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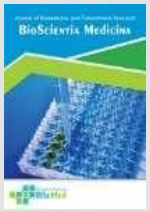

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Correlation of Absolute Lymphocyte Count with Severity of COVID-19 at Dr. Mohammad Hoesin General Hospital Palembang

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A B S T R A C T

Background: The rRT-PCR examination is very effective as a diagnostic tool for COVID-19 but cannot be a full reference as an evaluation examination because rRT-PCR is able to capture the genetic material of the virus without ensuring that the virus is still alive or only dead particles. This study aims to explore the correlation between absolute lymphocyte values and the severity of COVID-19 at Dr. Mohammad Hoesin General Hospital Palembang. **Methods:** This study is an observational study involving 413 research subjects at Dr. Mohammad Hoesin General Hospital. Data analysis was carried out univariate and bivariate. **Results:** The absolute number of lymphocytes with the severity of COVID-19 has a negative correlation, with a strong correlation strength, which is expressed by the value of r = -0.617 and the degree of significance of p = 0.000. **Conclusion:** There is a correlation between absolute lymphocyte count and the severity of COVID-19 at Dr. Mohammad Hoesin General Hospital Palembang.

1. Introduction

At the end of 2019, a new virus emerged in the city of Wuhan, China, and caused an outbreak of a highly contagious pneumonia virus that spreads rapidly throughout the world. This viral disease is also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] As of July 16, 2022, globally reported to the World Health Organization (WHO) there were 557,917,904 confirmed cases of COVID-19 (Coronavirus Disease 2019), including 6,358,899 deaths with a case fatality rate (CFR) of 1.13%.[2] Meanwhile, in Indonesia, there are 6,120,169 confirmed cases of COVID-19, and 156,818 deaths (CFR of 2.5%),[3] for the South Sumatra Province region, reaching 80,669 confirmed cases and 3,348 deaths (CFR of 4.1%),[4] and for the Palembang area there were 44,047 confirmed cases, and 1,322 cases died (CFR of 3.0%).[5]

Viral load examination is the gold standard in determining the amount of COVID-19 virus, but the inability to carry out this examination is expected to result in the CT value examination being able to represent the amount of virus in COVID-19 patients. Lymphopenia can occur in the early phase/phase of virus inoculation and replication. Lymphopenia describes a high viral load condition. CT value examination is only available in certain areas initially. Currently, more rRT-PCR examinations have been obtained in each region, but there are still limitations in terms of evaluation. The rRT-PCR examination is very effective as a diagnostic tool but cannot be a full reference as an evaluation examination because rRT-PCR is able to capture the genetic material of the virus without ensuring that the virus is still alive or only dead particles.[6,7] The study aims to explore the correlation between absolute lymphocyte values and the severity of COVID-19 in Dr. Mohammad Hoesin General Hospital Palembang.

2. Methods

This study is an observational study that aims to assess the correlation between absolute lymphocyte values and the severity of COVID-19 in Dr. Mohammad Hoesin General Hospital Palembang. A total of 413 research subjects took part in this study, where research subjects had met the inclusion criteria, namely patients with confirmed cases of COVID-19 from the SARS-CoV-2 RT-PCR test examination treated in July - December 2021, patients aged 18 - 80 years, willing to participate in the study. Participate in the study by signing informed consent. This study has been approved by the medical and health research ethics committee of Dr. Mohammad Hoesin General Hospital Palembang (No. 113/kepkrsmh/2021). Data analysis was carried out using SPSS version 26 software. Univariate analysis was carried out to present the test variable data in a tabulated distribution. Correlation analysis was carried out with Spearman analysis so that the r and p-values were obtained.

