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A Study of Incidence and Severity of Thrombocytopenia in Various Types of Malaria

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Abstract **Original Research Article**

Malaria continues to be a huge social, economic and health problem, particularly in the tropical countries. It still remains today as it has been for centuries, one of the most serious parasitic diseases of the world affecting 300-500 million people and causing over 1 million deaths each year. This prospective study was conducted to study the incidence of malaria, incidence & severity of thrombocytopenia in various types of malaria and how thrombocytopenia is associated with the severity of malaria. Total 145 cases of malaria, admitted in the Medicine Department between June 2012 to Oct. 2013 were studied. Patients were evaluated for the various clinical presentations as per a predefined proforma. Incidence of malaria in relation with age, sex, clinical features, types of species of malaria, baseline hematological profile of subjects with malaria in relation with various species of malaria, incidence of thrombocytopenia and its severity in relation with various species of malaria & how thrombocytopenia is associated with the severity of malaria was observed. In this study we found that Patients among reproductive age group are affected more than others, severe thrombocytopenia is seen more commonly with P. falciparum as compared to P. vivax and the patients having severe thrombocytopenia are more likely to have complicated malaria as compared to moderate and mild cases.

Keywords: Thrombocytopenia, types of malaria, species of malaria.

INTRODUCTION

Malaria is one of the oldest diseases known to mankind that has had profound impact on our history. It continues to be a huge social, economic 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 [1].

Malaria still remains today as it has been for centuries, one of the most serious parasitic diseases of the world affecting 300-500 million people and causing over 1 million deaths each year. It remains a serious public health problem in the south East Asia region with nearly 290 million people estimated to be at high risk. Although the reported mortality and morbidity showed a declining trend.

There are four identified species of this parasite causing human malaria, namely, Plasmodium vivax (PV), P. falciparum (PF), P. ovale (PO) and P. malariae (PM). It is transmitted by the female anopheles mosquito. It is a disease that can be treated in just 48 hours, yet it can cause fatal complications if the diagnosis and treatment are delayed. It is re-emerging as Infectious Killer and it is the Number 1 Priority Tropical Disease of the World Health Organization [1, 2].

A typical attack 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 the infection and also the presence of concomitant conditions such as malnutrition or other diseases. The febrile paroxysms occur with definite intermittent periodicity repeating every third or fourth day depending upon the species of the parasite involved [3].

Of the four species of plasmodia causing human malaria, P. falciparum has the potential for developing life threatening complications, which may result in fatality.

Infection with *Plasmodium falciparum* is more serious than with other malarial species, because of frequency of severe and fatal complications associated with it. This lethal parasite can be the basis to cerebral malaria, acute renal failure, acute malarial hepatitis, hypoglycemia, hyperpyrexia, non-cardiogenic pulmonary oedema, adult respiratory distress syndrome, adrenal insufficiency-like syndrome, hyperparasitemia, Blackwater fever, cardiac arrhythmias [1, 2].

The exact cause of thrombocytopenia in falciparum malaria is unknown but immune-mediated lysis, sequestration of platelets in spleen and dyspoietic process in the bone marrow leading to decreased platelet production, have all been postulated [1].

This prospective study was conducted to study the incidence of malaria, incidence & severity of thrombocytopenia in various types of malaria and how thrombocytopenia is associated with the severity of malaria.

MARERIALS & METHODS

This is a prospective study conducted in the Department of Medicine after taking permission from the Institute's local ethical committee. Total 145 cases of malaria, admitted in the Medicine Department between June 2012 to Oct. 2013 were included in the study.

Adult patients with age more than 12 yrs, patients presenting with fever, headache, bodyache, patients who were confirmed having malaria by slide method or MPFM (Malaria parasite by Fluorescence microscopy method) or Malaria kit & patients having platelet count less than 1.5 lacs were included in the study.

Patients who were negative by MPFM or slide method or Malaria kit, patients having platelet count more than 1.5 lacs, patients having dengue IgM elisa test positive, patient having thrombocytopenia because of diseases other than malaria like dengue, drugs like aspirin were excluded from the study.

All the patients were evaluated for the various clinical presentations as per a predefined proforma. All the patients were investigated for CBC, malaria by slide method or MPFM or malaria kit, dengue IgM elisa, S. bilirubin, SGOT, SGPT, Blood urea, serum creatinine, serum proteins, chest x-ray & ECG.

