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ORIGINAL ARTICLE

IMPORTANCE OF MALARIAL EXCLUSION IN A THROMBOCYTOPENIC FEBRILE PATIENT IN AN ENDEMIC AREA

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ABSTRACT: AIM OF THE STUDY: To evaluate the role of platelet count for predicting malarial infection and to determine the frequency and severity of thrombocytopenia in malarial parasite positive patients. **STUDY DESIGN:** The study included 150 patients who presented with fever in Santosh Medical College and Hospital, Ghaziabad. 97 patients with malaria were identified, rest were taken as control. Infection with both plasmodium vivax and plasmodium falciparum species was included. Thrombocytopenia was defined as platelet count less than 150000/cmm. **RESULTS:** Among 97 patients positive for malarial parasite, 78[80%] were found to have thrombocytopenia Overall 86 patients had plasmodium vivax while 8 patients had plasmodium falciparum infection and 3 had mixed infection. The frequency of thrombocytopenia was 78% [n=67] in vivax and 88% [n=7] in falciparum infection. Our study found the sensitivity of platelet count for diagnosing malaria was 80% and the specificity was 85%. Positive predictive value was 91% and negative predictive value was 83%. **CONCLUSION:** Platelet count can serve as an important initial screening tool in our setting. A finding of thrombocytopenia should increase the suspicion of malaria and more specific tests should be performed. Thrombocytopenia was a common haematological finding in patients with plasmodium infection, however its presence is not a distinguishing feature between the two types of malaria. Severe thrombocytopenia can occur in plasmodium vivax malaria although it is more common in plasmodium falciparum malaria.

KEYWORDS: Malaria; Thrombocytopenia; Plasmodium vivax; Plasmodium falciparum.

INTRODUCTION: Malaria continues to be a cause of high mortality and morbidity throughout the tropics and is endemic in many parts of India.[1] It is a vector born disease caused by the bite of female anopheles mosquito inoculating malarial sporozoites in the human blood stream leading to clinical disease manifestations.[2] Four species of plasmodium are recognized to cause disease in mankind. These include plasmodium falciparum, plasmodium vivax, plasmodium ovale, plasmodium malariae.[3] Malaria is a global disease with highest mortality in Africa. According to World Health Organization reports, about 40% of the world population is at risk of developing malaria. About 300-500million people are infected with it[4] and its fatality rate is about 2 million deaths per year.[5]

India has a high infectivity rate of malaria throughout the year with aggressive outbursts seen mainly during and after the rainy season. Falciparum malaria is associated with more severe life threatening multisystem disease in comparison to more benign course of plasmodium vivax. Considering the gravity of complications of this potentially treatable disease, it is important to diagnose and treat this disease before it is too late. Peripheral blood smear is the gold standard test in diagnosing malaria, but is time consuming and dependent on smear quality.

Thrombocytopenia has been reported to be quite frequently associated with malaria[6,7] with incidence ranging from 42%[8] to 85%.[9,10] As thrombocytopenia is also seen in some other common febrile acute conditions like viral fever, dengue therefore a significant correlation between malaria

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and presence of thrombocytopenia is necessary before taking it as a haematological parameter of the disease. This study was conducted to evaluate the role of platelet count, a routine test, as a marker for predicting malarial infection.

MATERIAL AND METHODS: This study was conducted at Santosh medical college and hospitals, Ghaziabad from May 2013 - May 2014. The study protocol included 150 patients who presented with fever. Samples were collected in EDTA containing tubes. Films were stained with Giemsa stain. Patients were divided into two groups-malaria group and non-malaria group. All the study subjects in the malaria group were identified positive for malarial parasite on peripheral smear examination, by conventional microscopy or tested positive with malarial parasite ELISA antigen cards [J. Mitra]. A patient was considered not to have malaria if three consecutive smears were negative and included in the non-malaria group which served as a control. Those 97 patients with a confirmed diagnosis of malaria were investigated for platelets, haemoglobin and total leucocyte on a Sysmex auto analyser.

