**Research**

**Open Access**

# Description of Hematological Parameters and Severity Levels of COVID-19 Patients and Disease Progression at Royal Prima Hospital, Medan, North Sumatera, Indonesia

**Yunita Wannur Azah, Chrismis Novalinda Ginting, Linda Chiuman, Sahna Ferdinand**

Department of Biomedicine, Faculty of Medicine, Dentistry and Health Sciences, Universitas Prima Indonesia, Medan

## ABSTRACT

**Background:** The severity of COVID-19 can be evaluated by checking several routine hematological parameters. Routine hematology examinations have an important role in early detection, diagnosis, disease management and disease progression. This study aims to determine the relationship between hematological parameters and disease progression and severity in COVID-19 patients.

**Subjects and Method:** This was a cross sectional study conducted at Royal Prima Hospital, Medan, North Sumatera, Indonesia, from January to February 2022. A total of 93 patients who had confirmed COVID-19 were selected using a simple random sampling technique according to the inclusion and exclusion criteria. The research was The dependent variables of this research were disease progression and severity of COVID-19 patients. The independent variables are hematological parameters based on hospital medical record data. Data analysis used the Chi-Square test and logistic regression.

**Results:** 75 people (80.6%) COVID-19 sufferers had severe disease. NLR and D-dimer levels were significantly related to disease progression in COVID-19 sufferers (p<0.05). Leukocyte, lymphocyte, NLR, CRP, D-dimer levels are related to the severity of COVID-19 sufferers (p<0.05). Leukocyte levels have the strongest relationship with the severity of COVID-19 with an OR value of 1.798.

**Conclusion:** NLR and D-dimer levels are significantly related to disease progression and leukocyte. Lymphocyte, NLR, CRP, D-dimer levels are related to the severity of COVID-19 sufferers.

**Keywords:** hematological parameters, severity level, disease progression

**Correspondence:**
Chrismis Novalinda Ginting. Faculty of Medicine, Dentistry and Health Sciences, Universitas Prima Indonesia. Jl. Sampul, Sei Putih Baru, Kec. Medan Petisah, Kota Medan, Sumatera Utara, Indonesia 20188. Email: chrismis@unprimdn.ac.id. Mobile: +6281370077795.

## BACKGROUND

Corona Virus Diseases 2019 (COVID-19) is an infectious disease caused by a new type of Corona Virus. This disease began with the emergence of cases of pneumonia of unknown etiology in Wuhan, China. Based on epidemiological results, the case is suspected to be related to the Seafood Market in

Wuhan. On January 7 2020, the Chinese Government then announced that the cause of the case was a new type of Coronavirus which was later named SARS CoV2 (Severe Acute Respiratory Syndrome Coronavirus 2) and the name of the disease as Coronavirus Disease 2019 (COVID-19). In recent years, coronaviruses have appeared periodically in various regions around the world and caused an increase in deaths. (Li et al, 2020).

Coronaviruses are enveloped, non-segmented, positive-stranded single-stranded RNA viral genomes ranging in size from 26 to 32 kilobases. There are 4 main protein structures in Coronavirus, namely protein N (nucleocapsid), glycoprotein M (membrane), glycoprotein S (Spike), and protein E (Envelope). (Li et al, 2020)

COVID-19 was diagnosed based on WHO guidelines. Confirmed COVID-19 cases were obtained from Real Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) from nasal and pharyngeal swab specimens.

Routine hematological examination and leukocyte count have an important role in early detection, diagnosis and treatment of disease. This examination is important because it can be used as supporting data for the gold standard examination, namely RT-PCR. Laboratory diagnostics are used to assess the severity of the disease, to determine the prognosis, for patient follow-up, treatment and monitoring therapy. Apart from early detection, laboratory examinations can be a tool for monitoring the course of COVID-19 (Wang et al, 2020).

Several blood test components that are widely used as monitoring tools and predictors of COVID-19 are leukocytes, lymphocyte levels, neutrophil levels, platelet levels, neutrophil lymphocyte ratio, C-Reactive Protein, and D-dimer. One of them is leukocytes, which are cells that have the main function of the body's immune system. Leukocytes consist of 5 types, namely eosinophils, basophils, neutrophils, lymphocytes and monocytes. The neutrophil value also plays a very important role in determining the severity of COVID-19. Likewise with lymphocytes, namely T cells, B cells and NK cells which play a role in maintaining the body's immune system, including viral infections. For this reason, many studies use this parameter for screening and monitoring the severity of COVID-19 disease (Ding et al., 2020).

