Monocytes and eosinophils in early positive COVID-19 patients

by Danny Ernest Jonas Luhulima, , Erida Manalu, Eirene Tomatala

Submission date: 07-Nov-2022 11:58AM (UTC+0700)
Submission ID: 1946748758
File name: Monocytesandeosinophilsinearlypositive.pdf (181.41K)
Word count: 5885
Character count: 31165

International Journal of Medical Science and Clinical Research
www.journalofmedical.com
Online-ISSN: 2664-7761, Print ISSN: 2664-7753
Received: 01-10-2022, Accepted: 17-10-2022, Published: 04-11-2022
Volume 4, Issue 2, 2022, Page No. 44-50

Monocytes and eosinophils in early positive COVID-19 patients

Dany Ernest Jonas Luhulima[1*], Erida Manalu[1], Eirene Tomatala[2]
[1] Medical Faculty, Universitas Kristen Indonesia, Jakarta, Indonesia
[2] Bhayangkara Tk. I Kramat Jati Hospital, Jakarta, Indonesia

Abstract
COVID-19 is a new disease designated by WHO as a pandemic. COVID-19 is caused by a new variant of the coronavirus called SARS-CoV-2. Monocytes and eosinophils are part of the innate immune system that is not specific to a particular antigen. This study set monocyte levels 3-8% and eosinophil levels 2-4% as normal values. This study aims to determine the profile of monocytes and eosinophils in COVID-19-positive patients. The design of this study was cross-sectional, using 68 medical records of patients who underwent PCR and complete blood tests. The results showed that there were 21 patients with normal monocyte counts (30.8%), 24 patients with decreased eosinophil counts (35.2%), and 15 patients with normal monocyte counts and decreased eosinophil counts (27.3%). Conclution: this study indicates that the examination of the number of monocytes and eosinophils cannot be used as screening material for COVID-19.

Keywords: COVID-19; monocytes; eosinophils

Introduction
At the end of December 2019, some patients were referred to the hospital with a diagnosis of pneumonia of unknown cause. The patients were linked to a fish market in Wuhan city, Hubei province, China [1, 2]. Several scientists in China found the cause of the pneumonia was a mutated Coronavirus named 2019 n-CoV. On February 11, 2020, WHO announced the name of the pneumonia disease as COVID-19, and the cause was SARS-CoV-2 [3].
COVID-19 infection causes a variety of symptoms. Common symptoms include respiratory system symptoms, such as coughing, sneezing, and shortness of breath. In some cases, COVID-19 infection causes systemic symptoms such as fever, fatigue, hypoxemia, headache, and others [1]. The various symptoms make COVID-19 challenging to diagnose the first time the patient meets the doctor, so a supportive examination is needed. The diagnostic test for COVID-19 is a PCR examination. Research from Sucahya, at the beginning of the pandemic, the Indonesian government only trusted one laboratory for COVID-19 examinations, but with increasing cases, the number of reference labs increased. Until April 29, 2020, 89 laboratories were referred for COVID-19 examination [4].
Wang *et al*. found that SARS-CoV-2 infects the body through the ACE2 receptor. Monocytes are leukocyte cells with ACE2 receptors so that SARS-CoV-2 can infect monocytes [5]. Monocytes infected with SARS-CoV-2 showed increased secretion of IL-6. Increased IL-6 will cause acute inflammatory conditions, which impact the production of other leukocytes in the bone marrow [6]. Eosinophils are leukocyte cells whose formation process is inhibited due to acute inflammatory conditions [7]. Based on the existing background, the problem in this study is formulated in the form of the following question "How do the COVID-19 cases compare with the number of monocytes?" and "How do COVID-19 cases compare to eosinophil counts?" with the aim of the study, namely to find out how the comparison of COVID-19 cases with the number of monocytes and to find out how the comparison of COVID-19 instances with the number of eosinophils.

Literature Review
Monocytes are mononuclear leukocytes that play a role in the innate immune system and makeup 3% to 8% of all human leukocytes. Monocytes have a nucleus shaped like a kidney with small vacuoles and a cytoplasm containing few granules. Monocytes are formed in the bone marrow and released into the blood vessels. Monocytes circulate in blood vessels or become tissue macrophages in the intestines, skin, heart, and lungs [8, 9].
Recently, several studies have found that monocytes have heterogeneous properties and can be divided into three subsets based on markers/receptors on the cell surface. Monocytes from 80% to 90% of monocytes with the marker CD14++CD16-. Monocytes from the remaining 10% to 20% with the markers CD14++CD16+ and CD14+CD16++. The three subsets have different functions [9, 10].

In general, monocytes have the function of phagocytes, mediators of inflammation and a source of macrophages and dendritic cells in blood vessels and tissues. The phagocytic abilities of monocytes, macrophages, and dendritic cells make up the MNP system. The MNP system plays a role in inflammation and tissue fibrosis. Monocytes that have differentiated into macrophages and dendritic cells can induce the proliferation of CD8+ T lymphocytes and regulate the activation of CD4+ T lymphocytes that play a role in the specific immune system [6, 11].

In a state of infection or tissue damage, the chemokine receptor CCR2 on the surface of monocytes will be stimulated by CCL2, which is secreted by infected or damaged tissue so that monocyte cells will move to that location. At the site of infection or damage, monocytes will phagocytize microorganisms and secrete cytokines such as IL-6 that modulate the inflammatory process. Some monocytes will enter the lymph channels, move to the lymph nodes, and stimulate T lymphocyte cells, thus starting the specific immune process [11, 12].

