ORIGINAL ARTICLE

Thrombocytopenia & Mean Platelet Volume in Plasmodium Vivax Malaria Cases Presenting at A Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of thrombocytopenia and mean platelet volume (MPV) cases reporting at a tertiary care hospital of Sindh

Methods: This cross sectional study was performed in the department of Medicine, Isra University Hospital, Hyderabad from Feb 2015 to Nov 2016. A sample of 312 P. vivax cases were studied according to the inclusion and exclusion criteria. Malaria was diagnosed on thick and thin blood smears by light microscopy. Complete blood counting was performed by Sysmex KX-21 hematology analyzer. Hemoglobin, hematocrit, platelets and MPV were counted on this fully automated hematoanalyzer. Data variables were analyzed by statistical software SPSS (ver 21.0) at 95% CI ($P \leq 0.05$).

Results: Thrombocytopenia was detected in 229 (73.4%) and normothrombocytosis in 83 (26.6%) (P=0.0001). Of 229 thrombocytopenia cases; the mild, moderate and severe thrombocytopenia were noted in 32 (13.9%), 157 (68.5%) and 40 (17.4%) respectively. MPV was raised in thrombocytopenia cases as 13.16±1.62 fl compared to 7.87±3.12 fl in normothrombocytosis cases (P=0.0001).

Conclusion: The present study observed high frequency of thrombocytopenia and elevated mean platelet volume in Plasmodium vivax malaria.

Key Words: Thrombocytopenia, MPV, Malaria, P. vivax

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INTRODUCTION:

Malaria is a mosquito vector-borne parasitic disease caused by genus plasmodium. Estimates show 3.2 billion people are suffering from malaria. World Health Organization reported 214 million cases of malaria with a mortality of 438000 deaths in 2015[1]. Vector for the spread of plasmodia is the Anopheles mosquito. There are four major species of plasmodia; P. vivax, P. falciparum, P. ovale and P. malariae[2]. A fifth species, P. knowlesi is also identified causing malaria in Southeast Asia[3]. Approximately 88% malaria cases are reported from Africa followed by 10% from South-East Asia and 2% from Eastern Mediterranean Region. In the South-East Asia, large number of malaria cases are reported from India, Pakistan, Myanmar and Indonesia (10%). Approximately 90% mortality occurred in African countries, followed by 7% in South-East Asia Region and 2% in the Eastern Mediterranean Region. Globally; malaria incidence declined by 37% globally and by 42% in the African countries. Similarly, malaria related mortality rates decreased by 60% throughout the globe and by 66% in the African countries[4].

Malaria is a clinical manifestation of proliferating damage to the cell in particular the red blood cells. As the plasmodia complete shizogony cycle; there is release of inflammatory mediators that induce fever. Typical malaria cases

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complaints of 3 peculiar stages; the chill (cold stage), hot stage followed by sweating. Clinical severity of malaria varies too much; ranging from mild feverish state to complicated unconsciousness as in cerebral malaria. This depends on the plasmodia species, infective dose of sporozoites, patient's immunity, % of red blood cell parasitized, nutritional status, drug resistance, and concomitant conditions and diseases[5,6]. Malaria parasite infects multiple organs such as brain, liver, gastrointestinal tract, spleen, gall bladder, pancreas, circulation and placenta. The clinical severity ranges from simple malaise to life threatening coma due to cerebral malaria. Anemia and thrombocytopenia are most common blood dyscrasias beside others[7,8]. Thrombocytopenia is caused by immunological and non-immunological destructions of platelets, splenic sequestration of infected platelets, and dyspoietic bone marrow. Abnormalities of platelet function have been described as a consequence of malaria such as the mean platelet volume (MPV). MPV is a qualitative measure of platelet physiology. In rare instances; platelets are invaded by malaria parasites[7,9]. The present study was conducted to analyze the platelet counts and mean platelet volume (MPV) in acute malaria cases presenting at our tertiary care hospital. The objective of study was to find frequency of thrombocytopenia and mean platelet volume (MPV) in patients with P.vivax malaria.