Incidence of malaria in relation with age, sex, clinical features, types of species of malaria was observed. Baseline hematological profile of subjects with malaria was observed in relation with various species of malaria. Incidence of thrombocytopenia and its severity was also observed in relation with various species of malaria & finaly observations were made how Thrombocytopenia is associated with the severity of malaria.

Aim & objectives

- To study the incidence of malaria in various age and sex groups.
- To study the incidence of thrombocytopenia among the malaria patients.
- To study the severity of the thrombocytopenia in various types of malaria.
- To study the risk of morbidity and mortality in patients of malaria.

RESULTS

In the present study, out of total 145 cases of malaria, 103 were males (71.03%) and 42 were female (28.97%) patients. Following observations were made from this study.

Population belonging to age group 12-20, 21-40, 41-60 yrs carry higher rate of incidence of malaria probably because of more contact with community and chances of travel to endemic areas (Table-I).

The common clinical features were fever with chills and rigors in 145 cases (100%), headache in 87 cases (60%), nausea & vomiting in 68 cases (46.9%), anaemia in 29 cases (20%), jaundice in 19 cases (13.1%), renal dysfunction in 7 cases (4.82%) and cerebral malaria in 4 cases (2.75%) (Table-II).

Table-I: Age distribution

Age in years	Number of patients	%
12-20	30	20.68
21-40	64	44.14
41-60	42	28.96
61-80	7	4.33
>80	2	1.38
Total	145	100

Table-II: Frequency of clinical features with malaria

Clinical Features	Number of patients		
	PV (80)	PF (60)	Mixed (5)
Fever	80	60	5
Headache	47	37	3
Nausea & Vomiting	34	32	2
Jaundice	6	11	2
Anaemia	12	14	3
Hepatomegaly/Splenomegaly	40	32	4
Renal dysfunction	2	4	1
Cerebral Malaria	1	3	0

Table-III: Distribution of physical Signs

Physical Signs	No. of patients		
	PV (80)	PF (60)	Mixed (5)
Splenomegaly	18	9	2
Anaemia	12	14	3
Icterus	6	11	2
Hepatomegaly	9	6	0
Hepatosplenomegaly	13	17	2
Hypotension	1	2	0

Commonest clinical sign among the cases was splenomegaly in 61 cases [29 isolated + 32 with hepatomegaly (42.07%)] followed by anaemia in 28 cases (19.31%) and icterus in 19 cases (13.1%) and three patients presented with Hypotension (2.06%).

Clinical spectrum of fever splenomegaly and pallor was commonaly associated with malaria.

Out of 145 cases, 80(55.17%) patients had P. Vivax malaria, 60(41.38%) had P. Falciparum malaria and 5(3.45%) cases had mixed malaria (Table-IV).

Table-IV: Type of species

Type of species	Number of patients	%
P. Falciparum	60	41.38
P. Vivax	80	55.17
Mixed	5	3.45
Total	145	100

Table-V: Incidence of thrombocytopenia

Degree of thrombocytopenia (Platelet count in lakhs)	Number of patients	%
Mild (1.0-1.5)	60	41.38
Moderate (0.5-0.99)	53	36.55
Severe (<0.5)	32	22.07
Total	145	100

In this study of 145 patients 60(41.38%) patients had mild thrombocytopenia while 53(36.55%) had moderate and 32(22.07%) cases had severe thrombocytopenia.

Table-VI: Baseline hematological profile of subjects with malaria

Hematological parameter	Species of malaria	Mean	Max. Value	Min. Value
WBC count	P. Vivax	7350.5	19600	2200
	P. Falciparum	8536.67	19700	2400
	Mixed	6680	15000	3500
Hemoglobin	P. Vivax	10.49	15.8	3.8
	P. Falciparum	9.315	14.2	2.4
	Mixed	7.03	10.56	3.7
Platelet count	P. Vivax	90612.5	149000	22000
	P. Falciparum	82793.33	149000	10000
	Mixed	51800	120000	13000

Above table revealed that the mean hemoglobin (9.315) & Platelet count (82793.33) in P. Falciparum cases was significantly lower than mean hemoglobin (10.49) and platelet counts (90612.5) in P. Vivax cases while mean WBC count is higher in P. Falciparum cases (8536.67) as compared to P. Vivax cases (7350.5).

