Hematologic Profiles of Plasmodium Vivax Malaria Patients

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Abstract

Background: Malaria infections cause various symptoms ranging from asymptomatic infections to severe disease complications. Plasmodium vivax malaria has been recognized as a disease that attacks blood cells, causing various hematologic changes, especially anemia, leukopenia, leucocytosis, neutropenia, neutrophilia, and thrombocytopenia with different percentages. Plasmodium vivax, formerly known to cause mild malaria, was later proven to cause severe malaria, even cerebral malaria such as Plasmodium falciparum. This study aims to determine the hematologic profile in patients with Plasmodium vivax malaria.

Method: This research use descriptive cross sectional design. This research was conducted in Puskesmas (PKM; Primary Health Care) Sukamaju and Puskesmas (PKM; Primary Health Care) Karang City in August until December 2017. Samples were taken by consecutive sampling. A total of 37 samples expressed positive Plasmodium vivax, examined their hematologic profiles specifically hemoglobin, erythrocytes, leucocytes, platelets, lymphocytes, neutrophils, monocytes and hematocrit using automatic hematology cell counter.

Results: Based on the results of this study, 56.76% of patients had anemia, 45.90% of patients had leukopenia, 89.20% thrombocytopenia, 2.70% neutrophilia, 10.80% neutropenia, 2.70% lymphocytosis, 35.10% lymphopenia, and 13.50% pancytopenia.

Conclusion: In patients with Plasmodium vivax malaria infection there may be a change in hematologic profiles, this change may be affected by the acute phase of infection and host immune system.

Keywords: Plasmodium vivax malaria, hematologic profiles

Background

Malaria remains a health problem worldwide, with an average of 300-500 million cases each year and nearly one million death.¹ Malaria affects almost all regions of the world, but malaria is endemic in the tropics to the subtropics region namely Asia, Africa, Central and South America. Based on the World Health Organization (WHO) report, the number of malaria cases worldwide from 2000 to 2015 was 212 million cases. By 2015, there are 174 million people in the world are at risk of developing malaria. Most malaria cases (90%) are in Africa, 7% in
Southeast Asia, and 2% in the Mediterranean region. There are five species of malaria that infect humans: *Plasmodium falciparum, Plasmodium ovale, Plasmodium malariae, Plasmodium vivax,* and *Plasmodium knowlesi.* Among the four species, *Plasmodium falciparum* and *Plasmodium vivax* are the highest prevalence of malaria in the world. Although *Plasmodium falciparum* is the most common cause of malaria associated with high mortality rates, geographically, *Plasmodium vivax* has a widespread distribution. Most cases of malaria occurring in Southeast Asia are caused by *Plasmodium vivax* which is 58% of cases. In addition, there are four countries with the main causes of malaria is *Plasmodium vivax* namely Ethiopia, India, Indonesia and Pakistan.

Malaria infections cause a variety of symptoms ranging from asymptomatic infections to severe disease complications. *Plasmodium vivax* malaria has been recognized as a disease that attacks blood cells, causing various hematological changes, especially anemia, leukopenia, leukocytosis, neutropenia, neutrophilia, and thrombocytopenia with different percentages. *Plasmodium vivax* previously known to cause mild malaria, was later proven to cause severe malaria, even cerebral malaria such as *Plasmodium falciparum.*

**Methods**

The type of this research is descriptive with cross sectional study design. This research has been conducted in August until December 2017. Blood sampling is done at *Puskesmas* Karang City and *Puskesmas* Sukamaju Bandar Lampung by consecutive sampling. Examination of the number of neutrophils conducted at the Central Laboratory of Lampung. Patients taken were confirmed patients infected with *P. vivax* by microscopic examination, aged 6 years or older and willing to be the subject of the study and sign the informed consent. Patients receiving mixed infection of *Plasmodium vivax* with other *Plasmodium* while in pregnancy, having chronic infections, such as tuberculosis, dengue disease, mumps, or measles, having a history of autoimmune disease and a history of malignant disease, and taking anti-inflammatory drugs, Isoniazid, and quinine is excluded this. The number of samples obtained according to inclusion and exclusion criteria was 37 samples.