3. Results

The research subjects included sociodemographic and clinical characteristics. The sociodemographic characteristics include age, sex, education, and occupation, which are shown in Table 1. At the same time, the clinical characteristics include body mass index, clinical symptoms, comorbidities, chest X-ray, CT value, and absolute lymphocyte count, which are shown in Table 2. Sociodemographic characteristics are based on the average age of the study subjects, with a median value of 49, a minimum value of 18, and a maximum value of 84. Ages 18-60 years had the largest percentage in mild-moderate degrees of 211 patients (77.3%), while age >60 years had the largest percentage in severe-moderate degrees. Critically in 45 patients (32.6%). In terms of gender characteristics, research subjects consisted of 167 (40.4%) males including 111 patients (40.4%) mild/moderate degrees, 56 patients (40.6%) with severe/critical grades, and 246 patients (59.6%) woman. Among them were 164 patients (59.6%) with mild/moderate grades and 82 patients (59.4%) with severe/critical grades. The educational background consisted of primary school with as many as 40 patients (9.69%), junior high school with as many as 20 patients (4.84%), and the highest educational background was high school consisting of 246 patients (59.56%), and diploma and undergraduate educational backgrounds consisted of 107 patients (25.91%). The largest number of job distributions was from the private group, with 157 patients (38.01%), housewives as many as 130 (31.48%), followed by civil servants, state-owned enterprises, Indonesian national police, as many as 64 patients (15.50%), then retired and not working as many as 36 patients (8.72 %), while doctors, paramedics as many as 14 patients (3.39%) and the least number of students, students as many as 12 patients (2.91%).

In clinical characteristics of research subjects based on BMI has a mean of 24.97 Kg/m^2, a minimum of 17.78 Kg/m^2 a maximum of 33.81 Kg/m^2. The highest distribution was in BMI 18.5 – 25 as many as 206 patients (49.9%), then BMI > 27 as many as 112

patients (27.1%), while BMI 25.1 – 27 as many as 83 patients (20.1%), the smallest with BMI <18,5 as many as 12 patients (2.9%). Patients with symptoms of fever/fever history were 181 patients (43.83%), while patients with no fever were 232 patients (56.17%). Patients with symptoms of fever/history of fever experienced severe-critical grades as many as 66 people (47.8%) while mild-moderate as many as 115 people (41.8%). Patients with symptoms of shortness of breath were 195 patients (47.2%), while patients with symptoms of not shortness of breath were 218 patients (52.8%). Patients with symptoms of shortness of breath experienced severe-critical degrees as many as 97 people (70.3%) while mild-moderate as many as 98 people (35.6%). Patients with cough symptoms were 154 patients (37.3%), while patients with no cough symptoms were 259 patients (62.7%). Patients with cough symptoms experienced mild-moderate degrees as many as 116 people (42.2%) while severe-critical as many as 38 people (27.5%). Patients with symptoms of decreased consciousness were 32 patients (7.7%), while patients with no symptoms of decreased consciousness were 381 patients (92.3%). There were 22 patients (15.9%) with symptoms of decreased consciousness who experienced severe-critical grades, while 10 patients (3.6%). Patients with symptoms of anosmia/ageusia were 26 patients (6.3%), while patients with symptoms of no anosmia/ageusia were 387 patients (93.7%). Patients with symptoms of anosmia/ageusia experienced mild-moderate degrees as many as 24 patients (8.7%) while severe-critical as many as 2 people (1.4%). The reported comorbidities in the study subjects were 116 patients (28.1%) and 297 (71.9%) patients (26.4%). Patients with comorbid hypertension experienced severe-critical grades as many as 47 people (34.1%) while mild-moderate as many as 69 people (25.1%). Patients with comorbid diabetes mellitus reached 68 patients (16.5%) and did not have diabetes mellitus reached 345 patients (83.5%). Patients with comorbid diabetes mellitus experienced severe-critical grades as many as 27 people (19.6%) while mild-moderate as many as 41 people (14.9%). Meanwhile, there were 32 patients (7.7%) with comorbid chronic kidney disease and 381 patients (92.3%). Patients with comorbid chronic kidney disease experienced mild-moderate degrees as many as 24 people (8.7%) while severe-critical as many as 8 people (5.8%). Patients with comorbid respiratory tract disorders (COPD) reached 27 patients (6.5%) and did not have respiratory disorders reached 386 patients (93.5%). Patients with comorbid respiratory tract disorders experienced severe-critical degrees as many as 18 people (13%) while mild-moderate as many as 9 people (3.3%). Patients with a chest X-ray of pneumonia were 243 patients (58.84%), while patients with a normal chest X-ray were 170 patients (41.16%). Patients with a chest x-ray of pneumonia experienced severe-critical COVID-19 as many as 128 patients (92.75%) while mild-moderate as many as 115 patients (41.82%). Based on the CT value, the severe-critical patient group had a mean CT value of 18, the minimum - maximum value (2.87-32.15). This severe-critical group had a lower CT value, statistically significant compared to the mild-moderate group has a mean CT value of 28, the minimum-maximum value (8-39.53). Similarly, the absolute lymphocyte value in the severe-critical group, the mean absolute lymphocyte value was 888.5 cells/mm^3, the minimum-maximum value (99-3332 cells/mm^3), and the value of the severe-critical group was statistically significantly lower than the mild-moderate group. Which has a mean absolute lymphocyte value of 1364 cells/mm^3, the minimum-maximum value (636-4388 cells/mm^3).