Several previous studies concluded that Leukocytosis, Neutrophilia, increased Neutrophil to Lymphocyte ratio, APTT, D-dimer, LDH, serum Ferritin and CRP were associated with the severity of COVID-19 disease (Taj et al, 2021). Dynamic changes in vital hematological parameters of severe and non-severe patients have been characterized during hospitalization. During hospitalization, NLR was found to have particular relevance to days of hospitalization and played a role in predicting disease prognosis for patients with COVID-19 (Ding et al, 2020). Increased NLR correlates with severity of COVID-19. NLR assessment can be proposed to identify high-risk individuals with COVID-19 (Matin et al, 2022). This study aims to determine the relationship between hematological parameters and disease progression and severity in COVID-19 patients.

## SUBJECTS AND METHOD

### 1. Study Design
This was a cross-sectional study conducted at the Medical Records Installation at Royal Prima General Hospital, Medan, Indonesia, from January to February 2022.

### 2. Population and sample
The population in this study were patients who had a confirmed diagnosis of COVID-19 at RSU Royal Prima Medan. Sampling was carried out using a simple random sampling

technique. The subjects in this study were 93 COVID-19 patients with a history of being treated from January to May 2021 who met the inclusion and exclusion criteria, namely patients who were diagnosed with COVID-19 from RT-PCR results and had complete hematology examination data.

Exclusion criteria include patients suffering from immunodeficiency, patients who are pregnant, have comorbidities, patients with blood disorders before suffering from COVID-19.

## 3. Study Variables
The dependent variables are disease progression and severity. The independent variables are hematological parameters.

## 4. Operational Definition of Variables
**The severity of COVID-19 patients** is the symptoms that appear after exposure to COVID-19.

**Disease progression** is the process of disease progressing, getting better or worse.

**Hematology parameters** are an examination of the types of cells in the blood through the results of hospital laboratory examinations.

## 5. Instrument
Data were obtained from patient's medical record data.

## 6. Data Analysis
Data from medical records were collected and analyzed using SPSS.

## 7. Research Ethics
This research has received approval from the Health Research Ethics Commission (KEPK) Faculty of Medicine, Prima Indonesia University, Medan with No: 003/-KEPK/UNPRI/III/2021 and research permission from the Head of Medical Records RSU Royal Prima Medan with No: 454.A/EXT/PP/RSURP/IV/2021.

## RESULT

### a. Characteristics of the patients
The subjects who participated in this study were 93 people suffering from COVID-19 with an average age of 47 years. The largest age group is 26-45 Years (Adults). More COVID-19 sufferers were female, namely 50 people (53.8%) with a length of stay ≥ 8 days, namely 65 people (69.9%). Sample characteristics can be seen in Table 1.

**Table 1. Distribution of Respondent Characteristics**

| Variable | Category | n | (%) |
|---|---|---|---|
| **Age** | 12-25 years (adolscent) | 9 | 9.6 |
| | 26-45 years (adult) | 40 | 43.0 |
| | 46-65 years (elderly) | 34 | 36.6 |
| | > 65 years (elderly) | 10 | 10.8 |
| **Gender** | Female | 50 | 53.8 |
| | Male | 43 | 46.2 |
| **Duration of treatment** | ≤ 8 days | 28 | 30.1 |
| | > 8 days | 65 | 69.9 |

### b. Hematology
**Table 2. Distribution of Patients Based on Hematological Parameters**

| Hematological Parameters | Mean | SD | Mean | SD |
|---|---|---|---|---|
| Leukosit | 7.0 | 2.9 | 8.5 | 3.7 |
| Trombosit | 219.1 | 79.7 | 280.3 | 101.3 |
| Limfosit | 23.1 | 9.2 | 21.1 | 10.7 |
| NLR | 4.4 | 4.7 | 7.5 | 9.0 |
| CRP | 31.8 | 25.0 | 25.8 | 26.9 |
| D-dimer | 1127.5 | 1212.4 | 861.4 | 1050.7 |