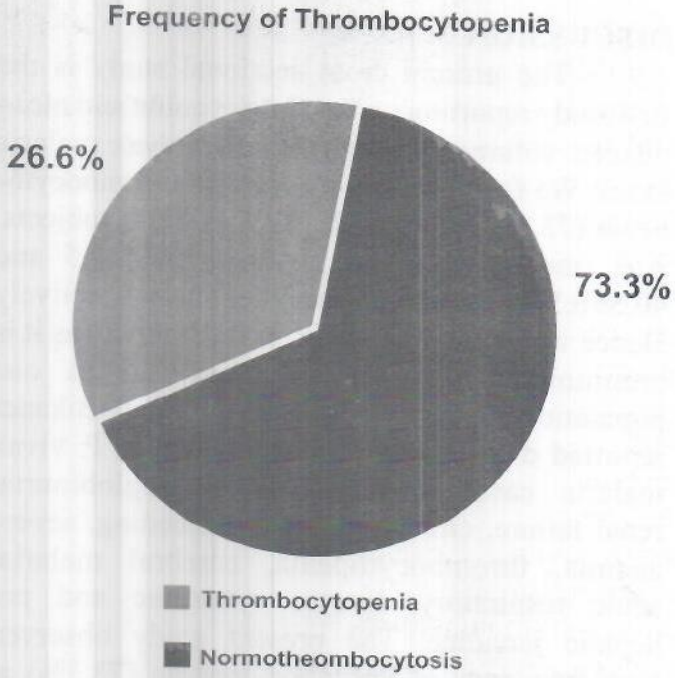
METHODS:

The present cross sectional study was conducted at Department of Medicine, Isra University Hospital Hyderabad from February 2015 to November 2016. Ethical approval of study protocol was taken from the ethical review committee of the institute. Sample was calculated by sampling-for- proportions. A sample of 312 P. vivax cases was studied according to the inclusion and exclusion criteria. The sample comprised of 195 male and 117 female subjects. Inclusion criteria were; age 20- 50 years, both gender, and malaria parasite P-vivax positive on peripheral smear. Subjects infected with other species of plasmodia, mixed infestation, typhoid and respiratory tract infections were excluded.

Volunteers were asked for the voluntary consent to abide by the protocol of study. A proper history, physical examination and blood testing were carried out for fulfilling the inclusion criteria. Volunteers were informed of the bio-data confidentiality. Medical officers were given task to segregate the patients to meet the inclusion criteria by proper history and physical examination and available laboratory investigations. Volunteer subjects were asked for blood sampling from a peripheral vein after area was sterilized and tourniquet was applied to make the vein prominent. Disposable syringe (BD, USA) was pricked into a prominent vein and 5 ml blood was collected. The area was covered with saniplast. Collected blood sample was poured into EDTA bottles. Malaria testing was performed on thick and thin blood smears by light microscopy. Thick and thin smears were stained by field stain and Leishman's stains. In field stain, the polychromated "methylene blue" and eosin dyes stained both the basophilic and acidophilic cell components to identify the blood cells and plasmodia. Complete blood counting was performed by Sysmex KX-21 hematology analyzer. Platelets and MPV were counted on this fully automated hematoanalyser. Platelet count was further confirmed by microscopic examination of thin blood smear slides. Platelet count was defined as number of thrombocytes measured by direct pulses of platelets, was multiplied by calibration constant and was expressed as thousands of thrombocytes per micro liter ($x10^6/\mu L$) of whole blood. Thrombocytopenia was graded as; mild thrombocytopenia defined as Platelet counts 50,000 to $\leq$1, 50,000 cells/μL), moderate thrombocytopenia as; Platelet counts 20,000 to <50000 cells/μL) and severe thrombocytopenia as; Platelet counts less than 20000 cells/μL) as referenced[1,10]. All data were preserved as in a Profroma. Age, gender, packed cell volume (PCV), hemoglobin, platelet counts and mean platelet volume were noted. Data variables were typed on Excel sheet and copied to statistical software SPSS (ver 21.0). Student t-test and Pearson`s Chi-square test were used for the analysis of continuous and categorical variables respectively. Confidence interval for data analysis was set at 95% CI ($P \leq 0.05$).

RESULTS:

Age (mean± SD) was observed as 39.5±9.5 and 40.5±6.5 years in male and female respectively (P=0.071). Of 312 sample, male and female comprised 195 (62.5%) and 117 (37.5%) respectively (P=0.035). M:F (male to female) ratio was 1.6:1. Table I show the demographic and blood findings. Platelets and MPV (mean± SD) were found as 151.6±56.7 vs. 157.15±49.3 $x10^6$ and 9.5±3.7 and 9.7±4.3 fl in male and female respectively. Thrombocytopenia was detected in 229 (73.4%) and normothrombocytosis in 83 (26.6%) of total sample (P=0.0001). Of 229 thrombocytopenic subjects, the mild, moderate and severe degree of thrombocytopenia were noted in 32 (13.9%), 157 (68.5%) and 40 (17.4%) respectively (Table-II). Mean platelet volume (MPV) was raised in thrombocytopenia group; noted as 13.16±1.62 fl and was 7.87±3.12 fl in normothrombocytosis group. The difference of MPV was found statistically significant (P=0.0001) (Table-III).



