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General Medicine

TO ASSESS SEVERITY OF THROMBOCYTOPENIA WITH TYPE OF MALARIA IN PATIENTS ADMITTED IN TERTIARY CARE HOSPITAL, NANDYAL

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ABSTRACT

Background: Malaria remains one of the major health problems in the tropics with increased morbidity & mortality. Thrombocytopenia is a common finding in malaria, but its correlation with the type of malaria and prognostic implications in context with severity of low platelet count has not been evaluated in large studies. In view of paucity of data from Indian studies, we attempt to correlate the low platelet count with type of malaria and outcome.

OBJECTIVES: To study the incidence of thrombocytopenia in malaria.

To correlate the severity with type of malaria and its prognostic significance

Methods: A total of 90 patients diagnosed to have Malaria over a period of three months admitted in Santhiram hospital were studied. All study subjects were identified positive for Malaria parasite on peripheral smear examination with conventional microscopy.Platelet count was done on a fully automated , quantitative analyzer. Daily platelet count was done for all those admitted with malaria. P.falciparum antigen test (PfHrp antigen test- Parascreen) was performed in subjects with P.vivax Malaria on the peripheral smear with a platelet count less than 20,000cells/cmm for more emphatic exclusion of associated P.falciparum infestation. P.falciparum antigen test was also performed in subjects with high index of clinical suspicion or multi organ involvement.

Results: In our study, a total of 90 patients were found to have malaria, 57(63.3%) were P.vivax, 31(34.4%) were P.falciparum and 2(2.7%) were mixed. 73(81.1%) patients had thrombocytopenia.17(23.3%) developed complicated malaria. Severe thrombocytopenia was noted in 58.8% of complicated malaria with $p<0.001$. 10 patients persisted to have thrombocytopenia on 6th day even after adequate therapy. 7(70%) patients out of 10 recovered and 3(30%) died in which one was P.falciparum and 2 were mixed infection.

Interpretation and conclusion: Thrombocytopenia is a common association of malaria with incidence of 81.1%. Severe thrombocytopenia is commonly seen in P.falciparum. Platelet count <25,000 was not seen in P.vivax. Out of 18 severe thrombocytopenia 17 developed complicated malaria with significant p value indicating that patients with severe thrombocytopenia at the time of admission are 8.5 times more prone to develop complications when compared to mild and moderate thrombocytopenia. Patients who persisted to have thrombocytopenia even after 6th day of therapy, their mortality increased by 30%.

KEYWORDS :

INTRODUCTION :

Malaria is probably one of the oldest diseases known to mankind that has had profound impact on our history. It is a protozoal disease caused by infection with plasmodium and transmitted to man by female anopheles mosquito.Malaria affects almost all blood components and is a true hematological disease.In endemic areas it has been reported as the major cause of thrombocytopenia.In some places it is used as an indicator of severity of malaria in patients presenting with fever. For centuries it prevented any economic development in vast regions of the earth. It continues to be a huge social, economical and health problem, particularly in the tropical countries. History of malaria and its terrible effects is as ancient as the history of civilization, therefore history of mankind itself.

Malaria was linked with poisonous vapours of swamps or stagnant water on the ground since time immemorial. This probable relationship was so firmly established that it gave the two most frequently used names to the disease mal'aria, later shortened to one word malaria, and paludisme. The term malaria (from the Italian mala "bad" and aria "air") was used by the Italians to describe the cause of intermittent fevers associated with exposure to marsh air or miasma. The term malaria, without the apostrophe, evolved into the name of the disease only in the 20th century. Up to that point the various intermittent fevers had been called jungle fever, marsh fever, paludal fever, or swamp fever.

Malaria affects more than 2400 million people, over 40% of the world's population, in more than 100 countries in the tropics from South America to the Indian peninsula. The tropics provide ideal breeding and living conditions for the anopheles mosquito, and hence this distribution. Every year 300 million to 500 million people suffer from this disease (90% of them in sub-Saharan Africa, two thirds of the remaining cases occur in six countries- India, Brazil, Sri Lanka, Vietnam, Colombia and Solomon Islands).