**Table 3. Distribution of Patients Based on Hematological Parameter Categories**

| Hematological Parameters | Examination 1 (days 1-7) | | Examination 2 (days 8-15) | |
|---|---|---|---|---|
| | Total | (%) | Total | (%) |
| Leukosit ($10^3$/µl) | | | | |
| Dropped | 21 | 22.6 | 12 | 12.9 |
| Normal | 59 | 63.4 | 54 | 58.1 |
| Raised | 13 | 14.0 | 27 | 29.0 |
| Trombosit ($10^3$/µl) | | | | |
| Dropped | 17 | 18.3 | 7 | 7.5 |
| Normal | 72 | 77.4 | 76 | 81.7 |
| Raised | 4 | 4.3 | 10 | 10.8 |
| Limfosit (%) | | | | |
| Dropped | 35 | 37.6 | 45 | 48.4 |
| Normal | 54 | 58.1 | 43 | 46.2 |
| Raised | 4 | 4.3 | 5 | 5.4 |
| Neutrofil Limfosit Ratio (NLR) (%) | | | | |
| Dropped | 54 | 58.1 | 44 | 47.3 |
| Raised | 39 | 41.9 | 49 | 52.7 |
| C-Reactive Protein (CRP) (ug /ml) | | | | |
| Dropped | 8 | 8.6 | 30 | 32.3 |
| Raised | 85 | 91.4 | 63 | 67.7 |
| D-dimer (ng /mL) | | | | |
| Dropped | 21 | 22.6 | 41 | 44.1 |
| Raised | 72 | 77.4 | 52 | 55.9 |

Disease progression in this study was seen through hematological parameters while the patient was undergoing treatment (Table 2). Then each hematological parameter seen based on laboratory tests was categorized (Table 3). The results of the study showed that COVID-19 sufferers had leukocyte levels for the first examination, namely a minimum of 2.11 $10^3$/µl and a maximum of 16.7 $10^3$/µl with an average value of 7.0 (SD= 2.9) $10^3$/µl and for the second examination, a minimum of 3.4 $10^3$/µl. µl and a maximum of 24.5 $10^3$/µl with an average value of 8.5 (SD= 3.7) $10^3$/µl and more with normal leukocyte levels.

COVID-19 sufferers had platelet levels for the first examination, namely a minimum of 98 $10^3$/µl and a maximum of 535 $10^3$/µl with an average value of 219.1 (SD= 79.7) $10^3$/µl and for the second examination, a minimum of 108.0 $10^3$/µl and a maximum of 586.0103 /µl with an average value of 280.3 (SD= 101.3) $10^3$/µl and more with normal platelet levels.

COVID-19 sufferers had lymphocyte levels for the first examination, namely a minimum of 4.8% and a maximum of 45.8% with an average value of 23.1% (SD= 9.2) and for the second examination, a minimum of 2.5% and a maximum of 48.7% with an average value of 21.1% (SD= 10.7) and more with normal lymphocyte levels for the first examination, namely 51 people (54.8%) while for the second examination it decreased more, namely 45 people (48.4%).

COVID-19 sufferers had NLR levels for the first examination, namely a minimum of 0.8% and a maximum of 23.8% with an average value of 4.4% (SD= 4.7) and at the second examination, a minimum of 0.7% and a maximum of 40.3% with an average value of 7.5% (SD= 9.0) and more with NLR levels decreasing for the first examination, namely 54 people (58.1%) while for the second examination it increased more, namely 49 people (52.7%).

COVID-19 sufferers have CRP levels for the first examination, namely a minimum of 2.5 ug/ml and a maximum of 119.0 ug/ml with an average value of 31.8 ug/ml (SD= 25.0) and for the second examination, a minimum of 2.5 ug/ml and a maximum of 96.0 ug /ml with an average value of 25.8 ug /ml (SD= 26.9) and more with increasing CRP levels for both the first and second examinations.

COVID-19 sufferers had D-dimer levels for the first examination, namely a minimum of 118.4 ng / mL and a maximum of 5041.3 ng/ mL with an average value of 1127.5 ng/ mL (SD= 1212.4) and for the second examination, a minimum of 112.0 ng / mL and maximum 5000.0 ng / mL with an average value of 861.4 ng/mL (SD= 1050.7) and more with increasing D-dimer levels for both the first and second examination.

