RESEARCH ARTICLE

THROMBOCYTOPENIA IN MALARIA: CORRELATION WITH VARIOUS PREVALENT SPECIES

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ABSTRACT

Background: Most of the patients suffering from malaria shows reduced Red cell count, leukopenia and varying degree of thrombocytopenia but it is rarely associated with haemorrhagic manifestations.

Aims & Objective: This study was undertaken to correlate the incidence and severity of thrombocytopenia with the prevalent species of malaria.

Material and Methods: Total 1480 Patients were included in this study after positive identification on PSMP. Platelet count was done by haematology analyser (Sysmax Kx 21).

Results: Incidence of thrombocytopenia was seen in 83.80% and 74% cases of P. falciparum and P. vivax malaria respectively. Severe thrombocytopenia in P. falciparum was found in 7.70% cases while in P. vivax 3.67% cases. No difference was observed in incidence of thrombocytopenia in both age groups in relation to both prevalent species. In paediatric age group, significant leukopenia was found in 22.22% Cases of P. falciparum in comparison to P. vivax (14.96%). Hb less than 10 mg/dl was found in 66.11% cases in P. Falciparum while in P. vivax it was found in 40.13% cases. In adults leukopenia was found in 27.46% Cases of P. falciparum in comparison to P. vivax 22.61% cases. Hb less than 10 mg/dl was found in 41.28% cases in P. falciparum while in P. vivax it was found in 28.57% cases.

Conclusion: Severe thrombocytopenia is commonly associated with P. falciparum malaria however severe thrombocytopenia also observed in P. Vivax malaria. In both species of malaria significant number paediatric patients present with low Hb level compared to adults. In P. vivax malaria significant number of adult patients presented with leukopenia as compared to paediatric patients.

Key-Words: Malaria; Thrombocytopenia; P. Vivax; P. Falciparum

Introduction

Malaria is one of the most prevalent human infections worldwide and among the oldest of diseases with far reaching repercussions in human history and still remains a major cause of mortality and morbidity. Malaria has been entrenched in India for countless years and the burden of disease is increasing.[1,2] Malaria is a vector born disease caused by the bite of the female Anopheles mosquito inoculating the sporozoites in the human blood stream leading to clinical manifestations. Four species of plasmodium cause malaria in human which includes Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale and Plasmodium malariae.

According to WHO approximately 219 million cases of malaria occurs annually with 6,60,000 death in 2010 with 80% of estimated death occurs in just 14 countries.[3] India contributes 75%-77% of total malaria cases in Southeast Asia region. 95% of the population of moderate to high risk of malaria in SEAR is living in India and highest numbers of death were reported from India.[3,4]

The main organs involved are liver, spleen and red blood cells. Most of the patients suffering from malaria shows reduced Red cell count, leucopenia and varying degree of thrombocytopenia but it is rarely associated with hemorrhagic manifestations.[5-8] Thrombocytopenia has been reported to be associated with malaria with incidence ranging from 40% to 85.5% irrespective of species of malaria.[9] In endemic area thrombocytopenia served as an indicator of malaria in a patients presented with high grade fever.[10] In the last five years the scenario shows an unexpected development in plasmodium vivax, apart from anemia and thrombocytopenia other complications like acute lung injury, acute kidney injury, cerebral malaria, shock and pulmonary edema is recently observed in P. vivax malaria.[1] Initially it was thought all of these were due to mixed infections but, in the study by Kocher et al showed that P. vivax was also responsible for

those complication which were never seen before in plasmodium vivax malaria.[11]

The mechanism of thrombocytopenia is poorly understood but shortened life span of platelets due to the immune mediated destruction of platelets by IgG antibodies directed against malarial antigen in platelet, elevated M-CSF level in malaria by increasing macrophage activity which induce platelet destruction, sequestration in spleen, increased cytokines, oxidative stress, and pseudothrombocytopenia due to platelet clumps has been postulated.[2,12,13] The present study was aimed to evaluate incidence and severity of thrombocytopenia and to correlate degree of thrombocytopenia with various species of malaria.