WHO forecasts a 16% growth in malaria cases annually .Malaria ranks third among the major infectious diseases in causing deaths- after pneumococcal acute respiratory infections and tuberculosis. It is expected that by the turn of the century malaria would be the number one infectious killer disease in the world.Malaria was nearly eradicated from most parts of the world by the early 60's, owing largely to anti malarial campaigns world over under the guidance of the World Health Organization.[1]

AIM AND OBJECTIVES :

- To study the incidence of thrombocytopenia in malaria.
- To correlate the severity of thrombocytopenia with type of malaria.
- To assess outcome in the study group

MATERIAL AND METHODS :

A Hospital-based Prospective study was conducted in the Department of General Medicine, Santhiram Medical College, and General Hospital for three months after taking approval from the Hospital Ethics and Research Committee.

- **Sampling Technique and Sample Size:** Universal Sampling Technique was used for the selection of study subjects. All the patients coming to the medicine department during the study period and fulfilling the inclusion and exclusion criteria were taken for study after taking prior informed consent. **90 cases during the study period were taken into study after satisfying**

the inclusion and exclusion Criterias.

Inclusion Criteria:
- All patients above 18 years whose blood smear or rapid kit is positive for malaria are included in the study.
- Platelet count < 1, 50,000 cells/ cmm
- Patients admitted in santhiram general hospital.
- Patients with informed written consent taken.

Exclusion criteria:
- Congenital & Hereditary Thrombocytopenia
- Immune induced thrombocytopenia
- Drug induced thrombocytopenia
- Thrombocytopenia due to other infections
- Patients without informed consent

Data Analysis:
Chi square test or Fisher Exact test and student 'T' test has been used to find the significant association of study characteristics (Thrombo cytopenia) with type of malaria.

RESULTS :
A total of 90 subjects who diagnosed to have Malaria over a period of three months were studied. The mean age of patients was 38.31 ± 12.25 years. The study included 75.6% males and 24.4% females. . A total of 90 subjects who had malaria, 57 were P.vivax , 31 were P.falciparum and 2 have mixed infection. Incidence of P.vivax was 63.3% , P.falciparum 34.4% and mixed infection 2.7%.Typical paroxysums were observered in 20 patients of P.Vivax and 5 patients of P.Falciparum. Under atypical manifestations ,vomiting was seen in 13 patients of P.Falciparum , 5 patients in P.Vivax and 2 in mixed infection; headache in 15 patients of P.Falciparum and 8 in P.Vivax; jaundice in 10 patients of P. falciparum,2 P.vivax and 2 mixed infection; altered sensorium in 8 patients of P.Falciparum and none in P.Vivax; pain abdomen in 6 patients of P.Falciparum and none in P.Vivax; cough and breathlessness in 8 patients of P.Falciparum and none in P.Vivax; joint pain in 3 patients in P.Falciparum 2 in P.Vivax. Commonest atypical symptom being headache and vomiting. Common clinical sign in decreasing order are splenomegaly(86.7%), pallor(46.6%), Icterus(13.3%), hepatomegaly(11%), altered sensorium(8.9%), petechiea(3.7%).

Table-1:Incidence of thrombocytopenia

Incidence of thrombocytopenia	Number (n=90)	%
Normal (>1.5 lakh)	17	18.9
Mild (1.0-1.5 lakh)	27	30.0
Moderate (0.50-0.99 lakh)	28	31.1
Severe (<0.5 lakh)	18	20.0

Incidence of Thrombocytopenia was 73(81.1%). with mild Thrombocytopenia 27(30%), moderate Thrombocytopenia 28(31.1%) and 18(20%) with severe Thrombocytopenia.

Normal platelet count was observered in 18.9% of patients indicating thrombocytopenia is a common association in malaria.73 out of 90 who had thrombocytopenia were taken up, to study its prognostic implication.

Table-2:Association of thrombocytopenia with species

Thrombocytopenia	Species			Total
	P. Falci	P. Vivax	Mixed	
Mild	9 (31%)	18(42.8%)	-	27
Moderate	12(41.3%)	16 (38%)	-	28
Severe	8 (27.5%)	8(19%)	2(100%)	18
Total	29	42	2	73

Mild Thrombocytopenia were 18(42.8%) in P.Vivax as against to 9(31%) in P.Falciparum .

