Asian Journal of Medicine and Health

15(3): 1-6, 2019; Article no.AJMAH.50309
ISSN: 2456-8414

Platelet Alteration in *Plasmodium vivax* Malaria Patients in Thailand

Mohammand Sami Hayat[1], Polrat Wilairatana[1*], Noppadon Tangpukdee[1], Srivicha Krudsood[2], Nalinrat Wilairat[3], Pichayapat Wilairat[3] and Pimjira Thebpatipat[4]

[1]Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.
[2]Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.
[3]Faculty of Education, Chulalongkorn University, Bangkok, Thailand.
[4]Faculty of Medicine, Thammasat University, Pathum Thani, Thailand.

Authors' contributions

This work was carried out in collaboration among all authors. Authors MSH and PW designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors SK, NT, NW and PW analyzed the study. Author MSH performed the statistical analysis and managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2019/v15i330125
Editor(s):
(1) Prof. Darko Nozic, University of Belgrade, Serbia.
Reviewers:
(1) Ahmed Tabbabi, Jichi Medical University, Japan.
(2) Abdu Umar, Usmanu Danfodiyo University, Nigeria.
(3) Franco Cervellati, University of Ferrara, Italy.
Complete Peer review History: http://www.sdiarticle3.com/review-history/50309

Original Research Article

Received 14 May 2019
Accepted 24 July 2019
Published 01 August 2019

ABSTRACT

Introduction: Malaria remains a global health problem. Malaria is often linked to thrombocytopenia as well as other hematological variations.
Objective: The aim of this study is to find the platelet changes in *Plasmodium vivax* malaria patients. This retrospective cross-sectional study included 204 malaria patients admitted to the Hospital for Tropical Diseases, Bangkok, Thailand.
Results: Thrombocytopenia (<150x10^3/µl) was seen in 170(83.3%) patients with a mean (SD) of 101x10^3/µl (56.5). Mild (150x10^3/µl-50x10^3/µl), moderate (50x10^3/µl-20x10^3/µl) and severe (<20x10^3/µl) thrombocytopenia were seen in 141 (69.1%), 25 (12.2%) and 4 (2%) patients

**Corresponding author: E-mail: polrat.wil@mahidol.ac.th;*

respectively. None of these patients with thrombocytopenia showed any sign of bleeding or required platelet transfusion.

Conclusion: This study showed thrombocytopenia as a classic feature of vivax malaria presenting more than 80% of cases. In patients with profoundly low thrombocyte counts there was no manifestation of bleeding nor was any platelet transfusion required.

Keywords: Malaria; Vivax; platelet; thrombocytopenia; Thailand.

1. INTRODUCTION

In 2017, an estimated 219 million cases of malaria occurred worldwide (95% confidence interval [CI]: 203–262 million), compared with 239 million cases in 2010 (95% CI: 219–285 million) and 217 million cases in 2016 (95% CI: 200–259 million). Most malaria cases in 2017 were in the WHO African Region (200 million or 92%), followed by the WHO South-East Asia Region with 5% of the cases and the WHO Eastern Mediterranean Region with 2%. The incidence rate of malaria declined globally between 2010 and 2017, from 72 to 59 cases per 1,000 population at risk. Although *Plasmodium falciparum* is the most prevalent malaria parasite in the WHO African Region, accounting for 99.7% of estimated malaria cases in 2017, *P. vivax* was reported in many areas: South-East Asia (37.2%), the Eastern Mediterranean (31%) and the Western Pacific (28.1%). *P. vivax* is the predominant parasite in the WHO Region of the Americas, representing 74.1% of malaria cases [1]. *P. vivax* infections affect people of all ages. Although the effects of repeated attacks of *P. vivax* through childhood and adult life are only rarely directly lethal, they can have major deleterious effects on personal well-being, growth, development and the economic performance at the individual, family and community. With invention of molecular diagnosis, it is now evident that *P. vivax* mono-infection could be involved in multiple organ dysfunction and severe life threatening disease as seen in *P. falciparum*. Severe *P. vivax* cases have been reported from several countries including India and Thailand [2]. Thrombocytopenia has been studied in malaria previously but its prognostic value in context of low platelet count with clinical presentation has not been evaluated in large studies.