Table-VII: Degree of thrombocytopenia in different species

Species of malaria	Mild thormbocy-topenia (Platelet Count 1-1.5 lakh)	Moderate thorombo-cytopenia (Platelet Count 50,000-1 lakh)	Severe thrombo-cytopenia (Platelet Count <50,000)	Total
P.Vivax	39 (65%)	28 (52.83%)	13(40.63%)	80
P. Falciparum	20 (33.33%)	24 (45.28%)	16 (50%)	60
Mixed	1 (1.66%)	1 (1.89%)	3 (9.37%)	5
Total	60 (100%)	53(100%)	32 (100%)	145

Out of 60 patients having mild thrombocytopenia 39(65%) were P. Vivax cases, 20(33.33%) were P. Falciparum and 1(1.66%) mixed malaria. Out of 53 patients having moderate thrombocytopenia 28(52.83%) were P. Vivax cases, 24(42.28%) were P. Falciparum and 1(1.89%) mixed malaria. Out of 32 patients having severe thrombocytopenia 13(40.63%) were P.Vivax cases, 16(50%) were P. Falciparum and 3(9.37%) mixed malaria.

Table-VIII: Association of Thrombocytopenia with severity of malaria

Severity of malaria	Mild Thrombocytopenia	Moderate Thrombocytopenia	Severe Thrombocytopenia	Total (%)
Uncomplicated	56 (93.33%)	42 (79.25%)	13 (40.62%)	111 (76.55%)
Complicated	4 (6.66%)	11 (20.75%)	19 (59.38%)	34 (23.45%)
Total	60 (100%)	53 (100%)	32 (100%)	145 (100%)

Mild vs Moderate - P = 0.0276 = Significant
Mild vs severe - P = < 0.0001 = Highly significant
Mod.vs severe - p = < 0.0001 = Highly significant

Out of the 34 complicated malaria cases only 4(11.76%) had mild thrombocytopenia while 11(32.35%) cases had moderate and 19(55.88%) cases had severe thrombocytopenia further analysis revealed P value < 0.001 which is statistically highly significant and proves that patients having severe thrombocytopenia are more likely to have complicated malaria as compared to moderate and mild cases.

Table-IX: Association of Species with severity of malaria

Species	Severity of malaria		Total
	Uncomplicated	Complicated	
P. Vivax	68 (61.26%)	12 (35.29%)	80 (55.17%)
P. Falciparum	41 (36.94%)	19 (55.88%)	60 (41.38%)
Mixed	2 (1.80%)	3 (8.82%)	5 (3.42%)
Total	111 (100%)	34 (100%)	145 (100%)

PV vs PF - P = 0.0188 = Significant

Out of 34 complicated cases 19(55.88%) had P. Falciparum Malaria revealing a statistically significant P value. Complication rate is higher in P Falciparum than P. Vivax.

Table-X: Association of Species with severity of malaria & degree of thrombocytopenia

Type of malaria	Degree of Thrombo-cytopenia	Uncompli-cated malaria	Complicated malaria	Death	Total
P. Vivax	Mild	37	2	1	39
	Moderate	24	4	0	28
	Severe	7	6	1	13
P. Falciparum	Mild	18	2	0	20
	Moderate	17	7	1	24
	Severe	6	10	2	16
Mixed	Mild	1	0	0	1
	Moderate	1	0	0	1
	Severe	0	3	0	3
Total		111	34	5	145

The above table revealed increase in the rate of complication with increasing degree of thrombocytopenia.

Table-XI: Association of species with outcome

Species	Outcome		No. of patients
	Died	Recovered	
P. Vivax	2 (2.5%)	78 (97.5%)	80
P. Falciparum	3 (5%)	57 (95%)	60
Mixed	0 (0%)	5 (100%)	5
Total	5(3.45%)	140(96.55%)	145

On association of species with outcome analysis shows P value > 0.05 which is not significant proving that mortality has no relation with species of malaria.

Table-XII: Association of thrombocytopenia with outcome

Degree of Thrombocytopenia	Outcome		No. of patients
	Died	Recovered	
Mild	1 (1.69%)	59 (98.31%)	60
Moderate	1 (1.89%)	52 (98.11%)	53
Severe	3 (9.38%)	29 (90.62%)	32
Total	5 (3.45%)	140 (96.55%)	145

On Association of mortality with thrombocytopenia also P value was found to be > 0.05 which is statistically not significant showing that alone thrombocytopenia has no relation with mortality.

DISCUSSION

Out of total of 145 cases of malaria, population belonging to age group 12-20, 21-40, 41-60 yrs carry higher rate of incidence of malaria probably because of more contact with community and chances of travel to endemic areas. This study includes 103 male (71.03%) and 42 female (28.97%) patients.

