

Thrombocytopenia in Malaria

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ABSTRACT

OBJECTIVE: Malaria is a major health problem in South Asia. It can be associated with many complications. Thrombocytopenia is the most common hematological complication of malaria. Our aim was to assess the severity and frequency of thrombocytopenia in malaria.

DESIGN: This was a descriptive case-series study. A total of 69 admitted patients diagnosed with malaria were assessed for thrombocytopenia using automated quantitative D3 Analyzer. The data was analyzed using SPSS version 16.0. The results were obtained in numbers and percentages. Data was expressed as means with standard deviation.

RESULTS: Out of the sample population 64 patients were diagnosed with vivax malaria and 3 with falciparum malaria while 2 patients had mixed infection. About 86% of patients with vivax malaria had thrombocytopenia while 66% of patients with falciparum malaria had thrombocytopenia. Mean platelet count in vivax malaria was $84.02 \times 10^3/\mu\text{L}$ with a range of $15-213 \times 10^3/\mu\text{L}$. Platelet count of $<20,000/\mu\text{L}$ was seen in only 2 patients with vivax malaria and none of the patients with falciparum malaria.

CONCLUSION: Thrombocytopenia is a common feature in malaria. In patients having fever with thrombocytopenia, malaria should be on top of differential diagnosis. Viral hemorrhagic fevers can also present as fever but in these cases the complete blood counts has other features such as high hematocrit and leucopenia along with thrombocytopenia. Our finding can have therapeutic implications in the context of avoiding unnecessary platelet transfusion with the relatively more benign course in vivax malaria.

In our study the commonest cause of thrombocytopenia in malaria was vivax malaria.

KEY WORDS: Thrombocytopenia, malaria, vivax.

INTRODUCTION

Malaria is a major health problem in Pakistan being one of the most common cause of acute fever. It is still one of the most common cause of mortality and morbidity throughout the developing world. It has an estimated incidence of 300-500 million cases worldwide and about 1-3 million deaths annually¹. In Pakistan 0.5 million cases occur annually and an estimated 50,000 deaths occurring per year. The mortality is mostly in infants, children and pregnant females². National malaria control program recorded a six fold rise in falciparum malaria in the last decade which now comprises 42% of all malaria cases.³

There are no fixed clinical criteria for diagnosis of malaria. The classic intermittent high grade fever with chills and rigors may not be seen very frequently and when present may be associated with some other disease⁴. The diagnosis is established by looking for the malarial parasite using thin and thick smears stained with Giemsa stain or by using antigen assay methods such as MP(ICT) to detect malarial antigen.

Hematological abnormality most commonly seen in malaria is thrombocytopenia followed by anemia. Both are seen with all types of malaria but most commonly

with falciparum malaria.⁴

Immune processes leading to lysis of platelets, sequestration in spleen and impaired thrombopoiesis in bone marrow are all thought to be responsible for the thrombocytopenia in malaria.⁵

The presence of thrombocytopenia with high grade fever should increase our suspicion of the probability of the diagnosis of malaria.⁶

Malarial parasites are not seen in the blood all the time, being present periodically with rupture of RBCs. In the current scenario of dengue epidemics occurring regularly in different regions of the country we need to be very vigilant about the diagnosis and should develop a policy of platelet transfusion; reserving it for patients at risk of bleeding. In malaria platelet counts go up with fever defervescence while with dengue as the fever goes down the possibility of significant vascular leakage and its associated complications like Dengue Haemorrhagic Fever and Dengue Shock Syndrome increases.⁷

This study also focuses on the point that a low platelet count with vivax malaria does not usually need platelet transfusion. Treatment of primary cause, i.e malaria, results in improvement of platelet count.

This study was conducted to find out the frequency of thrombocytopenia in patients with malaria, to assess its severity, incidence of bleeding episodes and the need of platelet transfusion in these patients.

MATERIALS AND METHOD

This descriptive case-series study was conducted in the Medical Ward of Sir Syed Hospital, Karachi, Pakistan, which is a secondary care center. The patients belonged to a low socioeconomic urban population of South Karachi. The sample population, through convenience sampling, comprised all the diagnosed malaria patients who presented to the hospital. This secondary care hospital drains a population of around 600,000 people; therefore the sample size was small. Thus 69 patients who were diagnosed with malaria, from 1-7-2011 till 30-6-2012, were included in the study. The diagnosis of malaria was made through observation of malarial parasite on peripheral smear examination stained with Giemsa on conventional microscopy or serological evidence of malarial infection (MP-ICT) through SD Bioline Malaria Antigen Pf/Pan Test (Standard Diagnostics, Inc., Korea) which is a one-step rapid qualitative and differential test for detection of Plasmodium species in human blood sample. Platelet count was done through automated cell count analyzer (D3 Analyzer). Baseline platelet counts were done on day of presentation. Repeat platelet counts were done in subjects with thrombocytopenia until normal or near normal counts were reached. Hemoglobin levels were measured on day of presentation and if low, was repeated till an upward trend was noticed. Dengue serology was done in patients with suspicion of dengue fever. Patients positive for dengue were excluded. Also pediatric patients, patients with other acute febrile illness negative for malarial parasite on peripheral film or MP (ICT) were excluded. Patients with localizing cause of fever, with history or clinical features of chronic liver disease, patients with bleeding disorders or idiopathic thrombocytopenic purpura were also excluded.