Moderate Thrombocytopenia were 16(38%) in P.Vivax as against to 12(41.4%) in P.Falciparum and Severe Thrombocytopenia were 8(19.1%) in P.Vivax as against to 8 (27.5%) in P.Falciparum, mixed infection 2(100%).

Table-3:Complicated malaria with species

Criteria	Number of patients	Species		
		P. Falciparum	P.Vivax	Mixed
Hb<5 gm/dl	12	10 (83.3%)	2 (16.7%)	-
S.Creatinine >3mg%	9	4 (44.4%)	3 (33.3%)	2(22.2%)
T.Bilirubin(>3 mg/dl)	12	10 (83.3%)	-	2 (16.7%)
M.acidosis.ph<7.2	11	8 (72.7%)	1(9.1%)	2(18.2%)
Spt bleeding and DIC	6	5(83.3%)	-	1(16.7%)
Coma >30min	3	1(33.3%)	-	2(66.7%)
Hyperparasitemia>5%	4	2(50.0%)	-	2(50.0%)
B.sugar<40mg%	1	-	-	1(100.0%)
Prostration	12	8(66.7%)	2(16.7%)	2(16.7%)
ARDS	4	2 (50.0%)	-	2 (50.0%)
Systolic BP<80mmhg	6	2 (33.3%)	2 (33.3%)	2 (33.3%)

According to the revised WHO guidelines of 2000, patients who had Thrombocytopenia were grouped into complicated and uncomplicated. In our study,out of 73 patients 17 cases had complicated malaria and 56 cases had uncomplicated malaria. In complicated malaria 12 patients had Hemoglobin <5gm% in which 10(83.3%) were P.Falciparum and 2(16.7%) were P.Vivax, 9 patients had s.creatinine >3mg% in which 4(44.4%) were P.Falciparum and 3 (33.3%) were P.Vivax, 12 patients had T.Bilirubin >3mg% in which 10(83.3%) were P.Falciparum and 2(16.7%) were mixed, 11 patients had metabolic acidosis (ph<7.2) ,8(72.7%) were P.Falciparum and 1(9.1%) were P.Vivax,and 2 mixed(18.2%). 6 patients had spontaneous bleeding with DIC in which 5(83.3%) were P.Falciparum and 1 (16.7%) in mixed, 3 patients had coma for > 30min, in which 1(33.3%) were P.Falciparum and 2(66.7%) were mixed, 4 patients had hyperparasitemia in which 2 (50%) in P.Falciparum and 2(50%) in mixed, 1 patient had hypoglycemia which was mixed infection, 12 patients had prostration in which 8(66.7%) were P.Falciparum,2(16.7%) P.Vivax and 2(16.7%) mixed, 4 patients had ARDS in which 2(50%) were P.Falciparum and 2(50%) were mixed, 6 patients developed shock in which 2 (33.3%) were P.Falciparum, 2(33.3%) were P.Vivax and 2(33.3%) were mixed .Complications were commonly seen in P.falciparum and mixed compared to P.vivax of which anemia and hyperbilirubinemia being the most common

Table-4:Association of thrombocytopenia with severity of malaria

Thrombocytopenia	Severity of malaria		Total
	Uncomplicated	Complicated	
Mild (1.0-1.5 lakh)	24 (42.9%)	3(17.6%)	27
Moderate (0.5-1.0 lakh)	24(42.9%)	4(23.5%)	28
Severe (<0.5 lakh)	8 (14.3%)	10(58.8%)	18
Total	56 (100.0%)	17(100.0%)	73
Inference	Patients with Severe thrombocytopenia are 8.5 times more likely to have complicated malaria with P<0.001** according to student 'T' test		

Relationship of degree of thrombocytopenia to severity of malaria.Out of 56 uncomplicated malaria, mild thrombocytopenia was noted in 24(42.9%), moderate thrombocytopenia in 24(42.9%), and severe thrombocytopenia in 8(14.3%). Out of 17 cases of complicated malaria mild thrombocytopenia was noted in 3(17.6%), moderate thrombocytopenia in 4(23.5%) and severe thrombocytopenia in 10(58.8%). P value <0.005, was noted in severe thrombocytopenia