Thrombocytopenia was defined as platelet count less than 150000/cmm. Thrombocytopenia was considered severe if less than 50,000 cells/cmm, moderate if 50,000-100000 cells/cmm and mild if platelet count was 100000-150000/cmm. The two groups were classified as: group A having thrombocytopenia and group B without thrombocytopenia. On the basis of haemoglobin, two groups were classified as group A having haemoglobin less than 10g/dl and group B having haemoglobin more than 10 g/dl. The normal range of leucocytes was taken as 4000-11000cells/cmm. Any deviation from this limit was noted as abnormal.

The unpaired t test was applied to evaluate statistical significance.

RESULTS: 150 patients were included in the study.97 patients were found to have malaria [71 males, 26 females] with a mean age of 35 years. The control group consisted of 53 patients [31 males, 22 females] with a mean age of 33 years. Platelet counts in the malaria group ranged from 18, 000-2, 80, 000 cells/cmm with a mean of 99000 cells/cmm. The difference in the platelet count between two groups was statistically significant [$p<0.001$].

Out of 97 patients in the malaria group 78[80%] patients had thrombocytopenia. 20 patients had severe thrombocytopenia, 42 patients had moderate thrombocytopenia and 16 had mild thrombocytopenia [Table 2].

The commonest manifestations were fever with chills and rigors, backache and headache. 86[89%] patients had plasmodium vivax infection and 8 [8%] suffered from plasmodium falciparum infection and 3[0.03%] subjects had mixed parasitemia of plasmodium vivax and plasmodium falciparum malaria. A non-significant difference was seen in gender distribution [$p=0.265$].

The mean platelet count in p. vivax malaria was 99000/µl with a range of 10,000-1, 98,000/µl as against p. falciparum malaria where the mean platelet count was 58,000/µl with a range of 10, 000-57,000/µl. Patients with falciparum malaria were found to have lower platelet count than patients with vivax malaria. Platelet count less than 20000/µl was noted only in 3 % cases of vivax malaria as against 25 % cases of p. falciparum malaria. None of the subjects with p. vivax infection has count less than 10000/µl. None of the subjects with p. vivax malaria and low platelet count had clinical manifestations of thrombocytopenia or bleeding from any site. Type of malaria and platelet count had a non-significant difference.

Haemoglobin analysis showed that 25[32 %] of thrombocytopenic patients had less than 10g/dl haemoglobin. [Table1]. Anaemia was normocytic and normochromic in 65 % of cases and it

correlated with degree of parasitemia. Mean haemoglobin concentration was 10g/dl in patients with p.falciparum malaria and 11g/dl in patients with p.vivax malaria and the lowest haemoglobin concentration was 5g/dl in p.falciparum infestation and 6g/dl in p.vivax infestation. The association between haemoglobin and platelet count was found to be statistically non-significant [p=0.786]

In 54% cases, total leucocyte count was within normal limits. 22% had leucocytosis and 24% had leucopenia. Polymorphonuclear leucocytosis was observed in 64% cases, some of whom had associated bacterial infection. Correlation between parasitemia and total leucocyte count was found to be non-significant.

Thus the sensitivity of platelet count for predicting malaria in our institution was 80% and the specificity was 85%, positive predictive value was 91% and negative predictive value was 83% [Table 3].

DISCUSSION: In tropical and subtropical areas, malaria is a cause of major health concern. Mortality and morbidity is mainly due to delayed diagnosis and treatment of this potentially treatable disease. Only small percentage of patient's exhibit classical pattern of disease. It is easily confused with other diseases like dengue fever, enteric fever or viral illness as there are no localizing signs and symptoms of malaria.

In the present study thrombocytopenia was taken as a haematological parameter. Thrombocytopenia is a common pathological feature of malaria.[11,12,13]

Two important findings were observed in this study-one that thrombocytopenia was a common laboratory feature in malaria, secondly both the plasmodium species [vivax, falciparum] were associated with it.

