

Correlation between parasitemia and spleen size in patients with *P. falciparum* infection

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ABSTRACT

Background Spleen is an important organ in immunity to malaria infection which is always affected in malaria patients. Enlargement of the spleen is one of the main clinical symptoms of malaria. Level of parasitemia is related to the risk of complications.

Objective To describe the correlation between parasitemia and spleen size in patients with *P.falciparum* infection.

Methods One hundred and four patients including children and adults with fever, pale, jaundice, diarrhea, and headache who visited public health centers in 5 villages in Mandailing Natal, North Sumatera were enrolled in this study. The diagnosis of malaria was based on blood smears stained by Giemsa method, while the spleen size was measured using Hackett method. Correlation between parasitemia and spleen size was tested by Spearman rank correlation.

Results Splenomegaly was found in 37 of 104 patients (35.6 %) with the size of H1 in 10.6 %, H2 in 15.4 %, H3 in 9.6 %. The mean parasite count between patients with and without splenomegaly was different, and the difference was significant between patients with spleen size of H0 and H3. The higher the parasitemia, the bigger the spleen size was ($r=0.291$; $p=0.03$).

Conclusion There was a correlation between parasitemia and spleen size in falciparum malarial infection [Paediatr Indones 2004;44:111-116].

Keywords: parasitemia, splenomegaly, falciparum malaria.

Malaria is still a public health problem in many countries, including in Indonesia. The symptoms are fever, shivering, anemia, jaundice, and hepatosplenomegaly.^{1,2} Diagnosis of malaria is established by the finding of malarial parasites in the blood. For the time being, the diagnosis is carried out by means of the conventional method using Giemsa staining of blood smears, either thick or thin. A thick

blood smear is made for detecting and counting the parasites, whereas a thin blood smear for identifying the species.³ The degree of parasitemia is useful as a prognostic factor. Parasites in blood of more than 100,000/microliter are associated with severe infection.^{4,5} Detectable parasitemia in immunocompromised patients causes significant symptoms, and the magnitude of parasitemia is related to the risk of death or complications.⁶

Spleen has an important role in defense mechanism against malarial infection. As the body's largest lymphoid organ, the spleen has a variety of immunologic functions including as a sieve for the blood removing blood cells, microorganisms, and immune complexes.⁷ The spleen is always affected in patients suffering from malaria; a palpable spleen is one of the main clinical symptoms. History of fever, anemia, and splenomegaly are predicting symptoms for clinical diagnosis of malarial infection in endemic areas.⁴ The purpose of this study was to describe the correlation between parasitemia and spleen size in patients with *P. falciparum* infection.

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Methods

A cross-sectional study was conducted in 5 villages in Mandailing Natal, North Sumatera, during the period of April 9th to 19th, 2001. Subjects were selected through a simple random sampling method. Sample size calculation using a formula⁸ revealed a sample size of 96 (95%CI, 0.5 proportion of falciparum malarial patients, 0.1 bound of error). Studied participants were all children and adults who visited the public health centers with complaints of fever, pale, diarrhea, headache, and jaundice. Patients who had antimalarial drugs one week before the study were excluded. Informed consent was obtained from the patients or their parents before study. This study was approved by the institutional review board of Adam Malik Hospital, North Sumatera.

A blood examination for counting the parasites was performed by taking a drop of blood sample from the finger or toe of the subjects to make thick and thin blood smears. Both thick and thin blood smears were prepared in a same film slide. Thick blood smears were directly stained using Giemsa method for 20 minutes, while thin blood smears were initially fixed with methyl alcohol for a few seconds and then stained for 30 minutes. Subsequently, clean water was poured

on the surface of stained films for 10–15 seconds and then the films were dried. The slide was examined under an ordinary light microscope. The result was considered negative when malarial parasite was not found in the blood smear, and positive if there was any. Parasite count per microliter of blood was defined as the number of malarial parasites found in every 100 white blood cells in the blood smear and multiplied by 80.⁴ Spleen enlargement was measured using Hackett method and classified as Hackett (H) 0–5 (Table 1).⁴