The aims of this study were to evaluate frequency and severity of thrombocytopenia exclusively in *P. vivax* patients. We also determined if laboratory values of severe thrombocytopenia corresponded to clinical severity in vivax malaria patients.

2. MATERIALS AND METHODS

This study was a retrospective cross-sectional study. Two hundred and four patients admitted to the Hospital for Tropical Diseases, Bangkok, Thailand from 2008 to 2012 were collected from medical records of the patients. For data collection we prepared case record forms and collected data of patients' records. The admitted patients had history of fever and other associated symptoms with positive blood films for vivax malaria. Inclusion criteria included in-patients with complete medical records of twenty-eight days, age ≥ 15 years, patients with confirmative diagnosis of *Plasmodium vivax* malaria nono-infection with thick or thin blood film by light microscopy. Exclusion criteria were patients with non-*P. vivax* or mixed infection, pregnant and lactating women or co-infections (with leptospirosis, scrub typus, dengue or melioidosis). Duration of the study was from October 2012 to April 2013. Data collection took place at the Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. The cut off point for thrombocytopenia was considered as platelet count less than 150,000/µl. According to previous articles the low thrombocyte count classification for mild, moderate and severe were considered as following [3]:

a. Mild thrombocytopenia: - having platelet counts between 50-150×10^3 cells/µl

b. Moderate thrombocytopenia: - having platelet counts between 20-50×10^3 cells/µl

c. Severe thrombocytopenia: - having platelet counts less than 20×10^3 cells/µl

Demographic data, clinical symptoms, physical examinations, baseline laboratory tests such as complete blood count and biochemistry profiles were collected. Information obtained from the patients' records were analyzed. Statistical Package for the Social Science (SPSS) version 15 software was used for statistical analysis. The

distribution of data was assessed for normality using the Kolmogorov-Simrnov test. Data were expressed as means and standard deviations (SD) if the data showed normal distribution. If the data did not show any normal distribution, the results were expressed as medians. Descriptive statistics were used for most of the data. For analytical part, non-parametric statistical tests such as Chi-square and Spearman's correlation tests were used. Microsoft Excel was used for descriptive statistics and graphic demonstration. The P-value was set at significance level of 0.05.

3. RESULTS

We included 204 vivax malaria patients. The male predominance in number was observed. 201 (98.5%) among 204 were males and 3 (1.5%) were females. Male comprised large number of patients with vivax malaria This indicated that majority of patients diagnosed and treated in this hospital for vivax malaria were male patients. The age of patients varied from 15 years to 60 with a mean (SD) of 26 (8.4). Patients regarding their age were classified to three subcategories of 15-30 years old, 31-45 years old, 45-60 years old and the number of patients in each category was 155 (76%), 42 (20.6%) and 7 (3.4%) respectively. This indicates the highest number of patients were between age 15 to 30 years. The frequency of some common symptoms reported by patients in our study were fever in 204 (100%) patients, headache in 172 (84%) patients, myalgia in 161 (78.9%), chill in 154 (75.5%), nausea in 39 (19.1%), abdominal pain in 35 (17.2%), vomiting in 29 (14.2%), arthralgia in 14 (6.9%) and cough in 1 (0.5%) patient. Others were myalgia in 161 (78.9%), nausea in 39 (19.1%) and abdominal pain in 35 (17.2%) patients respectively. Anemia, hepatomegaly, splenomegaly and jaundice were found in 98 (48%), 68 (33.3%), 40 (19.6%) and 19 (9.3%) respectively.

Using statistical program for further analyses we looked for correlation between platelet count and hematologic profile Tables 1 and 2; Figs. 1 & 2 of the patients. The result of our analyses showed significant correlation between platelet counts and some components of hematologic profiles in the patients. Hemoglobin changes were not seen to have any significant correlation with platelet changes with P=0.327 which was not significant. Similarly, hematocrit changes did not show any significant correlation with platelet count. Moving further to white blood cells (WBC), we found there was a significant statistical correlation with P<0.001 between WBC count and platelet count in vivax malaria patients. There was a strong positive correlation between platelet count and eosinophil count with P<0.001, on the contrary, a negative correlation between neutrophil count and platelet count was observed with P<0.005. Basophil count showed no correlation but monocyte count also showed a positive correlation with P<0.002 with the platelet count.