## c. Severity Level of COVID-19 Sufferers
**Table 4. Distribution of Sufferers Based on Severity Level**

| Level of Severity | Total | (%) |
|---|---|---|
| Medium | 75 | 80.6 |
| Severe | 18 | 19.4 |

The research results showed that more COVID-19 sufferers were observed through

### d. Correlation of Hematological Parameters with Disease Progression
Based on the levels of leukocytes, platelets and lymphocytes seen through the length of treatment, it is known that of the 93 COVID-19 sufferers for the first examination, most were in the normal category. Meanwhile, the levels of NLR, CRP and D-dimer varied, namely that NLR decreased more, CRP and D-dimer increased more. The results of the

medical records with moderate severity, namely 75 people (80.6%) (Table 4).

Pearson correlation test for the first examination of all hematological parameters obtained a p value of >0.05, indicating there was no relationship with disease progression.

On the second examination, the leukocyte levels, the platelets were more normal, but the lymphocytes were lower. Meanwhile, NLR, CRP and D-dimer levels increased more. The relationship between hematological parameters and disease progression can be seen in Table 5.

**Table 5. Correlation of Hematological Parameters with Disease Progression**

| Hematologi | Examination | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | I (day 1-7) | | | | II (day 8-15) | | | |
| | N | % | r | p | n | % | r | p |
| **Leukocytes** | | | | | | | | |
| Dropped | 21 | 22.6 | 0.09 | 0.400 | 12 | 12.9 | 0.22 | 0.032 |
| Normal | 59 | 63.4 | | | 54 | 58.1 | | |
| Raised | 13 | 14.0 | | | 27 | 29.0 | | |
| **Platelets** | | | | | | | | |
| Dropped | 17 | 18.3 | -0.05 | 0.664 | 7 | 7.5 | 0.26 | 0.013 |
| Normal | 72 | 77.4 | | | 76 | 81.7 | | |
| Raised | 4 | 4.3 | | | 10 | 10.8 | | |
| **Lymphocytes** | | | | | | | | |
| Dropped | 35 | 37.6 | -0.19 | 0.059 | 45 | 48.4 | -0.21 | 0.047 |
| Normal | 54 | 58.1 | | | 43 | 46.2 | | |
| Raised | 4 | 4.3 | | | 5 | 5.4 | | |
| **NLR** | | | | | | | | |

| Hematologi | Examination | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | I (day 1-7) | | | | II (day 8-15) | | | |
| | N | % | r | p | n | % | r | p |
| Dropped | 54 | 58.1 | 0.39 | <0.00 | 44 | 47.3 | 0.46 | <0.001 |
| Raised | 39 | 41.9 | | | 49 | 52.7 | | |
| **CRP** | | | | | | | | |
| Dropped | 8 | 8.6 | 0.14 | 0.184 | 30 | 32.3 | 0.22 | 0.038 |
| Raised | 85 | 91.4 | | | 63 | 67.7 | | |
| **D-Dimer** | | | | | | | | |
| Dropped | 21 | 22.6 | 0.19 | 0.066 | 41 | 44.1 | 0.21 | 0.048 |
| Raised | 72 | 77.4 | | | 52 | 55.9 | | |

### e. Correlation of Hematological Parameters with Severity Level

Based on the severity, leukocyte and platelet levels were more in the normal category, while lymphocyte levels were more decreased, while NLR, CRP and D-dimer levels were more increased. Th is a significant relationship of hematological parameters and severity.

**Table 6. Correlation of Hematological Parameters with Severity Level**

| Hematology | Level of severity | | | | p |
|---|---|---|---|---|---|
| | Moderate | | Severe | | |
| | n | % | N | % | |
| **Leukocytes** | | | | | |
| Dropped | 12 | 100.0 | 0 | 0.0 | <0.001 |
| Normal | 48 | 88.9 | 6 | 11.1 | |
| Raised | 15 | 55.6 | 12 | 44.4 | |
| **Platelets** | | | | | |
| Dropped | 7 | 100.0 | 0 | 0.0 | 0.108 |
| Normal | 62 | 81.6 | 14 | 14.4 | |
| Raised | 6 | 60.0 | 4 | 40.0 | |
| **Lymphocytes** | | | | | |
| Dropped | 30 | 66.7 | 15 | 33.3 | 0.004 |
| Normal | 40 | 93.0 | 3 | 7.0 | |
| Raised | 5 | 100.0 | 0 | 0.0 | |
| **NLR** | | | | | |
| Dropped | 43 | 97.7 | 1 | 2.3 | <0.001 |
| Raised | 32 | 65.3 | 17 | 34.7 | |
| **CRP** | | | | | |
| Dropped | 22 | 73.3 | 8 | 26.7 | 0.218 |
| Raised | 53 | 84.1 | 10 | 15.9 | |
| **D-Dimer** | | | | | |
| Dropped | 38 | 92.7 | 3 | 7.3 | 0.009 |
| Raised | 37 | 71.2 | 15 | 28.8 | |

