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Connection Inspection Blood Routine With Status History of Malaria at Ibnu Sina Hospital Makassar 2019-2024

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ABSTRACT

Malaria remains serious health problems in Indonesia, especially in the eastern region which has a high incidence . Routine blood tests are used to identify hematological abnormalities in malaria patients and the status of malaria history which is suspected to have a role in hematological changes , this is not fully understood . Therefore , it is necessary to explore the effect malaria history status on routine blood test results . To analyze the relationship between routine blood test results (hemoglobin, platelets , leukocytes) and malaria history status in patients at Ibnu Sina Hospital Makassar during the period 2019-2024. Observational analytical design with a cross-sectional approaches . There were 43 patients diagnosed with malaria. Data were analyzed using the chi-square statistical test . The majority of malaria patients were aged 21-30 years and were dominated by man while the most common type of plasmodium was P. vivax and occurred in patients without a previous history of malaria. Routine blood results found that most Patients had normal hemoglobin (76.70%), thrombocytopenia (83.70%), and normal leukocytes levels (72.10%). These results indicate a significant relationship between malaria history and hemoglobin levels (p = 0.020) and platelet count (p = 0.010) because malaria patients who have a history of malaria already have partial immunity that can minimize the occurrence of hematological disorders . However , in leukocytes , there was no significant relationship between malaria history and leukocyte count (p = 0.503). A significant relationship was found between hemoglobin and platelets with malaria history status .

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INTRODUCTION

Malaria Still become Wrong One problem health public Which Serious in low and middle income countries, so that control and elimination of this disease become priority main in region endemic . According to estimation World Health Organization (WHO) on year 2020, obtained 240 million case malaria Which cause more of the 600,000 deaths, the vast majority children under 5 years of age. In December 2022, Indonesia was declared malaria-

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free, but in eastern Indonesia there are still many cities that are endemic to malaria and contribute more than 90% of malaria cases reported nationally. Several provinces have high malaria cases in Indonesia, including West Papua, Papua, East Kalimantan, and East Nusa Tenggara. [1–3]

Malaria is disease infectious Which due to by parasite from genus *Plasmodium* . Disease This transmitted through bite mosquito female *Anopheles* Which infected. There is five species *Plasmodium* Which cause malaria, that is *P. falciparum* , *P. malaria* , *P. oval* , *P. vivax* , and *P. knowlesi* . These parasites infect human red blood cells and cause symptoms typical in the form of fever. Symptom general others include shivering, painful muscle, Sick head, and nauseous vomit. Species *P. falciparum* And *P. vivax* known can cause hematological disorders, caused by the interaction between the *Plasmodium parasite* and blood cells in malaria sufferers and the body's immune response . [4–6]

Routine blood tests are one of the important diagnostic methods in management. malaria. Parameter blood like level hemoglobin, platelets, And leukocytes frequently used For evaluate condition hematologist patient. Anemia, thrombocytopenia , And Changes in the number of leukocytes are hematological changes that are often found in malaria patients caused by damage to erythrocytes infected by the parasite. and will trigger the release of cytokines which cause anemia, thrombocytopenia and changes in the number of leukocytes in the blood [6.7]

Previous malaria status affects the immune response and can cause changes in blood test results. Patients with a history of malaria infection often show different blood test results compared to those who are newly infected, but this is not fully understood. Therefore, it is necessary to study the relationship between routine blood tests in malaria patients and previous malaria status . [8]

METHOD

Research use design observational analytic as well as approach cross-sectional . The research location was at Ibnu Sina Hospital Makassar in January-February 2024. The population of the study was the patient who diagnosed malaria during year 2019-2024. Data collected from medical records of patients who meet the inclusion criteria, and samples were taken by total sampling. The variables studied included hemoglobin levels, platelets, leukocytes and malaria history status. Data were analyzed using the chi-square test which aims to see the relationship between malaria history and routine blood test results.