Samples taken according to inclusion and exclusion criteria through anamnesis include symptoms experienced, history of previous illness and history of drug consumption. Blood samples were taken in the right or left arm cubital fossa (bassilica vein/ cephalic vein/medial
cubital vein) of 3 cc. The blood samples were subjected to a process of peripheral blood examination to confirm the type of malaria and laboratory examination for hematologic examination specifically hemoglobin, erythrocytes, leukocytes, thrombocytes, lymphocytes, neutrophils, monocytes and hematocrit using automatic hematology cell counter equipment in the Clinical Pathology Laboratory of UPTD (Unit Pelayanan Tranfusi Darah; Blood Transfusion Service Unit) Laboratory Hall Health of Lampung Province. The process of sending samples from the collection point to the checkpoint used a cooler at 4°C.

Results
Of the 37 respondents obtained, the majority are male (64.9%) and the age of most respondents was 26-45 years (48.6%). A total of 78.4% of respondents are indigenous. Based on history of malaria infection, 62.2% of new respondents were first infected with malaria. From 37 samples of blood of respondents examined hematologic profile obtained the average hemoglobin, leukocyte, erythrocytes, lymphocyte, monocyte, neutrophil and hematocrit have normal values and only slightly decreased thrombocyte value from the normal value of 104.21 ± 63.46 103/µL. However, when the result of hematologic profile of each individual, 56.76% of patients had anemia, 45.90% of patients had leukopenia, 89.20% with thrombocytopenia, 2.70% neutrophilia, 10.80% neutropenia, 2.70% lymphocytosis, 35.10% of lymphopenia, and 13.50% of pancytopenia. The hematologic profile of Plasmodium vivax malaria patients is presented in Table 1 and Table 2.

Table 1 Average Amount of Hematologic Profile of Malaria Plasmodium vivax Patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>37</td>
<td>12,8 ± 2,14</td>
</tr>
<tr>
<td>Leukocyte (10³/µL)</td>
<td>37</td>
<td>5,548 ± 1,71</td>
</tr>
<tr>
<td>Erythrocyte (million/ µL)</td>
<td>37</td>
<td>4,600 ± 0,78</td>
</tr>
<tr>
<td>Thrombocyte (10³/µL)</td>
<td>37</td>
<td>104,21 ± 63,46</td>
</tr>
<tr>
<td>Lymphocyte (/µL)</td>
<td>37</td>
<td>1366,21 ± 770,09</td>
</tr>
<tr>
<td>Monocyte (/µL)</td>
<td>37</td>
<td>365,67 ± 179,1</td>
</tr>
<tr>
<td>Neutrophil (/µL)</td>
<td>37</td>
<td>3810,81 ± 1485,8</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>37</td>
<td>39,10 ± 6,82</td>
</tr>
</tbody>
</table>
**Table 2 Hematologic Profile of Malaria *Plasmodium vivax* Patients**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Male</td>
<td>14</td>
<td>58.30</td>
</tr>
<tr>
<td>• Female</td>
<td>7</td>
<td>53.80</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>56.76</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>17</td>
<td>45.90</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>33</td>
<td>89.20</td>
</tr>
<tr>
<td>Neutrophilia</td>
<td>1</td>
<td>2.70</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>4</td>
<td>10.80</td>
</tr>
<tr>
<td>Lymphocytosis</td>
<td>1</td>
<td>2.70</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>13</td>
<td>35.10</td>
</tr>
<tr>
<td>Pancytopenia</td>
<td>5</td>
<td>13.50</td>
</tr>
</tbody>
</table>

**Discussion**

Based on the data, characteristic of the majority respondents are male (64.9%). The result of this research is almost the same with the result of a research conducted by Manas et. al (2017) that most of the respondents of malaria are male (64.1%). This can be happened because men are more likely to be in or working in malaria endemic areas such as miners, forest workers and fishermen.11

In this study obtained from 37 patients there were 56.76% of patients experiencing anemia. Research conducted by other researchers also showed similar results.7,8 The pathogenesis of anemia in malaria patients is complex, anemia may arise due to an imbalance between production and the destruction of red blood cells due to hemolysis, erythrocyte sequestration, and ineffective erythropoiesis due to high levels of TNF α in circulation.12,13 Increased destruction of these erythrocytes can be caused by parasitic hemoglobin digestion, parasitized red blood cell destruction (PRBC) during the schizogenic phase, and the destruction of the erythrocyte membrane. While the reduction in erythrocyte production may be due to suppression of erythropoiesis due to the production of excessive pro-inflammatory cytokines and diseritropoiesis.12