Correlation values between platelet count and biochemistry profiles in patients were evaluated. For the electrolytes, only sodium displayed a strong positive correlation with P<0.001, the other components of electrolytes including potassium, chlorine and bicarbonate showed no significant correlation with platelets. For the liver function tests, direct and total bilirubin levels were both showing a strong negative correlation with P<0.001. The negative correlation meaned that platelet drop was associated with rise of bilirubin values in vivax malaria patients. Unlike bilirubin, serum protein and serum albumin showed a strong positive correlation with platelet changes in malaria patients.

Table 1. Hematological profiles of the patients (N=204)

Parameter	Spearman's correlation of platelet count	P-value
Hemoglobin	-0.069	0.327
Hematocrit	-0.073	0.303
WBC	0.239	0.001
Neutrophils	-0.197	0.005
Lymphocytes	0.059	0.401
Eosinophils	0.386	<0.001
Basophils	0.063	0.374
Monocytes	0.215	0.002

WBC = white blood cells

Chi-square test showed association between clinical features and platelet status in the patients. From symptoms table we independently checked fever, chills, myalgia, arthralgia, nausea, abdominal pain, vomiting and cough with platelets to find if there was any correlation between them. No significant correlation was observed between symptoms with platelet count. Association of patients' clinical conditions including anemia, jaundice, hepatomegaly, and splenomegaly with platelet status showed no significant correlation with platelet count.