Table 1. Baseline characteristic

Characteristics	Research subjects (n=413)	Symptoms	
		Mild/moderate (n=275)	Severe/Critical (n=138)
Mean Age in (Years)	49 (18-84)	45.93 ±15.13	50 (35-65)
Age group			
18-60 years	304 (74.0%)	211 (77.3%)	93 (67.4%)
>60 years	107 (26.0%)	62 (22.7%)	45 (32.6%)
Gender			
Male	167 (40.4%)	111 (40.4%)	56 (40.6%)
Female	246 (59.6%)	164 (59.6%)	82 (59.4%)
Education			
Primary school	40 (9,7%)	27 (9.8%)	13 (9.5%)
Junior high school	20 (4,8%)	16 (5.8%)	4 (2.9%)
Senior high school	246 (59,6%)	162 (58.9%)	84 (60.8%)
Diploma, Undergraduate	107 (25,9%)	70 (25.5%)	37 (26.8%)
Job			
Civil servants, State-Owned Enterprises, Indonesian National Police	64 (15,5%)	41 (14.9 %)	23 (16.7%)
Doctor, Paramedic	14 (3,4%)	6 (2.2%)	8 (5.8%)
Private	157 (38,0 %)	106 (38.5%)	51 (37.0%)
Housewives	130 (31,5%)	88 (32.0%)	42 (30.3%)
Student, College student	12 (2,9 %)	9 (3.3 %)	3 (2.2%)
Retired, Not working	36 (8,7%)	25 (9.1%)	11 (8.0%)

Table 2. Clinical characteristics of research subjects

Characteristics	Research subjects (n=413)	Symptoms	
		Mild/moderate n=275)	Severe/Critical (n=138)
Mean Body Mass Index Kg/m^2	24.97 (13.78-38.81)	24.8 (13.78-38.81)	25.49.5±3.45
BMI Group			
<18.5	12 (2.9%)	9 (3.3%)	3 (2.2%)
18.5 – 25	206 (49.9%)	143 (52.0%)	63 (45.7%)
25.1 – 27	83 (20.1%)	55 (20 ,0%)	28 (20.3%)
> 27	112 (27.1%)	68 (24.7%)	44 (31.8%)
Symptoms			
Fever			
Yes	181 (43.8%)	115 (41.8%)	66 (47.8%)
No	232 (56.2%)	160 (58.2%)	72 (52.2%)
Shortness of breath			
Yes	195 (47.2 %)	98 (35.6%)	97 (70.3%)
No	218 (52.8%)	177 (64.4%)	41 (29.7%)
Cough			
Yes	154 (37.3%)	116 (42.2%)	38 (27.5%)
No	259 (62.7%)	159 (57.8%)	100 (72.5%)
Decreased consciousness			
Yes	32 (7.7%)	10 (3.6%)	22 (15.9%)
No	381 (92.3%)	265 (96.4%)	130 (84.1%)
Anosmia/ ageusia			
Yes	26 (6.3%)	24 (8.7%)	2 (1.4%)
No	387 (93.7%)	251 (91.3%)	136 (98.6%)
Comorbid			
Hypertension			
Yes	116 (28.1%)	69 (25.1%)	47 (34.1%)
No	297 (71.9%)	206 (74.9%)	91 (65.9%)
Diabetes mellitus			
Yes	68 (16.5%)	41 (14.9%)	27 (19.6%)
No	345 (83.5%)	234 (85.1%)	111 (80.4%)
Chronic kidney disease			
Yes	32 (7.7%)	24 (8.7%)	8 (5.8%)
No	381 (92.3%)	251 (91.3%)	130 (94.2%)
Airway Disorders			
Yes	27 (6.5%)	9 (3.3%)	18 (13%)
No	386 (93.5%)	266 (96.7%)	120 (87%)
X-ray of thorax pneumonia			
Yes	243 (58.8%)	115 (41.8%)	128 (92.7%)
No	170 (41.2%)	160 (58.2%)	10 (7.3%)
Absolute Lymphocyte Mean (cell/mm^3)* (min-max)	1147 (99-4388)	1364 (636-4388)	888.5 (99-3332)