Materials and Methods

The present study has been carried from June 2012 to December 2012 after obtaining permission from Institutional Ethics Committee. A total 1480 patients either hospitalized or treated on an outpatient basis were included in the study after positive identification for malarial parasites on PSMP. Complete blood count including platelet count was done on a 3 part cell counter (Sysmax Kx 21). All PSMP slides were stained with Giemsa stain and examined under microscope in oil emersion field.

All CBC data of PSMP Positive patients were analyzed for degree of thrombocytopenia along with Severity & type of malaria. Interpretation of platelet count in patients with positive PSMP were carried out from available CBC data. Thrombocytopenia was defined as Mild Thrombocytopenia: Platelet count between 100-150 x 10^3 cells/µl; Moderate Thrombocytopenia: Platelet count between 20 -100 x 10^3 cells/ul; and Severe Thrombocytopenia: Platelet counts less than 20 x 10^3 cells/ul. The CV of platelet count was < 10%. The patients with coexistent Dengue and Leptospirosis were excluded from the study as both conditions are known to contribute thrombocytopenia. All the data were entered on to excel 2007 spreadsheet and analysis was carried out by OpenEpi software.

Results

Present study included total of 1480 confirmed cases of malaria. P. vivax was found in 819 (55.33%) cases, P. falciparum was 636 (42.98%) and mixed infection of both P. vivax and P. falciparum were found in 25 (1.68%) cases. In our study males were affected in 979 (66.14%) cases while females were affected in 501 (33.86%) cases. Most common age group involved was 21-30 years which includes 460 (31.08%) cases. The mean age of presentation was 29.35 ± 17.26 years. Overall 1161 (78%) patients were found to have low platelet count. The mean platelet count was 71.634 ± 37.545 × 10^3 cells/µl (range 4-149× 10^3 cells/µl). There was significant difference in the incidence of thrombocytopenia, out of 636 cases of P. falciparum 433 (83.80%) had thrombocytopenia with mean platelet count was 67.242 ± 37.562 × 10^3 cells/µl (range 4-149× 10^3 cells/µl) while in 819 cases of P. vivax 606 (74%) had thrombocytopenia with mean platelet count 75.336 ± 37.347 × 10^3 cells/µl (range 9-149× 10^3 cells/µl) with P<0.001. Severe thrombocytopenia in P. falciparum was found in 49 (7.70%) cases while in P. vivax it was found in 30 (3.67%) cases (P<0.0001).

In younger and adults (>15 years), total 1220 (82.43%) cases of malaria were found while in pediatric age group (age <1 5 years) it was found in 260 (17.57%) cases.

Table-1: Incidence of Malaria with Thrombocytopenia among Various Age Groups

Age Group	No. of Cases	P. Falciparum	P. Vivax	Mixed Infection	Thrombocytopenia				Without Thrombocytopenia
					Mild	Moderate	Severe	Total	
≤10	179	71	103	5	35	88	4	127	52
11-20	264	102	158	4	66	118	14	198	66
21-30	460	188	265	7	95	245	26	366	94
31-40	265	134	124	7	46	160	19	225	40
41-50	182	88	93	1	41	92	9	142	40
51-60	81	37	43	1	13	45	3	61	20
61-70	37	14	23	0	10	18	4	32	5
71-80	12	2	10	0	0	9	1	10	2
Total	1480	636	819	25	306	775	80	1161	319

Table-2: Thrombocytopenia and Its Correlation with Age and Species of Malaria

Type of Malaria	Age (years)	Severe	Moderate	Mild	P value
P. Falciparum	<15	6	53	26	0.6*
	≥15	26	337	144	
P. Vivax	<15	4	64	31	0.05*
	≥15	43	305	100	