The mechanism of thrombocytopenia in acute malaria remains unknown. Different mechanisms are postulated including lysis, splenic sequestration, phagocytosis of platelets or decreased production from the marrow.[5] Disseminated intravascular coagulation was also suggested to be responsible for thrombocytopenia[14,15] but it was later shown that most patients with malaria do not have disseminated intravascular coagulation.[16] A direct interaction with platelets and plasmodium has been suggested as plasmodium vivax has been demonstrated by electron microscopy to exist inside the platelets with vivax malaria.[17] Immune mechanisms are considered to be the underlying cause of thrombocytopenia. Immune complex may play a role in peripheral destruction of platelets as well as red blood cells.[18] In case of plasmodium falciparum, immune reaction and complement activation are presumed to be the initiating steps leading to anaemia and thrombocytopenia.[19]

Thrombocytopenia was found in 78 out of 97 patients studied in this series. Contrary to general perception, plasmodium vivax can give rise to thrombocytopenia[20,21] as seen in this study. It was seen in 78% patients having p. vivax, while it was in 88 % patients with p. falciparum. Other researchers have also documented similar results.[22,23] As per our criteria 19 cases did not exhibit thrombocytopenia. Since baseline platelet counts were not taken into consideration thus prediction of thrombocytopenia in these cases could not be concluded.

In patients of vivax malaria, thrombocytopenia was usually mild to moderate, although occasionally platelet count was severely depressed. This was supported by Kakar A.[24] Jadhav and patkar[5] reported thrombocytopenia in both group of patients but severe thrombocytopenia [platelets less than 20000/µl] was more consistent with plasmodium falciparum malaria. Similar findings were seen in our study also.

Anaemia was another haematological indicator which was seen in 86% patients. It was difficult to ascertain whether anaemia was due to malaria or some other disease like nutritional deficiency anaemia or worm infestation or gastrointestinal bleeding as previous reports of haemoglobin were not available in most of the patients. Many workers have reported high incidence of anaemia[25,26,27] in falciparum malaria. Normocytic and normochromic morphology of red blood cells was observed in 78% of cases which was similar to findings of White NJ et al.[28]

The pathophysiology of anaemia in malaria could be multifactorial envolving a complex series of interactions envolving destruction of parasitized red blood cells, ineffective erythropoiesis or immune mechanisms.[29]

In this study leucopenia was seen in only 24% of patients. Low value of white blood cells in patients infected with malaria is also reported by Erhart et al.[30]

CONCLUSION: This study found thrombocytopenia, defined as platelet count less than 150,000cells/cmm, to be a highly sensitive test for malaria, with a high positive predictive value. Hence we suggest that in any patient with fever, platelet count may be an important clue to diagnosis of malaria. However presence of thrombocytopenia is not a distinguishing feature between two types of malaria. Patients with severe thrombocytopenia may be more likely to suffer from falciparum malaria than vivax malaria. Thrombocytopenia should increase the suspicion of malaria and multiple peripheral smears and or ELISA-for detection of parasite specific antigen level should be carried out. Patients with normal platelet count may suggest a wider spectrum of differential diagnosis for fever.

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Variables	Thrombocytopenia [n=78]	Without thrombocytopenia [n=19]	Total [n=97]
males	55	16	71
females	23	3	26
Platelet count			
p.vivax	67	19	86
p.falciparum	8	0	8
hemoglobin <10g%	25	7	32
hemoglobin >10g%	53	12	65
Three patients had mixed parasitemia			

TABLE 1: Distribution of variables in the malaria study group with or without thrombocytopenia

		Total [n-97]	Vivax malaria [n=86]	Falciparum malaria [n=8]	Mixed infection [n=3]
severe thrombocytopenia	<50000cells/cmm	20	16	4	0
moderate thrombocytopenia	50000-100000cells/cmm	42	35	4	3
mild thromocytopenia	100000-150000cells/cmm	16	16	0	0
no thrombocytopenia	>150000cells/cmm	19	19	0	0

TABLE 2: Platelet count in the malaria group patients

	Malaria		
	Present	Absent	Total
Thrombocytopenia			
Present	78	8	86
Absent	19	45	64
Total	**97**	**53**	**150**

Table 3: Association of malaria with thrombocytopenia in the study group

The sensitivity of thrombocytopenia in predicting malaria in our set up was 80% and the specificity was 85%, positive predictive value was 91% and negative predictive value was 83%.