The common clinical features observed were fever with chills and rigors in 145 cases (100%), headache in 87 cases (60%), nausea & vomiting in 68 cases (46.9%), anaemia in 29 cases (20%), jaundice in 19 cases (13.1%), renal dysfunction in 7 cases (4.82%) and cerebral malaria in 4 cases (2.75%). Commonest clinical sign among the cases was splenomegaly in 61 cases [29 isolated + 32 with hepatomegaly (42.07%)], followed by anaemia in 28 cases (19.31%) and icterus in 19 cases (13.1%) and three patients presented with hypotension (2.06%). Clinical spectrum of fever, splenomegaly and pallor was commonaly associated with malaria.

A study conducted by Murthy G L *et al*. [7] on "Clinical profile of falciparum malaria in a tertiary care hospital" found fever with chills and rigors (98.10%), altered sensorium (48.10%), algid malaria (18.35%) and jaundice (27.21%) in malaria patients. The other features were oliguria (6.96%) and bleeding manifestations due to disseminated intravascular coagulation (DIC) (4.43%).

Grobusch MP *et al*. [4] in their observational study on uncomplicated malaria noted that symptoms and signs of uncomplicated malaria are non-specific, as shared with other febrile conditions, and can occur early or later in the course of the disease. In endemic areas, the presence of hepatosplenomegaly, thrombocytopenia and anaemia is clearly associated with malaria. Fever, cephalgias, fatigue, malaise, and musculoskeletal pain constitute the most frequent clinical features in malaria.

In this study, incidence of P.vivax malaria was 55.17% and P.falciparum was 41.38%. Prevalence of P.vivax malaria is common in India, because of variation in climatic condition, breeding places of mosquito and genetic resistance of P.falciparum.

Jain M. *et al*. [5] on Comparative study of microscopic detection methods and haematological changes in malaria, observed that Anaemia was present in 66 (94.28%) samples of which 37 (56.06%) were Plasmodium falciparum, 21 (31.81%) were Plasmodium vivax and 8 (12.12%) had mixed infection (Plasmodium falciparum and Plasmodium vivax). Thrombocytopenia was found in 49 (70%) samples of which 33 (67.34%) were Plasmodium falciparum.

In this study of 145 patients 60(41.38%) patients had mild thrombocytopenia while 53(36.55%) had moderate and 32(22.07%) cases had severe thrombocytopenia. Out of 60 patients having mild thrombocytopenia 39(65%) were P. Vivax cases, 20(33.33%) were P. Falciparum and 1(1.66%) mixed malaria. Out of 53 patients having moderate thrombocytopenia 28(52.83%) were P. Vivax cases, 24(42.28%) were P. Falciparum and 1(1.89%) mixed malaria. Out of 32 patients having severe thrombocytopenia 13(40.63%) were P. Vivax cases, 16(50%) were P. Falciparum and 3(9.37%) mixed malaria.

A study conducted by Kumar A *et al*. [6] on Thrombocytopenia-an indicator of acute vivax malaria suggested that thrombocytopenia as an early indicator for acute malaria; a finding that is frequent and present even before anaemia and splenomegaly set in. The

possible mechanisms leading to thrombocytopenia in malaria includes immune mechanisms, oxidative stress, alterations in splenic functions and a direct interaction between plasmodium and platelets.

In the present study, among the 80 cases of P. Vivax malaria 39(48.75%) had mild thrombocytopenia, 28(35%) had moderate and 13(16.25%) cases had severe thrombocytopenia. Among the 60 cases of P. Falciparum malaria 20(33.33%) had mild thrombocytopenia, 24(40%) had moderate and 16(26.66%) cases had severe thrombocytopenia. Among the 5 cases of mixed malaria 1(20%) had mild thrombocytopenia 1(20%) had moderate and 3(60%) cases had severe thrombocytopenia.

In this study, the mean hemoglobin (9.315) & Platelet count (82793.33) in P. Falciparum cases was significantly lower than mean hemoglobin (10.49) and platelet counts (90612.5) in P. Vivax cases while mean WBC count is higher in P. Falciparum (8536.67) cases as compared to P. Vivax (7350.5) cases.