### f. Multiple Logistic Regression

Based on the results of the logistic regression test, the relationship between hematology and progression showed that NLR and D-dimer levels were related to disease progression, while leukocyte, platelet, lymphocyte and CRP levels were not related (p>0.05). The relationship between hematology and disease progression can be seen in Table 7.

**Table 7. Analysis of Logistic Regression Test Results for the Relationship between Hematology and Disease Progression**

| Independent Variables | OR | 95% CI | | p |
|---|---|---|---|---|
| | | Lower limit | Upper limit | |
| Leukocytes | 1.00 | 0.84 | 1.19 | 0.988 |
| Platelets | 1.00 | 0.99 | 1.01 | 0.358 |
| Lymphocytes | 1.05 | 0.99 | 1.12 | 0.096 |
| NLR | 1.09 | 1.01 | 1.19 | 0.030 |
| CRP | 0.99 | 0.97 | 1.01 | 0.339 |
| D-dimer | 1.00 | 1.00 | 1.00 | 0.019 |
| Constant | 0.04 | | | 0.033 |

Meanwhile, the results of the logistic regression test of the relationship between hematology and severity showed that leukocyte, lymphocyte, NLR, CRP and D-dimer levels were related to severity (p<0.05) while platelet levels were not related (p>0.05).

Leukocyte levels were a variable that dominantly related to the severity of COVID-19 with the largest OR (OR= 1.80). The relationship between hematology and severity can be seen in Table 8.

**Table 8. Analysis of Logistic Regression Test Results of the Relationship between Hematology and Severity Level**

| Independent Variables | OR | 95% CI | | p |
|---|---|---|---|---|
| | | Lower limit | Upper limit | |
| Leukocytes | 1.79 | 1.174 | 2.755 | 0.007 |
| Platelets | 1.00 | 0.995 | 1.012 | 0.429 |
| Lymphocytes | 1.16 | 1.008 | 1.335 | 0.038 |
| NLR | 1.34 | 1.109 | 1.615 | 0.002 |
| CRP | 0.89 | 0.833 | 0.971 | 0.007 |
| D-dimer | 1.00 | 1.000 | 1.002 | 0.009 |
| Constant | 0.01 | | | 0.002 |

## DISCUSSION

In this study, the largest age group was 26-45 years (Adults) compared to other age groups. Patients aged 26-45 years are included in the productive age group. The results of this research are not much different from research (Tyastuti, 2022) at Sultan Agung Hospital, Semarang, which concluded that patients in the productive age group dominate the frequency of COVID-19 incidents due to the high level of mobility in this age group. The proportion of COVID-19 sufferers is more female, namely 50 people (53.8%). The results of this study are not much different from the results of research (Ding et al, 2020) at Beijing YouAn

Hospital, concluding that more COVID-19 sufferers were women, namely 54.2%.

Referring to the results of research tests, bivariately, all hematological parameters obtained a value of p<0.05, indicating that there was a significant relationship with disease progression and in multivariate terms, only NLR and D-dimer levels were related to disease progression (p<0.05), while for leukocyte, platelet, lymphocytes and CRP were related but not significant.

NLR levels were significantly related to disease progression (OR= 1.09; 95% CI; 1.00 to 1.18; p= 0.030). This means that COVID-19 sufferers who have increased NLR levels are estimated to increase disease

progression against COVID-19 by 1.1 times. The results of this study are not much different from research (Ding et al, 2020) at Hunan Provincial People's Hospital, which concluded that patients with confirmed COVID-19 had NLR levels that correlated with hospitalization time gradually and increased significantly from day 5 after enter.