The correlation of absolute lymphocyte count with the severity of COVID-19 in this study was analyzed using Spearman. From the results of the analysis, it was found that the absolute number of lymphocytes with the severity of COVID-19 had a negative correlation, with a strong correlation strength, which was expressed by the value of r = -0.617 and the degree of significance of p = 0.000 (table 3). A higher absolute lymphocyte count correlates with a decrease in the severity of COVID-19 and vice versa.

Table 3. Correlation between absolute lymphocyte count and severity of COVID-19

Variable	Degree of disease	
Absolute Lymphocyte Count (ALC)	r = – 0,617**	p = 0,000*

* Spearman correlation test (p-value is meaningful when p < 0.05)
** When the value of r = 0.00-0.19 (correlation is very weak), r = 0.2-0.39 (weak correlation), r = 0.4-0.59 (moderate correlation), r = 0.60-0.79 (strong correlation), r = 0.80-0.99 (very strong correlation), r = 1 (perfect); with the sign "–" indicating the direction of the negative correlation.

4. Discussion

The results of this study are also in line with several studies that have been published. One of them is a study that obtained the results of the correlation between the number of lymphocytes and the severity of COVID-19 with significant results (p = 0.000) with a moderate correlation strength (r = 0.560).[8] Another study concluded that lymphopenia is a prominent feature of severe COVID-19, and an absolute lymphocyte count of 1,200 cells/mm^3 may be useful in predicting the severity of the clinical outcome of COVID-19.[9] Patients with poor clinical outcomes had very low lymphocyte counts compared to patients with good clinical outcomes. Subgroup analysis showed that patients who died, ARDS, or patients admitted to intensive care had low lymphocyte counts and concluded that lymphopenia was associated with severe COVID-19 severity. Another study reported lymphopenia was found in 80% of critical-degree COVID-19 cases.[10] Another study also reported that only 25% of mild COVID-19 patients had lymphopenia.[11-13]

Lymphocyte cells are cells that play a major role in the specific immune system. B cells in humoral immunity produce antibodies, while T cells in cellular play a role in helping B cells increase antibody production and initiate and increase inflammation through inflammatory mediators and lyse antigen target cells.[14] Early phase/viral phase is the phase during which the inoculation and formation of the virus occur. In this phase, the SARS-CoV-2 virus replicates and persists in the respiratory system by binding to the angiotensin-converting enzyme-2 (ACE-2) receptor. In the laboratory can be found lymphopenia. One study suggested that a decrease in a subset of peripheral T cells is characteristic in patients with the severe acute respiratory syndrome (SARS).[15] Peripheral T cell counts can serve as an accurate diagnostic and prognostic tool for SARS. Severe COVID-19 patients exhibit lymphopenia, lymphocyte activation and dysfunction, granulocyte and monocyte abnormalities, high cytokine levels, elevated immunoglobulin G (IgG), and total antibodies.[16]

5. Conclusion

There is a correlation between absolute lymphocyte count and the severity of COVID-19 at Dr. Mohammad Hoesin General Hospital Palembang.

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