IL-6 plays a role in regulating the differentiation of monocytes into macrophages, increasing the expression of GM-CSF receptors, and the differentiation of dendritic cells that have the ability of APCs to become inflammatory macrophages. IL-6 can bind to IL-6 receptors on brain endothelial cells to stimulate prostaglandin synthesis and increase inflammation. Furthermore, IL-6 can initiate a chronic inflammatory response by changing the leukocyte response from a neutrophil response to monocytes/macrophages [13].

Eosinophils are one of the polymorphonuclear leukocytes that play a role in the innate immune system and make up 2% to 4% of all human leukocytes. Eosinophils have a lobed nucleus (usually two lobes) and many red granules in their cytoplasm. Eosinophils are produced in the bone marrow and released into the blood vessels. Eosinophils have a half-life of 8 to 18 hours in the blood vessels. Generally, eosinophils can persist for several weeks in tissues [8, 14].

Eosinophils have multiple functions. The granules in eosinophils consist of a crystalloid nucleus, namely MBP, and a matrix, namely ECP, EPO, and EDN, which have parts [15]. The MBP crystalloid core is cytotoxic to respiratory tract tissue because it causes an increase in membrane permeability through surface charge interactions that disrupt the lipid bilayer layer. ECP and EDN matrices belong to the ribonuclease (RNAase), A gene superfamily that can degrade ssRNA substrates in microorganisms such as viruses [15, 16].

Under infectious conditions, eosinophils move to the infected tissue after being activated by IL-5. The IL-5 cytokine, produced by Th2 cells, maintains eosinophils in infected tissues, stimulating eosinophil movement and maturation. In infected tissue, eosinophils phagocytize infected cells and destroy infected cells with MBP crystalloids and ECP matrix. In addition to phagocytic abilities, eosinophils can kill infected cells extracellularly by secreting cytotoxins from degranulating eosinophils, thereby releasing the EPO matrix [15, 16].

COVID-19 is a new disease that emerged at the end of December 2019. The cause is a new variant of the coronavirus, which WHO SARS-CoV-2 was later named to avoid stigmatizing the virus's origin in terms of population, geography, or animal association [17]. SARS-CoV-2 causes COVID-19. The virus is a species of the coronavirus that infects humans. Coronavirus is a virus from the Coronaviridae family, which consists of 2 subfamilies: Orthocoronavirinae and Torovirinae. Orthocoronvirinae is divided into 4 genera, namely: alphacoronavirus, betacoronavirus, gammacoronavirus, and deltacoronavirus. The genera alphacoronavirus and betacoronavirus are reported to frequently infect mammals and cause respiratory and gastrointestinal infections in humans. Gammacoronavirus and delta coronavirus genera infect birds more often, but some can infect mammals [18].

Coronavirus is an RNA virus with a size of 120 nm to 160 nm. [3] Under the electron microscope, the coronavirus has a crown-like appearance. There are four structural proteins in the infectivity of the coronavirus, namely, spike (S), envelope (E), membrane (M), and nucleocapsid (N). The S protein is on the surface of the coronavirus and functions to bind to host cell receptors, a fusion of cell membranes with viruses, and virus internalization. The S protein in SARS-CoV-2 is similar to the S protein in SARS-CoV. Protein E plays a role in the formation and development of the viral envelope. Besides that, protein E has ion channels that play a role in the inflammatory activation process. The M protein gives the virus its shape and plays a role in viral assembly. M protein is mainly found in the viral envelope. N protein acts as an antagonist of the interferon pathway, making it difficult for the immune response to overcome infection [1, 18, 19].

On December 29, 2019, 4 patients with pneumonia of unknown cause were reported in Wuhan city, Hubei Province, China. The patients were linked to a local fish market in the city of Wuhan. On January 2, 2020, 41 patients with the same case were hospitalized. These patients were suspected of having a nosocomial infection and had severe symptoms. Cases of COVID-19 outside China were reported on January 13, 2020, in Bangkok, Thailand. As of January 30, 2020, there were 7736 cases of COVID-19 in China and 86 circumstances outside China. In Indonesia, the first 2 cases were reported on March 2, 2020. As of May 27, 2020, as many as 5.6 million cases of COVID-19 had been confirmed worldwide and caused more than 352,000 deaths [1, 19, 20].

The transmission of COVID-19 began at a local fish market in Wuhan, China. This started the presumption that COVID-19 came from animals and was zoonotic, so it infects humans. The increasing number of COVID-19 cases unrelated to the local fish market in the city of Wuhan supports the transmission of COVID-19 between humans [1]. There are three routes of transmission of COVID-19 between humans [19]:

First is droplet transmission, when a patient infected with COVID-19 coughs or sneezes. People around them can inhale droplets that come out. This transmission is the main transmission of COVID-19 transmission. The second is contact transmission, when someone touches a surface contaminated with the SARS-CoV-2 virus and then

touches the eye, mouth, or nose area. Third, aerosol transmission occurs when droplets are suspended in the air. In high doses, it can cause COVID-19 infection in people around it.