RESULTS AND DISCUSSION

Research result

This study discusses routine blood analysis in malaria patients at Ibnu Sina Hospital. Makassar. Data obtained from record medical patient Which visit on period January 2019 until May 2024. From data secondary Which collected, there is 43 patient Which become a research sample. The results of this study are explained in the form of a table as follows:

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Table 1. Characteristics research sample

	Amount (n)	Percentage (%)
Age		
15- 20	4	9.30
21- 30	19	44.20
31- 40	10	23.30
41- 50	5	11.60
51- 60	4	9.30
61- 70	1	2.30
Type Sex		
Man	32	74.40
Woman	11	25.60
Types of Malaria		
P. falciparum	17	39.50
P. vivax	20	46.50
Mixed Infection (P. falciparum & P. vivax)	5	11.60
P. malaria	1	2.30
History malaria		
There is	16	37.20
No There is	27	62.80

The age group that was most affected was 21-30 years old, 19 people (44.2%), 31-40 years old, year amount to 10 patient (23.3%), Then age 41-50 year as much as 5 patient (11.6%), then the age of 15-20 and 51-60 years old amounted to the same, namely 4 patients (9.3%) the last was the age of 61-70 years which amounted to 1 patient (2.3%). Based on the gender of the malaria sufferer, the majority were found to be male, namely 32 patients (74.4%), while women were 11 patients (25.6%) of the total number of malaria sufferers studied. Based on type plasmodium dominated by plasmodium vivax as much as 20 patients (46.5%), Based on the history of malaria, the majority of sufferers had no previous history of malaria, namely 27 patients (62.8%) and those who had a previous history of malaria were 16 patients (37.2).

Table 2. Characteristics research sample

		History of Malaria		Total
		There is	n't any	
Types of plasmodium	*P. falciparum*	6	11	17
	P. vivax	10	10	20
	Mix P.falciparum & P. vivax	1	4	5
	P. malaria	1	0	1
Total		18	25	43

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Based on table 2 obtained type plasmodium which to infect sufferer malaria with a history of previous malaria, the most common is *P. vivax* as many as 10 patients, after That *P. falciparum* 6 patient, Then mix *P. falciparum* & *P. vivax* only 1 patient, And *P. malaria* only there is 1 patient Also on sufferer malaria. Whereas obtained the type of plasmodium that infects malaria sufferers who have no previous history of malaria Which most Lots that is *P. falciparum* as much as 11 patient And *P. vivax* 10 patients, then *mix P. falciparum & P. vivax* only 4 patients.

Table 3. Characteristics results blood routine on sufferer malaria

	Number (n)	Percentage (%)
Hemoglobin		
Normal	33	76.70
Anemia	10	23.30
Platelets		
Normal	7	16.30
Thrombocytopenia	36	83.70
Leukocytes		
Normal	31	72.10
Leukocytosis	5	11.60
Leukopenia	7	16.30

Based on Table 3, it describes the results of routine blood tests on malaria patients, which where The hemoglobin results obtained were normal level hemoglobin was found in 33 patients (76.7%), while those with anemia (<10 g/dl) were 10 patients (23.3%). In routine blood tests of platelets in malaria patients, it was found that only 7 patients (16.3%) had normal platelet levels, while 36 patients (88.3%) had thrombocytopenia (<150,000 /µL). In routine blood tests of leukocytes in malaria patients, the highest number of normal leukocyte levels was found, namely 31 patients (72.1%), after that 7 patients (16.3%) had leukopenia (<4,000 /µL) and only 5 patients (11.6%) had leukocytosis (>9,000 /µL). In routine blood examination of neutrophils in malaria patients, the highest level of neutrophils was found in 36 patients (83.7%), while those experiencing neutrophilia (>1,700 /µL) were only 7 patients (16.3%). In routine blood examination of lymphocytes in malaria patients, the highest level of normal lymphocytes was found in 31 patients (72.2%), while those experiencing lymphopenia (<700 /µL) were only 12 patients (27.9%).

Table 4. Connection Hemoglobin with sufferer malaria Which own history previous malaria

		History of malaria			Mark test Chi square
		There is	There isn't any	Total	P
Hemoglobin	Normal	17	16	33	0.020
	Anemia	1	9	10	
Total		16	27	43	

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Based on table 4, the results of the chi-square test square found p value = 0.020 indicating there is correlation Which very significant that is between status history malaria with hemoglobin in malaria patients.

Table 5. Connection level platelets with sufferer malaria Which own history previous malaria

		History of Malaria			Test Value chi square
		There is	There isn't any	Total	P
Platelets	Normal	6	1	7	0.010
	Thrombocytopenia	12	24	36	
Total		18	25	43	

Results of the chi test square found p value = 0.010 shows a significant correlation between level platelets sufferer malaria with status history malaria previously.