Table-5:Association of complicated malaria with type of malaria

Species	Type of Malaria		Total	P value
	Uncomplicated	complicated		

P Falciparum	19 (33.9%)	10(58.8%)	29	0.066+
P. Vivax	37(66%)	5(29.4%)	42	0.007**
Mixed	-	2 (11.7%)	2	0.062+
Total	56(100%)	17(100%)	73	-

Relationship of severity of malaria to species, out of 56 uncomplicated cases of malaria 19 (33.9%) were P.Falciparum and 37(66%) were P.vivax. Out of 17 cases of complicated malaria 10(58.8%) were P.falciparum, 5(29.4%) were P.vivax and 2(11.7%) were mixed infection Daily platelet count was done for all patients from the day of admission to 6th day of discharge, and underwent specific treatment. On an average 6th day was considered as last day . On day one 73 patients had low platelet count, on day two 61 patients had low platelet count, on day three 58 patients had low platelet count, on day four 45 patient had low platelet counts, on day five 28 patients had low platelet counts, on day six 10 patients persisted to have low platelet count despite of adequate therapy.

Table-6:Association of species with outcome

Species	Outcome		Number of patients
	Died	Recovered	
P. Falciparum	1 (3.4%)	28(96.6%)	29
P. Vivax	-	42(100.0%)	42
Mixed	2(100.0%)	-	2
Total	3 (4.1%)	70(95.9%)	73

Out of 73 cases 3 died with the overall mortality of 4.1%.10 patients who persisted to have thrombocytopenia on 6th day 7 recovered and 3 died in which 1 was P.falciparum and 2 were mixed infection with an increase in mortality rate of 30%.

DISCUSSION :

Falciparum malaria presents with protean manifestations and is associated with a variety of complications and has a high mortality. Thrombocytopenia is a common feature of acute malaria and occurs in both P. falciparum and P. vivax infections regardless of the severity of infection. The absence of the normal quantity of platelets on a peripheral smear in a case of fever is often a clue to the presence of malaria as seen in this study also. Thrombocytopenia is rarely accompanied by clinical bleeding or biochemical evidence of DIC. Platelet counts can fall to below 25,000/µl but this is uncommon.[2] Platelet counts rise rapidly with recovery. The prevalence of thrombocytopenia was 81.1% of the cases studied in our series and highlights the fact that a persistent normal platelet count is unlikely in the laboratory findings of malaria. Thrombocytopenia was seen in 40-90 percent of patients infected with P. falciparum infection in India[3,4.] Maximum thrombocytopenia occurred on the fifth or sixth day of infection, and gradually returned to normal within 5-7 days after parasitemia ceased. The mechanism of thrombocytopenia in malaria could be due to peripheral destruction and consumption by DIC.[5,6] Profound thrombocytopenia with platelet count as low as 5000/µl has been reported in the Indian literature in a 43-year old female patient with vivax malaria.[7] Although none of the subjects suffering from vivax malaria had a platelet count less than 5000/µl in our series, counts ranging from 5,000 to 20,000/µl were noted without any evident bleeding. This must be considered in the context that very low platelet counts can be transient in the course of malaria illness and may not necessarily have prognostic implications or merit platelet infusions. Most severe malaria patients have thrombocytopenia; however, platelet concentrate transfusion is indicated only in patients with systemic bleeding. Clinical bleeding in severe malaria is not a common feature and occurs in less than 5-10% of individuals with severe disease. Platelet and fibrin deposition are rarely seen in the capillaries of patients at postmortem and despite numerous studies indicating elevated levels of fibrin degradation products, clinical DIC is rare. A host of other indicators of intravascular coagulation may be found to be outside the normal range, but this appears to be only a reflection of the severity of the disease. Thrombocytopenia , per se cannot be a distinguishing feature in a particular case of malaria, although there is a statistical significant difference in the prevalence and severity of thrombocytopenia between the two types of malaria. The mechanism of thrombocytopenia in malaria is uncertain. Immune-mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have all been postulated. Abnormalities in platelet structure and function have been described as a consequence of malaria, and in rare instances platelets can be invaded by malarial parasites themselves. Thrombopoietin (TPO) is the key growth factor for platelet production and is elevated in states of platelet depletion. TPO serum levels have been shown to be significantly higher in subjects with severe malaria, normalizing within 14-21 days of therapy.[8] 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 malarial parasites themselves. Two types of changes in platelet dysfunction are seen in malaria. Initially there is platelet hyperactivity, this is followed by platelet hypoactivity. Platelet hyperactivity results from various aggregating agents like immune complexes, surface contact of platelet membrane to malarial red cells and damage to endothelial cells. The injured platelets undergo lysis intravascularly. The release of platelet contents can activate the coagulation cascade and contributes to DIC. Transient platelet hypoactivity is seen following this phase and returns to normal in 1 to 2 weeks.[9,10] In many studies undertaken, the significance of haemostatic abnormalities as a consequence of malaria has been difficult to assess as a result of the presence of various associated complications such as liver dysfunction, uraemia and treatment with low molecular weight dextran, dexamethasone and heparin. Quinine-associated thrombocytopenia may present rapidly with symptoms of profound thrombocytopenia. Center for Drug Evaluation and Research (CDER) CDER, USA continues to receive reports of thrombocytopenia in association with quinine in use for nocturnal leg cramps and should evoke interest in context with therapy of malaria and thrombocytopenia.[11] However, there are no literature reports of quinine-induced thrombocytopenia in malaria.