In the present study, among 145 cases of malaria, 34(23.45%) had complicated malaria and 111(76.55%) had uncomplicated malaria. Among 34 cases of complicated malaria, 19 (55.88%) were P. falciparum, 12 (35.19%) were P.vivax and 3 (8.82%) were mixed infection. Among 34 complicated malaria, 15 patients had severe anaemia (Hb<5gm%) 7 patients had renal dysfunction (creatinine > 3mg%), 8 patients had hepatic dysfunction & altered sensorium and 4 patients developed coma, out of which 3 patients died within 1 week which shows very high mortality rate in cerebral malaria.

Murthy G L *et al*. [7] observed that the frequently encountered complications were anaemia (74.68%), jaundice (40.50%), cerebral malaria (45.56%), thrombocytopenia (40.50%) and renal failure (24.68%).

In this study, out of the 34 complicated malaria cases only 4(11.76%) had mild thrombocytopenia while 11(32.35%) cases had moderate and 19(55.88%) cases had severe thrombocytopenia further analysis revealed P value < 0.001 which is statistically highly significant and proves that patients having severe thrombocytopenia are more likely to have complicated malaria as compared to moderate and mild cases.

Guha HA *et al*. [8] found that predominant complication was severe malarial anemia (45.4%), followed by convulsions (21%), cerebral malaria (16. 4%) and hypotension (11.8%). Severe malaria was recognized in all age groups, but 44.5% of patients were aged 2 to 4 years. The mean ages of patients with severe anemia (5.6 years) and convulsions (5.9 years) were significantly lower than the mean ages of patients with cerebral malaria (14.1 years) or hypotension (35.2 years).

In this study, out of 34 complicated cases, 19(55.88%) had P. Falciparum Malaria revealing a statistically significant P value. Significant no. of cases, 19(31.67%) out of total 60 P. Falciparum cases were having complicated malaria. Complication rate is higher in P Falciparum than P. Vivax.

Severe thrombocytopenia is commonly associated with complicated malaria, 19 cases (59.38%) as compared to mild and moderate based on student 'T' test showing P value < 0.001 which is statistically highly significant. So there is increase in the rate of complication with increasing degree of thrombocytopenia.

A study conducted by Krishnan A *et al*. [9] on Severe falciparum malaria: an important cause of multiple organ failure in Indian intensive care unit patients, concluded that Malaria is an important cause of multiple organ failure in India. Mortality rate is 6.4% when one or fewer organs fail but increases to 48.8% with failure of two or more organs. However, outcomes are better than for similar degrees of organ failure in sepsis.

Murthy G L *et al*. [7] in their study observed that most of the patients i.e., 126 (79.74%) recovered with treatment and 32 (20.25%) succumbed. Higher mortality was associated with higher parasite count, presence of complications like anaemia, jaundice, renal failure, DIC, adult respiratory distress syndrome (ARDS), and septicemia.

CONCLUSION

In the present study, we found that patients among the age group 12-20, 21-40, 41-60 yrs are affected more than others. In this study, 103 patients were male (71.03%) and 42 were female (28.97%).

The common clinical features observed were fever with chills and rigors in 145 cases (100%), headache in 87 cases (60%), nausea & vomiting in 68 cases (46.9%), anaemia in 29 cases (20%), jaundice in 19 cases (13.1%), renal dysfunction in 7 cases (4.82%) and cerebral malaria in 4 cases (2.75%). Commonest clinical sign among the cases was splenomegaly in 61 cases [29 isolated + 32 with hepatomegaly (42.07%)], followed by anaemia in 28 cases (19.31%) and icterus in 19 cases (13.1%) and three patients presented with hypotension (2.06%).

Out of 145 cases 80(55.17%) had P.vivax malaria, 60(41.98%) patients had P.falciparum, and 5(3.45%) had mixed infection. Out of 145 cases 60(41.38%) patients had mild thrombocytopenia while 53(36.55%) had moderate and 32(22.07%) cases had severe thrombocytopenia.

The mean hemoglobin (9.315) & Platelet count (82793.33) in P. Falciparum cases was significantly lower than mean hemoglobin (10.49) and platelet counts (90612.5) in P. Vivax cases. Mean WBC count was higher in P. Falciparum (8536.67) cases as compared to P. Vivax (7350.5) cases.

Thrombocytopenia is a common complication of malaria. There is increase in the rate of complication with increasing degree of thrombocytopenia. Complicated malaria is common in P.falciparum infection. Severe thrombocytopenia is seen more commonly with P. falciperum as compared to P. vivex.

Severe thrombocytopenia is good predictor of mortality and mobidity as compared to mild and moderate thrombocytopenia.

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