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Thrombocytopenia as a Clue of Vivax Malaria in Endemic Region, Sudan

By Bakri Y. M. Nour, Elgaily M. Elgaily & Albadawi A. Talha

University of Gezira, Sudan

Abstract- Reduction in circulating platelets is observed relatively frequently in cases of malaria due to P. vivax. 61 patients with confirmed vivax malaria were enrolled in this study and the platelets were counted by hematological analyzer. our study revealed that 77.1% had platelets count less than 150,000/ µl , thrombocytopenia grade 1 represent 43%, grade 2 represent 19.8%, grade 3 represent 9.8% and grade 4 represent 4.9%. Thrombocytopenia should be a consideration as a clue to the presence of malaria in endemic region.

Keywords: *vivax malaria; thrombocytopenia; sudan.*

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Thrombocytopenia as a Clue of Vivax Malaria in Endemic Region, Sudan

Bakri Y. M. Nour [α], Elgaily M. Elgaily [σ] & Albadawi A. Talha [ρ]

Abstract- **Reduction in circulating platelets is observed relatively frequently in cases of malaria due to P. vivax. 61 patients with confirmed vivax malaria were enrolled in this study and the platelets were counted by hematological analyzer. our study revealed that 77.1% had platelets count less than 150,000/ µl , thrombocytopenia grade 1 represent 43%, grade 2 represent 19.8%, grade 3 represent 9.8% and grade 4 represent 4.9%. Thrombocytopenia should be a consideration as a clue to the presence of malaria in endemic region.**

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I. Introduction

Plasmodium vivax cause a major global health problem in endemic regions, this species of parasite has the broadest geographic distribution of the five malaria species known to infect humans (Guerra *et al* 2009). There are about 2.85 billion people at risk of malaria and an estimated 80 to 300 million clinical cases of *P. vivax* annually (Guerra CA et al 2009, Mendis K *et al* 2001). Although *P. vivax* is mainly endemic in Southeast Asia and Latin America (Mueller I *et al* 2009) but, *P. vivax* was recently increased in Sudan and Ethiobia (Yohannes AM *et al* 2011, Abdalla SI *et al* 2007). *P. vivax* represent 6.1% of malaria cases in Central and Eastern Sudan (Albadawi A. Talha 2014). Malaria is one of the leading causes of morbidity and mortality in Sudan. Reported malaria cases account for 9.3% of outpatients´ clinic visits and approximately 8.7% of hospital admissions. The malaria mortality is about 2.6% and fatality rate about 0.64% (FMOH 2014). Malaria is commonly associated with various degrees of hematological complications like anemia and thrombocytopenia. The anemia is usually due to varied reasons ranging from haemolysis to other complications like parasitic infections, folate, iron, and vitamin B12 deficiencies in endemic areas, antimalarials and further complicated by the coexistence of thalassemia andother haemoglobinopathies [K. Ghosh and K. Ghosh 2007, S. N. Wickramasinghe et al 2000].

Author α ρ: Department of Parasitology, Faculty of Medical Laboratory Sciences, - University of Gezira P.O. Box 20 - Wad Medani – Sudan. e-mail: bakrinour@hotmail.com

Author σ: Department of Pathology, Faculty of Medicine - University of Gezira- P.O. Box 20 - Wad Medani – Sudan.

Author ρ α σ: Department of Parasitology, Blue Nile Research National Institute for Communicable Diseases - University of Gezira- P.O. Box 20 - Wad Medani – Sudan.

Thrombocytopenia is reported especially in severe *P. falciparum* malaria and few repots in isolated *P. vivax* infection [Pal Singh Makkar 2002]. Thrombocytopenia is less studied in vivax malaria causes neg¬ligible of hidden mortality. The pathogenesis of thrombocytopenia in malaria is unclear, although increased platelet destruction rather than decreased production appears to be responsible [Piguet P. F. *et al* 2002]. In general, the underlying mechanisms of thrombocytopaenia in malaria are peripheral destruction, excessive sequestration of platelets in spleen, and excessive use of platelets associated with the disseminated intravascular coagulation phenomenon [Gupta NK *et al,* 2013]. In addition to the reduction in the number of platelets, platelet function is also compromised in malaria [Greisenegger S, *et al* 2004]. In most laboratories, a normal platelet count is between 150,000 to 450, 000/µl. By definition, 5% of the population will have counts outside the "normal" range. No generally accepted definition of mild, moderate or severe thrombocytopenia exists. For cancer patients receiving treatment, the National Cancer Institute (NCI) has developed the Common Toxicity Criteria to describe severity of thrombocytopenia. Platelet counts of 75,000 to 150,000/ µl are defined as grade 1 thrombocytopenia, 50,000 to <75,000/ µl as grade 2, 25,000 to <50,000/ µl as grade 3, and below 25,000/ µl as grade 4 thrombocytopenia. (CTCAE v3.0; www.ctep.cancer.gov/reporting/ctc.html), here we use this criteria for the classification of thrombocytopenia in vivax malaria patients.