D-Dimer levels were significantly associated with disease progression (p = 0.019; OR = 1.001; 95% CI; 1.000-1.001). This means that COVID-19 sufferers who have increased D-Dimer levels are estimated to increase disease progression against COVID-19 by 1.0 times. The results of this study are not much different from research (Shi et al, 2021) in China, which concluded that the majority of COVID-19 patients experienced a decrease in D-dimer levels when they were discharged from the hospital.

This study concluded that NLR and D-dimer levels were significantly related to disease progression in COVID-19 sufferers. Referring to the research results, leukocyte, lymphocyte, NLR, CRP and D-dimer levels were related to severity (p<0.05) while platelet levels were not related (p>0.05).

Leukocyte levels were significantly related to severity (p = 0.007; OR = 1.798; 95% CI; 1.174-2.755). This means that sufferers who have increased leukocyte levels are estimated to have an increased risk of severity of COVID-19 by 1.8 times. The results of this study are in line with research (Shi et al, 2021); (Zhao et al, 2020); (Taj et al,); (Waris et al, 2021) concluded that higher leukocyte levels (OR, 1.34; 95% CI, 1.05–1.71) were associated with severity.

Platelet levels were related but not significant to severity (p = 0.429; OR = 1.003; 95% CI; 0.995-1.012). The results of this study are in line with research (Taj et al, 2021) concluding that platelet levels do not

show a significant relationship with the severity of COVID-19 disease.

Lymphocyte levels were significantly related to severity (p = 0.038; OR = 1.160; 95% CI; 1.008-1.135). This means that sufferers who have increased lymphocyte levels are estimated to have an increased risk of severity of COVID-19 by 1.2 times. The results of this study are in line with research (Gong et al, 2020); (Waris et al, 2021) concluded that lymphocyte levels show a significant relationship with the severity of the disease.

NLR levels were significantly related to severity (p = 0.002; OR = 1.338; 95% CI; 1.109-1.615). This means that sufferers who have increased NLR levels are estimated to have an increased risk of severity of COVID-19 by 1.3 times. The results of this study are in line with research (Taj et al, 2021); (Waris et al, 2021); (Ding et al, 2020) and (Fristiani et al, 2022) concluded that NLR levels show a significant relationship with disease severity.

CRP levels were significantly related to severity (p=0.007; OR= 0.899; 95% CI; 0.833-0.971). This means that sufferers who have increased CRP levels are estimated to have an increased risk of severity of COVID-19 by 0.9 times. The results of this research are in line with research (Taj et al, 2021); (Sun et al, 2020); (Gong et al, 2020) which concluded that CRP levels show a significant relationship with disease severity.

D-dimer levels were significantly related to severity (p=0.009; OR= 1.001; 95% CI; 1.000-1.002). This means that sufferers who have increased D-dimer levels are estimated to have an increased risk of severity of COVID-19 by 1.0 times. The results of this research are in line with research (Taj et al, 2021); (Sun et al, 2020); (Li et al, 2020) and (Yu et al, 2020) which concluded that D-dimer levels showed a

significant relationship with disease severity.

This study concludes that the levels of leukocytes, lymphocytes, NLR, CRP, D-dimer are related to the severity of COVID-19 sufferers.

## AUTHOR CONTRIBUTION:

Chrismis Novalinda, Linda Chiuman, Sahna Ferdinand as supervisors and providers of input regarding literature reviews, research methods, as well as providers of input in discussing the results. Yunita Wannur Azah as a writer and thinker analyzing data and discussing results.

## FINANCIAL SUPPORT AND SPONSORSHIPS

This study is self-funded.

## ACKNOWLEDGEMENT:

We would like to express our gratitude for the facility support provided by RSU Royal Prima Medan for the provision of research space in the Medical Records Installation section of RSU Royal Prima Medan.

## CONFLICT OF INTEREST

There is no conflict of interest in this study.

## REFERENCE

Matin S, Safarzadeh E, Rezaei N, Negaresh M, Salehzadeh H, Matin S, Sharifiazar AH, et al. (2022). Hematological Parameters as Diagnostic Factors: Correlation with Severity of COVID-19. Acta Biomed: 93(2), e2022061. doi:10.23750/abm.v93i2.12320

Ding X, Yu Y, Lu B, Huo J, Chen M, Kang Y, Lou J, Liu Z (2020). Dynamic profile and clinical implications of hematological parameters in hospitalized patients with coronavirus disease 2019. Clin Chem Lab Med. 58(8), 1365-1371. doi: 10.1515/cclm-2020-0411.