Table 6. Connection level leukocytes with sufferer malaria Which own previous history of malaria

		History of Malaria			Test Value Chi square
		There is	No There is	Total	P
Leukocytes	Leukocytosis	3	2	5	0.503
	Normal	13	18	31	
	Leukopenia	2	5	7	

Based on table 6, results from test chi square found mark p = 0.503 Which weight there is no correlation significant that is between level leukocytes sufferer malaria with status previous history of malaria.

Discussion

Based on secondary data that obtained from 43 patients, this study identified sample characteristics based on age group, gender, type of malaria, and history of malaria. In table 1 There are most patients suffering from malaria at Ibnu Sina Hospital Makassar in the age group of 21-30 years, as many as 19 patients (44.2%). This is consistent with the analysis of data from Riskesdas 2013, indicating the age range category of 25-34 years. year is group age Which very prone to to infection malaria. Group this age is at in age Which productive, in where they very active Work And often moving places. for work purposes. According to the literature, the spread of malaria is greatly influenced by type work, migration, as well as factor other. Age productive This related with the increase activity move place Work or traveling to region endemic malaria, which increases the possibility of being infected with malaria through the bite of the Anopheles mosquito sp [9,10]

Study Which done in RS Ibn Sina Makassar on year 2019-2024 showed that the majority of malaria patients were male, with a total of 32 out of 43 samples (74.4%). The findings This in line with research that done by Chart A (2018) in HOSPITAL Panglima Sebaya, Paser Regency, where the number of male malaria patients is higher, namely 105 people (87.5%).

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This is due to higher risk factors in men due to their activities which are more often outside the home, such as farming, raising livestock, managing ponds Which is habitat mosquito vector, as well as habit culture local For out of the house on Evening day. Besides That, man tend more often do journey or migration Work, especially to regions endemic malaria. Data study This showed that most of the samples had a history of traveling to Papua, which is one of the malaria endemic areas , so the risk of being infected with malaria increases. [9,11]

At Ibnu Sina Hospital Makassar, the type of malaria most commonly found in patients is that caused by *Plasmodium vivax infection* , with a total of 20 people (46.5%), followed by *P. falciparum infection.* as many as 17 patients (39.5%). Furthermore, there were 5 patients with mixed infections (mixed infection) (11.6%), and only 1 patient had *P. malariae infection* (2.3%). This finding is consistent with the research of Putu and Alan (2020) at the Hanura Health Center, Pesawaran Regency, which showed that *Plasmodium vivax infection* was the most common, with 33 cases (86.8%). *P. vivax infection* usually occurs in areas with high malaria transmission unstable, while *P. falciparum* more often found in malaria endemic areas with stable transmission. Most of the samples in this study had a history of travel to Papua, one of the malaria endemic areas , so the number of *P. falciparum infections* and *P. vivax* at Ibnu Sina Hospital Makassar is relatively balanced. [12,13]

Based on the history of malaria, most sufferers had no history of malaria before, amounting to 27 patients (62.8%) and those who had a history of malaria before were 16 patients (37.2%). When sufferers are exposed to malaria, the body will develop anti-malaria antibodies that provide resistance to future infections. The sufferer who previously infected malaria And healed. Matter This will create vulnerability sufferer malaria to infection in time upcoming will reduce. On first infection time, system immunity body respond with activate mechanism innate defenses, including phagocytic cells such as macrophages that engulf and destroy malaria parasites. An inflammatory response also occurs, in which cytokines such as IFN- γ and TNF- α (NCBI) are released to help control the infection, and T cells (especially CD8+ and CD4+ T cells) activated For recognize And destroy cell Which infected And cell B activated to produce specific antibodies against malaria parasite antigens. The antibodies produced by cell B can tie parasite malaria, mark it For destroyed by cells immunity other. Antibody Also can prevent parasite to infect cell blood red new. After several exposures, the body develops partial immunity, this immunity is not complete. protect from infection repeat, but reduce severity of symptoms And prevent serious complications. Therefore, just because someone has had malaria, it does not mean they are protected from being infected with malaria again and does not make someone immune. By Because That results study This obtained 16 person (37.2%) suffer malaria who have a history of malaria. [14,15]