TABLE 1. SPLEEN SIZE BY HACKETT METHOD

H0	Normal spleen, not palpable even in deep inspiration
H1	Spleen was palpable below the costal margin, usually on deep inspiration.
H2	Spleen was palpable below the costal margin, but not projected beyond a horizontal line half way between the costal margin and the umbilicus measured along a line dropped vertically from the left nipple.
H3	Spleen with lowest palpable point projected more than half way to the umbilicus but not below a line drawn horizontally through it.
H4	Spleen with lowest palpable point below the umbilical level but not projected beyond a horizontal line situated half way between the umbilicus and the symphysis pubis.
H5	Spleen with the lowest point palpable beyond the lower limit of class 4.

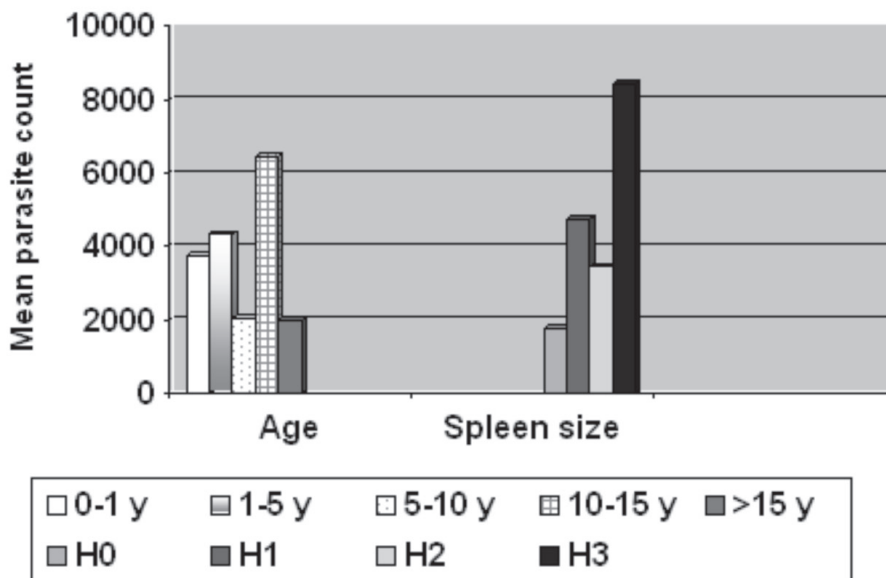


Figure 1. Mean parasite count according to age group and spleen size

Statistical analysis was conducted using a computer program (SPSS version 10.5). The correlation between parasitemia and spleen size was assessed by Spearman rank correlation. Differences were considered as statistically significant if p was <0.05.

Results

One hundred and four patients, including children and adults with fever, pale, jaundice, diarrhea, and headache, were enrolled during the study period. There were 46 (44.2 %) males and 58 (55.8 %) females. The most affected age group was adults and children more than 15 years old (41.3%), followed by children >5-10 years (23.1%), >1-5 years (19.2%), 10-15 years (9.6%), and <1 year (6.8 %).

Table 2 shows the clinical findings of malarial patients. The most frequent clinical symptoms were fever (98.1%), headache (75 %), pale (62.3 %), diarrhea (28.8%), and jaundice (7.7%). Thirty seven patients (35.6%) had splenomegaly, 64.4 % of H0, 10.6 % H1, 15.4 % H2, and 9.6 % H3. No splenomegaly of H4 and H5 were found. Most splenomegaly were found in the age group of 5-10 years old (11 patients). **Table 3** presents the distribution of spleen size according to the age groups.

Figure 1 shows the mean parasite count according to age group and spleen size. Although the highest mean of parasite count was in the age group of 10–15 years, statistical analysis showed no significant difference among the age groups. The mean parasite count in patients with splenomegaly was higher than those without splenomegaly. There were differences in the means of parasite count between H0, H1, H2, and H3. The difference was significant between H0 and H3.

