Original Research Article

A cross sectional study of thrombocytopenia in malaria positive cases in a tertiary care hospital of Bareilly

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ABSTRACT

Background: To find out correlation of thrombocytopenia with malaria. Malaria is a protozoal disease caused by infection with parasite of genus *Plasmodium*. Thrombocytopenia is a common and early sign of malarial infection and 60-80% thrombocytopenia is observed in malarial cases and present more frequently and severe in complicated P. falciparum malaria.
Methods: A cross sectional study done in Central Pathological Lab of Department of Pathology, RMCH, Bareilly. Blood samples collected in ethylenediaminetetraacetic acid vial and blood smear was examined for malaria parasite within red blood cells. Malaria rapid test was done for detection of *Plasmodium* species and platelet count was done.
Results: 780 cases of malaria was studied from September 2018 to December 2018, male predominance of 54.5%, maximum malarial positive cases 26.92% in the age group of 21-30 years, maximum 86.28% cases were of *P. vivax*, and thrombocytopenia was observed in 91.54% cases.
Conclusions: Mostly developing countries with limited resources and trained health manpower are malaria-endemic region of world. Thrombocytopenia is associated with both *P. vivax* and *P. falciparum* infections. In our study significance association between malaria and thrombocytopenia has been observed. We suggest malaria should be a consideration in all patients with fever and thrombocytopenia.

Keywords: Malaria, *P. vivax*, Thrombocytopenia

INTRODUCTION

Malaria is a protozoal disease caused by infection with parasite of genus *Plasmodium* and transmitted to man by bite of infected female Anopheles mosquito. Five species of *Plasmodium* (*Plasmodium vivax, P. falciparum, P. malariae, P. ovale and P. knowlesi*) cause malaria in human.[1] Malaria has emerged as top 10 killer diseases around globe.[2,3] As per the World Health Organization report 2015, South East Asian Region (SEAR) bears the second largest burden of malaria (10%), only being next

to African region (88%). Malaria caused 214 million infections and 4,38,000 deaths worldwide. Most of them occurred in Africa region (90%) followed by SEAR (7%).[4] among SEAR India shared two third of burden (66%) followed by Myanmar (18%) and Indonesia (10%).[5] Approximately 2.48 million cases are reported annually from South Asia, of which 75% cases from India alone.[6]

Thrombocytopenia is a common and early sign of malarial infection. Anaemia and thrombocytopenia are

the most prominent alterations during both *P. falciparum* and *P. vivax* infection.[7-9] Thrombocytopenia is observed in 60-80% of malaria cases and present more frequently and severe in complicated *P. falciparum* malaria.[10]

The most common complication during malaria infection is thrombocytopenia.[11,12] All complications seen in falciparum malaria are now reported with *P. vivax* also.[13-15] Malaria is infected patients tended to have significant lower platelets, WBCs, lymphocytes, eosinophils, RBCs and Hb level.[16-18]

Severe malaria is 4.2 times less common in patient with mixed *P. falciparum* and *P. vivax* infections than among those with falciparum infection alone, suggesting that co-infection with *P. vivax* decreases the severity of *P. falciparum* malaria.[19]

Typically microscopic slide examination of peripheral blood remains the most widely used test and is the gold standard for detecting malaria infection.[20] In symptomatic individuals, early diagnosis based on microscopy or rapid diagnostic test, all suspected cases of symptomatic *Plasmodium* infection should be biologically confirmed to treatment.[21-26]

We conducted this study to find out the frequency and degree of thrombocytopenia in patients with malaria.

METHODS

It is a cross sectional study, was done in Central Pathological Lab of Department of Pathology, RMCH, Bareilly and was conducted from September 2018 to December 2018.

Selection criteria

The study included 780 suspected malaria patient attended in outpatient department and inpatients department. Informed consent was taken.

Procedure

Laboratory investigations

Blood sample is collected in ethylenediaminetetraacetic acid (EDTA) vials by venepuncture and thin blood film was made by method described by Dacie and Lewis.[27] Blood smear stained with leishmen stain, and is examined microscopically under oil immersion lens for the presence of type of malaria parasite (*P. falciparum or P. vivax*) within RBCs

Malaria rapid diagnostic test (MAL CARD by J. Mitra and company Pvt. Ltd.)