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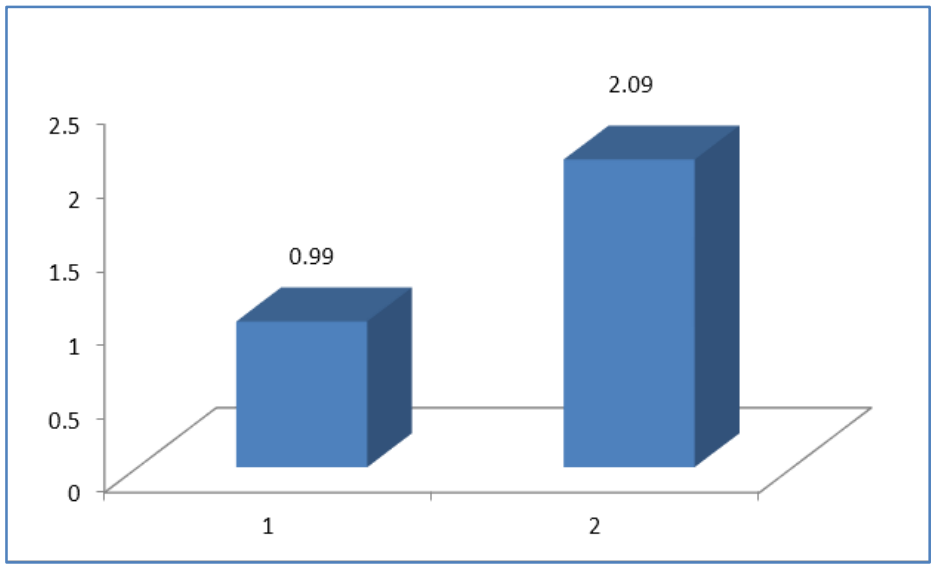

Fig. 1: Mean Platelets count in malaria Patients and in control group (p<0.001)

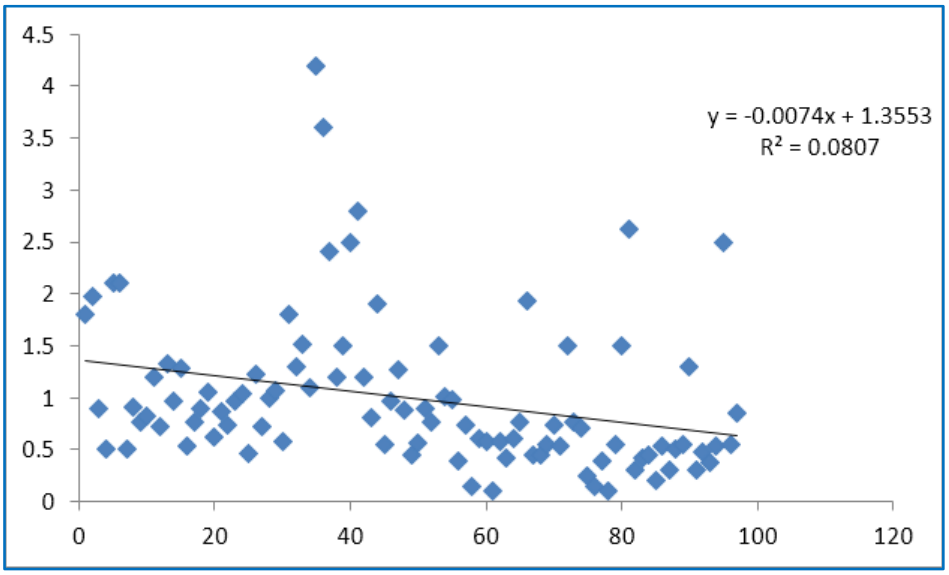

Fig. 2: Statistically significant correlation between thrombocytopenia and malaria positive cases

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