ORIGINAL
PROF-1678

THROMBOCYTOPENIA;
FREQUENCY AND DEGREE IN PATIENTS WITH FALCIPARUM MALARIA

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ABSTRACT: Background: Malaria is usually associated with reduction in blood cell counts and mild to moderate thrombocytopenia is a common feature of falciparum infection. This study has been conducted to find out frequency and degree of thrombocytopenia in patients suffering from falciparum malaria at a tertiary care hospital of Abbottabad. **Methods:** It was a descriptive case-control study being carried out at Ayub teaching hospital and Northern institute of Medical Sciences (NIMS) Abbottabad over a period of ten months. All patients with acute febrile illness without localizing signs were considered for study. A total 250 patients having falciparum malaria diagnosed by peripheral blood film examination have been studied. Complete blood counts were performed by Automated Beckman Coulter Analyzer. Blood films were examined by clinical pathologist for plasmodium falciparum via light microscopy using oil-immersion lens. **Results:** Out of 250 patients, 155(62%) were females and 95(38%) males with M:F ratio of 1:1.5. Mean age was 36±1.2 years (range 17-58 years). Out of 250, 175(70%) had thrombocytopenia ($p<0.05$) while 75(30%) had normal platelet counts. Thus mild, moderate and severe thrombocytopenia had been observed in 121(48.4%), 41(16.4%) and 13(5.2%) respectively ($p<0.05$). Fever appeared to be most common symptom observed in all patients (100%) followed by vomiting and nausea (88%). Anemia was the commonest sign present (80%) during our study. **Conclusions:** We discovered high frequency of mild thrombocytopenia in falciparum malaria. Therefore, thrombocytopenia can be supportive in diagnosis of plasmodium falciparum infection.

Keywords: Frequency, Falciparum malaria, Field's stain, thrombocytopenia.

INTRODUCTION

Malaria is a global threat to health and socio-economic development. Worldwide an estimated 300-500 million people suffer from malaria each year with 20 million of deaths annually[1]. In Pakistan, half million of malaria cases occur annually and an estimated 50,000 deaths per year. Main victims were infants, children and pregnant women. Therefore, malaria is an important public health problem of our country[2]. In previous decade, there is a six fold rise in falciparum malaria comprising 42% of all malaria cases recorded by National Malaria Control Program[3]. Severe malaria has been a major cause of mortality throughout the world and plasmodium falciparum is the main species for most of these deaths[4]. Malaria is usually associated with a variable degree of reduction in blood cell counts and mild to moderate thrombocytopenia is a common feature of falciparum infection, but rarely associated with bleeding tendencies[5]. Hence thrombocytopenia is an important marker for diagnosis of malaria in acute febrile patients living or visiting an endemic area[6]. 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[7].

We conducted this study to find out frequency and degree of thrombocytopenia in patients with falciparum malaria at a tertiary care hospital of Abbottabad.

PATIENTS AND METHODS

This descriptive case-control study was conducted at Ayub teaching hospital and Northern Institute of Medical Sciences (NIMS) Abbottabad from 20th August 2009 to 20th June 2010. All patients with acute febrile illness without localizing signs were considered for study. A total 250 patients positive for plasmodium falciparum via

peripheral blood film examination were included. Complete blood counts have been performed by Automated Beckman Coulter Analyzer. Thin blood films were prepared with Field's staining and examined by clinical pathologist for plasmodium falciparum through light microscopy using oil immersion lens 100. A blood smear has been considered negative if no parasite found on examination under 100 high power microscope. Patients with decreased platelet counts (thrombocytopenia) were re-evaluated by manual method. According to severity, patients with thrombocytopenia have been divided into three main groups:-

1. Mild thrombocytopenia:- having platelet counts between 50-150×10^3 cells/µl.
2. Moderate thrombocytopenia:- having platelet counts between 20-50×10^3 cells/µl.
3. Severe thrombocytopenia:- having platelet counts less than 20×10^3 cells/µl .

This study has been designed to include demographics and clinical information of the patients having falciparum malaria. Other laboratory investigations were carried out wherever necessary.

Patients with acute febrile illness and negative MP on peripheral blood film in three consecutive samples at interval of 12 hours were excluded. Similarly patients with history of chronic liver disease, bleeding disorder, cerebral malaria or acute renal failure and those taken anti-malarial drugs were excluded from this study. Data has been analyzed by using SPSS version 10.0. Pearson Chi-square test was used to test the significance, statistically significance was set at the p-value <0.05.

RESULTS

A total of 250 patients with falciparum malaria were studied. Out of which 155 (62%) were females and 95 (38%) males with M: F ratio of 1:1.5.

