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Clinical Study

Thrombocytopenia as an Indicator of Malaria in Adult Population

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Objectives. To evaluate the predictive value of thrombocytopenia in malaria. *Patients and Methods*. It was a prospective observational study on all febrile patients with thrombocytopenia presenting to the Medical Unit of Hayat Abad Medical Complex during November 2008 to November 2010. *Results*. Of the total of 228 patients with fever and thrombocytopenia, 121 patients (53%) proved to be suffering from malaria. Of them 82 patients (68%) had *falciparum* malaria while 39 patients (32%) had *vivax* infection. Of these 121 patients, platelet counts ranged between 25,000 and 150,000/dL with a mean value of 101,000/dL (SD $\pm$ 47,500) and a median of 75,000/dL. Of the 107 patients who were not suffering from malaria, the counts ranged between 10,000 and 150,000/dL with a mean value of 58,000/dL (SD $\pm$ 54,000) and median of 50,000/dL. *Conclusions*. The presence of thrombocytopenia may be a predictor of malaria in adult population.

1. Introduction

Malaria is commonly associated with various degrees of hematological complications like anemia and thrombocytopenia. The anemia is usually due to varied reasons ranging from hemolysis to comorbidities like parasitic infections, folate, iron, and vitamin B12 deficiencies in endemic areas, antimalarials and further complicated by the coexistence of thalassemia and other haemoglobinopathies [1]. Anemia and thrombocytopenia are the most frequent malaria-associated hematological complications [2].

The hematopoietic response is, however, also somewhat blunted, and there is reduced platelet count and sometimes reduced WBC counts as well. Thrombocytopenia is a very common association of malaria. In the past it was thought that malaria is rarely associated with clinical features of thrombocytopenia like bleeding disorders and is usually an incidental finding on blood testing. Recent scientific evidences have invalidated this anecdote. It is pertinent that the finding of thrombocytopenia in patient may be an indication for a thorough lookout into the blood smear to rule out malaria as the cause. This fact is especially important in the workup for thrombocytopenia in febrile patients. Thrombocytopenia may be associated with bleeding tendency which is one of the important severe manifestations of *P. falciparum* malaria.

The presence of thrombocytopenia in acute febrile travelers returning from tropical areas has become a highly sensitive clinical marker for malaria diagnosis [3].

A number of observational studies have confirmed the association of thrombocytopenia to malaria but till date the cause of thrombocytopenia is poorly understood. The speculated mechanisms leading to thrombocytopenia are coagulation disturbances, splenomegaly, bone marrow alterations, antibody-mediated platelet destruction, oxidative stress, and the role of platelets as cofactors in triggering severe malaria [4–6].

In an animal model of cerebral malaria, platelet's role has been implicated. In autopsy studies of children dying of cerebral malaria, clumps of platelets with or without infected RBC's have been found in the brain capillaries [7, 8].

The platelet counts usually are normalized quickly in a matter of few weeks when malaria is treated successfully.

2. Patients and Methods

It was a prospective observational study conducted at Hayat Abad Medical Complex, Postgraduate Medical Institute,

Table 1: Thrombocytopenia in patients with malaria and without malaria.

Grade	Platelet count	Malaria positive patients (% age)			Malaria negative patients (% age)	Total ($n = 228$)
		Total (% age)	Plasmodium *falciparum* positive (% age)	Plasmodium *vivax* positive patients (% age)		
3	25,000–50,000 dL	27 (12)	22 (18)	05 (4)	46 (20)	81 (35.5%)
2	50,000–75,000 dL	46 (20)	30 (25)	16 (13)	47 (20.6)	93 (41%)
1	75,000–150,000 dL	48 (21)	30 (25)	18 (15)	06 (2.6)	54 (23.7)
	Total	121 (53)	82 (68%)	39 (32%)	107 (47)	228 (100%)

Peshawar. All patients with thrombocytopenia presenting to the medical B unit of Hayat Abad Medical Complex during November 2008 to November 2010 were included in the study.

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 25,000/dL as grade 4 thrombocytopenia.