Fristiani R, Warida W, Edward H (2022). Hubungan Nilai Neutrophil-Lymphocyte Ratio (NLR) Dan Kadar C-Reactive Protein (CRP) Dengan Tingkat Keparahan Penyakit Pada Pasien COVID-19. AMHJ. 2(2): 68–74. doi: 10.53770/amhj.v2i2.121.

Gong J, Dong H, Xia QS, Huang ZY, Wang DK, Zhao Y, Liu WH, et al. (2020). Correlation analysis between disease severity and inflammation-related parameters in patients with COVID-19: a retrospective study. BMC Infec Dis. 20(1) 1-7.doi:10.1186/s12879-020-05681-5.

Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, Pan P, et al. (2020a). Coronavirus infections and immune responses. J Med Virol. 92(4), 424-432. doi:10.1002/jmv.25685.

Li X, Geng M, Peng Y, Meng L, Lu S (2020b). Molecular immune pathogenesis and diagnosis of COVID-19. J Pharm Anal, 10(2), 102-108. doi:10.1016/j.jpha.2020.03.001.

Li Y, Zhao K, Wei H, Chen W, Wang W, Jia L, Liu Q, et al. (2020c). Dynamic relationship between D-dimer and COVID-19 severity. Br J Haematol, 190(1), e24-e27. doi:10.1111/bjh.16-811.

Shi S, Nie B, Chen X, Cai Q, Lin C, Zhao G, Zhang X (2021). Clinical and laboratory characteristics of severe and non-severe patients with COVID-19: a retrospective cohort study in China. J Clin Lab Anal. 35(1), e23692. doi: 10.1002/jcla.23692.

Sun Y, Dong Y, Wang L, Xie H, Li B, Chang C, Wang FS (2020). Characteristics and prognostic factors of disease severity in patients with COVID-19:

The Beijing experience. J Autoimmun. 112, 102473. doi:10.1016/j.-jaut.2020.102473.

Taj S, Fatima SA, Imran S, Lone A, Ahmed, Q (2021). Role of hematological parameters in the stratification of COVID-19 disease severity. Ann Med Surg (Lond). 62, 68-72. doi:10.1016-/j.amsu.2020.12.035.

Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, Jiang X, Li X (2020). C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol. 92(7), 856-862. doi: 10.1002/jmv.25871.

Tyastuti AD (2022). Hubungan Antara Kadar C-Reactive Protein Dengan Derajat Keparahan Covid-19 Studi Observasional Analitik pada Pasien Rawat Inap di RS Islam Sultan Agung Semaran (The Relationship Between C-Reactive Protein Levels and Severity of Covid-19 Analytical Observational Study of Inpatients at Sultan Agung Islamic Hospital Semarang) (Doctoral dissertation, Universitas Islam Sultan Agung).

Wang X, Tan L, Wang X, Liu W, Lu Y Cheng L, Sun Z (2020). Comparison of nasopharyngeal and oropharyngeal swabs for SARS-CoV-2 detection in 353 patients received tests with both specimens simultaneously. Int J Infect Dis. 94, 107-109. doi: 10.10-16/j.ijid.2020.04.023.

Waris A, Din M, Khalid A, Lail RA, Shaheen A, Khan N, Nawaz M, et al. (2021). Evaluation of hematological parameters as an indicator of disease severity in Covid-19 patients: Pakistan's experience. J Clin Lab Anal. 35(6), e23809. doi: 10.1002/jcla.23809.

Yu HH, Qin C, Chen M, Wang W, Tian DS (2020). D-dimer level is associated with the severity of COVID-19. Thromb Res. 195, 219-225. doi: 10.1016/j.thromres.

Zhao K, Li R, Wu X, Zhao Y, Wang T, Zheng Z, Zenge S, et al. (2020). Clinical features in 52 patients with COVID-19 who have increased leukocyte count: a retrospective analysis. J Clin Microbiol Infect Dis. 39, 2279-2287. doi: 10.1007/s10096-020-03976-8.