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Thrombocytopenia in Malaria: A hospital based study

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Introduction

Malaria is an infectious vector borne parasitic disease of the genus *plasmodium* and transmitted by the bite of infected *Anopheles* mosquitoes. There are four recognized and distinct species are: *Plasmodium vivax*, *Plasmodium falciparum*, Plasmodium *ovale*, *Plasmodium malaria* [1]. However, a fifth species, *Plasmodium knowlesi*, has been identified as a cause of human malaria in almost all countries in Southeast Asia [2] and extending to the Nicobar and Andaman Islands in India [3]. According to the latest estimates from world health organization, there were 214 million new cases of malaria worldwide in 2015 (range 149–303 million). The African Region accounted for most global cases of malaria (88%), followed by the South-East Asia Region (10%) and the Eastern Mediterranean Region (2%). Among South East Asia region, India shares two-thirds of the burden (70%) followed by Myanmar (16%) and Indonesia (10%). In 2015, there were an estimated 438 000 malaria deaths (range 236 000–635 000) worldwide. Most of these deaths occurred in the African Region (90%), followed by the South-East Asia Region (7%) and the Eastern Mediterranean Region (2%). Between 2000 and 2015, malaria incidence rates (new malaria cases) fell by 37% globally, and by 42% in Africa. During this same period, malaria mortality rates fell by 60% globally and by 66% in the African Region.[4]

A typical attack of malaria comprises three distinct stages: cold stage, hot stage and sweating stage. The clinical features of malaria vary from mild to severe, and complicated, according to the species of parasite present, the patient's state of immunity, the intensity of infection and also the presence of concomitant conditions such as malnutrition and other disease [5]. Severity of the disease depends on the interaction of a number of factors. These include the size of the infective dose of sporozoites, nutritional status of the host, level of acquired immunity, host genetic factors, parasite growth rate, drug resistance status, socio-economic condition, availability of health care and education [6]. Malaria parasite affects multiple organs of the body such as liver, spleen, brain, gastro intestinal tract, gall bladder, pancreas, blood vessels and placenta. Hence the clinical picture could be of wide spectrum ranging from simple malaise to life threatening central nervous symptoms like coma [7-8]. Hematological abnormalities have been observed in patients with malaria, with anemia and thrombocytopenia being the most common [8-9]. Both non-immunological as well as

immunological destruction of platelets have been implicated in causing thrombocytopenia but the mechanisms involved are still not completely clear. Immune-mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have all been postulated in the cause for thrombocytopenia. Abnormalities in platelet structure and function have been described as a consequence of malaria, and in rare instances platelets can be invaded by malaria parasites.[10,11,12] We conducted this study to find out the frequency and the degree of thrombocytopenia in patients with malaria.

Material and Method

The blood investigations were carried out in Rama medical college Hospital & Research Centre, Mandhana, Kanpur (East part of U.P) to those patients who were referred to Microbiology laboratory for malaria test from various departments especially, from medicine. This prospective study was carried out from 01/01/2016 to 31/12/2016. A total 230 patients were included for studies that were found the positive for malaria parasite. Malaria test was carried out by thin and thick smear examination. Thin smear was stained by Leishmen stain and thick smear was stained by field stain. In field stain polychromated methylene blue and eosin stains specifically to basophilic and acidophilic cellular elements to demonstrate blood cells and hemoparasites. All patients undergone for complete blood count by "sysmex KX-21" a fully automated hematology analyzer. Grading of thrombocytopenia was carried out according to NCI Common Terminology Criteria for Adverse Events Version 3.0.[9] According to that patients with thrombocytopenia have been divided into following five grades:

- Grade 0: With in normal limit, platelet count 150,000 or above.
- Grade I: Platelet count between 75,000 and 150,000.
- Grade II: Platelet count between 50,000 and 75,000.
- Grade III: Platelet count between 25,000 and 50,000.
- Grade IV: Platelet count less than 25,000.