TABLE 2. CLINICAL FINDINGS IN MALARIAL PATIENTS

Clinical findings	Total	
	n	%
Symptoms		
Fever	102	98.1
Pale	69	66.3
Jaundice	8	7.7
Diarrhea	30	28.8
Headache	78	75.0
Physical examination		
Fever	101	97.1
Pale	71	68.3
Icterus	6	5.8
Splenomegaly	37	35.6
H0	67	64.4
H1	11	10.6
H2	16	15.4
H3	10	9.6
H4	0	0
H5	0	0
Hepatomegaly	11	10.6

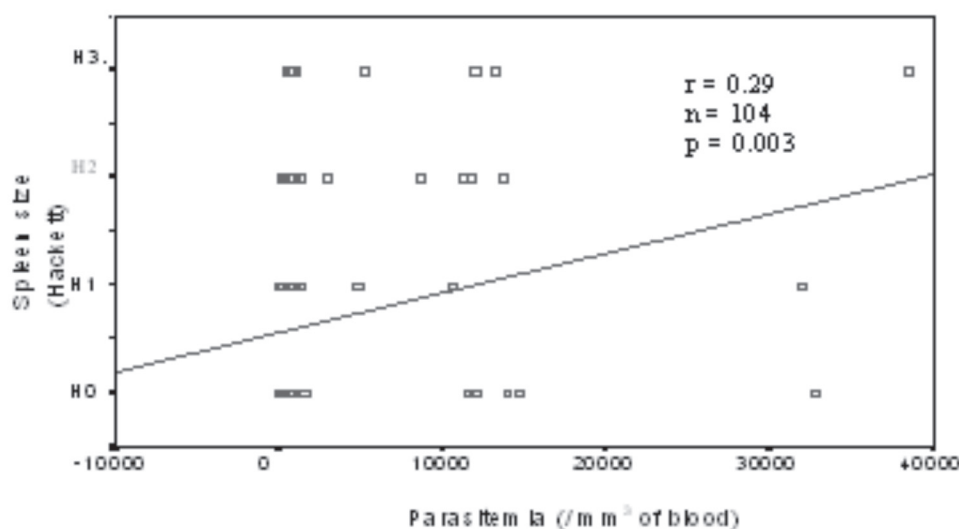


Figure 2. The correlation between parasitemia and spleen size in falciparum malarial patients.

TABLE 3. DISTRIBUTION OF SPLEEN SIZE ACCORDING TO AGE

Age	Spleen size								Total	
	Ho		H1		H2		H3			
	n	%	n	%	n	%	n	%	n	%
0–1 years	4	3.9	2	1.9	1	1.0	0	0	7	6.8
>1–5 years	10	9.6	2	1.9	2	1.9	6	5.8	20	19.2
>5–10 years	13	12.5	3	2.9	7	6.7	1	1	24	23.1
>10–15 years	6	5.8	2	2.9	3	1.9	0	0	10	9.6
>15 years	34	32.7	2	2.9	4	3.8	3	2.9	43	41.3
Total	67	64.4	11	10.6	16	15.4	10	9.6	104	100

Figure 2 shows the correlation between parasitemia and spleen size in falciparum malarial patients. Increase in spleen size was parallel with increase in level of parasitemia with a weak correlation coefficient ($r=0.291$). This result was statistically significant with a p value of 0.003.

Discussion

This study found that the most age group that suffered from malaria was >15 years of age. This was in accordance with other studies conducted in Nias⁹ and Aceh Langsa Hospital.^{9,10} Our study revealed females were affected more than males, but Albar in Ternate,¹¹ found that males were affected more than females. This distinction might be influenced more by the composition of gender for each population rather by other factors.