Graph I: Frequency of Thrombocytopenia in study subject

Table-I: Demographic & Blood Findings of Study Subjects (n=312)

Variables	Male	Female	P-Value
Age (Years)	39.5±9.5	40.5±6.5	0.071
Gender	195 (62%)	117 (38%)	0.035
PCV (Hct) %	40.5±5.5	41.5±5.7	0.047
Hemoglobin (g/dl)	12.7±1.1	11.6±2.1	0.051
MPV (fl)	9.5±3.7	9.7±4.3	0.085
Platelet Counts (x109)	151.6±56.7	157.1±549.3	0.01

Table-II: Frequency and Degree of Thrombocytopenia

Variables	Male	Female	Total	P-Value
Thrombocytopenia				
Thrombocytopenia	133 (58.1%)	96 (41.9%)	229 (73.4%)	0.0001
Normothrombocytosis	62. (74.7%)	21 (25.3%)	83 (26.6%)	
Total	195 (62.5%)	117 (37.5%)	312 (100%)	
Degree of Thrombocytopenia ($x10^6/\mu L$)				
Mild (0.5-1.5)	17 (53.1%)	15 (49.9%)	32 (13.9%)	
Moderate (0.2-<0.5)	95 (60.5%)	62 (39.5)	157 (68.5%)	
Severe (<0.20)	21 (52.5%)	19 (47.5%)	40 (17.4)	
Total	133 (58.1%)	96 (41.9)	229 (100%)	

DISCUSSION

The present cross sectional study is the first study reporting on the platelet count and mean platelet volume in a sample of P. vivax malaria cases. We found high frequency of thrombocytopenia (73.3%) and raised MPV in these subjects. Age (mean± SD) was noted as 39.5±9.5 and 40.5±6.5 years in male and female respectively Hence we conducted study on the P. vivax as it is common species causing malaria in our population. A previous study[20] from Bikaner reported data of eleven cases of severe P. vivax malaria cases and reported hemoglobinuria, renal failure, circulatory shock, bleeding, severe anemia, thrombocytopenia, cerebral malaria, acute respiratory distress syndrome and pre hepatic jaundice. The present study observed high frequency of thrombocytopenia (73.3%) in a sample of 312 cases of P. vivax malaria. A previous study[21] from the Aga Khan University Hospital reported thrombocytopenia in 89% of P. *vivax* cases. Another study[22] from JPMC Karachi reported very high frequency of thrombocytopenia of 93.33% of P. *vivax* cases. The findings of above study showed very high frequency of thrombocytopenia that is in contrast to the present study. In present study; Platelets counts were observed as 151.6±56.7 vs. 157.15±49.3 x10^6 in male and female respectively. And thrombocytopenia was noted in 229 (73.3%) compared to normothrombocytosis in 83 (26.6%) of total sample (P=0.0001). These findings are in agreement with previous studies.[20-23]. Of 229 thrombocytopenic subjects, the mild, moderate and severe degree of thrombocytopenia were noted in 32 (13.9%), 157 (68.5%) and 40 (17.4%) respectively. These findings are in agreement with previous studies.[21,22] Prajapati et al[23] (2018) reported frequency of 66.03% of thrombocytopenia in malaria cases. Another study Nadeem et al[9] (2014) reported low frequency of 59.52% and 45.45% from CMH Sibi and Malir hospitals. The findings are in opposition to the present and previous studies.[7,11-13] It is reported that the P. *vivax* related thrombocytopenia rarely may prove fatal.[24] In present study the MPV was raised in thrombocytopenia group; noted as 13.16±1.62 fl and was 7.87±3.12 fl in normothrombocytosis group (P=0.0001). The findings are in agreement with a recent study by Ahmed et al[7] (2015) from Karachi. They reported that the thrombocytopenia is common in P. vivax malaria cases noted in 108 (76.1%) patients. MPV in P. vivax malaria cases was higher than control group. These findings are agreement with the present study. The evidence based findings of present study observations show high frequency of thrombocytopenia that may sometime prove fatal hence patients should be scrutinized for the platelet counts. Elevated MPV is a new findings being reported for the first time by the present study from our hospital. As the literature is lacking on the platelet counts and mean platelet volume despite malaria being common, hence is a need to conduct more studies on the topic. The limitations of present study are sample size was small hence it may not be not representative of total population of the study area. However, the strength of present is evident from its prospective study design with inclusion and exclusion criteria.

CONCLUSION

The present hospital based study reports 73.3% frequency of thrombocytopenia and elevated mean platelet volume in Plasmodium vivax malaria. Mild, moderate and severe degree of thrombocytopenia were noted in 32 (13.9%), 157 (68.5%) and 40 (17.4%) respectively. Mean platelet volume (MPV) was elevated in cases of thrombocytopenia. The finding may improve the diagnosis of malaria as thrombocytopenia in acute febrile illness increases the possibility of malaria in the tropical areas.

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