* P Value <0.05 is significant

Table-3: Correlation of Hb and Leucocyte Count with Age and Species of Malaria

Type of Malaria	Age (Years)	Hb (%)		P Value	Leucocyte Count (%)		P Value
		<10	≥10		<4000	≥4000	
P. Falciparum	<15	66 (61.11)	42 (38.89)	0.0001*	24 (22.22)	84 (77.78)	0.13*
	≥15	218 (41.28)	310 (51.72)		145 (27.46)	383 (72.54)	
P. Vivax	<15	59 (40.13)	88 (59.87)	0.002*	22 (14.96)	125 (85.04)	0.03*
	≥15	192 (28.57)	480 (71.43)		152 (22.61)	520 (77.39)	

* P Value <0.05 is significant

In pediatric age group among 260 cases of malaria, 147 (56.54%) cases were of P. vivax, 108 (41.54%) cases were of P. falciparum and 5 (1.92%) cases were of mixed infection. Males are more affected than females, 154 (59.23%) vs 106 (40.77%). Incidence of thrombocytopenia in pediatric patients were found in 99 (67.35%) cases with P. vivax while in P. falciparum were 85 (78.70%) cases (P<0.002). Significant leucopenia was found in 24 (22.22%) cases of P. falciparum in comparison to P. vivax 22 (14.96%) cases (P 0.07). Hb less than 10 mg/dl was found in 66 (66.11%) cases in P. falciparum while in P. vivax it was found in 59 (40.13%) cases.

In younger and adults (>15 years), total 1220 cases of malaria were found. Among 1220 cases males were more affected than female, 825 (67.62%) Vs 395 (32.68%). P. vivax and P. falciparum cases were 672 (55.08%) and 528 (43.28%) respectively while mixed infection was seen in 20 (1.63%) cases. 507 (75.44%) cases of P. vivax and 438 (82.95%) cases of P. falciparum showed thrombocytopenia (P<0.0001). 145 (27.46%) cases of P. falciparum showed leucopenia while in P. vivax it was seen in 152 (22.61%) cases.

Statistically no significant difference was found in degree of thrombocytopenia between age group and type of malaria as mentioned in table no 2.

Discussion

In the present study males were predominantly (66.14%) infected in comparison with females mostly due to more active outdoor activities. The females in India are better clothed so less exposed.[14] Similar results were documented in study by Jagnami Srikanth in Andhra Pradesh (65% males, 35% females).[15] In the study by K. Kuladeepa Anand Vaidya (139 males, 11 females) shows higher no. of males were infected in compared to females.[5]

In our study incidence of P. vivax was higher (55.33%) as compared to P. falciparum (42.98%). It was comparable to study by Maya P. Dhungat et al showed P. vivax in 54% and P. falciparum in 26%.[13] Study by Neeru Singh et al also showed increased number of P. vivax malaria in their study conducted in central India.[15]

Anemia and thrombocytopenia is most common hematological finding in patients with malaria.[16] Thrombocytopenia in malaria is usually mild to moderate and very rarely symptomatic and not associated with bleeding tendency.[2] Our study was aimed to correlate incidence of thrombocytopenia with prevalent species of malaria as thrombocytopenia complicate many cases of malaria and its occurrence also provide diagnostic clue for malaria.[10,17,18] Our study showed 78% cases of malaria having thrombocytopenia. Study by Mumtaz Ali et al showed 85.5%, Solanki Rajan et al showed 87.09%, Clonel et al showed 72% cases and Qurban H. Shah showed 80.6% cases having thrombocytopenia.[9,19-21]

Higher number of cases with P. falciparum (83.80%) showed thrombocytopenia as compared to P. vivax (74%). Similar results were reported in study by Charulata S. Limbaye et al in their study which showed incidence thrombocytopenia in 73% cases of P. falciparum and 68% cases in P. vivax.[22] while in study by D.K. Kochar et al showed 85.71% cases of P. vivax having thrombocytopenia which was higher than our observation.[23]