In this study also found the presence of thrombocytopenia as much as 89.20%. Thrombocytopenia is a hematological change that is common in acute malaria. Thrombocytopenia in malaria can be caused by several factors including increased platelet pooling in the spleen due to splenomegaly, platelet activation and aggregation, platelet
phagocytosis, platelet adhesion to erythrocytes, oxidative stress leading to premature platelet death and hyper-reactive malaria splenomegaly (HMS).\textsuperscript{14,15}

Another hematological parameter that undergoes a change in this study was leukocytes, as many as 17 patients (45.90\%) had leukopenia. Leukocytes play an important role in the body's defense against malaria. Changes in leukocytes in malaria patients are influenced by many factors such as the acute phase of malaria, parasitemia, severity of the disease, immune status of the host against malaria and other infections.\textsuperscript{16}

Based on the results of this study obtained the average result of the number of neutrophils is normal that is $3810.81 \pm 1485.8/\mu l$. Of 37 patients, 86.5\% of normal neutrophils were found, 10.8\% neutropenia and 2.7\% neutrophilia. In malaria patient there is a change in hematologic parameters of neutrophils that may be neutropenia or neutrophilia, but the most common neutropenia.\textsuperscript{12,17,18} The average number of neutrophils in malaria infection depends on the phase of infection. Neutrophil activation occurs early in the malaria infection. In the acute phase the number of neutrophils will increase and return to normal during the convalescent phase. This is due to the acceleration of the production and or the release of neutrophils into the circulation.\textsuperscript{19,20} Neutrophilia in malaria can be caused by the circulating pooling mechanism from circulation pools to an enlarged marginated pool due to infection so that the number of circulating neutrophils in the malaria patient is reduced, spleen activity during infection, lymphotoxic serum factor and neutrophil sequestration due to increased expression of cell adhesion molecules (ICAM-1 and VCAM-1) in malaria.\textsuperscript{21,22,23} Neutrophilia in malaria patients is usually found in severe malaria or secondary infection by bacteria.\textsuperscript{24} The number of neutrophils in the blood is maintained in a stable amount through the process of hematopoiesis in the bone marrow, the neutrophil distribution from the marginated pool to the blood and the number of neutrophils coming out of the blood into the tissues. After entering the circulation, the neutrophil half-life is only 6 to 8 hours.\textsuperscript{25} The production of neutrophils in the bone marrow is regulated by three major glycoprotein or cytokine hormones, namely interleukin-3 (IL-3), granulocyte-Monocyte Colony Stimulating Factor, and Granulocyte Colony-Stimulating Factor (G-CSF).\textsuperscript{26} Granulocyte Colony-Stimulating Factor (G-CSF) is a predominant factor of regulation of the neutrophil life cycle by increasing cell proliferation, cell survival, differentiation, and neutrophil cell mobilization.\textsuperscript{27}

As with neutrophils, the number of lymphocytes in malaria patients may be decreased, normal or increased in acute malaria.\textsuperscript{28} In this study, the average number of normal lymphocytes
was 1366.21 ± 770.09/μl. Of 37 patients, 35.10% of patients had lymphopenia and 2.70% lymphocytosis. Lymphopenia can occur due to redistribution of lymphocytes to tissues from the circulating pool to the marginated pool and the destruction of lymphocytes due to Fas-induced apoptosis.21,29,30

The condition of pancytopenia was also found in this study, as many as 5 patients (13.5%), in accordance with previous studies, showing pancytopenia in malaria P. vivax as much as 17.1% and 13.68%.7,8 Suspected occurrence of pancytopenia in malaria infection is caused by the hemophagocytosis syndrome.12 This result proves that a single infection of P. vivax can cause pancytopenia as well as P. falciparum.

Conclusion

In patients with Plasmodium vivax malaria there may be a change in hematologic profile. Many factors that affect it include the phase of malaria infection and host immune system.

Bibliography


