Association of thrombocytopenia with splenomegaly in malaria patients in East Kalimantan: A cross-sectional, retrospective study [version 1; referees: awaiting peer review]

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Abstract

Background: Malaria still presents as a major health problem in Indonesia and specifically in East Kalimantan. One common finding in malaria is thrombocytopenia, the mechanism of which is still unclear. Several studies have suggested some mechanisms, one of which is splenomegaly. This study aimed to discover the association between thrombocytopenia and splenomegaly of malaria patients in East Kalimantan.

Methods: This study was a descriptive retrospective study with clinical and laboratory data obtained from the medical records of malaria patients in four major public hospitals from January 2015 to July 2018. The association between thrombocytopenia with splenomegaly was analysed using Chi-Square test.

Results: A total of 215 patients were included; 189 male (87.9%) and 26 female (12.1%). The most common aetiology were Plasmodium vivax (43.2%), P. falciparum (42.8%), and mixed infection (P. falciparum and P. vivax) (4.6%). The distribution of thrombocyte count were normal in 28 patients (13%) and decreased in 187 patients (87%). Among patients with thrombocytopenia, the percentage of mild, moderate and severe thrombocytopenia was 18.2%, 43.8% and 33%, respectively. Splenomegaly was found in only 11 patients (5.1%). We found no association between thrombocytopenia with splenomegaly (p=0.61).

Conclusions: We conclude that thrombocytopenia is not associated with splenomegaly in these malaria patients.

Keywords
thrombocytopenia, splenomegaly, malaria, East Kalimantan
This article is included in the ICTROPS 2018 collection.

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Author roles: Siagian LRD: Conceptualization, Funding Acquisition, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing;
Lumbantoruan VM: Data Curation, Writing – Review & Editing; Hasanah N: Data Curation, Writing – Original Draft Preparation; Sihotang FA: Data Curation, Writing – Original Draft Preparation, Writing – Review & Editing; Gunawan C: Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The Islamic Development Bank funded this study.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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How to cite this article: Siagian LRD, Lumbantaruan VM, Hasanah N et al. Association of thrombocytopenia with splenomegaly in malaria patients in East Kalimantan: A cross-sectional, retrospective study [version 1; referees: awaiting peer review] F1000Research 2018, 7:1832 (https://doi.org/10.12688/f1000research.16606.1)

First published: 21 Nov 2018, 7:1832 (https://doi.org/10.12688/f1000research.16606.1)
Introduction
Malaria is still a serious health problem in Indonesia, with the prevalence of malaria in Indonesia increased from 2.5% to 6.0%.

Data from the East Kalimantan Provincial Health Office showed that there were 7,045 cases of malaria in 2010. This number fluctuated in the following years, with 3,021 cases in 2011, 9,966 cases in 2012 and 2,603 cases in 2013. In terms of Annual Parasite Incidence (API), in 2014 East Kalimantan was still above the national average with an API of 2.04 per 1000 population, leading to it being categorized as a low cumulative incidence area.

One common finding in malaria is decreased platelet count or so-called thrombocytopenia. This laboratory finding is often confused with other infectious diseases, especially dengue infection in which thrombocytopenia is a major diagnostic parameter. There are many studies that demonstrate thrombocytopenia in malaria patients, and this is found in both infection with Plasmodium falciparum and Plasmodium vivax. The results from our previous study demonstrated that from [104] patients in East Kalimantan, 5% presented with thrombocytopenia of varying degrees. Therefore, thrombocytopenia in malaria has been suggested as one important diagnostic parameter in malaria. The mechanism of thrombocytopenia in malaria is still unclear. Several theories, such as mechanical trapping of thrombocytes inside the spleen and immune response that attacks thrombocytes, has been proposed. A study by Coelho et al. found that platelet phagocytosis may contribute to thrombocytopenia in vivax malaria.

