrease in the number of neutrophils and Natural Killer (NK) cells, T cell dysregulation, to variations in production. Antibodies from B cells (15). Another study concluded a decrease in the overall leukocyte count in mild cases of Covid-19 compared to severe cases, with an increase in the overall leukocyte count (16). The study conducted by Li et al. (2020) showed a picture of lymphocytes and leukocytes during the incubation period (generally 37 days). Leukocytes and lymphocytes were not significantly reduced (normal or slightly lower. In the next phase, around 7-14 lymphocytes decreased significantly, including T lymphocytes and B Lymphocytes (15). The decrease or change that occurred went straight with the severity of the patient (17).

However, the results showed a moderate and positive relationship between leukocytes (p = 0.000; r = 0.350) and the outcome of Covid 19 patients. In line with the study, there was a significant relationship between leukocyte count and clinical severity of Covid-19 patients at two Covid-19 referral hospitals in Ambon City in 2020 (p = 0.029) (18).

CONCLUSIONS AND SUGGESTIONS

The results showed that most Covid-19 patients were early elderly, normal category lymphocytes, normal neutrophils, and leukocytes. The majority of Covid-19 patients have recovered. There is a weak and positive relationship between lymphocytes and the outcome of Covid-19 patients. There is a moderate and positive relationship between neutrophils and the outcome of Covid 19 patients. There is a moderate and positive relationship between leukocytes and the outcome of Covid-19 patients.

Further research is needed with large groups by assessing the severity of the disease and length of stay.

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