The clinical presentation of the patient was also recorded. Any bleeding episode before and during hospital stay was given special attention.

Data was entered on Excel spreadsheet and statistical analysis was performed with SPSS version 16.0. The results were obtained in numbers and percentages. Data was expressed as means with standard deviation.

RESULTS

In this study 69 patients with malaria were analyzed with 64 having vivax malaria and 3 having falciparum malaria and 2 patients had a mixed infection, both vivax and falciparum malaria.

Out of these patients 41 were male and 28 were female. The mean age of the patients was 34.7 years with a standard deviation of 13.8 range (13-65 years). Most patients had history of 5 days illness and the most frequent presenting complaint was fever followed by vomiting and headache.

In patients with vivax malaria 55 patients had thrombocytopenia i.e 85.9%. The lowest counts seen with vivax were 15,000/ μ L. Mean platelet count was $86.4 \times 10^3 / \mu$ L (Range 15-213 $\times 10^3 / \mu$ L).

Out of the 3 patients with falciparum malaria 2 had thrombocytopenia (66.6%). Lowest count seen with falciparum malaria was 20,000/ μ L. The mean platelet count was $70.6 \times 10^3 / \mu$ L, (range 20-168 $\times 10^3 / \mu$ L).

The platelet counts started improving within a day of achieving normal body temperature and achieved normal counts within 5-7 days after treatment. The time period required for normalization of platelet count was directly proportional to the initial platelet count, being prolonged to two weeks in patient with platelet count of 15,000/ μ L at presentation.

Patients with malaria had a mean hemoglobin of 11.9g/dl and a range of 3.8-17.7 g/dl. The lowest hemoglobin level was seen in a pregnant patient with falciparum malaria.

Platelet count <20,000/ μ L was noted in 2 patients with vivax malaria and in none of those who had falciparum malaria.

None of the patients with either falciparum or vivax malaria had clinical manifestations of thrombocytopenia such as bleeding from any site or purpura. None of the patients received platelet transfusion.

TABLE I: FREQUENCY OF PATIENTS BY GENDER AND TYPE OF MALARIA

		Frequency	Percentage
Gender	Female	28	40.6
	Male	41	59.4
Malaria type	Vivax	64	92.8
	Falciparum	3	4.3
	Vivax, Falciparum	2	2.9

TABLE II: PLATELET COUNTS IN MALARIA PATIENTS

Criteria	Type of malaria	Mean x $10^3 / \mu$ L	Range x $10^3 / \mu$ L	Patients with thrombocytopenia
Platelets	Vivax Malaria	86.473	15--213	55 (85.9%)
	Falciparum Malaria	70.666	20--168	2 (66.66%)

DISCUSSION

Malaria is caused by protozoal parasite of genus *Plasmodium* which infects and lyses red blood cells. Four species of *Plasmodium* cause malaria in humans, i.e. *P. vivax*, *P. malariae*, *P. ovale* and *P. falciparum*. Of these *P. falciparum* is most likely to affect multiple organs like liver, spleen, brain, gastrointestinal tract, placenta etc. So it may present with different manifestations ranging from fever to life threatening multi-system disease⁸. Studies have been published which have reported severe disease caused by *P. vivax*. The manifestations are similar to *P. falciparum* albeit rarer.⁹

Thrombocytopenia and anemia are the most common hematological manifestations of malaria. In endemic areas malaria has been reported to be a common cause of low platelet count. In some regions it is used as an indicator of malaria in patients presenting with fever.¹⁰ Thrombocytopenia is a common feature of acute malaria and occurs in both *P. falciparum* and *P. vivax* infections regardless of severity of infection.¹¹ Thrombocytopenia has been reported to be associated with malaria, with incidence ranging from 40-85%. With some studies reporting a lower incidence in vivax malaria as compared to falciparum malaria.¹²

In Pakistan some studies have shown an incidence of thrombocytopenia of around 72% in patients suffering from malaria caused by *P. vivax*.^{13,14}