Based on table 2, the type of plasmodium that most frequently infects malaria sufferers with a history of previous malaria is *P. vivax.* as many as 10 people. Plasmodium vivax has the unique ability to form hypnozoites , a dormant form of the parasite that hides in the liver and can remain inactive for several months, or several year before become active return. And cause relapse malaria without the presence of a new mosquito bite, which means a person was previously infected by *P. vivax* can experience malaria return without exposure new to mosquitoes that infected. This be the cause most Lots *P. vivax* to infect sufferer malaria Which

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own history previous malaria. Sufferer malaria Which Once infected Possible develop partial immunity that is more effective against P. falciparum , but the immune response to P. vivax tends to be milder, and therefore insufficient to prevent reactivation. hypnozoites , causing recurrent infections more frequently in individuals with a previous history of malaria. In some areas, the Anopheles mosquito that bring P. vivax may be more common or more adaptive in environment certain. Matter This means that in areas that mosquitoes carrying P. vivax are more common or more effective in transmitting the parasite. As a result, every person Which is at in area the will own risk more tall to recurrent malaria infections due to *Plasmodium vivax* . Adaptation of Anopheles mosquitoes to the local environment can include factors such as breeding site preferences, biting habits, and the ability to survive in certain climatic conditions, all of which can affect the extent of malaria transmission in the area and increase the likelihood of recurrent infections in the region. [16]

The results of routine blood tests on malaria patients, where the hemoglobin results obtained were normal hemoglobin levels in 33 people (76.7%) with hemoglobin levels in the range (12 g/dl – 18 g/dl), while those with anemia were 10 people (23.3%) with hemoglobin levels (<10 g/dl). This study is consistent with the findings of Junarli and Somia (2017) in Atambua , which reported that the majority of malaria patients had normal hemoglobin levels, as many as 46 people (64.8%). Anemia due to malaria happen Because process hemolysis on erythrocytes Which infected and Which not infected. This is caused by changes in the body's environment and the immune response in the form of phagocytosis erythrocytes; moment surface erythrocytes changed, cells This will destroyed by phagocytes. In addition, malaria can also cause inhibition of erythropoiesis , where the inflammatory process during malaria infection interferes with the production of new erythrocytes in the bone marrow due to the action of inflammatory cytokines such as TNF- α , interferon -γ , and IL-6. This results in a number of hemoglobin in circulation decrease , Which on Finally cause anemia which is normocytic and normochromic . Other studies have shown that hemoglobin levels decrease around 0.1 g/ dL per day before diagnosis malaria enforced, However decline this is not fully Enough For become cause anemia on part big patient malaria. [7.17]

Then inspection blood routine platelets on sufferer malaria in can Which The platelet levels were normal, namely only 7 people (16.3%) who ranged from (150,000 – 350,000 / µL) while those who experienced thrombocytopenia were 36 people (88.3%) where the platelet count was (<150,000 / µL) . This study is in line with the findings of Mulianingsih (2018) in North Penajam Paser which showed that 171 patients (84.2%) of malaria experienced thrombocytopenia . Thrombocytopenia occurs when the number of platelets in the blood decreases below the normal limit, which is less than 150,000 cells/ µl . This condition is one of the hematological disorders that is often observed besides anemia, because it can be an early sign of diagnosis. malaria And indicator prognosis Which bad, especially on infection *P. falciparum* And

P. vivax . A decrease in the number of platelets in cases of malaria can be caused by several factors, such as platelet activation . causes platelets to become active and quickly damaged, enlargement spleen (splenomegaly) Which make platelets trapped And destroyed in there, and a shorter platelet lifespan. Normally, platelets live for 7-10 days, but in malaria,

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their lifespan can be reduced to 2-3 days due to the interaction between malaria antigens and platelets, which are then destroyed by the immune system through antibody-mediated phagocytosis. In acute malaria, there is an increase in platelet-associated antibodies (PAIgG), which cause platelets to bind to parasite antigens on their surface, forming immune complexes in situ and triggering platelet destruction. In addition, macrophages also play a role in destroying platelets, with an increase in Macrophage Colony Stimulating Factor (M-CSF) that activates macrophages to destroy platelets in the liver and spleen, which causes thrombocytopenia.. [17]