Thrombocytopenia was thus divided into these groups. The counts were visually confirmed by a clinical hematologist after the counts were done by an auto analyzer machine. The thick and thin slides were prepared according to the WHO guidelines and studied by a hematologist. Thick smears using Geimsa stain and thin smears using Wright stain were used and the patient was labeled as nonmalaria only if three consecutive smears were negative. Thus these patients were divided further into two groups: malaria and non-malaria group. The non-malaria group was further evaluated for other causes of thrombocytopenia which was not part of this study. Laboratory tests done on these patients consisted of full blood counts, liver enzymes, renal function, vitamin B12 levels, folic acid levels, erythrocyte sedimentation rate, and peripheral blood smear. In undiagnosed cases and where suspicion of immune thrombocytopenia was high, bone marrow biopsy was done to differentiate whether the low platelet count is due to decreased production or peripheral destruction.

Statistical calculation was done using Word Excel and SPSS version 11 for diagnostic accuracy between the two groups, that is, between platelet count from 25,000/dL to 50,000/dL, 50,000/dL to 75,000/dL and 75,000/dL to 150,000/dL using the Wilson score with 95% confidence interval.

3. Results

Of the total 228 patients with thrombocytopenia, 121 patients (53%) proved to be suffering from malaria. Of them 82 patients (68%) had *falciparum* malaria while 39 patients (32%) had *vivax* infection. In these 121 patients, platelet counts ranged 25,000 to 150,000/dL with a mean value of 101,000/dL and median of 75,000/dL. Of the 107 patients who were not suffering from malaria, the counts ranged between 10,000 to 150,000/dL with a mean value of 58,000/dL and median of 50,000/dL.

Table 2: Accuracy parameters between level 1 (platelets from 25,000 to 50,000 dL) and level 2 (platelets from 50,000 to 75,000 dL) using Wilson score.

Parameter	Estimate	Lower-upper 95% confidence interval
Sensitivity	77.69%	(69.48, 84.19)
Specificity	50.47%	(41.14, 59.76)
Positive predictive value	63.95%	(55.92, 71.26)
Negative predictive value	66.67%	(55.85, 75.97)
Diagnostic accuracy	64.91%	(58.52, 70.81)

Table 3: Accuracy parameters between level 1 (platelets from 50,000 to 75,000 dL) and level 2 (platelets from 75,000 to 150,000 dL) using Wilson score.

Parameter	Estimate	Lower-upper 95% confidence interval
Sensitivity	39.67%	(31.4, 48.57)
Specificity	94.39%	(88.3, 97.4)
Positive predictive value	88.89%	(77.81, 94.81)
Negative predictive value	58.05%	(50.62, 65.13)
Diagnostic accuracy	65.35%	(58.97, 71.23)

The numbers of patients who had and had not malaria after the evaluation are mentioned in Table 1.

The accuracy parameters between different levels of platelet counts are given in Tables 2 and 3.

4. Discussion

Thrombocytopenia often accompanies malaria and is usually mild to moderate. It may however be symptomatic and severe [9–18]. Fifty-three percent of patients with malaria showing thrombocytopenia in our study is close to others reporting low platelets as 57% [9] and 48% [10].

In Liberia, Mahmood and Yasir [11] studied a total of 145 patients who had *P. falciparum* malaria. Out of these 109 (75.18%) had thrombocytopenia. The sensitivity of the platelet count was considered as a predictor of malaria was 80.11% while specificity was 81.36%. The positive predictive value was 63.87% and the negative predictive value was 90.86%. Another study has reported 60% sensitivity and

88% specificity of thrombocytopenia for malaria diagnosis in acute febrile patients [12].

In another important study from India, Patel et al. reports the sensitivity of thrombocytopenia together with the acute febrile syndrome as 100% for malaria diagnosis, with a specificity of 70%, a positive predictive value of 86% and a negative predictive value of 100% [13].

In our study we have calculated the sensitivity, specificity, positive and negative predictive value and diagnostic accuracy at different levels of platelet counts and have concluded that the sensitivity and negative predictive value is high at low platelet counts (78% sensitivity and 67% negative predictive value 40% and 58% resp.) while the specificity and positive predictive value is high at relatively higher platelet counts (94% specificity and 89% positive predictive value against 50% and 64% resp.). The diagnostic accuracy remains almost the same at both counts (around 65%). Mahmood and Yasir [11] concluded an extended search for malarial parasite in patients having thrombocytopenia on smear. Mild-to-severe thrombocytopenia observed in hospitalized patients was considered enough to alert the possibility of malarial infection, as *P. falciparum* was found to be common species in these patients. Our study also connotes that *falciparum* malaria is more common at lower platelet counts as compared to *vivax* infection and overall the chances of finding falciparum malaria are almost twice than that of finding *vivax* malaria in thrombocytopenic patients.