The pathogenesis of SARS-CoV-2 is still not fully understood, but the similarity of SARS-CoV-2 with SARS-CoV and MERS-CoV helps to understand the pathogenesis of SARS-CoV-2. Interim research on the pathogenesis of COVID-19 states that there are five stages for SARS-CoV-2 to infect humans [19, 20].

WHO reports that the incubation period for COVID-19 is 2 to 10 days, with an average of 5 days. Several other studies have reported that the incubation period for COVID-19 can be more than 14 days. The period from symptom onset to death ranged from 6 to 41 days, with a median of 14 days. The period depends on the patient's age and immune status. The period will be shorter in patients over 70 years of age than in patients under 70 years [1, 19].

Symptoms of COVID-19 range from asymptomatic to respiratory system damage and requiring ventilatory assistance to systemic manifestations such as septic shock and MODS. Common symptoms in COVID-19 patients are fever (>38°C), cough, sneezing, shortness of breath, headache, sore throat, and rhinorrhea. Symptoms of COVID-19 depend on the patient's age and immune status, so elderly and immunocompromised patients, may develop severe complications of pneumonia (characterized by tachypnea, severe respiratory distress, or oxygen saturation <90%) [19, 21].

Patients with mild symptoms are reported to have recovered after seven days, while patients with severe symptoms experience decreased respiratory function due to alveolar damage, which can lead to death. Cases of COVID-19 deaths generally occur in patients with previous diseases (such as diabetes mellitus, hypertension, and coronary heart disease) [20].

In Indonesia, diagnosing COVID-19 is done by PCR examination. The diagnosis of COVID-19 is based on epidemiological history, clinical manifestations, PCR examination, and additional examinations such as a CT-scan radiological examination [22]. The study recommended by WHO is the PCR examination. The patient is declared positive for COVID-19 if the PCR examination finds at least two target genomes (N, E, S, or RdRP) specific for SARS-CoV-2 or if PCR is positive for betacoronavirus [3]. The samples used in the PCR examination are sputum, throat swabs, and lower respiratory tract secretions [19, 20].

COVID-19-positive patients exhibit dysregulation of the innate immune response in the presence of excessive inflammation, as evidenced by a cytokine storm. Cytokine profiles in severe COVID-19 positive patients showed similarities to cytokine profiles in macrophage activation syndrome and secondary hemophagocytic lymphohistiocytosis. An increase in cytokines IL-2, IL-6, IL-7, GM-CSF, and TNF-α. The cytokine storm is caused by excessive macrophage proliferation and activation [6, 22].

Examination of bronchoalveolar fluid in COVID-19 patients showed an increase in the number of MNPs, which reached 80% of the total BAL cells. The MNP composition had a decrease in the number of alveolar macrophages and an increase in the number of macrophages derived from blood vessels. On peripheral blood examination of COVID-19-positive patients an increase in the number of intermediate monocytes that produce IL-6 was found. Macrophages containing SARS-CoV-2 particles were found to express IL-6. Several studies reported that an increase in IL-6 macrophages was associated with a decrease in the number of lymphocytes [6, 18].

Several reports indicate that cases of COVID-19 are rare in patients with a history of asthma. A report on 140 COVID-19 patients in Wuhan showed none had a history of asthma or another atopic disease. Of these 140 patients, 53% had decreased eosinophil counts (absolute eosinopenia = <0.02x109 cells/L) at the time of first admission. Another study on 548 COVID-19 patients in Wuhan reported that only five patients had an asthma history. A study examining 85 severe COVID-19 patients showed that as many as 81% of patients experienced a decrease in eosinophils at first admission [23].

Blood tests in COVID-19 patients show eosinopenia, and samples from lung tissue biopsies and BAL of COVID-19 patients showed decreased eosinophil counts. The condition of eosinopenia correlates with a decrease in the number of lymphocytes. In addition, the condition of eosinopenia is associated with a poor prognosis in COVID-19. The worsening of the COVID-19 condition could be caused by a decrease in the number of ECP and EDN eosinophils that can degrade ssRNA substrates in SARS-CoV-2 [16, 24].

Low eosinophil conditions or eosinopenia are generally caused by acute infection. Various reports state that in acute infectious conditions, there is eosinopenia, but the certainty is not known. The hypothesis of eosinopenia in acute infectious conditions, according to Espinosa V *et al*., eosinopenia in acute infectious conditions occurs because white blood cells that move first to fight antigens are neutrophils, macrophages, and monocytes. Therefore, the production of these three white blood cells increases, but the production of other white blood cells, such as eosinophils and basophils, decreases [25].

Research Method

The study was conducted with a cross-sectional descriptive design, using patient medical records to determine the description of monocytes and eosinophils in patients who had their first PCR examination and complete blood count. The collection of medical record data was carried out at a private hospital in the East Bekasi area. The time processing, collecting, and carrying out the research was conducted during June - December 2020. The population in this study were all patients in a private hospital in the East Bekasi area. The samples in this study were all patients in a private hospital in the East Bekasi area who carried out PCR examination for COVID-19 diagnostic tests and performed complete blood tests. This study uses secondary data, namely medical records of

patients suspected of COVID-19 infection and conducting PCR examinations and blood tests. Data collection was carried out in the medical record section of a private hospital in the East Bekasi area. Furthermore, the medical record data will be recorded according to the research variables. The data that will be used are the results of the PCR examination, the number of monocytes, the number of eosinophils, gender, and age. All data obtained will be filtered again according to the inclusion and exclusion criteria set to produce data that will be used in the results of this study. Processing of data collected through medical records is processed using Microsoft Office Excel 2016 and SPSS 16.0 for Windows programs.

