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Hematological Profile of Malaria Patients at the Southeast Minahasa, North Sulawesi, Indonesia

Diana Shintawati Purwanto[1, 2, *], Juliet Merry Eva Mamahit[1]

[1]Entomology Study Program, Postgraduate Program, Sam Ratulangi University, Manado, Indonesia
[2]Department of Biochemistry, Faculty of Medicine, Sam Ratulangi University, Manado, Indonesia

Email address:
dianashintapurwanto@unsrat.ac.id (Diana Shintawati Purwanto)
[*]Corresponding author

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Abstract: Malaria remains a public health concern in Indonesia. Several types of district and private hospitals play a very important role in treating malaria sufferers and their complications. Hematological alterations are the most prevalent consequences of malaria. Therefore, this study aimed to compile a hematological profile of malaria patients treated at Mitra Sehat Regional General Hospital, Southeast Minahasa Regency, North Sulawesi, Indonesia. A total of 92 patients with clinical symptoms of fever and positive for malaria after examining their peripheral blood smear, were included in this cross-sectional study. The data from the hematology examination was then analyzed. There were 65 cases caused by *P. falciparum,* followed by 21 cases of *P. vivax,* and 6 cases of *P. falciparum* and *P. vivax* co-infection. The most frequent hematological abnormality seen in malaria patients in this study was thrombocytopenia (91%). Furthermore, leukopenia was found in 33%, followed by anemia in 20%. While females had greater levels of white blood cells and platelets count, male patients had significantly higher averages for hemoglobin, red blood cells count, and hematocrit profiles. In conclusion, the hematological alterations associated with malaria patients include thrombocytopenia, leukopenia, and anemia, therefore people living in highly endemic locations, like Southeast Minahasa, can use these markers to strengthen their suspicion of malaria.

Keywords: Malaria, Plasmodium, Anemia, Leukopenia, Thrombocytopenia

1. Introduction

Malaria is caused by plasmodium infection which is transmitted from the female *Anopheles* mosquitoes, as the disease vector [1]. Approximately 3.2 billion people on the earth reside in regions where malaria can spread easily. An estimated 350–500 million cases of clinical malaria are reported each year, with *P. falciparum* and *P. vivax* infections accounting for the majority of cases. Severe malaria results in the death of 1.1–2.7 million people annually. It is the second greatest cause of death in Africa and the fifth cause of infectious disease-related deaths globally [2].

Due to endemic areas in some areas, malaria remains a public health concern in Indonesia. Data from the Indonesia Ministry of Health shows that there were 415,140 cases of malaria in Indonesia in 2022. This number has increased by 36.29% compared to the previous year which was 304,607 cases [3]. Given all of those details, North Sulawesi is Indonesia's third-most malarial-case-counting province. Malaria is also among the top ten illnesses that are most frequently seen in North Sulawesi's hospitals and medical facilities. Several type of private and district hospitals, play a very important role in treating malaria sufferers and their complications [4]. Furthermore, *Plasmodium falciparum* accounts for 71.5% of infections and is the most common parasite found in North Sulawesi [5].

Hematological alterations are the most prevalent consequences of malaria since the parasites that cause the disease are blood parasites. Consequently, they represent a number of the key factors in the pathophysiology of malaria [6]. Certain hematological indicators have not been characterized consistently as a criterion for evaluating malaria

burden, despite their direct and indirect impact on the disease. Hemoglobin, leukocyte, and platelet counts are examples of such standard laboratory results [7].

Southeast Minahasa is one of the districts in North Sulawesi Province and located around 80 km from Manado, as the capital city of North Sulawesi. The area of Southeast Minahasa district covers an area of 730.62 km^2, which is administratively divided into 12 sub-districts, and had a total population of 117,079 at the 2021 census. The main occupations of the residents of this area are related to the fields of agriculture, forestry and fisheries, and mining and quarrying. According to data from North Sulawesi Province's Central Statistics Agency, in 2020 and 2021, this region had the greatest number of malaria cases per 1,000 people in North Sulawesi. Therefore, this study aims to compile a hematological profile of malaria patients treated at Mitra Sehat Regional General Hospital, Southeast Minahasa Regency, North Sulawesi during the 2023 period.

2. Material and Methods

2.1. Data Collection

The study was conducted in the Mitra Sehat Regional General Hospital, Southeast Minahasa Regency, as a government hospital that provides data on malaria cases in this area. The data from fever patients who had their blood smears examined under a microscope and tested positive for malaria during the 2023 period were incorporated into this study.

