RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

Hematological Profile in Plasmodium Vivax Malaria in Western Rajasthan.

KEYWORDS: vivax malaria, thrombocytopenia, bleeding manifestation

Rajesh Chetiwal
Associate Professor Depatt. of Medicine ESI PGIMSR, New Delhi.

Rahul Gupta
Resident Deptt. of Medicine Dr. SN Medical College and attached hospitals, Jodhpur

Jyoti Bagla
Associate Professor Depatt. of pediatrics ESI PGIMSR, New Delhi.

Manoj Lakhotia
Professor Deptt. of Medicine Dr. SN Medical College and attached hospitals, Jodhpur

ABSTRACT

Background: *As the target of malaria parasite is RBC, it can cause haematological abnormalities that range from anemia, pancytopenia and hemostatic abnormalities ranging from asymptomatic thrombocytopenia to fulminant disseminated intravascular coagulation (DIC).*

Objective: *Hematological disturbances in relation to anaemia, leukopenia, thrombocytopenia, and pancytopenia in Plasmodium vivax malaria.*

Study design: *A prospective observational study was done in 782 patients with positive plasmodium vivax malaria, attending tertiary care teaching hospital in western Rajasthan, India.*

Methodology: *Patients with acute febrile illness admitted in a tertiary care hospital, from January 2010 to January 2011, diagnosed as plasmodium vivax malaria. The diagnosis of malaria was established on peripheral blood film examination, Malarial Parasite Qunatitative Buffy Coat or rapid diagnostic test detecting antigen. Hematological parameters were observed. Thrombocytopenia and its association with bleeding manifestation was also looked for.*

Results: *In this prospective observational study 782 patients were enrolled, 64.7 % male and 35.3% were female. Majority (55.6%) of patients were in younger age group (11 to30 years old). In vivax malaria, anaemia was observed in 75.44% patients, more in female(83.33%)than in males (71.14%).Thrombocytopenia was present in 85.29% and leukopenia in 27.66% and pancytopenia in 13.68% patients. Majority(80%) were having mild to moderate thrombocytopenia and only 7% patient had platelet count <20000. Less than 1/5 of patients with platelet count <20,000/µl showed bleeding manifestations.*

Conclusion: *P.vivax malaria, though considered as benign malaria, is giving rise to many hematological abnormalities sometimes adding to the growing morbidity and mortality. Thus if hematological changes are noticed in time, the management and the outcome can surely be modified.*

Introduction:

In spite of worldwide efforts to reduce malaria transmission, it is still the major cause of morbidity and mortality, with overall fatality rate of 10-30 % [(1)] was seen. The main areas where disease predominates are the rural and remote areas, where prompt treatment is not available or not detected in time. [(2)]

Malaria can cause hemostatic abnormalities leading to bleeding manifestations that range from asymptomatic thrombocytopenia to fulminant disseminated intravascular coagulation (DIC).[(3)] In recent years clinicians have recognized thrombocytopenia as a common and early sign of *P. vivax* or *P.falciparum* malaria infection, whereas DIC is rare[(4).] The mechanism of thrombocytopenia in malaria is uncertain. Coagulation disturbances, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production, antibody mediated destruction, oxidative stress, platelet destruction have all been postulated ***(Lacerda et al).***[(7)]

There is no extensive local literature available on such topic, therefore by keeping and considering such debate in mind the present study was conducted at a tertiary care teaching hospital that cover rural as well as urban population of western Rajasthan and provide all health related emergency facilities. The present study evaluates the hematological disturbances in relation to thrombocytopenia, anaemia, leukopenia, pancytopenia in *P. vivax* malaria. The present study also evaluates the complications in *P. vivax* malaria.

Material and Methods:

This was a prospective observational study done in a tertiary care teaching hospital from January 2010 to Jan 2011. After taking ethical committee approval patients history, examination and personal data were entered on predesigned proforma. 782 patients admitted to the medicine wards with fever of acute onset (less than 7 days) or nonspecific symptoms like headache, fatigue, myalgia, pain abdomen, chest pain, diarrhoea, convulsion and diagnosed as plasmodium vivax malaria were enrolled.

Detailed history taken for fever, chills and rigor, associated sympotoms and bleeding manifestation. Past and family history including drug history were noted. The diagnosis of malaria was established on peripheral blood film examination and/or Quantitative Buffy coat (MP,QBC) and/or rapid diagnostic test detecting antigen *Plasmodium falciparum (P.F.)* or mixed *(P.V., P.F.)* malaria cases were excluded .