It is a general consensus that thrombocytopenia is very common in malaria [14, 15] and previously it was believed that it is more common in *F. malaria*. Recent studies have shown that thrombocytopenia is equally or even more common in *P. vivax* malaria contrary to the popular belief that it may be observed in *P. falciparum* malaria [16–23]. More recent data in India has shown how thrombocytopenia exhibited a heightened frequency and severity among patients with *P. vivax* infection [24].

Recent studies conducted from the Indian subcontinent have found significant thrombocytopenia in *P. vivax* malaria [25, 26].

Similar results have been reported from Qatar and Venezuela [27, 28]. Studies from Brazil have shown a similar trend [29].

A recent 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* [30].

Though we have found significant thrombocytopenia in more than half of our patients with malaria, the fact that it was seemingly more common in *P. falciparum* malaria needs to be validated by larger studies.

5. Conclusion

Malaria should be a consideration in all patients with low platelets and after excluding this common and easily treatable cause, further evaluation of thrombocytopenia should be undertaken.

References

[1] K. Ghosh and K. Ghosh, "Pathogenesis of anemia in malaria: a concise review," *Parasitology Research*, vol. 101, no. 6, pp. 1463–1469, 2007.

[2] S. N. Wickramasinghe and S. H. Abdalla, "Blood and bone marrow changes in malaria," *Bailliere's Best Practice and Research in Clinical Haematology*, vol. 13, no. 2, pp. 277–299, 2000.

[3] V. D'Acremont, P. Landry, I. Mueller, A. Pécoud, and B. Genton, "Clinical and laboratory predictors of imported malaria in an outpatient setting: an aid to medical decision making in returning travelers with fever," *American Journal of Tropical Medicine and Hygiene*, vol. 66, no. 5, pp. 481–486, 2002.

[4] S. S. Jamal Khan, F. R. Khan, M. Usman, and S. Zahid, "Malaria can lead to thrombocytopenia," *Rawal Medical Journal*, vol. 33, no. 2, pp. 183–185, 2008.

[5] T. S. Faseela, R. A. Roche, K. B. Anita, C. S. Malli, and Y. Rai, "Diagnostic value of platelet count in malaria," *Journal of Clinical and Diagnostic Research*, vol. 5, no. 3, pp. 464–466, 2011.

[6] A. Rasheed, S. Saeed, and S. A. Khan, "Platelet count in malaria," *Pakistan Journal of Phytopathology*, vol. 19, no. 3, pp. 86–88, 2008.

[7] G. E. Grau, C. D. Mackenzie, R. A. Carr et al., "Platelet accumulation in brain microvessels in fatal pediatric cerebral malaria," *Journal of Infectious Diseases*, vol. 187, no. 3, pp. 461–466, 2003.

[8] A. Pain, D. J. P. Ferguson, O. Kai et al., "Platelet-mediated clumping of *Plasmodium falciparum* erythrocytes is a common adhesive phenotype and is associated with severe malaria," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 98, no. 4, pp. 1805–1810, 2001.

[9] G. A. Niazi, "Haematological aspect of malaria in a population based hospital, Saudi Arabia," *Journal of the Egyptian Society of Parasitology*, vol. 25, no. 3, pp. 787–793, 1995.

[10] A. Mert, R. Ozaras, F. Tabak, M. Bilir, R. Ozturk, and Y. Aktuglu, "Malaria in Turkey: a review of 33 cases," *European Journal of Epidemiology*, vol. 18, no. 6, pp. 579–582, 2003.

[11] A. Mahmood and M. Yasir, "Thrombocytopenia : a predictor of malaria among febrile patients in Liberia," *Infectious Diseases Journal*, vol. 14, pp. 41–44, 2008.

[12] T. B. Lathia and R. Joshi, "Can hematological parameters discriminate malaria from nonmalarious acute febrile illness in the tropics?" *Indian Journal of Medical Sciences*, vol. 58, no. 6, pp. 239–244, 2004.

[13] U. Patel, G. Gandhi, S. Friedman, and S. Niranjan, "Thrombocytopenia in malaria," *Journal of the National Medical Association*, vol. 96, no. 9, pp. 1212–1214, 2004.