2.2. Laboratory Analysis

Hematology examination was carried out with a Sysmex XP-300 hematology instrument using 3 mL EDTA blood. The definition of anemia and leukopenia was based on laboratory reference values according to different genders and age groups, while thrombocytopenia was defined as platelets count <150 × 10^3/μL [1].

Malaria was diagnosed using blood film microscopy (peripheral blood smear examination). Blood from a finger prick was used to create thick and thin blood films on slides. Methanol was used to fix the thin film for half a minute. After that, the blood film was stained for 15 minutes with 3% Giemsa stain and inspected by experienced analyst using an oil immersion objective with a 100× magnification [2].

2.3. Data Analysis

Data collected was analyzed using Microsoft Excel and Statistical Package for Social Science (SPSS) version 26.0, and then presented as frequency, percentages, and mean±standard deviation (SD). The statistical difference between two means of nonparametric datasets was tested using the Mann-Whitney test, as in Table 2. One-way ANOVA and Kruskal-Wallis test were employed to determine statistical difference among the means of more than two independent variables of parametric and nonparametric datasets, respectively, as shown in Tables 3. A p value of ≤0.05 was considered statistically significant.

3. Results

A total of 263 patients with clinical symptoms of fever and suspected malaria had their peripheral blood smears examined, and 92 of them were positive for malaria, of which males constituted 84 (91%) of the patients who tested positive. The age range of all participants was 3–85 years, with an average of 32.4 years. There were 65 cases caused by *P. falciparum,* followed by 21 cases of *P. vivax,* and 6 cases of *P.falciparum* and *P.vivax* co-infection.

The most frequent hematological abnormality seen in malaria patients in this study was thrombocytopenia. Of the total malaria patients studied, 91% experienced thrombocytopenia, while the remaining 9% had normal platelet counts. No cases of malaria with thrombocytosis were found. Furthermore, leukopenia was found in 33%, followed by anemia in 20% (Table 1).

Table 1. *Hematological alterations in malaria patients.*

Hematological abnormalities	Frequency	%
Anemia	18	20
Leukopenia	30	33
Thrombocytopenia	84	91

Table 2. *The profile of hematological parameters according to gender.*

Parameter	Total	Male	Female	*p-value*
	mean ± SD	mean ± SD	mean ± SD	
WBC (10^3/μL)	5.7 ± 1.9	5.7 ± 1.9	6.4 ± 1.9	0.147
RBC (10^6/μL)	4.9 ± 0.6	5.0 ± 0.6	4.0 ± 0.4	0.000*
HGB (g/dL)	14.0 ± 2.0	14.4 ± 1.5	9.9 ± 2.0	0.000*
HCT (%)	41.2 ± 5.8	42.1 ± 4.8	30.9 ± 4.8	0.000*
PLT (10^3/μL)	78.9 ± 48.8	77.3 ± 44.8	96.4 ± 82.3	0.798
MCV (fL)	84.1 ± 4.8	84.5 ± 4.6	79.9 ± 5.9	0.047*
MCH (pg)	28.5 ± 2.0	28.8 ± 1.8	26.0 ± 2.2	0.002*
MCHC (g/dL)	33.9 ± 1.1	34.0 ± 1.0	33.0 ± 1.4	0.054

Note: WBC= white blood cells count, RBC= red blood cells count, HGB= hemoglobin, HCT = hematocrit, PLT= platelets count, MCV= mean corpuscular volume, MCH= mean corpuscular hemoglobin, MCHC= mean corpuscular hemoglobin concentration.

Table 2 indicates that the male patients had substantially higher means (x) for haemoglobin, red blood cells, and haematocrit profiles (14.4 g/dl, 5.0×10^6/μL, and 42.1%) than their female counterparts (9.9 g/dl, 4.0×10^6/μL, and 30.9%),

respectively. On the other hand, the means (x) of white blood cells and platelets were found to be higher in females (6.4x10³/µL and 96.4×103/µL, respectively) than in males (5.7×103/µL and 77.3×103/µL), although this difference was not statistically significant.

Based on the differences in the type of plasmodium that infects, it can be seen that only red blood cells count, haemoglobin, and haematocrit have significant differences between the three groups, while the other parameters, namely white blood cells count, platelets, and erythrocyte index, have no statistical differences (Table 3).