Samples were collected in ethylene diamine tetra acetic

Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

acid (EDTA) and citrated tubes for complete blood count (CBC), Total leukocyte count (TLC), Platelet count, ESR, Peripheral smear, Blood urea, Serum creatinine, electrolytes, Liver function tests (LFT) ,blood sugar and prothrombin time (PT) analysis. Thin and thick films were stained with Leishman's stain and Giemsa stain for identification of species and grading of parasitemia respectively as described by Dacie and Lewis. [9] Grading is as follows: 1-10 parasites per 100 thick film high power field (HPF): +; 11-100 parasites per 100 thick film HPF: ++; 1-10 parasites per one thick film HPF: +++; >10 parasites per one thick film HPF: ++++.

All the enrolled subjects were evaluated for hematological profile. Anaemia was defined as haemoglobin (Hb) level <12g/dl in female and <13g/dl in male according to WHO criteria. [6] Thrombocytopenia was defined as platelet count <150000/µl and leukopenia as total leukocyte count <4,000/µl.

The severe complicated malaria was defined according to WHO criteria. These were severe anaemia (Hb <5mg/dl with parasitemia >1,00,000/µl), renal failure (creatinine >3mg/dl), jaundice (bilirubin >3mg/dl), convulsion (>2 seizures in 24 hours), significant bleeding and shock (systolic blood pressure 80/mmHg).

Quantitative data tabulated in Microsoft excel sheet and presented in proportion.

Results :

In this prospective observational study 782 patients (506 males and 276females) were enrolled. Majority (55.6%) of patients were in younger age group (11 to30 years old).

Mean value of Hb was 10.79 ± 2.69 g/dl,(male 11.71±2.22 g/dl and female 9.10±2.64 g/dl).Mean platelet count was 79442.45 ± 63605.91/µl (male 80369.56 ± 68468.13/µl and female 77742.80 ± 53515.70/µl). Mean leukocyte count was 6003.17(3080.02)/µl.

In vivax malaria, anaemia was observed in 75.44% patients, more in female(83.33%)than in males (71.14%).(Table 1) Thrombocytopenia was present in 85.29% and leukopenia in 27.66% of patients. Pancytopenia was present in 13.68% patients.

Majority of patients (81%) had anaemia of mild to moderate grade (≥8 g/dl), but 19% had anaemia of severe grade (<8 g/dl). Of total anaemic male patients 7% had severe anaemia while of total anaemic female patients 38% had severe anaemia.

Eighty five percent patient (667) of vivax malaria had thrombocytopenia and majority(80%) having mild to moderate (Table 1). 7% patient had platelet count <20000 but only 18 (2.69%) had bleeding manifestation. Out of these patients 15 showed frank bleeding and 3 had petechial rashes. The mean platelet count of patients with bleeding manifestations was 63333/µl. 8/46 (17.4%) patients with platelet count <20,000/µl showed bleeding manifestation. 1.35% patients with platelet count >20,000/µl showed bleeding manifestation and 98.5% did not show bleeding manifestation.

Discussion:

In our study the majority of patients were of younger age group 56.6% (in 11-30 years). This can be attributed to the high endemicity of malaria in our area where the burden of disease in childhood is high. In adulthood most malarial infection are asymptomatic because of immunity developed from infected mosquito bite in early childhood repeatedly. Male predominance (64.7 %) was seen, can be attributed to the male dominated social system where a sick male gets preferential medical attention.

Mean haemoglobin level was 10.79 g/dl in 9.1g/dl in female as compare to 11.71g/dl in male (p value <0.001). Anaemia was seen in 75% of total patients with slightly higher rate in female (83%) in comparison to male (71%). It was lower than observed by ***Rodrı´guez-Morales et al.*** (96.6%) in 2000-02. The severity of anaemia was also higher in female than in male, hemoglobin <8 g/dl was in 6.66% and hemoglobin ≥8g/dl was in 93.33% males while in females hemoglobin <8 g/dl was seen in 38.26% and hemoglobin ≥8 g/dl in 61.7%. Leukopenia was present in 27.66% of patients with mean leukocyte count of 6000/µl, similar in male and female. Pancytopenia was present in 13.68% of patients.

Thrombocytopenia was observed in 88% of patients, mean platelet count was 7,9442/µl. The minimum platelet count was 7,000/µl and maximum was 4,28,000/µl. Similarly results were observed in 82% of patients in the study done by ***Srivastava et al*** in 2011. Where it was seen in 31% of patients in the study done by ***Kochar DK et al in 2010*** this lower percentage of thrombocytopenia in this study because of both inpatients and outpatients were included. In another study done in outpatients by ***Silva et al*** [8] in 2009, 77% of patients had low platelets ,. This high incidence in our study as well as of others highlights the fact that a persistent normal platelet count is unlikely in the laboratory findings of malaria.