Profound thrombocytopenia with platelet count less than 20,000/ µl was seen in 5.40% of cases of

malaria. Other studies in India showed higher incidence of severe thrombocytopenia.[24,25] Lowest platelet count reported in our study was 4000/µl in patient with P. falciparum While in P. vivax lowest platelet count was 7000/ µl. In India few recent study showed platelet count less than 5000/ µl and 8000 / µl.[26,27] Study by UM Jadhav showed 1.5% and 8.5% cases of thrombocytopenia with P. vivax and P. falciparum respectively.[28] Solanki Rajan et al showed 8.9% and 12.85% cases with severe thrombocytopenia in P. vivax and in P. falciparum in their study.[18] AS Hayat observed 5.2 % cases having severe thrombocytopenia in P. falciparum.[29] Our study showed statistically higher incidence of thrombocytopenia in P. falciparum (7.70%) than P. vivax (3.67%).

In our study we had attempted to study characteristic of platelet count, Hb and Leucocyte count in pediatric and adult age group in relation to species of malaria prevalent in our region.

In pediatric age group P. vivax was most common species than P. falciparum (56.54% Vs 41.54%) similar result was observed by Guruprashad Shetty et al in their study.[4]

Incidence of thrombocytopenia in this pediatric age group was 70.79% in cases of malaria. Prusun Bhattacharyjee reported 75% of patients with thrombocytopenia in their study.[30] Thrombocytopenia in P. falciparum and in P. vivax was 78.70% and 67.35% respectively. Various Indian literature showed 61.54% to 73.92 % cases with thrombocytopenia in P. vivax.[11,31]

Severe thrombocytopenia in pediatric patients was observed in both P. falciparum and P. vivax malaria. In our present study severe thrombocytopenia was observed in 2.72% and 5.55% cases in P. vivax and P. falciparum respectively. Similar result was observed in the study by HA Joshi.[31] But few study showed higher number of patients (7.1% patients) having severe thrombocytopenia in P. vivax malaria.[30]

In our present study males are predominantly affected than females and incidence of P. vivax was higher than P. falciparum in both age groups. Significant difference was observed in occurrence of thrombocytopenia in both age group affected by both species of malaria. Significant association was observed in Hb value in relation with age group and species of malaria. In P. falciparum malaria higher number of paediatric patients (61.11%) showed less than 10 mg/dl Hb in comparison to adults which showed 41.28% patients. In P. vivax malaria similar result was observed as in P. falciparum, 40.13% paediatric patients with Hb less than 10mg/dl Vs 28.57% in adults. In reference to leucocytes count leukopenia was observed in both age groups in both species of malaria. But in P. falciparum malaria no significant difference was observed in both age groups. P. vivax malaria showed significant difference in leukopenia with predominantly adult patients 22.61% as compared to paediatric patients 14.96%.

Conclusion

It is usually believed thrombocytopenia is more common in P. falciparum but it was observed that thrombocytopenia was common finding in both species of malaria. Severe thrombocytopenia is more commonly associated with P. falciparum malaria however severe thrombocytopenia also observed in P. vivax malaria. So thrombocytopenia is not a distinguishing feature between these two prevalent species in our study. There was no difference in expression of thrombocytopenia in both age groups. In both species of malaria significant number of paediatric patients presented with low Hb level as compared to adults. In P. vivax malaria significant number of adult patients presented with leukopenia as compared to paediatric patients. In P. Falciparum malaria there was no significant difference observed in percentage of leukopenia in both age groups.

So with Hb level (low in paediatric patients), Leucocyte count (Low in Adults with P. vivax) and thrombocytopenia (more in P. falciparum in both age group) help us to differentiate malaria from other cases of PUO. Only thrombocytopenia is not helpful to differentiate species of malaria in both age groups.

ABBREVIATION

WHO: World Health Organization; SEAR: South East Asia Region; M-CSF: Macrophage Colony Stimulating Factor; Hb: Haemoglobin; P. Vivax: Plasmodium Vivax; P. Falciparum: Plasmodium Falciparum; PUO: Pyrexia of Unknown Origin

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