Result and Discussion

In this chapter, the researcher will present the results of data collection obtained from one of the private hospitals in the East Bekasi area. Data collection was carried out from November 2020 to December 2020. The data used in this study came from patient medical records. Some of the limitations of this study are that this data does not have a record of the patient's disease phase and the length of time the patient was infected with SARS-CoV-2. The data collection method was carried out by random sampling, where the researcher took data from medical records that met the inclusion criteria. The data collection obtained as many as 77 patients according to the inclusion criteria. There were 34 negative COVID-19 patients and 43 positive COVID-19 patients.

The result of the Kolmogorov-Smirnov normality test in this sample is 0.000, and it can be concluded that the data distribution is not normal, so the statistical calculation used is the Wilcoxon statistical test. Researchers conducted the Wilcoxon statistical test to determine whether there was a comparison between PCR-negative patients and PCR-positive patients. The comparison is seen in the number of monocytes and the number of eosinophils. The number of data used was 68 of 77 patients because the number of positive and negative PCR patient data obtained was not the same, so the researchers took the least amount of PCR data, namely negative PCR data, as many as 34 patients and took 34 patients from 43 positive PCR patients. This is done so that the results obtained are more objective. The selection of 34 patients from 43 positive PCR patients was based on the order in which researchers received patient medical record data from the relevant hospital.

Table 1: Comparison of PCR by age group

Age Group	Age Range	COVID-19 Negative	COVID-19 Positive	Total
1	<6 years	1 (1,5%)	0	1 (1,5%)
2	7-19 years	1 (1,5%)	0	1 (1,5%)
3	20-29 years	2 (2,9%)	1 (1,5%)	3 (4,4%)
4	30-39 years	6 (8,8%)	8 (11,8%)	14 (20,6%)
5	40-49 years	11 (16,2%)	10 (14,6%)	21 (30,9%)
6	50-59 years	8 (11,8%)	10 (14,6%)	18 (26,5%)
7	>60 years	5 (7,3%)	5 (7,3%)	10 (14,6%)
Total		34 (50%)	34 (50%)	68 (100%)

The results of the PCR examination based on the patient's age showed that the age group 5 (age range 40 to 49 years) was the age group that performed the most PCR examinations, with as many as 21 patients. Of the 21 patients, 11 had negative PCR results, and ten had positive PCR results.

Table 2: PCR comparison by sex

Gender	COVID-19 Negative	COVID-19 Positive	Total
Man	19 (27,9%)	18 (26,5%)	37 (54,4%)
Woman	15 (22,1%)	16 (23,5%)	31 (45,6%)
Total	34 (50%)	34 (50%)	68 (100%)

The results of the PCR examination based on gender showed that of 37 male patients, 19 patients had negative PCR results, and 18 patients had positive PCR results. Of the 31 female patients, 15 had negative PCR results, and 16 had positive PCR results.

Table 3: PCR comparison based on monocyte count

PCR Result	Decreased Monocytes	Normal Monocytes	Monocytes Rise	Asymp. Sig. (2-tailed)
Positive	1 (1,5%)	21 (30,9%)	12 (17,6%)	0.000
Negative	2 (2,9%)	19 (28,0%)	13 (19,1%)	
Total	3 (4,4%)	40 (58,9%)	25 (36,7%)	

The results of the PCR examination based on the number of monocytes showed that there were three patients with decreased monocyte counts, two patients had negative PCR results, and one patient had positive PCR results. A total of 40 patients had normal monocyte values, 19 patients with negative PCR results, and 21 patients with positive PCR results. As well as 25 patients with increased monocyte counts, 13 patients with negative PCR results and 15 with positive PCR results. From the data collected, it was found that there were 21 patients with normal monocyte counts, with a percentage of 30.9%. Wilcoxon test results show the value of Asymp. Sig. (2-tailed) of 0.000.

Table 4: Comparison of PCR based on the number of eosinophils

PCR Result	Decreased Eosinophils	Normal Eosinophils	Eosinophils Rise	Asymp. Sig. (2-tailed)
Positive	24 (35,2%)	9 (13,2%)	1 (1,5%)	0.622
Negative	19 (28,0%)	10 (14,7%)	5 (7,3%)	
Total	43 (63,2%)	19 (27,9%)	6 (8,8%)	

Table 8 shows that from the data collected, it was found that 24 patients had decreased eosinophil counts, with a percentage of 35.2%. Wilcoxon test results show the value of Asymp. Sig. (2-tailed) of 0.622. The results of the PCR examination based on the number of eosinophils showed that there were 43 patients with decreased eosinophil counts, 19 patients had negative PCR results, and 24 patients had positive PCR results. A total of 19 patients had normal eosinophil values, ten had negative PCR results, and nine had positive PCR results. As well as six patients with increased eosinophil counts, five patients with negative PCR results and one with positive PCR results.