Mean age was 36±1.2 years (ranging from 17-58 years). In our study, 175 (70%) of patients had thrombocytopenia (p<0.05) while 75 (30%) had normal platelet counts. Thus mild, moderate and severe thrombocytopenia had been observed in 121 (48.4%), 41(16.4%) and 13(5.2%) respectively and p-values less than 0.05. This has been shown in table no I. Mean platelet count has been found 157,000 ± 51,300/µl (ranging from 16,000-350,000/µl). The mean values of hemoglobin 11.9±2.3g/dl and white blood cell counts 12,100±310/µl were observed during this study.

Table-I. Distribution of variables in patients with and without thrombocytopenia having falciparum malaria (n=250)

Variables	Thrombocytopenia (n=175)	without Thrombocytopenia (n=75)	P-value
Age (years)	34±13	38±9	-
Sex			
Male	70	25	0.35
Females	105	50	
Platelets counts			
Mild	121	-	
Moderate	41	-	0.02
Severe	13	-	
Hemoglobin			
>10g/dl	125	13	0.01
<10g/dl	50	62	
White blood cell Count (WBC count)			
>11,000 cells/: l	125	13	0.01
<11,000 cells/: l	50	62	

In this study, all patients have acute febrile illness at time of presentation and fever appeared to be most common symptom observed in all patients (100%) followed by vomiting and nausea (88%). The most common sign was anemia present in (80%) of our patients. Other clinical features and their frequencies have been shown in table no II.

Table-II. Frequency of clinical features in patients with falciparum malaria (n=250)

Clinical Features	No. of Patients	%age
Fever	250	100%
Vomiting and nausea	220	88%
Anemia	200	80%
Splenomegaly	40	16%
Jaundice	20	8%
Hepatosplenomegaly	15	6%
Diarrhea	10	4%

DISCUSSION

Falciparum malaria is one of the most common causes of acute febrile illness in Pakistan but clinical diagnosis is often difficult. It is a major community health problem of our country having high mortality and morbidity with varied manifestations. Hematological abnormalities are common finding in falciparum malaria. Thrombocytopenia often accompanies falciparum infection and is usually mild to moderate but very rarely symptomatic. In acute febrile illness finding of thrombocytopenia along with anemia is an important clue for diagnosis of malaria[8,9].

The exact mechanism of thrombocytopenia in falciparum malaria is unknown but decreased thrombopoiesis, sequestration of platelets by macrophages in the spleen, immune-mediated lysis[7] and hypersensitive platelets, have all been postulated. The hypersensitive (hyperactive) platelets produce increased quantities of platelet-specific proteins such as beta thromboglobin (β-TG), platelet factor 4 (PF_4), thromboxane A_2 and prostacyclin[10]. The hyperactive platelets may enhance hemostatic responses and that is why bleeding episodes are very rare in acute malarial infections, despite significant thrombocytopenia[11].

The frequency of thrombocytopenia in falciparum malaria ranges 60-80% according to previous studies[12]. In our study, 70% of the patients have shown some degree of thrombocytopenia ranging from mild to severe in intensity. This is comparable to results of studies by Robinson et al[13], Memon AR[17], Ansari S[14] and Rodriguez et al[15], showing thrombocytopenia in 71%, 70%, 69% and 59% respectively. In Liberia, Mahmood A[16] studied 145 patients having falciparum malaria. He found 109 (75%) of patients with thrombocytopenia. The sensitivity of the platelet counts has been considered as a predictor of falciparum infection, and it was 80% sensitive and 81.3% specific. The positive predictive value considered 63.8%, while negative predictive value 99.9%. Finding of mild to severe thrombocytopenia may alert the possibility of plasmodium falciparum infection[17].

In this study, we found mild degree of thrombocytopenia in majority of our patients (69.1%) which is closer to results of study by Memon AR[17]. But it is in contrast to study by Ansari S[14] who found moderate thrombocytopenia in 70% of their patients. Hence from this study, it is now concluded that patients with acute febrile illness in an endemic area without localizing signs and having mild thrombocytopenia, may alert treating physician towards the possibility of falciparum malaria, which can be confirmed by specific laboratory tests.

CONCLUSIONS

On conclusion, we discovered high frequency of mild thrombocytopenia in falciparum malaria. Hence patients with acute febrile illness in an endemic area with thrombocytopenia may raise suspicion of falciparum infection until proven otherwise. Therefore, thrombocytopenia can be supportive in diagnosis of plasmodium falciparum infection.

ACKNOWLEDGMENT

We are thankful to pathology departments of Ayub Teaching Hospital and Northern Institute of Medical Sciences (NIMS) Abbottabad for their cooperation in this

research. We are also thankful to Mr. Zohaib Ahmed Khan for his participation in typing of this article.

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Article received on: 07/07/2010 Accepted for Publication: 12/12/2010 Received after proof reading: 00/00/0000

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Article Citation:
Hayat AS, Siddiqui MS, Shaikh N. Thrombocytopenia; frequency and degree in patients with falciparum malaria. Professional Med J Mar 2011;18(1):75-79.

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