Antigen histadine release protein II test, for detection of *P. falciparum* pLDH (parasite lactate dehydrogenase) for any *Plasmodium* species (*P. vivax*). It is an immunoassay

based on the sandwich principle. The conjugate contains colloidal gold conjugated to monoclonal anti-pan specific pLDH antibody. The test uses monoclonal anti-Pf pLDH antibody

Platelet count

Haemogram was done by a fully automated haematology blood cell analyser (five part) model XS-1000i supplied by Transasia (SYSMEX MACHINE).

Grading of thrombocytopenia

Grading of thrombocytopenia was carried out according to National Cancer Institute common terminology criteria for adverse events version 3.0 according to that patients with thrombocytopenia have been divided into following 5 grades:[28]

Grade 0: within normal limit, platelet count 1,50,000 or above.

Grade I: platelet count between 75,000 -1,50,000.

Grade II: platelet count between 50,000-75,000.

Grade III: platelet count between 25,000 -50,000.

Grade IV: platelet count <25,000.

Ethical approval

Ethical approval was taken from college ethical committee, RMCH, Bareilly.

Statistical analysis was done by SPSS version 21.

RESULTS

Maximum malarial cases were in 21-30 years age group and minimum cases were in 71-80 years age group. Maximum cases of malaria were found among males.

Maximum thrombocytopenia of all grades was found in 21-30 yrs age group. Maximum thrombocytopenia in males was of grade IV and maximum thrombocytopenia of grade III was found in females.

Maximum *P. vivax* cases was found in 21-30 yrs age group while maximum cases of *P. falciparum* was found in 11-20, 21-30 and 41-50 yrs age group and maximum cases of mixed infection in 31-40 yrs age group.

Maximum cases of *P. vivax* and mixed infection were found among males while *P. falciparum* was found equal in both sexes.

Maximum cases of grade I thrombocytopenia was found in both (*P. vivax* and *P. falciparum*) while grade III thrombocytopenia was found in mixed infection.

Table 1: Demographic profile (n=780).

Demographic profile	Number	%
Age group (yrs)		
0-10	78	10.00
11-20	157	20.13
21-30	210	26.92
31-40	142	18.20
41-50	72	09.23
51-60	74	09.49
61-70	43	05.52
71-80	04	00.51
Sex		
Male	425	54.50
Female	355	45,50

Table 2: Correlation of demographic profile with platelets.

Correlation with platelets	Thrombocytopenia with different grades						P value/ Chi square
	Normal (%)	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)	Total (%)	
Age group (yrs)							
0-10	7 (10.61)	11 (06.55)	17 (11.64)	24 (11.27)	19 (10.16)	78 (10.00)	
	08.97	14.10	21.79	30.77	24.37	100.00	
11-20	20 (30.30)	28 (16.67)	28 (19.18)	44 (20.66)	37 (19.79)	157 (20.13)	
	12.78	17.82	17.82	28.02	23.56	100.00	
21-30	17 (25.76)	51 (30.36)	47 (32.19)	51 (23.94)	44 (23.53)	210 (26.92)	
	08.11	24.31	22.40	24.31	20.97	100.00	
31-40	09 (13.64)	36 (21.43)	30 (20.55)	36 (16.90)	31 (16.58)	142 (18.20	0.153/35.6
	04.29	02.11	21.13	25.35	21.83	100.00	
41-50	03 (04.55)	10 (05.95)	15 (10.27)	22 (10.33)	22 (11.76)	72 (09.230	
	04.17	13.89	20.82	30.56	30.56	100.00	
51-60	05 (07.57)	18 (10.71)	05 (03.42)	22 (10.33)	24 (12.83)	74 (09.360	
	06.76	24.32	06.76	29.73	32.43	100.00	
61-70	05 (07.57)	12 (07.14)	03 (02.06)	14 (06.57)	09 (04.81)	43 (09.49)	
	11.63	27.92	06.96	32.56	20.93	100.00	
71-80	00 (00.00)	02 (01.19)	01 (00.69)	00 (00.00)	01 (00.54)	04 (00.51)	
	00.00	50.00	25.00	00.00	25.00	100.00	
Total	66 (100.00)	168 (100.00)	146 (100.00)	213 (100.00)	187 (100.00)	780 (100.00)	
	08.46	21.54	18.72	27.31	23.97	100.00	
Sex							
Male	38 (57.58)	90 (53.57)	92 (63.01)	99 (46.48)	106 (56.68)	425 (54.49)	
	08.94	21.88	21.65	23.29	24.94	100.00	
Female	28 (42.42)	78 (46.43)	54 (36.99)	114 (53.52)	81 (43.32)	355 (45.51)	10.5/0.033
	07.89	21.97	15.21	32.11	22.82	100.00	
Total	66 (100.00)	168 (100.00)	146 (100.00)	213 (100.00)	187 (100.00)	780 (100.00)	
	08.46	21.54	18.72	27.31	23.97	100.00	