Table 5: Comparison of the number of monocytes based on the number of eosinophils

Monocyte Count	PCR	Decreased Eosinophils	Normal Eosinophils	Eosinophils Rise	Asymp. Sig. PCR -	Asymp. Sig. PCR +
Decreased	-	2 (2,9%)	0	0	1.000	0.068
	+	1 (1,5%)	0	0		
Normal	-	7 (10,2 %)	8 (11,7%)	4 (5,8%)		
	+	15 (22,0%)	5 (7,3%)	1 (1,5%)		
Rise	-	10 (14,7%)	2 (2,9%)	1 (1,5%)		
	+	8 (11,7%)	4 (5,8%)	0		

Table 9 showed that from the data collected, 15 patients with normal monocyte counts and decreased eosinophils were found in the positive PCR group. There were also ten patients with increased monocyte counts and decreased eosinophils from the negative PCR group. Wilcoxon test results show the value of Asymp. Sig. (2-tailed) of 1.000 from the negative PCR group and 0.068 from the positive PCR group. The comparison of the number of monocytes based on the number of eosinophils in the negative PCR group showed as many as ten patients with increased monocyte counts and decreased eosinophils. The comparison of the number of monocytes based on the number of eosinophils in the positive PCR group showed as many as 15 patients with normal monocyte counts and decreased eosinophils.

The results of this study indicate that the most positive COVID-19 patients were found in patients in age group 4 (age range 30 years to 39 years) and age group 5 (age range 40 years to 49 years), with as many as ten patients in age group 4 and 10 patients. Age group 5 out of a total of 34 COVID-19-positive patients. This can be caused because a person's age is a risk factor for COVID-19 infection. With age, the immune system declines, so older people are more susceptible to disease. The age group 4, aged 30 to 39 years, was the group that most reported positive cases of COVID-19 [26]. Other reports indicate that age group 3, ranging from 20 to 29 years, is the group that reports the most positive cases. After these two age groups, followed by the age group 6, the age range of 50 years to 59 years. This can happen because these age groups are included in the productive age group, so many people in these age groups are often outside the home, increasing the risk of SARS-CoV-2 infection [27].

This study showed that the positive patient for COVID-19 was found in the male patient gender. There were 18 male patients with positive PCR results from 34 patients with positive PCR results. This can be caused because more men work outside their homes. Thus, men are more at risk for infection with COVID-19. A report by Jin *et al*. from the journal "Gender Differences in Patients with COVID: Focus on Severity and Mortality" said that the prevalence of COVID-19 in men and women was almost the same. Of the 425 COVID-19 positive patients, 56% were male [28]. The report by WHO stated that of 1,434,793 positive COVID-19 patients, 47% were women and 51% were men [29]. Other results found by Jin JM *et al*. The mortality rate of COVID-19 patients is higher in male patients than in female patients. This can occur due to lifestyle factors because men's lifestyles are more likely to be associated with various substances that can lower the immune system, such as lifestyle smoking, drinking alcoholic beverages, and severe stress. These three things can cause complications in organs in the body that can cause various diseases and make patients more susceptible to COVID-19 infection [30].

The normal value for the number of monocytes in humans is 3-8% of total white blood cells. In conditions of viral infection, the number of monocytes will increase. This is because monocytes have several roles in the innate immune system besides being phagocytic cells, namely cells that induce the inflammatory process by releasing inflammatory cytokines. The inflammatory process is one of the innate protective mechanisms in the body when it experiences tissue damage. Inflammation is divided into 2, namely: acute inflammation, inflammation that lasts for a few days to several weeks, and chronic inflammation, which lasts for months to years. The most important white blood cells in acute inflammatory conditions are neutrophils and macrophages.

Meanwhile, the most important white blood cells in chronic inflammatory conditions are macrophages and lymphocytes [8, 23, 31].

In this study, the Wilcoxon statistical test showed a value of 0.000, so that it could be found a difference between the number of monocytes in PCR negative patients and PCR positive patients, so it could be concluded that there was a relationship between the number of monocytes and the patient's PCR results. The standard value for the number of eosinophils in humans is 2-4% of the total white blood cells. In conditions of parasitic infection, the number of eosinophils will increase. This happens because APC cells stimulate the adaptive immune system, Th2 cells, and will facilitate eosinophils from the bone marrow to the site of infection. After eosinophils are at the site of parasitic infection, eosinophils will degranulate and release granules in their cytoplasm, which will damage the infecting parasite. The same is true for viral infections [15]. In SARS-CoV-2 disease, the number of eosinophils decreases. The cause of the decreased eosinophil count in the COVID-19 condition is unknown.

The theory from Lindsey AW *et al*. states that eosinopenia or decreased eosinophil count (eosinophil count below 2% of total white blood cells) in COVID-19 patients is caused by a decrease in lymphocyte count [24]. Another theory says that eosinopenia occurs because eosinophils move to the site of infection so that on blood examination, the number of eosinophils appears to decrease, and eosinopenia occurs due to acute inflammation [26]. On examination of lung tissue, various reports stated that COVID-19 patients did not experience an increase in eosinophils either early in the infection phase or during postmortem analysis [16, 24]. A report from Zhang *et al*. showed that out of 140 COVID-19 patients, 53% had eosinopenia when the patient was first admitted to the hospital [32]. Another report by Rodriguez *et al*. and Du *et al*. stated that eosinopenia was associated with a poor prognosis [16, 33].