[14] M. N. Akhtar, S. Jamil, S. I. Amjad, A. R. Butt, and M. Farooq, "Association of malaria with thrombocytopenia," *Annals of King Edward Medical College*, vol. 11, pp. 536–537, 2005.

[15] Z. U. Rehman, M. Alam, A. Mahmood, A. Mubarik, A. Sattar, and K. A. Karamat, "Thrombocytopenia in acute malarial infection," *Pakistan Journal of Pathology*, vol. 10, pp. 9–11, 1999.

[16] A. Aggarwal, S. Rath, and Shashiraj, "*Plasmodium vivax* malaria presenting with severe thrombocytopenia," *Journal of Tropical Pediatrics*, vol. 51, no. 2, pp. 120–121, 2005.

[17] N. M. Anstey, B. J. Currie, and M. E. Dyer, "Profound thrombocytopenia due to *Plasmodium vivax* malaria," *Australian and New Zealand Journal of Medicine*, vol. 22, no. 2, pp. 169–170, 1992.

[18] V. Bhatia and J. Bhatia, "Severe thrombocytopenia with bleeding manifestations in two children secondary to *Plasmodium vivax*," *Platelets*, vol. 21, no. 4, pp. 307–309, 2010.

[19] R. Harish and S. Gupta, "Plasmodium vivax malaria presenting with severe thrombocytopenia, cerebral complications and hydrocephalus," *Indian Journal of Pediatrics*, vol. 76, no. 5, pp. 551–552, 2009.

[20] U. M. Jadhav, V. S. Patkar, and N. N. Kadam, "Thrombocytopenia in malaria—correlation with type and severity of malaria," *Journal of Association of Physicians of India*, vol. 52, pp. 615–618, 2004.

[21] A. Kakar, S. Bhoi, V. Prakash, and S. Kakar, "Profound thrombocytopenia in *Plasmodium vivax* malaria," *Diagnostic Microbiology and Infectious Disease*, vol. 35, no. 3, pp. 243–244, 1999.

[22] D. Kaur, V. Wasir, S. Gulati, and A. Bagga, "Unusual presentation of *Plasmodium vivax* malaria with severe thrombocytopenia and acute renal failure," *Journal of Tropical Pediatrics*, vol. 53, no. 3, pp. 210–212, 2007.

[23] A. Kumar and Shashirekha, "Thrombocytopenia—an indicator of acute vivax malaria," *Indian Journal of Pathology and Microbiology*, vol. 49, no. 4, pp. 505–508, 2006.

[24] D. K. Kochar, A. Das, A. Kochar et al., "Thrombocytopenia in *Plasmodium falciparum*, *Plasmodium vivax* and mixed infection malaria: a study from Bikaner (Northwestern India)," *Platelets*, vol. 21, no. 8, pp. 623–627, 2010.

[25] S. Srivastava, S. Ahmad, N. Shirazi, S. Kumar Verma, and P. Puri, "Retrospective analysis of vivax malaria patients presenting to tertiary referral centre of Uttarakhand," *Acta Tropica*, vol. 117, no. 2, pp. 82–85, 2011.

[26] P. George and L. M. Alexander, "A study on the clinical profile of complicated *Plasmodium vivax* mono-infections," *Asian Pacific Journal of Tropical Medicine*, vol. 3, no. 7, pp. 560–562, 2010.

[27] F. Yousef Khan, A. K. Lutof, M. A. Yassin et al., "Imported malaria in Qatar: a one year hospital-based study in 2005," *Travel Medicine and Infectious Disease*, vol. 7, no. 2, pp. 111–117, 2009.

[28] B. González, H. Rodulfo, M. De Donato, M. Berrizbeitia, C. Gómez, and L. González, "Hematologic variations in patient with malaria caused by *Plasmodium vivax* before, during and after treatment," *Investigacion Clinica*, vol. 50, no. 2, pp. 187–201, 2009.

[29] S. B. R. Silva, *Avaliação da frequência e dos fatores associados à plaquetopenia causada pelo Plasmodium vivax [MSc Thesis]*, Universidade Federal do Mato Grosso, Mato Grosso, Brazil, 2009.

[30] M. Metanat and B. Sharifi-Mood, "Malaria vivax and severe thrombocytopenia in Iran," *Iranian Journal of Parasitology*, vol. 5, no. 3, pp. 69–70, 2010.