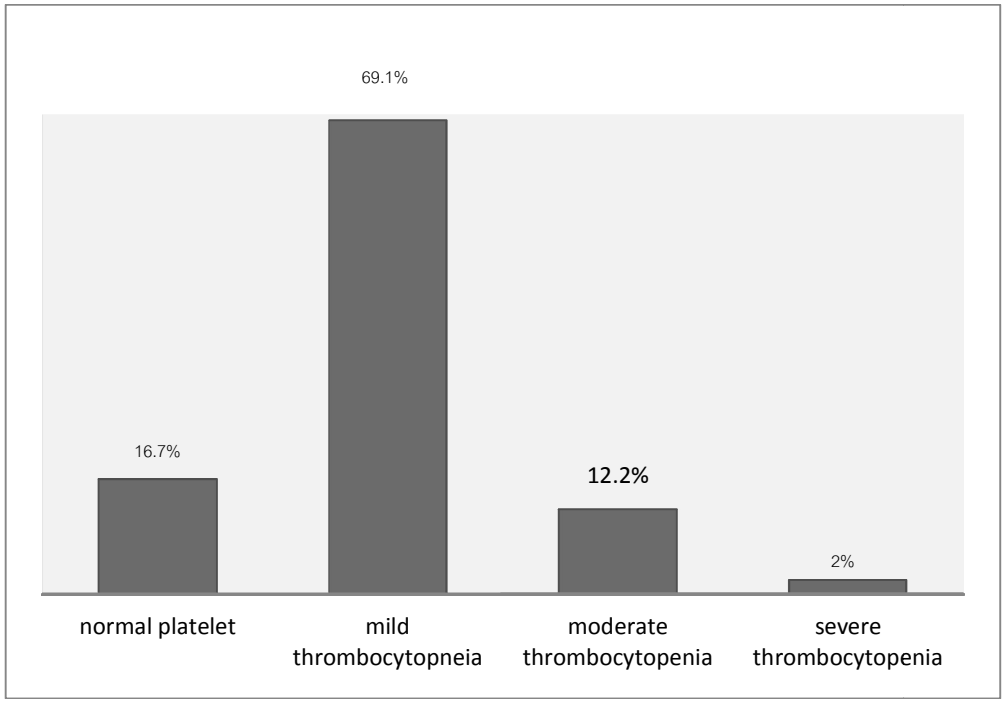

Fig. 1. Platelet levels regarding to severity in *vivax* malaria patients

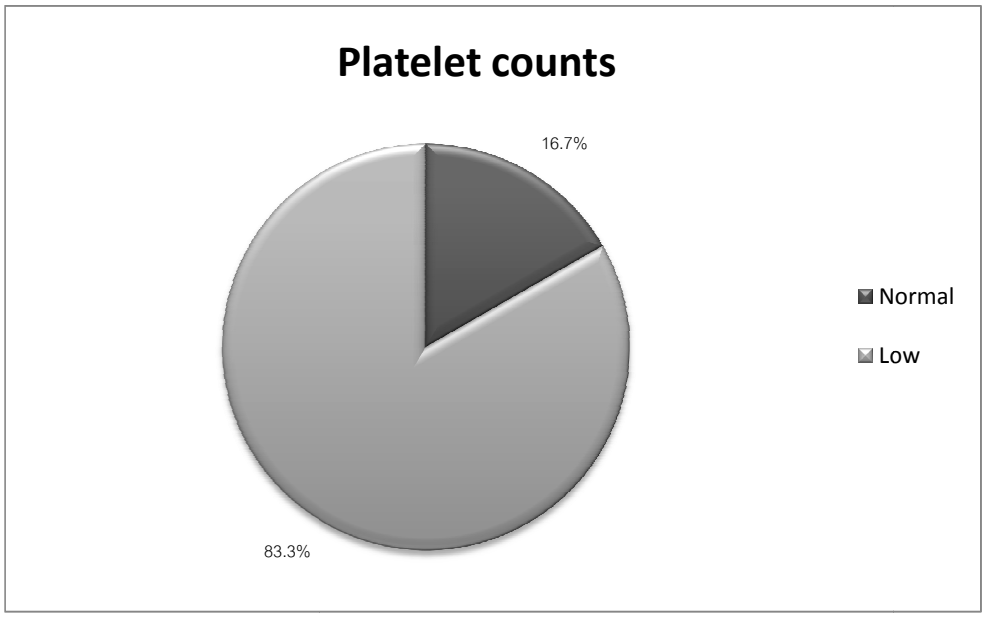

Fig. 2. Normal and low platelet counts in *vivax* malaria patients (N=204)

4. DISCUSSION

To evaluate frequency and severity of thrombocytopenia in vivax malaria patients, the range for normal platelet was considered as platelet count of 300,000±150,000/µl. In this study, platelet count varied among patients, ranging from 14,000/µl to 357,000/µl with a mean of 101,000/µl. We later classified thrombocytopenia to three categories of mild, moderate and severe groups. The normal platelet count was seen in 34 (16.7%) patients.

Thrombocytopenia was seen in 170 (83.3%) patients. Mild thrombocytopenia was observed in 141 (69.1%), moderate thrombocytopenia in 25 (12.2%) and severe thrombocytopenia in only 4 (2%) patients. Our study showed thrombocytopenia as a very common phenomenon occurring in 83.3% of vivax malaria patients. The frequency did not correlate with severity of the patients. In our study more than eighty percent of patients were detected with low platelet count but among them the largest portion was seen in the mild group. The severe group (platelet count below 20×10^3 cells/µl) comprised only four patients. Patients with thrombocytopenia were not seen with any bleeding manifestation. Mild or moderate thrombocytopenia is a common feature of malaria and is rarely associated with hemorrhagic manifestations or a component of disseminated intravascular coagulation. In most clinical studies, thrombocytopenia is not usually associated with mortality in malaria.

Table 2. The table showed correlation values between platelet counts and biochemical profiles of patients in the study (N = 204)

Parameter	Spearman's correlation of platelet count	P-value
Bicarbonate	0.12	0.083
Sodium	0.271	<0.001
Potassium	0.157	0.025
Chlorine	0.11	0.119
Direct bilirubin	-0.535	<0.001
Total bilirubin	-0.429	<0.001
AST	-0.153	0.03
ALT	-0.41	0.558
Total protein	0.41	<0.001
Albumin	0.353	<0.001

Using statistical analysis, we looked for correlation between WBC count and platelet count. There was a significant statistical correlation between WBC and platelet count (P< 0.001). Positive correlation meant that platelet drop was associated with a drop of WBC count in vivax patients. As patients tended to develop thrombocytopenia their WBC meanwhile tended to drop to minimally normal or lower than normal count. This positive correlation confirmed our finding of malaria associated with low WBC count. Later, when we subsequently looked for correlation between platelet count and differential WBC count, we found significant positive correlation with eosinophil count and negative correlation with neutrophil count. The statistical correlations could sometimes correspond to clinical correlations with significant outcomes or they could occur without any clinical importance.