The patients who had severe thrombocytopenia (platelet count <20,000/µl) were 6.9% [46/667], as comparison to 18.18% in the study by ***Kochar DK et al in 2010.*** The patients who had bleeding manifestations were 2.3% in our study as comparison to 0.6% of patients in the study of ***Kochar DK et al in 2010.***

It was also observed that patients with severe thrombocytopenia, majority of them are asymptomatic and 17% of them had bleeding manifestations. 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 bleeding manifestation or merit platelet infusions. [10]

Cause of thrombocytopenia in malaria is uncertain however Coagulation disturbances, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production, antibody mediated destruction, oxidative stress, platelet destruction have all been postulated ***(Laccerda et al).***[7] 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. [5, 6]

In many studies undertaken, the significance of hemostatic 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 further studies are required to address this.

Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

Conclusion:

In conclusion, absence of thrombocytopenia is uncommon in the laboratory diagnosis of malaria. Despite severe thrombocytopenia platelet concentrate transfusion is indicated only in patients with systemic bleeding.

Table 1: Hematological parameter

Parameter	Total 782 (%)	Male n = 506	Female n = 276
No Anemia	192 (24.6%)	146 (28.86%)	46 (16.67%)
Anemia	590 (75.4%)	360 (71%)	230 (83%)
Hemoglobin mg/dl			
8 -12/13mg/dl	478 (81%)	336 (93.4%)	142 (61%)
<8mg/dl	112 (19%)	24 (6.6%)	88 (38%)
No thrombocytopenia Platelet >1.5 lac/µl	115 (14.7%)	83 (26.3%)	32 (11.6%)
Thrombocytopenia Platelet <1.5 lac/µl	667 (85.3%)	423 (83.6%)	244 (88.4%)
No Leukopenia	574 (73%)	366 (72.3%)	208 (75.4%)
Leukopenia	208 (26%)	140 (27.6%)	68 (24.6%)
Pancytopenia	107 (13.68 %)	68 (13.43)	39 (14.13%)

TABLE 3: SEVERITY OF THROMBOCYTOPENIA

PLATELET COUNT	TOTAL n = **667** (%)
<20,000/µl	46 (6.9%)
≥20,000 TO <50,000/µl	267 (40%)
≥50,000 TO <1,00,000/µl	268 (40.2%)
>1,00,000 TO <1,50,000/µl	86 (12.9%)
TOTAL	(100%)

Table 2: RELATION OF BLEEDING MANIFESTATION WITH PLATELET COUNT

PLATELET COUNT (/µL)	TOTAL	PATIENTS WITH BLEEDING	PATIENTS WITHOUT BLEEDING
<20,000	46	8 (17.4%)	38 (82.6%)
≥20,000 TO < 50,000	160	4 (2.5%)	156 (97.5%)
≥50,000 TO <1,50,000	361	6 (1.6%)	355 (98.4%)
≥1,50,000	115	NIL	115 (100%)
TOTAL	782	18 (2.3%)	764 (97.7%)

REFERENCE

1. Kumar, A.K. and Shashirekha, P.B. Thrombocytopenia- an indication of acute vivax malaria. Indian J Pathol Microbiol, 2006; 49:505-508. 2. Park, K.S.: Arthropod born infection, Park's textbook of Preventive & Social Medicine, Jabalpur,2007; 5:209-220. 3. Rodriguez A.J., Morales E., Sanchez M., Vargas C., Piccolo R., Colina M., Clinical infectious disease, 2005; 41:130-131 4. Sharma S.K., Das R.K., Das B.K. Das P.K. Hematological profile in acute falciparum malaria. J. Assoc. Physicians India, 1992; 40:581-583 5. Kakar A., Bhoi S., et al. Profound thrombocytopenia in plasmodium malaria. Diagn Microbiol Infect Dis.1999; 35:243-244 6. Nicholas J. White, Joel G. Breman: Malaria. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J.eds. Harrison' principles of internal medicine,18th editionVol 1. Newyork: Mc Graw Hill 2011: 1688-1705. 7. Lacerda MVG 2007. Manifestações clínicas e patogênese da plaque¬topenia na malária, PhD Thesis, Universidade de Brasília, 439 pp. 8. Silva IBA 2004. Malária vivax: manifestações clínicas e laboratori¬ais relacionadas com o fator de necrose tumoral alfa, PhD The¬sis, Universidade Federal do Pará, Belém, 128 pp. 9. Dasci, S.J., and Lewis, S.M.: Reference ranges and normal values, Practical hematology, 10th edition,U.K., Churchill Livingstone Pub., 14-17 (2006). 10. Jadhav UM, Patkar VS, Kadam NN et al. Thrombocytopenia in Malaria-Correlation with Type and Severity of Malaria. JAPI. 2004. 52(2): 615-618.