On infection *P. falciparum* , erythrocytes Which infected easy attached with erythrocytes other, platelets, and capillary endothelium. This adhesion contributes to thrombocytopenia . In addition, malaria infection stimulates the liver to release hydroxyl (OH) in response to oxidative stress to fight the infection. The parasite also produces H_2O_2 and O_2 , which increases stress oxidative And cause lysis platelets Because membrane platelets cannot withstand this condition. Overall, the combination of these factors causes a decrease in the number of platelets in the blood of malaria sufferers. [17]

The number of leukocytes in malaria patients at Ibnu Sina Hospital, Makassar, was mostly found in the range normal, that is as much as 31 person (72.1%) with level leukocytes between 4,000 – 9,000 /µL. Followed by the patient who experiencing leukopenia as many as 7 people (16.3%) with leukocyte levels below 4,000/µL, and leukocytosis was only found in 5 people (11.6%) with leukocyte levels of more than 9,000/µL. These results are in line with Annisa's (2018) research at Panglima Sebaya Hospital which also found that the majority of malaria patients had normal leukocyte counts, namely 46 people (71.09%). The number of leukocytes in patients with uncomplicated malaria usually is at in range normal or A little decrease. A number of factor which influence amount leukocytes This including duration infection malaria, level parasitemia , immune system body, level severity disease, And existence infection other. Leukocytosis on Malaria patients appear as an immune system response to infection, where the body increases the production of leukocytes to fight the parasite. Malaria infection also triggers the release of pro-inflammatory cytokines that encourage the bone marrow to produce more leukocytes, causing leukocytosis.

On the other hand, leukopenia is often found in malaria patients, especially in falciparum malaria infection compared to vivax malaria . This decrease in leukocytes can be caused by increased phagocytosis of leukocytes by macrophages triggered by increased levels of TNF-α and IL-1α . In addition, a decrease in the number of leukocytes can also occur due to ineffective hemopoiesis, which is caused by increased TNF, cytokine imbalance , and macrophage dysfunction that interferes with the process of stimulation and inhibition of hemopoietic growth factors , thus affecting leukocyte production and causing leukopenia. [18,19]

The data in this study shows that there is a significant correlation between history of malaria with hemoglobin on test chi square got with mark p = 0.020. Seen In table 4, there was only 1 malaria patient who experienced anemia with a previous history of malaria, while there were 9 malaria patients who experienced anemia with no previous history of malaria out of 43 samples of malaria patients.

In the first malaria infection, the body faces significant stress because it does not yet

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have adaptive immunity to the malaria parasite. Plasmodium parasites infect and destroy red blood cells, which can cause acute anemia. In addition, in the first infection, individuals may experience higher levels of parasitemia due to the lack of developed immunity. This hyperparasitism increases red blood cell destruction. The body's immune response to malaria infection involves the release of inflammatory cytokines such as TNF- α and IFN- γ , which interfere with red blood cell production in the bone marrow and shorten the life span of erythrocytes, contributing to anemia. More specific mechanisms include direct intravascular hemolysis due to the rupture of erythrocytes infected, as well as extravascular hemolysis through phagocytosis of infected red blood cells by macrophages in the spleen. Furthermore, pro-inflammatory cytokines can cause endothelial dysfunction and increase capillary permeability, which can worsen hemolysis and lead to further red blood cell loss. The combination of this hemolysis and impaired red blood cell production results in a significant decrease in hemoglobin in the first malaria infection. [20]

Individuals who have a history of malaria previously may have developed partial immunity to the malaria parasite. This immunity allows the body to control the level of parasitemia , thereby reducing red blood cell destruction. The body may have adapted to reduce the impact of repeated infections by increasing production cell blood red And repair mechanism Which reduce hemolysis. Cell B and memory T cells formed during previous infections can recognize and respond to parasites more quickly, thereby reducing the severity of the infection and red blood cell damage. Memory B cells produce antibodies that specifically recognize parasite antigens, which accelerates the elimination of parasites from the bloodstream. Memory T cells, especially cytotoxic T cells, are able to kill infected red blood cells before the parasites have a chance to multiply further. In recurrent infections, the body is more efficient in maintaining hemoglobin production thanks to a faster and more effective immune response. Hematopoietic mechanisms in the bone marrow can also be optimized to increase the production of new red blood cells. In addition, anti-inflammatory cytokines such as IL-10 help suppress the response inflammation excessive, with thus prevent damage more carry on on cell red blood and other body tissues. With this combination of adaptations, individuals with a history of malaria tend experience anemia Which more light or even No experience anemia compared to individuals who were newly infected. [19,20]