Thrombocytopenia associated with malaria is not commonly accompanied by clinical bleeding. Maximum thrombocytopenia usually occurs on the fifth or sixth day of infection and gradually rose after fever came down to normal. Platelets can fall to below 25,000/ μ L but this is not very common. Platelet counts rise rapidly with recovery.¹⁵

Thrombocytopenia was seen in 40-90% of patients infected with *P. falciparum* in India.^{16,17} The prevalence of malaria patients having a low platelet count highlights a fact that normal platelet counts are unlikely to be seen in malaria. Profound and severe thrombocytopenia with platelets as low as 5,000/microliter has been seen in *P. vivax* malaria.¹⁸

There is a case report from India with a patient having spontaneous mild gum bleeding with low platelet count i.e. 8,000/cubic mm in a patient with vivax malaria.¹⁹

Mechanism of thrombocytopenia is not very clear. Immune mediated lysis, splenic sequestration, a shortened platelet survival and dyserythropoiesis in marrow with decreased platelet production have all been postulated. In some cases parasitization of platelets has also been implicated as a cause. Abnormalities of platelet structure and function may also be caused by malarial infection. Thrombopoietin levels are raised in patients with severe malaria and it normalizes in 14-21

days. Platelets containing *P. vivax* have been seen on electron microscopy postulating lysis as a cause of thrombocytopenia. Thus lytic destruction and lysis because of platelet specific IgG antibodies that bind to the antigen of *P. vivax* in platelets have been implicated in the production of a low platelet count.²⁰⁻²⁴

Our study emphasizes the fact that in patients with acute febrile illness having low platelet counts, *P. vivax* malaria should also be kept as a differential diagnosis and should be treated according to the local drug resistance pattern prevalent in the area.

In our study none of the patients suffering from vivax malaria had platelets lower than 10,000/ μ L; counts less than 20,000/ μ L were seen with no evidence of bleeding. The prevalence of thrombocytopenia was 85.9% in patients with vivax malaria and 66.6% in patients with falciparum malaria in our study. Data suggests that platelet counts go down in majority of the patients suffering from malaria. This finding is consistent with the results from other studies.⁵

Platelet counts kept falling until normal body temperature was achieved. The lowest platelet counts were seen usually on the fifth or sixth day of infection. The count started to improve after normalization of body temperature, improved daily and was within the normal range a few days after recovery. The improvement was dependent on the lowest platelet count observed in the patient, taking a longer time with patients who had a lower platelet count initially.

In a study in India hemoglobin levels in the subjects with thrombocytopenia with vivax malaria were low i.e. mean hemoglobin 8.87 g/dl and hemoglobin levels were higher in patients with normal platelet counts where the mean hemoglobin was 11.89 g/dl.⁵ In dengue fever hemoglobin level may paradoxically rise with a low platelet count. In our study the patients had mean hemoglobin of 11.99 g/dl which is comparable to another study conducted in Pakistan.²

We could not compare the hematological values in different types of malaria because of low incidence of falciparum malaria in urban setting in Pakistan. Among the 69 patients analyzed in our study only two patients had falciparum malaria. Falciparum is commoner in rural areas of Pakistan while vivax malaria is seen more frequently in the urban areas.

Dengue fever is emerging as one of the causes of thrombocytopenia. It is a challenge to differentiate vivax malaria, falciparum malaria and dengue fever clinically. Usually dengue is associated with a low WBC count and a normal or high hemoglobin level and a high hematocrit along with thrombocytopenia. Studies reflecting the incidence and severity of thrombocytopenia in such cases of fever may be of great help to clinicians in diagnosing the disease. High or increasing hematocrit, very low or rapidly decreasing

platelet counts are important to recognize as they may indicate impending complications of dengue.²⁵

In our study a large majority of patients with vivax malaria had thrombocytopenia but none needed platelet transfusion as there was no evidence of systemic bleeding. At platelet levels lower than 20,000/ μ L the patient was cross matched and platelet transfusions kept ready but all patients improved their platelet counts without any episode of bleeding and without the need for platelet transfusion.

In patients with acute febrile illness and thrombocytopenia, malaria should be kept in the differential diagnosis and platelet transfusion should be withheld until there is clinical evidence of bleeding or platelet counts go below internationally recognized levels at which platelet transfusion is recommended.

CONCLUSION

Low platelet counts are common in all types of malaria especially *P. vivax* and *P. falciparum* malarias. These counts are transient and may not merit platelet infusion. Most severe malarias have low platelet counts. Platelet infusion is required in those cases which show evidence of systemic bleeding. Clinically evident bleeding is not very common in malaria, even in severe illness. In conclusion, absence of thrombocytopenia is uncommon in the laboratory diagnosis of malaria.

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