Splenomegaly is also one common clinical finding in malaria patients. The spleen is part of the reticuloendothelial system, which becomes active in order to get rid of Plasmodium infected erythrocytes. Splenomegaly can also contribute to increased destruction of thrombocytes due to mechanical trapping. Therefore, the aim of this present study was to determine the association of thrombocytopenia with splenomegaly in malaria patients in East Kalimantan.

Methods
Study design and participants
This study was a cross-sectional retrospective study. This study was approved by the Ethical Committee for Health Research at Abdul Wahab Syahranie Hospital Samarinda, East Kalimantan (approval number 124/KEPK/AWS/V/2018). This ethical approval also covers the research conducted at all hospitals included in our study. Patient consent for the use of their data records was waived by the ethical committee due to the retrospective nature of the study.

Data collection
Data were collected between June and August 2018 from the medical records of patients with malaria during the period of January 2015 to July 2018. Clinical and laboratory data of both outpatients and inpatients diagnosed with malaria from four major hospitals in East Kalimantan were collected. These hospitals were: Abdul Wahab Syahranie Hospital in Samarinda, Aji Putri Botung Hospital in Penajam Paser Utara, Abdul Rivai Hospital in Tanjung Redeb and Panglima Sebaya Hospital in Tanah Grogot.

All patients with malaria, both paediatric and adult patients, were included in the study. Patients were excluded from the study if the necessary data were incomplete or patients discharged themselves during treatment.

In order to collect data, first, the hospital’s database was searched for patients diagnosed with malaria. Second, after identifying these patients, the relevant medical records were retrieved which contained age, gender, type of Plasmodium, thrombocyte count and presence of splenomegaly.

Discussion
We found that the incidence of malaria was higher in males than females in this group of patients, and the parasite infecting the majority of patients was Plasmodium vivax (42.0%). This study found that thrombocytopenia affected the majority of malaria patients; thrombocytopenia occurred in 87.8% of patients, with moderate thrombocytopenia (43.8%) as the majority. This result is in concordance with another study by Arif et al. in India, that found that 79% of patients had moderate thrombocytopenia, while Ansari et al. found 69.18%. In the present study, the degree of thrombocytopenia classified to mild, moderate and severe was 18.2%, 43.8%, 33.0%, respectively. If we compare to study of Arif et al. that found 33.96%, 51.15% and 14.89%, respectively, we find that...
patients had splenomegaly, but there are no information about thrombocyte count in those malaria patients with splenomegaly.

In our study, we describe the thrombocyte count in malaria patients with splenomegaly. We found that there was no association between thrombocytopenia with splenomegaly ($p=0.611$). Therefore, we propose that thrombocytopenia is not caused by the mechanical trapping of thrombocytes in the spleen. This result suggests another mechanism of thrombocytopenia that involves immune process, as proposed by Coelhoe et al. in 2013. Until now, the definitive mechanism of thrombocytopenia in malaria was unclear; however, some factors that contribute to thrombocytopenia have been reported, such as decreased thrombopoiesis, peripheral destruction induced by *P. falciparum* and disseminated intravascular coagulation.

This study has its limitations. Different types of automatic haematology analysers were used in the hospitals and this might contribute to variations in thrombocyte count. Therefore, we suggest the use of a single haematology analyser across hospitals to improve accuracy. In addition, we did not exclude other causes of thrombocytopenia that could coexist with malaria infection, such as viral infection and autoimmune diseases, which would be required to further validate our findings. Finally, the examination of splenomegaly was conducted by different physicians, which might contribute to subjective factors in determining splenomegaly, such as physician’s expertise and thoroughness, especially in cases with minor or subclinical splenomegaly.

Overall, we conclude that thrombocytopenia is not associated with splenomegaly in this set of malaria patients.

### Data availability

F1000Research: Dataset 1. Data retrieved from the medical records of malaria patients in East Kalimantan, Indonesia, including age, gender, type of *Plasmodium*, thrombocyte count, and presence of splenomegaly. [https://doi.org/10.5256/f1000research.16606.d22512](https://doi.org/10.5256/f1000research.16606.d22512).

### Grant information

The Islamic Development Bank funded this study.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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### References


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