In this study, the Wilcoxon statistical test showed a value of 0.622, so there was no difference between the number of eosinophils in PCR negative patients and PCR positive patients, so it can be concluded that there is no relationship between the number of eosinophils and the results of PCR patients.

In a comparison study of the number of monocytes and eosinophils in the negative PCR group, the Wilcoxon statistical test showed a value of 1,000, so there was no difference between the number of monocytes and eosinophils in the PCR negative patient [34]. So, it could be concluded that there was no relationship between the number of monocytes and eosinophils in the negative PCR group. In comparison, in the study of the number of monocytes and eosinophils in the positive PCR group, the Wilcoxon statistical test showed a value of 0.068, so there was no difference between the number of monocytes and eosinophils in the positive PCR group. So, it could be concluded that there was no relationship between the number of monocytes and eosinophils in the positive PCR group.

This research has several limitations. First, this study only used data the first time the patient underwent a PCR and complete blood count. So the changes that occurred after the examination were not included in this study. Second, the data did not have the results of the patient's radiological examination, so the phase and severity of the disease could not be known. Third, from the data collected, there are no other diseases that the patient may experience because the number of monocytes and the eosinophils is an innate immune system that will react to all antigens that can stimulate these two cells. Therefore, the examination of the number of monocytes and the number of eosinophils is not specific to COVID-19 disease.

Conclusion

From the results of the research shown in previous chapters, it is concluded that this study indicates that the examination of the number of monocytes and eosinophils cannot be used as screening material for COVID-19.

References

1. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. Journal of autoimmunity,2020:109:102433.
2. Chang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. Transfusion medicine reviews,2020:34(2):75-80.
3. Susilo A, Rumende CM, Pitoyo CW, Santoso WD, Yulianti M, Herikurniawan H *et al*. Coronavirus disease 2019: Tinjauan literatur terkini. Jurnal penyakit dalam Indonesia,2020:7(1):45-67.
4. Sucahya PK. Barriers to covid-19 RT-PCR testing in Indonesia: a health policy perspective. Journal of Indonesian Health Policy and Administration,2020:5(2).
5. Wang J, Jiang M, Chen X, Montaner LJ. Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection: review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts. Journal of leukocyte biology,2020:108(1):17-41.
6. Merad M, Martin JC. Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. Nature reviews immunology,2020:20(6):355-62.
7. Wibrow BA, Ho KM, Flexman JP, Keil AD, Kohrs DL. Eosinopenia as a diagnostic marker of bloodstream infection in hospitalised paediatric and adult patients: a case-control study. Anaesthesia and intensive care,2011:39(2):224-30.
8. Maharani EA, Noviar G. Imunohematologi dan Bank Darah. Kementrian Kesehatan Republik Indonesia,2018:11(3):322.
9. Guilliams M, Mildner A, Yona S. Developmental and functional heterogeneity of monocytes. Immunity,2018:16:49(4):595-613.

10. Yang J, Zhang L, Yu C, Yang XF, Wang H. Monocyte and macrophage differentiation: circulation inflammatory monocyte as biomarker for inflammatory diseases. Biomarker research,2014:2(1):1-9.
11. Karlmark K, Tacke F, Dunay I. Monocytes in health and disease—Minireview. European Journal of Microbiology and Immunology,2012:1:2(2):97-102.
12. Shi C, Pamer EG. Monocyte recruitment during infection and inflammation. Nature reviews immunology,2011:11(11):762-74.
13. Gómez-Rial J, Rivero-Calle I, Salas A, Martinon-Torres F. Role of monocytes/macrophages in Covid-19 pathogenesis: implications for therapy. Infection and Drug Resistance,2020:13:2485.
14. Sheeler R. Cardiovascular Diseases, An Issue of Primary Care Clinics in Office Practice. Elsevier Health Sciences, 2013.
15. Ramirez GA, Yacoub MR, Ripa M, Mannina D, Cariddi A, Saporiti N *et al*. Eosinophils from physiology to disease: a comprehensive review. BioMed research international, 2018.
16. Rodriguez C, Veciana C. Asthma and Covid-19: The Eosinophilic Link. Qeios, 2020.
17. Di Gennaro F, Pizzol D, Marotta C, Antunes M, Racalbuto V, Veronese N *et al*. Coronavirus diseases (COVID-19) current status and future perspectives: a narrative review. International journal of environmental research and public health,2020:17(8):2690.
18. Tufan A, Güler AA, Matucci-Cerinic M. COVID-19, immune system response, hyperinflammation and repurposingantirheumatic drugs. Turkish journal of medical sciences,2020:50(9):620-32.
19. RI K. Pedoman Pencegahan dan Pengendalian Coronavirus Disease (COVID-19). Jakarta: Kementerian Kesehatan RI.
20. Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. Journal of pharmaceutical analysis,2020:10(2):102-8.
21. Burhan E, Isbaniah F, Susanto AD, Yoga Y, Tjandra A, Sugiri T *et al*. Pneumonia COVID-19 Diagnosis & Penatalaksanaan di Indonesia. Jakarta: Perhimpunan Dokter Paru Indonesia,2020, 1-49.
22. Gómez-Rial J, Martinón-Torres F. A strategy targeting monocyte-macrophage differentiation to avoid pulmonary complications in SARS-Cov2 infection. Clinical Immunology (Orlando, Fla.),2020:216:108442.
23. Lindsley AW, Schwartz JT, Rothenberg ME. Eosinophil responses during COVID-19 infections and coronavirus vaccination. Journal of Allergy and Clinical Immunology,2020:146(1):1-7.
24. Hirosawa T, Harada Y, Morinaga K, Takase H, Nin M, Shimizu T. Eosinopenia as a diagnostic marker of bloodstream infection in a general internal medicine setting: a cohort study. BMC infectious diseases,2020:20(1):1-7.
25. Espinosa V, Rivera A. First line of defense: innate cell-mediated control of pulmonary aspergillosis. Frontiers in microbiology,2016:3:7:272.
26. Pratiwi VP, Nofrima S, Purwaningsih T. Central Government Communication With Regions in Handling Covid-19 in Dki Jakarta Through Social Media. WACANA: Jurnal Ilmiah Ilmu Komunikasi.,2021:30:20(1):14-24.
27. Boehmer TK, DeVies J, Caruso E, van Santen KL, Tang S, Black CL *et a*l. Changing age distribution of the COVID-19 pandemic—United States, May–August 2020. Morbidity and Mortality Weekly Report,2020:2:69(39):1404.
28. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM *et al*. Gender differences in patients with COVID-19: focus on severity and mortality. Frontiers in public health, 2020, 152.
29. World Health Organization (WHO). Gender and COVID-19; Advocacy Brief. World Health Organization, 2020.
30. Gebhard C, Regitz-Zagrosek V, Neuhauser HK, Morgan R, Klein SL. Impact of sex and gender on COVID-19 outcomes in Europe. Biology of sex differences,2020:11(1):1-3.
31. Hannoodee S, Nasuruddin DN. Acute inflammatory response. InStatPearls [Internet]. StatPearls Publishing, 2021.
32. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ *et al*. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy,2020:75(7):1730-41.
33. Pahwa R, Goyal A, Bansal P, Jialal I. Chronic inflammation. StatPearls. Treasure island (FL). [Internet] StatPearls Publishing, 2021.
34. Du Y, Tu L, Zhu P, Mu M, Wang R, Yang P *et al*. Clinical features of 85 fatal cases of COVID-19 from Wuhan. A retrospective observational study. American journal of respiratory and critical care medicine,2020:1:201(11):1372-9.