CONCLUSION :

Thrombocytopenia is common in the laboratory diagnosis of malaria and presence of thrombocytopenia is not a distinguishing feature between the two types of malaria. Its presence in patients who present with acute febrile illness in the tropics, increases the probability of malaria. This may be used in addition to the clinical assessment, to heighten the suspicion of this disease. If thrombocytopenia is present, malaria has to be ruled out before performing expensive tests to rule out other febrile conditions, so that a prompt treatment can be initiated.[25] Thrombocytopenia less than 20,000/ µl can occur in P. vivax malaria although statistically more significant with P. falciparum malaria.

REFERENCES

1. New Delhi: DGHS, Ministry of Health and Family Welfare; 2009. Government of. India Strategic Action Plan for Malaria Control in India 2007-2012
2. Sharma SK, Das RK, Das BK, Das PK. Haematological and coagulation profile in acute falciparum malaria. J Assoc Physicians India 1992; 40: 581-3.
3. Krishna S, Waller D, ter-Kuite F, et al. Lactic acidosis and hypoglycemia in children with severe malaria: pathophysioligical and prognostic significance. Trans R Soc Trop Med Hyg 1994; 88:67-73.
4. Sharma SK, Das RK, Das BK, Das PK Haematological and coagulation profile in acute falciparum malaria. J Assoc Physicians India 1992;40:581-3.
5. Skudowitz R, Katz J, Lurie A, et al. Mechanisms of thrombocytopenia in malignant tertian malaria. BMJ 1973;1:151-8.
6. Looareesuwan S, Davis J, Allen D, et al. Thrombocytopenia in malaria. South Asian J Trop Med Publ 1993;23:44-50.
7. Kakar A, Bhoi S, Prakash V, Kakar S. Profound thrombocytopenia in Plasmodium vivax malaria. Diagn Microbiol Infect Dis 1999;35:243-4.
8. Kreil A, Wenisch C, Brittenham G, Looareesuwan S, PeckRadosavljevic M. Thrombopoietin in Plasmodium falciparum malaria. Br J Haematol 2000;109:534-6.
9. Srichaikul T, Pulket C, Sirisatepisan T, Prayoonwiwat W. Platelet dysfunction in malaria. Southeast Asian J Trop Med Pub Health 1988;19:225-33.
10. Mohanty S, Marwaha K, Ghosh S, et al. Functional and ultrastructural changes of platelets in malaria infection. Trans R Soc Trop Med Hyg 82:369-75, J Clin Invest 1988;71:832-6.
11. Brinker AD, Beitz J. Spontaneous reports of thrombocytopenia in association with quinine: clinical attributes and timing related to regulatory action. Am J Hematol 2002;70:313-7.