Table 3. *Hematological parameters according to the type of plasmodium.*

Parameter	*P. falciparum*	*P. vivax*	Mixed (*P. falciparum* & *P. vivax*)	*p-value*
	mean ± SD	mean ± SD	mean ± SD	
WBC (10^3/µL)	5.6 ± 2.0	5.9 ± 1.8	6.4 ± 1.7	0.064
RBC (10^6/µL)	5.0 ± 0.6	4.5 ± 0.6	5.0 ± 0.7	0.012*
HGB (g/dL)	14.4 ± 1.9	12.9 ± 2.1	14.0 ± 2.0	0.010*
HCT (%)	42.2 ± 5.4	38.0 ± 5.9	40.7 ± 6.0	0.012*
PLT (10^3/µL)	76.4 ± 42.3	82.0 ± 60.8	96.0 ± 71.9	0.831
MCV (fL)	84.3 ± 4.5	84.2 ± 5.2	81.2 ± 6.6	0.487
MCH (pg)	28.8 ± 1.8	28.1 ± 2.4	27.7 ± 2.5	0.363
MCHC (g/dL)	34.0 ± 1.0	33.6 ± 1.3	33.8 ± 1.2	0.583

Note: WBC= white blood cells count, RBC= red blood cells count, HGB= hemoglobin, HCT = hematocrit, PLT= platelets count, MCV= mean corpuscular volume, MCH= mean corpuscular hemoglobin, MCHC= mean corpuscular hemoglobin concentration.

4. Discussion

Based on the results of research at the Mitra Sehat Regional General Hospital, it was found that there were 92 cases of malaria in 2023. From the gender distribution, it can be seen that malaria cases are more common in males. This matches what was previously reported by Awoke at Tercha General Hospital, Dawuro Zone, South Ethiopia [2] and Kumbhar et al, at a tertiary care hospital, Karad, India [8]. This result relates to behavioral aspects, which are assumed to be important. The majority of men in this region who suffered from malaria are more engaged in work-related activities; many of them are miners. This activity makes it easier for males to come into contact with vectors [4].

This study showed that *P. falciparum* was the most common species of malaria, followed by P. vivax. Similarly, Tafesse and Amenu reported that *P. falciparum* was most prevalent in Sibu Sire Woreda, East Wollega Zone, and Western Ethiopia [9]. When *P. falciparum* is infected, anemia, leukopenia, and thrombocytopenia are frequently observed; this is likely because these patients have greater levels of parasitaemia [1].

Thrombocytopenia is most commonly seen in malaria infection, as individuals with platelet counts below 150,000/µL have a 12–15 times higher chance of contracting malaria than those with counts over 150,000/µL [1, 6]. The result of this study was higher when compared with the findings from the studies by Gebreweld [10] and Awoke [2]. There were several theories on the possibility of thrombocytopenia during a malaria infection. Increased peripheral destruction, excessive spleen pooling, and platelet consumption through the course of disseminated intravascular coagulopathy (DIC) are thought to be the causes of thrombocytopenia [6].

Leukopenia was the second hematological abnormality noticed in this research. This is comparable to another study that found leukopenia to be present in 39% of cases with malaria [11]. Among the leukocytic alterations linked to malaria infection, lymphocyte and neutrophil counts were the most significant. The reduction in lymphocyte numbers linked to malaria that was seen in this study might be the result of lymphocytes being redistributed after being sequestered in the spleen. Previous research suggested that stimulated neutrophil generation or release from the marrow or repressed peripheral clearance could be the cause of the increased neutrophil count associated with malaria infection [6, 12].

One of the most frequent side effects of malaria infection is anemia, which is more common in younger children and pregnant women living in high transmission areas. It is unclear what exactly causes anemia during a malaria infection, however it is thought to be caused by the parasite's main target, the red blood cell, which leads to the destruction of red blood cells, rapid elimination of parasitized and non-parasitized cells, bone marrow malfunction, and a high degree of parasitemia [6, 13]. The red blood cells count, hemoglobin, and hematocrit counts of the two genders were also shown to differ significantly in this study, with the male individuals having higher levels than the female subjects. However, the gender differences in reference ranges may be the cause of this [14].

The absence of prior medical histories for conditions including hemoglobinopathies, anemia, bacterial or viral infections, or other conditions that could introduce bias into the analysis were among the study's limitations and could have an impact on how the results were interpreted.

5. Conclusion

According to the study's findings, *P. falciparum* was the most prevalent species in the examined area, with males accounting for the majority of cases. Malaria patients should be examined for hematological abnormalities such as anemia, leukopenia, or thrombocytopenia. People who live in highly endemic areas, like Southeast Minahasa, can use these

markers to raise their suspicion of having malaria. If any abnormalities are found, effective treatment should be started to lessen the patient's risk of sequelae.

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Conflicts of Interest

All the authors do not have any possible conflicts of interest.

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