DISCUSSION

Age distribution

In our study, out of total 780 study population maximum 210 (26.92%) cases were in 21-30 year age group, followed by 157 (20.13%) in 11-20 year age group and minimum 04 (0.51%) in 71-80 year age group. Similar finding 56% cases in 15-40 year age group, 38% in 18-30 year age group was observed by Gupta et al, 38.20 % in 21-30 year age group, 20.00% in 31-40 year age group, 2.6% in 61-80 year age group was observed by Jairajpuri et al, 34.61% in 21-30 years age group by Khuraiya et al while maximum 43.33% cases were under the age of 20 years was found by Gill et al.[29-32]

Sex distribution

In our study, out of 780 malarial patients 54.50% were males while 45.50% were females. 52% males and 48% females was observed by Ahmad et al, 63.33% males and 36.66% females was found by Gill et al, 65.22% males and 34.78% females by Gupta et al, 67% males and 33% females was found by Aundhakar et al, 69% males and 31% females was reported by Jairajpuri et al, 77.15% males and 22.85% females was reported by Kalavathi et al.[29,30,32-35] The males thought to be at a higher risk due to more outdoor activity and less protection from mosquito bites.

Type of malaria

Out of 780 cases of malaria we found 86.28% cases of *P. vivax*, 02.31% cases of *P. falciparum* and 11.41% mixed infection.

Similar finding *P. vivax* (87.74%) *P. falciparum* (03.77%) and mixed infection (08.49%) was found by Jairajpuri et al.[30] *P. vivax* (57.14%, 56.51%, 51.69%, 41.00% and 40.00%), *P. falciparum* (37.14%, 39.13%, 01.12%, 59.00% and 50.00%) mixed (05.72%, 05.72%, 04.34%, 47.19%, 0.90% and 10.00%), was reported by Kalavathi et al, Gupta et al, Faseela et al, Patel et al, and Kashikunti et al respectively and higher *P. falciparum* (70.6%) and *P. vivax* (28.7%) was found by Agravat et al.[29,35-39]

Correlation of malaria with platelets

In our study out of 780 malarial cases thrombocytopenia was found in 91.54% cases. Normal platelet was observed in 08.46% out of which 07 .18% were in *P. vivax*, 0.26% in *P. falciparum* and 01.03% in mixed infection. Maximum 27.31% thrombocytopenia grade III was found in our study followed by 23.97% grade IV than 21.54% in grade I and minimum18.72% in grade II.

Table 3: Correlation of demographic profile with type of malaria parasite.

Correlation with platelets	Malaria parasite with different types				P value/ Chi square
	P. vivax	*P. falciparum*	Mixed	Total	
Age group (yrs)					
0-10	67 (09.96)	01 (00.06)	10 (11.24)	78 (10.00)	
	85.90	1.28	12.82	100.00	
11-20	134 (19.91)	04 (22.22)	19 (21.35)	157 (20.13)	
	85.35	2.55	12.10	100.00	
21-30	198 (29.42)	03 (16.67)	09 (10.11)	210 (26.92)	
	94.29	01.43	04.29	100.00	
31-40	117 (17.3)	04 (22.22)	21(23.60)	142 (18.21)	
	82.39	2.82	14.79	100.00	
41-50	58 (08.62)	04 (22.22)	10 (11.24)	72 (09.23)	0.051/23.625
	80.56	5.56	13.89	100.00	
51-60	62 (09.210	01 (05.56)	11 (12.36)	74 (09.49)	
	83.78	01.35	14.86	100.00	
61-70	33 (04.90)	01 (05.56)	09 (10.11)	43 (05.51)	
	76.74	02.33	20.93	100.00	
71-80	04 (00.06)	00 (00.00)	00 (00.00)	04 (00.51)	
	100.00	00.00	00.00	100.00	
Total	673 (100.00)	18 (100.00)	89 (100.00)	780 (100.00)	
	86.28	2.31	11.41	100.00	
Sex					
Male	363 (53.94)	09 (50.00)	53 (59.55)	425 (54.49)	
	85.41	02.12	12.47	100.00	
Female	310 (46.06)	09 (50.00)	36 (40.45)	355 (45.51)	0.563/1.148
	87.32	02.54	10.14	100.00	
Total	673 (100.00)	18 (100.00)	89 (100.00)	780 (100.00)	
	86.28	02.31	11.41	100.00	