Monocytes and eosinophils in early positive COVID-19 patients

ORIGINALITY REPORT

20%	14%	13%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	aging-us.com Internet Source	1%
2	Fillaux, J.. "Accuracy of a routine real-time PCR assay for the diagnosis of Pneumocystis jirovecii pneumonia", Journal of Microbiological Methods, 200810 Publication	1%
3	repository.stikim.ac.id Internet Source	1%
4	journal.unnes.ac.id Internet Source	1%
5	Andrew E. Williams. "Immunology", Wiley, 2011 Publication	1%
6	www.frontiersin.org Internet Source	1%
7	Submitted to Universitas Teuku Umar Student Paper	1%

8	Lina Dewi Anggraeni, Widiyanti Widiyanti. "DISTRACTION TECHNIQUES: TELLING STORIES TO DECREASE PAIN FOR PRESCHOOL CHILDREN DURING INFUSION", Jurnal Keperawatan Indonesia, 2019 Publication	1 %
9	www.ijmsdr.com Internet Source	1 %
10	link.springer.com Internet Source	1 %
11	www.dovepress.com Internet Source	1 %
12	www.medrxiv.org Internet Source	1 %
13	www.journalofmedical.com Internet Source	1 %
14	Alain Meyer. "Safety and efficacy of anti-tumor necrosis factor α therapy in ten patients with recent-onset refractory reactive arthritis", Arthritis & Rheumatism, 05/2011 Publication	<1 %
15	Maja Mitrašinović-Brulić, Amela Dervišević, Asija Začiragić, Muhamed Fočak et al. "Vitamin D3 attenuates oxidative stress and regulates glucose level and leukocyte count in a semi-chronic streptozotocin-induced	<1 %

diabetes model", Journal of Diabetes & Metabolic Disorders, 2021
Publication

16	academic.oup.com Internet Source	<1 %
17	journals.tubitak.gov.tr Internet Source	<1 %
18	Xiaowei Li, Manman Geng, Yizhao Peng, Liesu Meng, Shemin Lu. "Molecular immune pathogenesis and diagnosis of COVID-19", Journal of Pharmaceutical Analysis, 2020 Publication	<1 %
19	bmcinfectdis.biomedcentral.com Internet Source	<1 %
20	Miriam Merad, Jerome C. Martin. "Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages", Nature Reviews Immunology, 2020 Publication	<1 %
21	J. Gómez-Rial, Martinón-Torres. "A strategy targeting monocyte-macrophage differentiation to avoid pulmonary complications in SARS-Cov2 infection", Clinical Immunology, 2020 Publication	<1 %

jonuns.com

22	Internet Source	<1%
23	openaccesspub.org Internet Source	<1%
24	www.nature.com Internet Source	<1%
25	repository.uki.ac.id Internet Source	<1%
26	Submitted to Universiti Brunei Darussalam Student Paper	<1%
27	journalijdr.com Internet Source	<1%
28	TANAKA. "Surface phenotype analysis of CD16+ monocytes from leukapheresis collections for peripheral blood progenitors", Clinical & Experimental Immunology, 4/1999 Publication	<1%
29	Submitted to University of Sunderland Student Paper	<1%
30	Claudia Pérez - Rivera, Humberto Ramírez - Mendoza, Susana Mendoza - Elvira, Rene Segura - Velázquez et al. "First report and phylogenetic analysis of porcine deltacoronavirus in Mexico", Transboundary and Emerging Diseases, 2019 Publication	<1%