II. Patints and Methods

It was a cross sectional observational, hospital based study conducted at Wad Medani Paediatric teaching hospital and Wad Medani teaching hospital in central Sudan, All patients with vivax malaria presenting to the two hospitals during august 2013 to December 2013 were included in the study after written consent. The thick and thin blood smears were prepared and stained with Giemsa according to the WHO guidelines and studied by a medical parasitologist. and the platelets counts were done by an auto analyzer machine (Hematological analyser SysMix-KXN21, Roche, German) and rechecked by peripheral blood smear. Platelet counts of 75,000 to 150,000/dL are defined as grade 1 thrombocytopenia, 50,000 to <75,000/dL as grade 2, 25,000 to <50,000/dL as grade 3, and below

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25,000/dL as grade 4 thrombocytopenia according to NCI criteria.

III. Result

Sixty one Thin & Thick blood film from febrile cases showed positive P. vivax mono-infection by light microscope and the parasitaemia ranged from 1,070 to 42,800 parasites /µl of blood, most of the cases have different asexual stages from young trophozoite to schizont. The mean of platelets count were 112,016 /µl. And (47/61 77.1%) of total cases had platelets count < 150,000/ µl. About 14.7% of total cases had platelets count ≤ 50,000 / µl. Three patients had platelets count 14,000, 12,000 and 9,000 / µl respectively. Statistically no correlation was found between the severity of thrombocytopenia and parasite count. The severity of thrombocytopenia according to NCI criteria were indicated in table 1.

Table 1 : Thrombocytopenia using NCI sc.ore and mean parasite count in patients infected with vivax malaria

Platelets grade	N-of patients (%)	Mean of parasite count/ µl
>75,000 >150,000	26 (43%)	10338
>50.000 <75,000	12(19.8)	14283
>25,000 <50,000	6 (9.8%)	13671
< 25,000	3(4.9%)	4096

IV. Discussion

Thrombocytopenia is very common in severe falciparum malaria [M.N. Akhtar et al 2005, Z. U. Rehmanet al 1999]. Some studies have shown that thrombocytopenia is equally or even more common in P. vivax malaria in contrast to the popular observation in *P. falciparum* malaria [A. Aggarwal et al 2005, A. Kumar and Shashirekha 2006]. Our study revealed that 77.1% had platelets count less than 150,000/ µl , thrombocytopenia grade 1 represent 43%, grade 2 represent 19.8%, grade 3 represent 9.8% and grade 4 represent 4.9%. Mild reduction in circulating platelets is observed relatively frequently in cases of malaria due to *P. vivax* but cases of severe thrombocytopenia are quite rare. (Daily JP *et al* 2003). Similar study of 101 symptomatic patients with vivax malaria revealed that 85% had platelet counts less than 150,000/ µl (Oh M-D *et al* 2001) Published data in India has shown thrombocytopenia among patients with *P. vivax* infection [D. K. Kochar et al 2010]. A studies conducted from the Indian have found significant thrombocytopenia in *P. vivax* malaria [S. Srivastava *et al* 2011, P. George and L. M. Alexander et al 2010]. Similar results have been reported from Qatar and Venezuela [F. Yousef Khan et al 2009, B. Gonz´alez *et al* 2009]. In Horstmann's series [Horstmann R.D et al 1991], the lowest count of platelets in 39 cases of vivax malaria was 44,000/µl. Pukrittayakamee *et al* described a case of a volunteer experimentally infected with the Chesson's strain of *P. vivax* with a platelet count of 20,000/µl [Pukrittayakamee S et al 1989]. Also a case of vivax malaria associated with an initial platelet count of 5,000/µl was reported from India [Kakar A *et al* 1999]. Studies from Brazil have shown a similar result [S. B. R. Silva *et al* 2009]. A study from Iran confirms that they are getting more cases of thrombocytopenia due to *P. vivax* than Falciparum and attributes this to the possible development of a new genotype of P. vivax [M. Metanat and B. Sharifi-Mood 2010]. Thrombocytopenia were found in most cases with acute vivax malaria (A. Kumar and Shashirekha 2006, A. Aggarwal, S. Rath, and Shashiraj2005). In this study statistically no correlation was found between the severity of thrombocytopenia and parasite count, it is similar to the study conducted by Dhanpat Kumar Kochar *et al* [Dhnpat Kumar Kochar *et al* 2012]. The thrombocytopenia that found in most cases in this study and profound thrombocytopenia may indicated that the traditional view of vivax malaria as benign infection were changed as vivax malaria can cause severe manifestations.

V. Conclusion

Thrombocytopenia should be a consideration as a clue to the presence of malaria in endemic region and after excluding this easily treatable cause, further evaluation of thrombocytopenia should be undertaken.

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