In our study we found thrombocytopenia (91.54%). Similar finding 92% thrombocytopenia was observed by Jairajpuri et al, 81.9% thrombocytopenia was found by Agravat et al, 77.83% by Gupta et al, 71.61% was found by Akthar et al.[29,30,39,40] In our study we found normal platelets in *P. vivax* (07.18%), *P. falciparum* (00.26%) and in mixed infection 01.03%), while normal platelets was found only in *P. vivax* (07.90%) and normal platelets was not found in *P. falciparum* and mixed infection by Jairajpuri et al.[30] while normal platelets in *P. vivax*

(05.23%, 13.04%, and 10.81%),in *P. falciparum* normal platelets (13.24%, 08.69%, 13.51%) and in mixed infection 00.00%, 00.43% and 2.70%) by Agravat et al, Gupta et al and Akthar et al.[29,39,40] In our study we found grade I thrombocytopenia (21.54%) while 16.51% grade I thrombocytopenia was observed by Jairajpuri et al and 26.13% by Agravat et al.[30,39] In our study grade II thrombocytopenia was found (18.72%) while 31.01%

grade II thrombocytopenia was found by Agravat et al and 2.83% by Jairajpuri et al, in our study Grade III thrombocytopenia (27.31%) was found, while 21.31% was observed by Agravat et al and and 41.03% was found by Jairajpuri et al, Grade IV thrombocytopenia was found in our study (23.97%). 21.23% by Jairajpuri et al and in contrast 3.14% was found by Agravat et al.[30,39]

Table 4: Correlation of type of malaria parasite with platelets.

Malaria parasite	Grade normal	Grade I	Grade II	Grade III	Grade IV	Total	P value/ Chi square
P. vivax	56 (84.85)	137 (81.55)	126 (86.30)	180 (84.51)	174 (93.05)	673 (86.28)	
	08.32	32.47	18.72	26.75	25.85	100.00	
P. falciparum	02 (03.03)	07 (04.17)	01 (00.69)	06 (02.82)	02 (01.07)	18 (02.31)	0.076/ 14.218
	11.11	38.89	05.56	33.33	11.11	100.00	
Mixed	08 (12.12)	24 (14.28)	19 (13.01)	27 (12.67)	11 (05.88)	89 (11.41)	
	00.90	26.97	21.35	30.34	12.36	100.00	
Total	66 (100.00)	168 (100.00)	146 (100.00)	213 (100.00)	187 (100.00)	780 (100.00)	
	08.46	21.54	18.72	27.31	23.97	100.00	

Table 5: Correlation of malaria with platelets.

		Our study (n=780) (%)	Jairajpuri et al[30] (n=230) (%)	Agravat et al[39] (n=287) (%)	Gupta et al[29] (n=230) (%)	Akthar etal[40] (n=74) (%)
Thrombocytopenia		91.54	92	81.5	77.83	71.61
Normal platelets	*P. vivax*	07.18	07.80	05.23	13.04	10.81
	P. falciparum	00.26	00.00	13.24	08.69	13.51
	Mixed	1.03	00.00	-	00.43	2.70
	Total	08.46	7.80	18.47	22.17	27.03
Grade I	*P. vivax*	17.56	14.62	08.71		
	P. falciparum	00.90	00.47	17.42		
	Mixed	03.07	01.42	-		
	Total	21.54	16.51	26.13		
Grade II	*P. vivax*	16.15	18.40	19.86		
	P. falciparum	00.13	00.94	11.15		
	Mixed	02.44	01.89	-		
	Total	18.72	02.83	31.01		
Grade III	*P. vivax*	23.08	37.26	02.09		
	P. falciparum	00.77	00.94	19.13		
	Mixed	03.46	02.83	-		
	Total	27.31	41.03	21.31		
Grade IV	*P. vivax*	22.30	17.45	01.05		
	P. falciparum	00.26	01.42	02.09		
	Mixed	01.41	02.36	-		
	Total	23.97	21.23	3.14		

CONCLUSION

Mostly developing countries are with limited resources and trained health personnel. The haematological aspects of malarial infection constitute a very interesting area and may be used in addition to the clinical assessment, to heighten the suspicion of disease. Thrombocytopenia is associated with both *P. vivax* as well as *P. falciparum*

infections. So thrombocytopenia with acute febrile illness in the tropics, increases probability of malaria, as in our study we found thrombocytopenia in about 92% in malarial cases.

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