31	Debora Natalia, Dina Keumala Sari, Rizky Ardiansyah, Wulan Fadinie. "Knowledge Regarding Coronavirus Disease-19 Related to Nutritional Practices in Residents of Medan City, Indonesia", Open Access Macedonian Journal of Medical Sciences, 2021 Publication	<1 %
32	www.freepatentsonline.com Internet Source	<1 %
33	Sukma Widayani, Wahyu Nuraini Hasmar. "APPROPRIATE USE OF ORAL ANTIHYPERTENSIVE DRUGS EVALUATION IN NONDIALYSIS CHRONIC KIDNEY DISEASE PATIENT OF PRIVATE HOSPITAL IN EAST BEKASI 2018-2020", Jurnal Mitra Kesehatan, 2021 Publication	<1 %
34	ijisrt.com Internet Source	<1 %
35	jlb.onlinelibrary.wiley.com Internet Source	<1 %
36	www.cdc.gov Internet Source	<1 %
37	Ping Yi, Xiang Yang, Cheng Ding, Yanfei Chen et al. "Risk factors and clinical features of deterioration in COVID-19 patients in	<1 %

Zhejiang, China: a single- centre, retrospective study", Research Square Platform LLC, 2020
Publication

38	Sotir, M. J., D. L. Cappozzo, D. M. Warshauer, C. E. Schmidt, T. A. Monson, J. L. Berg, J. A. Zastrow, G. W. Gabor, and J. P. Davis. "Evaluation of Polymerase Chain Reaction and Culture for Diagnosis of Pertussis in the Control of a County-Wide Outbreak Focused among Adolescents and Adults", Clinical Infectious Diseases, 2007. Publication	<1 %
39	blogs.iu.edu Internet Source	<1 %
40	content.iospress.com Internet Source	<1 %
41	e-epih.org Internet Source	<1 %
42	iopscience.iop.org Internet Source	<1 %
43	matriksbiotek.com Internet Source	<1 %
44	www.longdom.org Internet Source	<1 %
45	www.sciencegate.app Internet Source	<1 %

46	"Poster presentations", European Geriatric Medicine, 2016 Publication	<1 %
47	Dipo Aldila, Sarbaz H.A. Khoshnaw, Egi Safitri, Yusril Rais Anwar et al. "A mathematical study on the spread of COVID-19 considering social distancing and rapid assessment: The case of Jakarta, Indonesia", Chaos, Solitons & Fractals, 2020 Publication	<1 %
48	Federico Martinón-Torres, Adolfo García-Sastre, Andrew J. Pollard, Carlos Martín et al. "TIPICO XI: report of the first series and podcast on infectious diseases and vaccines (aTIPICO)", Human Vaccines & Immunotherapeutics, 2021 Publication	<1 %
49	Janna Riechmann, Laurent M. Willems, Rainer Boor, Matthias Kieslich et al. "Quality of life and correlating factors in children, adolescents with epilepsy, and their caregivers: A cross-sectional multicenter study from Germany", Seizure, 2019 Publication	<1 %
50	Seema Patrikar, Deepti Poojary, D.R. Basannar, Renuka Kunte. "Projections for novel coronavirus (COVID-19) and evaluation	<1 %

of epidemic response strategies for India", Medical Journal Armed Forces India, 2020
Publication

51	Y. Wang, S. Oeztuerk, W. Kratzer, B. Boehm. "A Nonclassical Monocyte Phenotype in Peripheral Blood is Associated with Nonalcoholic Fatty Liver Disease: A Report from an EMIL Subcohort", Hormone and Metabolic Research, 2015 Publication	<1 %
52	Yasir Mokodompis, Dr. Irwan M.Kes. "DETECTION OF ANTI-SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2) ANTIBODY IGM AND IGG IN ADOLESCENTS IN GORONTALO", International Journal of Health Science & Medical Research, 2022 Publication	<1 %
53	Yingzheng Tan, Juan Zhou, Qing Zhou, Lingli Hu, Yunzhu Long. "Role of eosinophils in the diagnosis and prognostic evaluation of COVID‐19", Journal of Medical Virology, 2020 Publication	<1 %
54	indjst.org Internet Source	<1 %
55	journal.fkm.ui.ac.id Internet Source	<1 %

56	lib.fjmu.edu.cn Internet Source	<1 %
57	portalfield.com Internet Source	<1 %
58	pure.rug.nl Internet Source	<1 %
59	uokerbala.edu.iq Internet Source	<1 %
60	www.ecdc.europa.eu Internet Source	<1 %
61	www.researchsquare.com Internet Source	<1 %
62	Siti Roudhotul Jannah, Aini Ahmad. "Examination of Pregnant Woman (Antenatal Care) during the Covid-19 Pandemic. A Literature Review", International Journal of Advanced Health Science and Technology, 2022 Publication	<1 %

Exclude quotes	On	Exclude matches	Off
Exclude bibliography	On		