Results

In our study, 53 patients with malaria positive were investigated with platelet count. Out of 53 patients 26 (49.05%) were males and 27 (51.94%) were female. Majority of the patients were between 11-30 years (26 patients). **[Table 1]**

Table1: Age and sex distribution of patients

Age group (years)	Male	Female	Total (n=53)
<10	04	00	04
11-20	07	06	13
21-30	05	08	13
31-40	04	06	10
41-50	05	05	10
>50	01	02	03
Total	26	27	53
Mean age 29.54 years, SD±14.70			

All the patients had fever (100%) at the time of presentation, followed by weakness (92.45%), and vomiting (75.47%). Most common sign was anemia (66.03%) followed by splenomegaly (28.30%) and hepatomegaly (1.88%). **[Table2]**

Table 2: Frequency of clinical features in patients with malaria

Symptoms /signs	Clinical features	No. of Patients	Percentage
Symptoms	Fever	53	100%
	Weakness	49	92.45%
	Vomiting	40	75.47%
Signs	Anemia	35	66.03%
	Splenomegaly	15	28.30%
	Hepatomegaly	01	1.88%

Out of 53 cases detected with vivax malaria, 35 (66.03%) cases had thrombocytopenia, 18 (33.96%) cases had normal platelet count. 08 (15.09%) cases had Grade I thrombocytopenia, 10 (18.86%) cases had Grade II thrombocytopenia, 15 (28.30%) cases had Grade III thrombocytopenia and 02 (3.77%) cases had Grade IV thrombocytopenia.[**Table3**]

Table 3: Frequency of thrombocytopenia according grade

Grade	Platelet count	No. of Patient
Grade 0	150000 or above	18 (33.96%)
Grade I	75000-150000	08 (15.09%)
Grade II	50000-75000	10 (18.86%)
Grade III	25000-50000	15 (28.30%)
Grade IV	25000	02 (3.77%)
Total		53 (100%)

Discussion

Malaria caused by P. vivax and P. falciparum is endemic in many parts of India. Malaria affects almost all blood components and is a true hematological disease. Thrombocytopenia and anemia are the most frequently malaria associated hematological complications. In endemic areas malaria has been reported as the major cause of low platelet counts. This is so characteristic of malaria, that in some places, it is used as an indicator of malaria in patients presenting with fever. Platelets count of less than 150,000/cumm increases the likelihood of malaria 12-15 times.[13,14,15]

In our study, 66.03% patients with malaria presented with thrombocytopenia which is in close approximation to other studies reporting low platelets of 57% and 48%. [16, 17]

The mechanism of thrombocytopenia in malaria is not clearly known. Fajardo and Tallent in 1974 demonstrated P. vivax within platelets by electron microscopy and suggested a direct lytic effect of the parasite on the platelets [18]. Both non-immunological destruction as well as immune mechanisms involving specific platelet-associated IgG antibodies that bind directly to the malarial antigen in the platelets has been recently reported to play a role in the lysis of platelets and the development of thrombocytopenia. In clinical trials, recombinant – macrophage colony stimulating factor (M-CSF) has been known to cause a reversible dose dependent thrombocytopenia. Elevated M-CSF levels in malaria, by increasing macrophage activity may mediate platelet destruction in such cases [19]. Oxidative stress damage of thrombocytes has also been implicated in the etiopathogenesis based on the finding of low levels of platelet superoxide-dismutase and glutathione peroxidase activity and high platelet lipid peroxidation levels in malaria patients, when compared to those of healthy subjects [20].

Conclusion

Higher frequency of mild to severe thrombocytopenia was observed in-hospitalized patients suffering from malaria. The above finding can have improve therapeutic implications in context of avoiding unnecessary platelet infusion. Presence of thrombocytopenia in a patient with acute febrile illness in the tropics increases the possibility of malaria. This may be used in addition to the clinical and microscopic parameters to heighten the suspicion of this disease and prompt initiation of the treatment.

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