The data in this study shows that there is a significant correlation between history of malaria with hemoglobin on test chi square got with mark p = 0.010. Seen on the table 5 sufferer malaria Which experience thrombocytopenia with have history Previously, there were only 12 malaria sufferers, while malaria sufferers experienced thrombocytopenia with No There is history malaria previously there is as much as 24 person from 43 samples of malaria sufferers.

On infection malaria First time, body Not yet own immunity adaptive to malaria parasites, so that the body's immune response is rapid and aggressive, causing activation and consumption platelets Which excessive, Which end on thrombocytopenia . On individual those first infected with malaria, parasitemia levels may be higher due to lack of immunity, Which known as hyperparasitism , Which increase consumption platelets and interfere with platelet production in the bone marrow. The body's immune response to malaria infection

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also involves the release of inflammatory cytokines such as TNF- α and IFN- γ , which can cause endothelial dysfunction and increase capillary permeability, further exacerbating platelet consumption. During malaria infection, dendritic cells activate T cells through presentation antigens, cause proliferation And activation cell T helper (Th1). Cell Th1 then releases IFN- γ , which enhances phagocytosis by macrophages and induces the production of nitric oxide, a substance that is toxic to parasites but also damages endothelial cells and platelets. In addition, NK (Natural Killer) cells are also activated and release cytokines such as TNF- α , which exacerbate tissue damage and platelet consumption. The combination of these mechanisms leads to thrombocytopenia that significant in patients who experience malaria for the first time. [21]

In a second or subsequent infection, this trained adaptive immune system is able to control the infection more efficiently, thereby reducing excessive inflammation and activation. platelets Which No need, that can cause thrombocytopenia . Antibody produced during previous infection recognize and bind parasites rapidly, facilitating phagocytosis by macrophages and other immune cells, helping to reduce the number of parasites in the blood and reducing excessive platelet activation . Overall, the process development immunity adaptive Which involving activation And formation cell T and B memory and specific antibody production are very important in minimizing the occurrence of thrombocytopenia in malaria reinfection. [23]

Discussion connection leukocytes on sufferer malaria with sufferer Which have a previous history of malaria.

Based on Chi-square correlation test , p value = 0.553, indicates that there is no significant correlation between malaria history and leukocyte count in malaria patients. As seen in table 6, malaria patients who experience leukocytosis have... history malaria previously there is 3 person Which experience leukocytosis with no There is history malaria previously only 2 person, then Which experience leukopenia with have history malaria previously there is 2 person Which experience leukocytosis with And Which No There is history malaria previously 5 person person , with total sample 43 malaria sufferers.

Overall, differences in leukocyte responses to recurrent malaria infections are due to a combination of immunological, genetic, environmental factors, and specific characteristics of the infection itself. Not only because of previous infection, but also because of other factors that may reduce the likelihood of abnormal leukocyte changes. When somebody infected with malaria for the first time, the body develops an adaptive immune response. Memory T and B cells produced during the first infection can recognize And respond infection repeat with more fast And efficient, Which can reducing the need for a large inflammatory immune response, thereby reducing the likelihood of leukocytosis or normal leukocyte levels. The research by Tran et al. (2014) found that individuals who are frequently exposed to malaria in endemic areas develop partial immunity that can reduce the severity of reinfection and less virulent strains may not trigger an excessive leukocyte response because the adaptive immune system is ready to respond efficiently. [23,24]

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CONCLUSION

Based on the results of the study, it was found that of the 43 malaria patients studied, the majority were aged 21-30 years and dominated by men, with the most common type of plasmodium being Plasmodium vivax , especially in patients without a history of previous malaria. Routine blood tests showed that most patients had normal hemoglobin levels (76.70%), experienced thrombocytopenia (83.70%), and normal leukocyte levels (72.10%). In addition, there was a significant relationship between hemoglobin and platelet levels with malaria history status, while leukocyte levels did not show a significant relationship with malaria history.

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