In the present study, malaria was uncommon among infants (<1 year). This finding is supported by Lubis.¹⁰ In endemic areas where transmission occurs severely throughout the year, infection among infants is uncommon since there were transplacental antibodies from mothers. The existence of fetal hemoglobin (HbF) in infants is also the reason of protective effect against parasite's growth.⁷ The mechanism of this protective effect is still unclear. It is probably associated with the oxygen content, intercellular acidity and rigidity of the cellular membrane, which are different from adult hemoglobin (HbA).^{4,7}

We found that the most common symptoms in this study were fever, headache, and pale. Fever is the most common symptom in malaria, and presumably it is associated with pyrogens such as TNF, IL-1, and IL-6.¹² Jacobsen reported that the level of TNF was higher in symptomatic malarial patients compared with that of asymptomatic patients, and this TNF level was correlated with the

level of parasitemia and body temperature.¹³ In this study, we did not measure the level of this cytokine.

In endemic areas, children aged 1–5 year-old are in a high risk period of having malarial infection due to the absence of the immunity. Infection in children older than 5 years is usually mild and will be asymptomatic in adults. Prolonged exposure to malaria results in the development of antibodies, therefore the immunity is increased by time.^{14,7} We found that there was no significant difference in mean parasite count/mm³ blood among the age groups in this study (**Figure 1**). To our knowledge, there had been no study about the correlation between age and level of parasitemia.

In the case of parasite count above 10%, exchange transfusion may be beneficial. It can reduce parasitemia more rapidly and in addition, it can restore red cell mass, platelets, clotting factors, albumin, as well as remove the harmful toxins. However the procedure may still be in trial for patients who are severely ill, did not respond adequately to antimalarial therapy especially newer drugs such as artemisin, and had parasite count of more than 10%.¹ In this study the parasite count was not more than 2%.

Hepatomegaly was found in 10.6% of subjects, while splenomegaly was found in 35.6%. This finding was supported by the study of Annobil *et al.*¹⁵ Hepatomegaly occurs early in malaria and usually can be palpable in the first week after the onset. Hepatic sinusoids are dilated and show hypertrophy of Kupffer cells.¹² Liver is an alternative organ besides the spleen as a place for eliminating the parasitized red cells.¹⁶

We found splenomegaly in 37 (35.6 %) patients. This result was smaller than that of other study which found splenomegaly in 45% to 75% of patients.^{10,15,17} Spleen enlargement in malaria is related to the lysis of

red blood cells that are infected by merozoite. There are edemas of the pulps and lymphoid and reticuloendothelial hyperplasia with the increase of hemolytic and phagocytic functions of the organ.¹² In this study, splenomegaly was found predominantly in children under 10 years of age. This finding was supported by the result of Sutanto's study.¹⁸ Rita Marletta in Nias found splenomegaly predominantly in the age of 5–11 year-old.⁹ Splenomegaly is common in children aged 1–10 years where the immune response is performed.⁴

Considering the fact that Indonesia is a tropic country and Mandailing Natal is an endemic area, we were not able to conclude whether splenomegaly in our patients could be included as a *tropical splenomegaly syndrome* or not since the highest spleen size in this study was only of Hackett 3 and we did not examine the level of IgG and IgM.^{19,20}

Total parasitemia is associated with prognosis of patients. Parasite count more than 100,000 per microliter blood indicates severe infection and bad prognosis. This study was conducted to compare parasite counts for each degree of spleen size in patients with malaria. We found that the highest spleen size was Hackett 3. The comparison of mean parasite counts for each degree of spleen size showed that mean parasite counts in subjects with or without splenomegaly (H0 vs. H1, H2, and H3) were different. Differences were also found among different degrees of splenomegaly (H1, H2, H3). The most significant difference was found between the groups of H0 and H3 (**Figure 1**).

In conclusion, our findings showed the correlation between parasitemia and the degree of spleen size. The higher the parasite count, the bigger the spleen size is. In endemic areas, we can use these findings to predict patients with high parasitemia and prevent development into severe complications.

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