We also evaluated correlation values between platelet and biochemistry profile in patients. For the liver function tests, both direct and total bilirubin levels showed strong negative correlation with P <0.001. The negative correlation implied that decrease in platelet was associated with a rise of bilirubin value in vivax malaria patients. This finding was consistent with a previous case control study where they found malaria association with an increase in bilirubin value when compared to control group [4]. Unlike bilirubin, serum protein and serum albumin displayed a strong positive correlation with platelet changes in malaria patients. This positive correlation in vivax malaria patients indicated the relationship between serum protein and platelet level in a manner that decrease in platelet was associated with a decrease in total protein and albumin level in the serum and vice versa. Previous studies done on evaluating serum protein and albumin level showed malaria was associated with low serum total protein and albumin level [5]. Patients with *P. vivax* infections had minimal abnormalities in liver profiles, increased levels of bilirubin, aminotransferases, alkaline phosphatases, and hypoalbuminemia [6]. Although, the mean value for total protein and albumin were normal in this study, nevertheless we found a very strong positive correlation (P<0.001) of platelet count with serum protein and albumin levels.

5. CONCLUSION

Thrombocytopenia is a characteristic feature of malaria patients. Our study showed the frequency of thrombocytopenia in vivax malaria as common as in falciparum malaria patients. Thrombocytopenia was usually mild, however some patients might present with severe thrombocytopenia. Severe thrombocytopenia usually did not correspond to any clinical severity in malaria. Patients usually had no bleeding manifestation and platelet transfusion was rarely required [7-10]. This explained a rather benign nature of thrombocytopenia in vivax malaria patients in Thailand.

CONSENT

As per international standard, informed and written participant consents have been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard, this study was approved by the Ethics Committee, Faculty of Tropical Medicine, Mahidol University, Thailand (Approval number: FTM ECF-019-02).

ACKNOWLEDGEMENTS

This study was supported by Faculty of Tropical Meidicine, Mahidol University, Thailand.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. WHO. World malaria report 2018. Geneva: WHO; 2018.
2. Mendis K, Sina BJ, Marchesini P, Carter R. The neglected burden of *Plasmodium vivax* malaria. Am J Trop Med Hyg. 2001;64(1-2 Suppl):97-106.
3. Hayat AS. Thrombocytopenia; frequency and degree in patients with falciparum malaria. Professional Med J. 2011;18(1): 75-9.
4. Khan SJ, Abbass Y, Marwat MA. Thrombocytopenia biomarkers among malaria infected patients in Ikeja Lagos State, Nigeria. Curr Res J Biol Sci. 2011;3(3):172-4.
5. Adebisi SA, Soladoye AO. Serum protein fractions of Nigerians with *Plasmodium* infections. Afr J Clin Exp Microbiol. 2002;3(2):82-4.
6. Tangpukdee N, Thanachartwet V, Krudsood S, Luplertlop N, Pornpininworakij K, Chalermrut K, et al. Minor liver profile dysfunctions in *Plasmodium vivax, P. malaria* and *P. ovale* patients and normalization after treatment. Korean J Parasitol. 2006;44(4):295-302.
7. Khan SJ, Abbass Y, Marwat MA. Thrombocytopenia as an indicator of malaria in adult population. Malar Res Treat. 2012;405981.
DOI: 10.1155/2012/405981
Epub 2012 Jul 2
8. Punnath K, Dayanand KK, Chandrashekar VN, Achur RN, Kakkilaya SB, Ghosh SK, et al. Association between inflammatory cytokine levels and thrombocytopenia during *Plasmodium falciparum* and *P. vivax* infections in south-western coastal region of India. Malar Res Treat. 2019;4296523.
DOI: 10.1155/2019/4296523
eCollection 2019
9. Gupta P, Guddattu V, Saravu K. Characterization of platelet count and platelet indices and their potential role to predict severity in malaria. Pathog Glob Health. 2019;113(2):86-93.
DOI: 10.1080/20477724.2019.1600855
10. Awoke N, Arota A. Profiles of hematological parameters in *Plasmodium falciparum* and *Plasmodium vivax* malaria patients attending Tercha General Hospital, Dawuro Zone, South Ethiopia. Infect Drug Resist. 2019;12:521-7.
DOI: 10.2147/IDR.S184489
eCollection 2019

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle3.com/review-history/50309